

Pulse Oximetry References List

This document outlines the pulse oximeter journal articles provided for your review. The articles have been categorized below into the following topics: Fetal Applications, Neonatal Applications, Reflectance Applications, Transmittance Applications, Comparison of Reflectance and Transmittance and Transcutaneous Oxygen, and Fetal Hemoglobin. A brief summary is listed below each reference for your convenience. Also, please note that the all the articles have been sequentially numbered in the lower center of the page.

Fetal Applications

- Page 1 *Effect of location of the sensor on reflectance pulse oximetry*, A. Dassel (1997)
Calls into question the reliability of reflectance oximetry in the fetus. Uses light of wavelengths, 660 and 940 nm (same as transmittance).
- Page 8 *Does the hemoglobin concentration in fetal blood interfere with the accuracy of fetal reflection pulse oximetry?*, G. Arikan (1998)
The Hb concentration in fetal blood does not interfere with the accuracy of fetal pulse oximetry and need not be taken into consideration in calibration curves. The reflectance system used light wavelengths of 660 and 920 nm, the same wavelengths used for transmittance oximetry.
- Page 13 *Accuracy of fetal pulse oximetry and pitfalls in measurements*, R. Nijland (1997)
Sources of inaccuracies – blood volume fraction differences, hematocrit, and blood flow.

Neonatal Applications

- Page 20 *Pulse oximetry: an alternative method for the assessment of oxygenation in newborn infants*, M. Jennis (1987)
Reports oxygen measurements according to % HbF (fetal hemoglobin) and the effect on SaO₂.
- Page 25 *The accuracy of pulse oximetry in neonates: effects of fetal hemoglobin and bilirubin*, J. Anderson
Early oximeters (OB 3700 and N100) accurately reflect measured oxyhemoglobin independent of bilirubin and HbF levels.

- Page 26 *The uses, benefits, and limitations of pulse oximetry in neonatal medicine: consensus on key issues*, W. Hay (1987)
Fetal hemoglobin is theoretically significant but not clinically significant in determining pulse oximeter accuracy.
- Page 29 *Pulse oximetry in newborn infants with birth weights of 620 to 4285 grams receiving dopamine and dobutamine*, S. Sardesai (1996)
Pulse oximetry can be used reliably from 80 to 100% SaO₂ for those receiving dopamine and dobutamine.
- Page 33 *Neonatal pulse oximetry: accuracy and reliability*, W. Hay (1989)
Effects of nursing and other factors on the accuracy of SpO₂.

Reflectance Applications

- Page 39 *The effect of pulsating arteries on reflectance pulse oximetry: measurements in adults and neonates*, R. Nijland (1995)
Pulsating arteries can affect the reliability of reflectance pulse oximetry.
- Page 44 *Reflectance pulse oximetry in neonates*, K. Faisst (1995)
Tested custom reflectance oximeter in neonates.
- Page 50 *Wavelength selection for low-saturation pulse oximetry*, P. Mannheimer (1995)
Wavelengths of 735 and 890 nm are better for low saturation (fetal) values.
- Page 61 *Limitations of forehead pulse oximetry*, J Jorgensen (1995)
Spurious differences observed during mechanical ventilation between forehead reflectance and transmission oximetry. Attributed to valodilatation and pooling of venous blood.

Transmittance Applications

- Page 65 *Accuracy of pulse oximeters: the European multi-center trail*, P. Wouters et. al. (2001)
Large clinical study (2694 recordings from 1483 patients) shows that observed accuracies are generally in agreement with claims. Main determinants of inaccuracy are skin color, peripheral temperature, hemoglobin levels and finger thickness. Sparse data below 85 % SpO₂.

- Page 69 *Accuracy of two pulse oximeters at low arterial hemoglobin-oxygen saturation*, B. Carter (1998)
- The ability of pulse oximeters (an Ohmeda and an Hewlett Packard) to reliably predict change in SaO₂ based on change in pulse oximetry was limited. Recommends measurement of PaO₂ or SaO₂ for important clinical decisions.
- Page 75 *Pulse oximetry-clinical implications and recent technical developments*, L Lindberg (1995)
- Review articles. Reported a conclusion that pulse oximeters were unaffected by fetal hemoglobin.
- Page 84 *Accuracy of pulse oximetry in cyanotic congenital heart disease*, V. Lazzell (1987)
- Page 85 *Noninvasive pulse oximetry in children with cyanotic congenital heart disease*, R. Boxer (1987)
- Pulse oximetry is accurate in infants and children with cyanotic CHD.

Comparison Of Reflectance And Transmittance And Transcutaneous Oxygen

- Page 88 *Reflectance pulse oximetry from core body in neonates and infants: comparison to arterial blood oxygen saturation and to transmission pulse oximetry*, A. Kugelman (2004)
- Neither technology very good at low saturations (< 85%).
- Page 94 *Forehead pulse oximetry compared with finger pulse oximetry and arterial blood gas measurement*, E. Cheng (1988)
- When signal strength is weak causing poor pulse detection, there will be problems associated with accurate SpO₂ determination.
- Page 98 *Pulse oximetry in pediatric intensive care: comparison with measured saturations and transcutaneous oxygen tension*, S. Fanconi (1985)
- Pulse oximetry is reliable and effective.
- Page 103 *Noninvasive arterial hemoglobin oxygen saturation versus transcutaneous oxygen tension monitoring in the preterm infant*, R. Deckardt (1984)

Fetal Hemoglobin

- Page 108 *Effects of fetal hemoglobin on pulse oximetry*, J. Pologe, D. Raley (1987)
Any errors due to HbF are insignificant for saturations > 90%. The *co-oximeter* had an error of approximately 1% at an SaO₂ of 70%.
- Page 111 *Absorption characteristics of human fetal hemoglobin at wavelengths used in pulse oximetry*, A. Harris, M Sendak, et. al. (1987)
Fetal and adult hemoglobin have nearly identical absorption characteristics over the wavelength range of 600 – 1050 nm.
- Page 114 *Variations in optical absorption spectra of adult and fetal hemoglobins and its effect on pulse oximetry*, Y. Mendelson (1989)
No difference in the optical absorption spectra of fetal and adult hemolized blood from wavelengths of 650-1000 nm commonly used in pulse oximetry.
- Page 119 *Effects of fetal hemoglobin on the accuracy of pulse oximetry in preterm infants*, V. Rajadurai (1991)
N200 pulse oximeter was unaffected by HbF in preterm infants.
- Page 123 *Absorption spectra of human fetal and adult oxyhemoglobin, deoxyhemoglobin, carboxyhemoglobin, and methemoglobin*, W. Zijlstra (1991)
Oximeters based on 660 and 940 nm wavelength LEDs are so insensitive to the presence of fetal hemoglobin that they can be used safely in neonates.

Effect of location of the sensor on reflectance pulse oximetry

*A. C. M. Dassel *Research Fellow*, †R. Graaff *Senior Scientist (Biophysics)*, *M. Aardema *Student*,
‡W. G. Zijlstra *Professor*, *J. G. Aarnoudse *Professor (Obstetrics and Perinatal Medicine)*

*University Hospital Groningen, *Department of Obstetrics and Gynaecology,
†Centre for Biomedical Technology and ‡Department of Pediatrics, Groningen, The Netherlands*

Objective The influence of the location of the sensor on reflectance pulse oximetry during fetal monitoring in labour was investigated using the newborn infant as a model.

Methods Seven healthy infants were studied between 19 and 48 hours after term delivery. Recordings of reflectance pulse oximetry were obtained from eight different sites on the infant's head. The relative changes in red to infrared light (R/IR) were determined. In pulse oximetry R/IR values are converted to arterial oxygen values by means of an empirically derived calibration curve.

Results Significantly lower R/IR values were found at the forehead compared with the fontanelle, the parietal and occipital position, and the temporal area. Conversion to oxygen saturation values revealed a difference of up to 13.4% in oxygen saturation between the forehead and the occipital area.

Conclusion Assuming that the arterial blood oxygen saturation did not change substantially, our findings indicate that in reflectance pulse oximetry there is no unique relation between R/IR and arterial oxygen saturation. The differences in reflectance pulse oximetry at the various sites are explained by differences in optical properties (scattering and absorption) of the tissue underneath the sensor. These will affect the red and infrared light reaching the detectors in a different way, and consequently R/IR changes. Because during intrapartum monitoring exact positioning of the sensor on the fetal head is usually impossible, the accuracy of fetal reflectance pulse oximetry is impaired.

INTRODUCTION

Reflectance pulse oximetry has been introduced as a potential method for continuous noninvasive monitoring of fetal arterial oxygen saturation during labour¹⁻³. Although the results of the initial fetal reflectance pulse oximetry studies were encouraging, the method is not yet suitable for routine clinical use^{4,5}. Several problems must be solved before pulse oximetry can be safely used for reliable intrapartum fetal monitoring. One of the issues requiring more investigation is the application of the pulse oximetry probe^{6,7}. Where should the probe be applied to the fetal skin without causing any harm to fetus and mother? How to keep the probe in close contact to the skin? To what extent do the red and infrared pulsatile waveforms and the derived oxygen saturation values depend on the location of the probe⁸⁻¹⁰?

In the initial studies on pulse oximetry in the human fetus, the probe was placed at the presenting part of the head and attached to the skin by glueing, suction or by a clip, the latter being used simultaneously for heart rate monitoring⁶. These methods were sometimes hampered

by disturbance of the local skin circulation underneath the probe (e.g. through caput formation)^{11,12}. More recently, others have used a probe which is placed at the fetal temple or cheek. This probe is thought to be kept in place by the static force of the uterine wall exerted on the fetal skin and on the probe¹³. This method, however, implies practically blind application of the probe, which carries the risk of damaging the fetus, the placenta or the mother, as does inadvertent movement of the probe in the course of labour.

We suggest that the site of application of the probe is likely to influence fetal reflectance pulse oximetry^{14,15}. The structure of the tissue underneath the probe depends on the locations on the fetal head: considerable variations occur in thickness of the skin, subcutaneous tissue and the skull. The same holds for the local arterial and venous circulation. Such local variations may result in variations in red and infrared pulse waves due to differences in light propagation at the various sites. These effects may be more pronounced in reflectance pulse oximetry than in transmission pulse oximetry. As a consequence, the relation between red to infrared light (R/IR) and the actual oxygen saturation of the arterial blood may vary with the different sites of application of the probe. We therefore suggest that the currently used

Correspondence: Professor J. G. Aarnoudse, Department of Obstetrics and Gynaecology, University Hospital Groningen, Hanzeplein 1, 9713 GZ Groningen, The Netherlands.

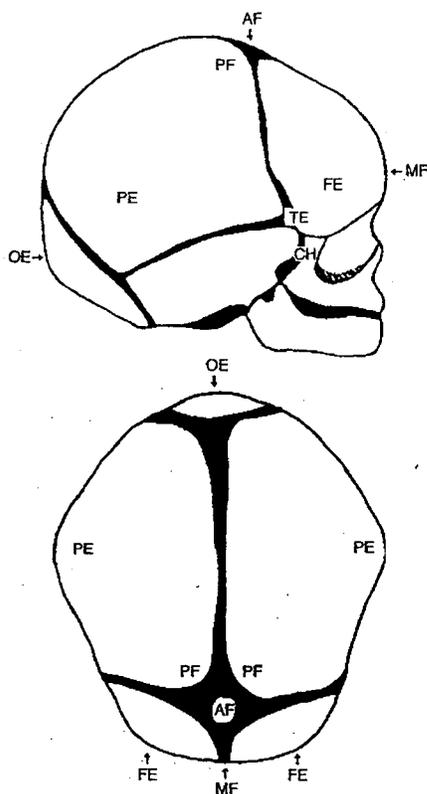


Fig. 1. Schematic presentation of the eight locations where reflectance pulse oximetry recordings were performed on the infant's head: AF = anterior fontanelle; PF = os parietale just beside the fontanelle; PE = parietal eminence; OE = just above the occipital eminence; MF = in the mid frontal line at the glabella; FE = frontal eminence; TE = temple; CH = cheek.

method of conversion of the R/R values to oxygen saturation values by using a single empirically derived calibration curve is essentially not correct and may lead to unacceptably high inaccuracy.

In the present study we have addressed the question of the influence of the localisation of the probe on reflectance pulse oximetry on the fetal head. The healthy term newborn infant was used as a model for this investigation, and reflectance pulse oximetry was compared at eight different sites on the infants' head. The reflectance pulse oximetry equipment used for this study was developed in our department and is provided with a sensor with three detectors at different distances from the light sources, thus allowing better insight into the physics underlying this procedure.

METHODS

Reflectance pulse oximeter recordings were made at eight locations on the head of seven newborn babies. The infants were healthy 19 to 48-hours old caucasian infants born by vaginal delivery ($n = 6$) or by caesarean section ($n = 1$), with Apgar scores of 9 after 1 min and of 10 after 3 min. The mean birthweight was 3632 g

Table 1. Differences in tissue under the sensor at the eight locations on the neonatal head. Key as for Fig. 1; NVS = near venous sinus.

Location	Hair	Blood supply	Tissue under skin	NVS
AF	+	A.temp.sup R.parietalis	Aponurosis subarachnoid space	+
PF	+	A.temp.sup R.parietalis	Thin bone subarachnoid space	-
PE	+	A.temp.sup R.parietalis	Thick bone	-
OE	+	A.occipitalis R.occipitalis	Thick bone	+
MF	-	A.ophtalmica* A.supraorbitalis A.supratrochlearis	Thin bone suture	+
FE	-	A.temp.sup R.frontalis	Thick bone	-
TE	-	A.temp.sup R.frontalis A.zygomatico-orbitalis	Thin bone	+
CH	-	A.temp.sup A.transv.faciei R.auricularis ant	Zygomatic bone **	-

*The opthalmic artery derives from the internal carotid artery, whereas the superior temporal artery and the occipital artery derive from the external carotid artery.

**At this location the skin is thicker and contains more adipose tissue.

(range 3310–3970) and the mean gestational age was 40.1 weeks (range 38.6–42.3). Recordings were made while the infants were sleeping in their cots at least 30 min after feeding. During the recordings room temperature (24°C) and humidity were constant. The parents of each baby were informed about purpose and procedure of the study and were asked for their consent.

The reflectance pulse oximeter probe was positioned successively at the following locations (Fig. 1, Table 1): over the anterior fontanelle (AF); over the parietal bone just beside the fontanelle (PF); over the parietal eminence (PE); just above the occipital eminence (OE), at the glabella in the mid-frontal line (MF); over the frontal eminence (FE); at the temple (TE); and at the upper part of the cheek in front of the ear (CH). The probe was held in place with a pressure of 30 to 40 mmHg exerted on the probe by the finger of the investigator. At each location a pulse oximetry recording was made for 2 min to 3 min.

In six of the seven infants we also had a standard transmission pulse oximeter at our disposal, which was attached to a hand, for simultaneous recording (Datex, Intrumentarium Corp, Helsinki, Finland, software version 1987). Because fetal or neonatal calibration values were not available, only changes in oxygen saturation could be measured. The individual changes, however, were always small (<2% SO₂).

The reflectance pulse oximeter developed in our department determines blood oxygen saturation by comparing light intensity changes at 660 nm (red) and

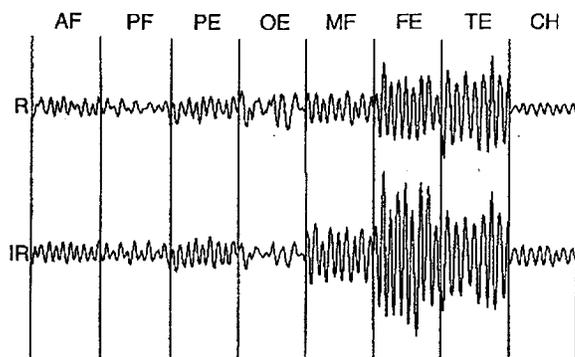


Fig. 2. Representative example of the red (R) and infrared (IR) plethysmographic waveforms derived from the second detector at each of the eight locations. All samples are 3 s out of 15-s periods derived from the recording of one infant. Key as for Fig. 1.

940 nm (infrared) resulting from changes in absorption and multiple scattering in tissue¹⁶. The probe contains two light sources (light emitting diodes, CR 10 SR and CR 10 IR, ELCOS, Pfaffenhofen, Germany) on one side of an optical barrier and three photodiodes (BPX 90, Siemens, Munich, Germany) on the opposite side of the optical barrier. The distances between the light emitting diodes and the photodiodes are 4 mm, 7 mm, and 9 mm for detectors 1, 2 and 3, respectively. Red and infrared signals were measured at the three detectors separately but simultaneously. The measurements were done in this way in order to determine the influence of light emitting diode detector distance on the measurements and to provide a deeper understanding of the underlying physics of the procedure so that eventually a broader and more secure application of reflectance pulse oximetry may be obtained.

For each detector the red and infrared pulsatile variation of the logarithm of the measured intensity is measured as a function of time. The variations in photon flux, which are plethysmographic waveforms, give an impression of the quality of the detected signals. R and IR, the relative pulse sizes which can be expressed as the standard deviation of the intensity fluctuations divided by the average intensity, are related to pulsatile blood volume fluctuations of the vessels in the tissue underneath the probe. The calculated mean light intensity is a measure of the fraction of emitted photons which return to the detector after being scattered in the tissue under the sensor. An increase in light absorption in the tissue will result in a decrease in detected mean light intensity. Therefore, the mean light intensity changes when there is a change in the scattering and absorption properties of the tissue underneath the probe. When the mean light intensity is low, the influence of noise on the signal increases, resulting in a less favourable signal-to-noise ratio. The ratio of the relative changes of the intensities, R/IR, is used to determine the

arterial oxygen saturation. R/IR is calculated by

$$R/IR = \Delta \ln(I_R) / \Delta \ln(I_{IR})$$

where I is intensity. Both light emitting diodes illuminate the skin alternately during 20- μ s pulses with a repetition rate of 1 kHz. Every 40 ms the signals are converted to 12-bit digital values. Further processing is performed with a personal computer and red and infrared signals are visualised at the computerscreen. Each measurement contains data over a 15-second period. In previous reports detailed information on the construction of the oximeter has been presented¹⁴. The signals were stored in a personal computer.

The light intensity fluctuations (the plethysmographic waveforms) were analysed visually to detect motion artefacts which, if present, were excluded. R/IR, the relative pulse sizes and mean light intensities were calculated for the remaining signals. Data from four measurements from each location were averaged to eliminate the influence of short lasting changes, resulting in eight datasets for each subject. Statistical analysis was performed on these datasets with repeated measures ANOVA, in which measurements obtained from the middle of the forehead were compared with the other locations. A P value < 0.05 was considered significant.

RESULTS

Red and infrared pulsatile waveforms varied considerable in size and form with the site of measurement. A representative example of the pulsatile signals obtained from one infant at the eight locations is shown in Fig. 2. A pulsatile pattern can easily be recognised at all sites, except at the occipital location where the signal quality is poor.

The R/IR values and standard deviations of the seven infants at the various locations are shown in Table 2 and Fig. 3 for all three detectors. With the probe applied at the forehead, the lowest R/IR values were measured at all three detectors. Of the two forehead locations, R/IR values in the midline were slightly lower than at the frontal eminence. Compared with the forehead midline values, the greatest differences in R/IR were observed with the temple (detectors 1 and 2) and with the AF, PE and OE sites (detectors 2 and 3). Of these, the most pronounced deviating R/IR values were measured at detector 3 at the occipital eminence location. The R/IR values at the cheek were only slightly higher than those at the forehead locations, and the differences were not statistically significant.

Considerable differences in variability of R/IR values were observed at the various sites. Standard deviations of R/IR were higher at the parietal site, at the occipital site and at the temple, whereas the lower standard deviations were found at the frontal locations, at the fontanelle and at the cheek. It appeared that the differ-

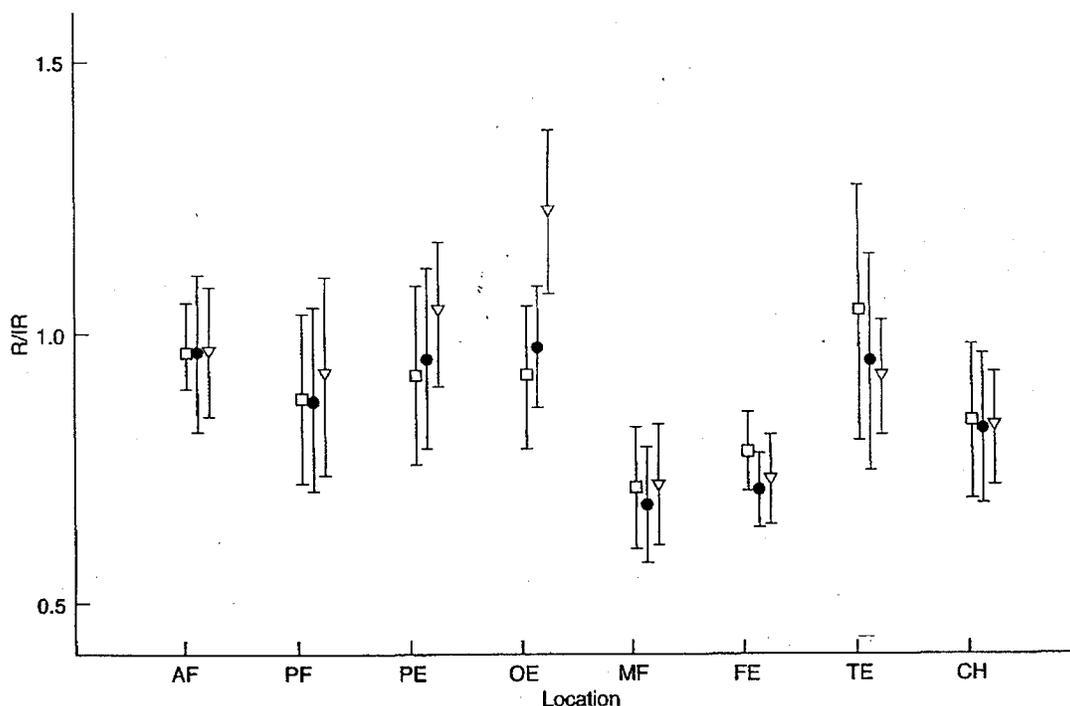


Fig. 3. R/IR (y axis), average and standard deviations for seven infants, versus location (x axis). Curves are presented for the first (\square), second (\bullet) and third detector (∇) placed at respectively 4, 7 and 10 mm from the light emitting diodes.

Table 2. R/IR and SD derived from eight locations at the neonatal head, measured at three light emitting diode detector distances simultaneously. From the R/IR values, arterial oxygen saturations were estimated and differences between the locations calculated (ΔSO_2). Values in parentheses are SD; ΔSO_2 are given as percentages. Key as for Fig. 1; Loc = location.

Loc	Detector 1		Detector 2		Detector 3	
	R/IR	$\Delta\text{SO}_2\%$	R/IR	$\Delta\text{SO}_2\%$	R/IR	$\Delta\text{SO}_2\%$
AF	0.98 (0.08)	7.1	0.97 (0.15)*	7.6	0.97 (0.12)*	6.6
PF	0.88 (0.16)	4.5	0.88 (0.17)	5.3	0.92 (0.19)	5.3
PE	0.93 (0.17)	5.8	0.96 (0.17)*	7.4	1.04 (0.14)†	8.4
OE	0.92 (0.13)	5.5	0.98 (0.11)*	7.9	1.23 (0.15)†	13.4
MF	0.71 (0.12)	—	0.68 (0.11)	—	0.72 (0.11)	—
FE	0.78 (0.07)	1.8	0.71 (0.07)	0.8	0.73 (0.08)	0.3
TE	1.05 (0.24)*	9.0	0.95 (0.20)*	7.1	0.92 (0.11)*	5.3
CH	0.84 (0.15)	3.4	0.83 (0.14)	4.0	0.83 (0.11)	2.9

§Difference in oxygen saturation (%) calculated towards R/IR at the midfrontal location.

*Significant difference in R/IR value compared with R/IR obtained from the midfrontal location, $P < 0.05$; † $P < 0.01$.

ences in variability could be attributed to both intra- and inter-individual differences in variability.

The relative pulse sizes of the plethysmographic changes in red and infrared light showed a tendency to be larger at the forehead frontal eminence than at the other locations, at all three detectors whereas the smallest pulse sizes were observed at the cheek and at the occiput (Fig. 4). The distance between the detector and the light source was also relevant for the pulse wave amplitude: the greater the distance, the larger the pulse

size. However, the differences in pulse sizes were not statistically significant.

Mean light intensity values for red and infrared light were determined for each detector. Figure 5 shows these values at the various sites measured by the second detector. The highest intensities were found at the cheek, at the forehead and at the parietal bone near the fontanelle. The lowest values were found at the parietal and occipital eminences. Comparable differences were observed at the other two detectors. For all detectors the red and infrared light intensities at the occiput were significantly lower compared with the light intensities measured at the parietal bone besides the fontanelle, at the forehead and at the cheek. The red light intensity at the occiput was also significantly lower compared with the fontanelle and the temple. The light intensities detected at the cheek were significantly higher than at the fontanelle, the parietal and occipital eminence and the temple.

DISCUSSION

In the present study we performed reflectance pulse oximetry at eight locations on the head of newborn infants. These locations are potentially accessible for application of a reflectance pulse oximetry sensor for fetal monitoring in labour. R/IR values were significantly lower with the sensor at the forehead than at the other locations, as was R/IR variability. This means that with reflectance pulse oximetry, using a single calibra-

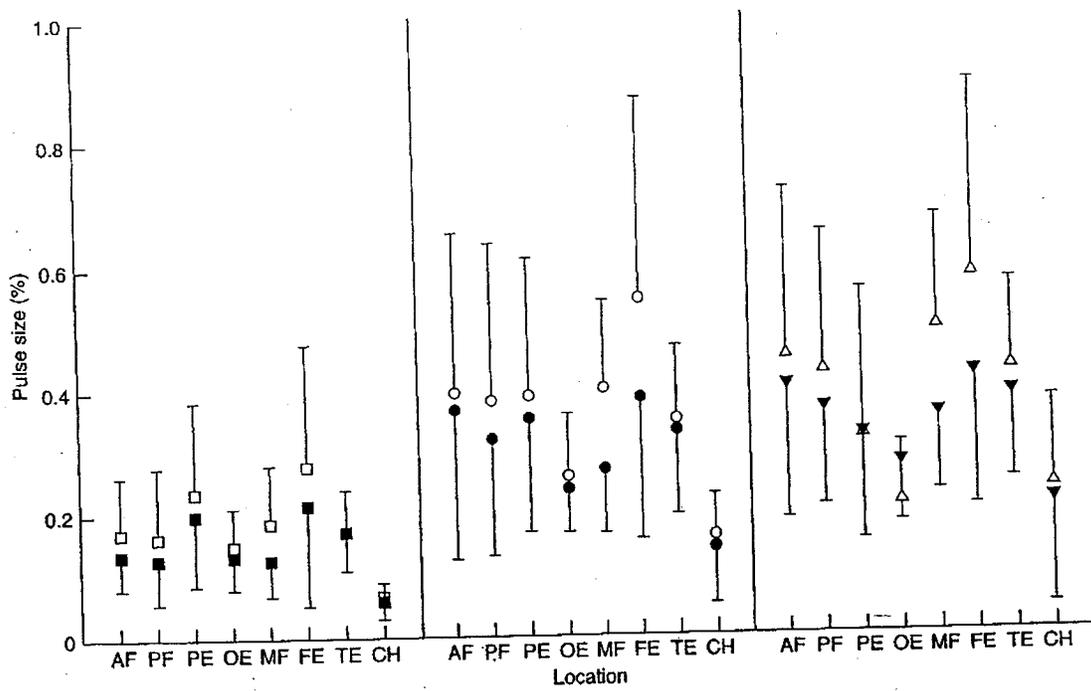


Fig. 4. Pulse size (y -axis), average and standard deviation, versus location. Red (R) and infrared (IR) pulse sizes are shown for each detector: detector 1 (\blacksquare = R; \square = IR), detector 2 (\bullet = R; \circ = IR), and detector 3 (\blacktriangledown = R; \triangle = IR).

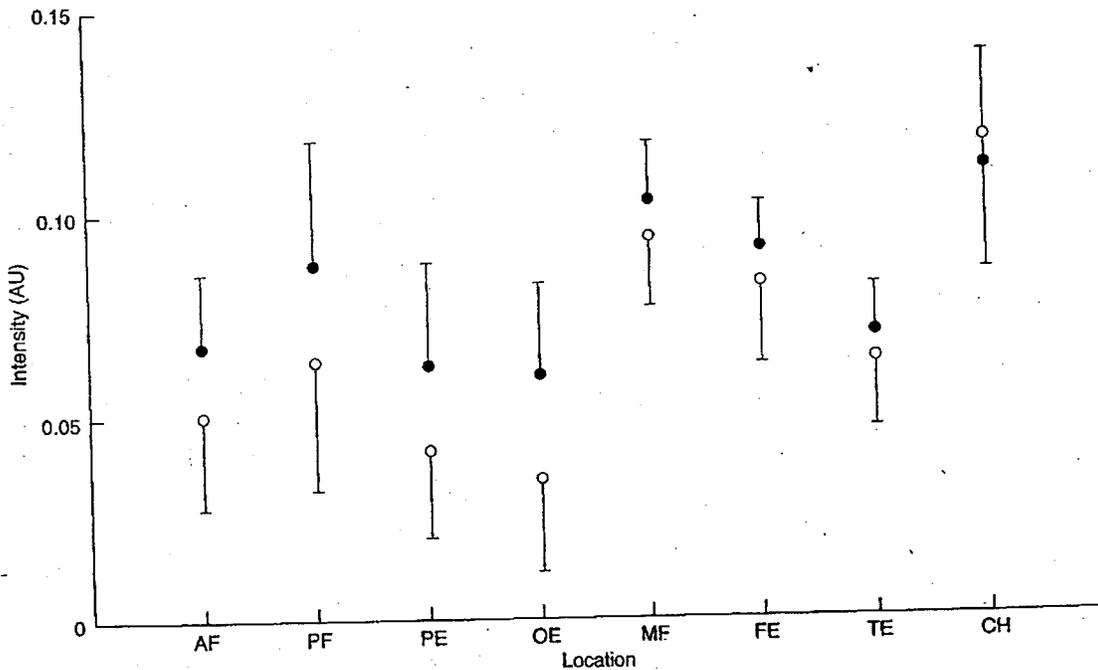


Fig. 5. Mean light intensities (y -axis), average and standard deviation versus location for the second detector (\bullet = IR; \circ = R).

tion curve, higher oxygen saturation values would be determined at the forehead. The estimated differences in oxygen saturation between the forehead and the remaining sites varied depending on the detector location and differences up to 13.4% were observed (Table 2). These

estimations were based on a previously derived calibration curve for the conversion of R/IR to arterial oxygen saturation values. Because it is practically impossible to calibrate an oximeter in the human fetus, this calibration curve was obtained in the near term ovine fetus,

using the same instrument over a wide range of arterial oxygen saturation values (15% to 80%)¹⁶.

In general, pulse oximetry in reflectance mode is less accurate than in transmission mode. This is partly explained by the lower signal-to-noise ratio in reflectance pulse oximetry, which is due mainly to the smaller pulse signals and the smaller fraction of the emitted light that reaches the detector. This is supported by Figs 4 and 5 which show that an increased standard deviation in R/IR is often found at the locations where the pulse sizes are small and the light intensities are low. However, the reflectance pulse oximetry findings at the cheek suggest that the effect of a small pulse size can be compensated for by a relatively high light intensity at the detector. As shown in Fig. 2 the quality of the plethysmogram detected at the cheek is much better than that at the occiput. At the occiput the pulse sizes are small and the mean light intensities are low; this may explain the high R/IR values at the third detector.

Differences in the composition of the tissue underneath the probe are the most likely explanation for the differences in R/IR values derived from the various locations. Both absorption and scattering properties of blood and tissue underneath the sensor influence the path length of the photons on their way to the detector. These influences can be different for red and for infrared light and affect both the pulsatile and the nonpulsatile part of the signals⁴. Evidence has been provided that the influence of differences in scattering and absorption properties exists in reflectance pulse oximetry, and might be of importance in transmission pulse oximetry^{3,17}. Previous studies in pulse oximetry as well as in near-infrared spectroscopy have shown that Lambert Beer's law cannot be simply applied under these circumstances^{2,15,18}. Consequently, at each location a unique relationship exists between R/IR and the actual oxygen saturation of the arterial blood: in other words, each location needs its own calibration curve.

Table 1 summarises some of the most relevant characteristics of the tissue and the circulation at the various locations¹⁹ which may have contributed to the observed differences in R/IR values. We have considered the following aspects: presence of hair whether or not pigmented; thickness of the skin; tissue underneath the skin including both subcutaneous and bony tissue (the latter lacking at the fontanelles); and composition of the vascular bed in the tissue sampled.

In newborns vellus hair is present all over the body²⁰. The scalp is covered with more or less pigmented hair. This could possibly explain the lower R/IR values found at the locations in the face (e.g. forehead and cheek) compared with those measured at the scalp. It does, however, not explain the higher R/IR values found at the temporal area, where hair is also unpigmented. In another study, comparing reflectance pulse oximetry at

the forehead and temporal area, higher R/IR values were also reported at the temporal area when the detector of the sensor was placed over the temporal artery¹⁰. The authors of this study¹⁰ suggested that the pulsating temporal artery is the cause of the falsely high R/IR values at this location.

The slight difference between the R/IR values at the forehead and those found at the cheek area may be explained by the thicker skin and/or the thicker subcutis of the cheeks²¹. The adipose tissue of the subcutis causes less scattering of the incident light and high intensity levels are detected in this area.

We did not observe a demonstrable influence of the presence of bony tissue on the R/IR values as virtually no difference was found between the R/IR values measured at the fontanelle and those at the adjacent scalp. It is possible that the optical properties of the aponeurosis covering the fontanelles and the periosteum covering the bone are similar and that light propagated through deeper located tissue hardly reaches the detectors.

Finally, the possible influence of differences in the amount of venous blood at the various locations might explain some of the differences in R/IR values. The sagittal sinus is located in the midline underneath the skin surface. Using ultrasound Doppler, we observed heart beat synchronous waveforms in this sinus in newborns of similar age. This pulsatile venous blood will contribute to the reflectance pulse oximetry by increasing the resulting R/IR level. As shown by others²²⁻²⁵, the fluctuations in venous blood volume caused by ventilation can also influence pulse oximetry.

In this study the healthy newborn was used as a model to investigate the influence of various locations of the probe during fetal monitoring by reflectance pulse oximetry. Studies in the human fetus are not suitable for this purpose for a variety of reasons: exact location of the probe is rather difficult and in the course of labour the probe is likely to change its position. Moreover, caput formation and the effects of varying pressure on the probe and on the fetal head will affect reflectance pulse oximetry⁶. Finally, the arterial oxygen saturation of the fetus itself shows considerable fluctuations in the course of labour. We assumed that in the newborns studied the arterial oxygen saturation levels in blood remained almost constant during individual experiments which was supported by the stable transmission pulse oximeter values during the measurements. Recordings were obtained between 18 and 48 hours after birth, during which period the cardiovascular system still shows some adaptive changes: arterio-venous mixing is eliminated and the skin circulation becomes involved in thermoregulation^{26,27}. The ensuing small differences in arterial blood oxygen saturation between the newborns are likely to be responsible for the inter-individual differences in R/IR values found.

Compared with the fetus, the newborn infant has considerably increased arterial oxygen saturation levels. With regard to the S-shaped oxygen-haemoglobin equilibrium curve, the position of the curve will be only slightly more to the left in the fetus than in the newborn. The fetus, however, 'uses' the steep part of the curve whereas the newborn infant uses the flat upper part of the curve. As a consequence, oximetry in the fetus has a higher sensitivity to detect changes in oxygen tension than in the neonate. The observed differences in reflectance pulse oximetry at the various locations at the neonatal head in the present study are neither dependent on the position of the oxygen-haemoglobin equilibrium curve nor on the place at the curve and therefore will be also expected in the fetus.

At present, we do not know at what critical arterial oxygen saturation level the human fetus is jeopardised during labour. Moreover, it is reasonable to assume that not only the degree of hypoxemia but also the duration of hypoxemia is relevant. A study of fetal sheep revealed that arterial oxygen saturation values below 30% corresponded with serious fetal distress. However, it remains to be seen whether this also applies to the human fetus during labour. Clinical studies are needed to determine the validity of pulse oximetry for fetal monitoring. A prerequisite for producing reliable results from these clinical studies is the capability to measure fetal arterial oxygen saturation accurately by reflectance pulse oximetry.

Our findings indicate that with the currently used reflectance pulse oximetry technique the relationship between R/IR and the actual arterial blood saturation (the calibration curve) varies with the location of the probe at the neonatal head. Assuming that this is also true for reflectance pulse oximetry at the fetal head, it has consequences for fetal monitoring by reflectance pulse oximetry. Reliable monitoring by reflectance pulse oximetry requires the sensor to stay at the same position. In clinical practice, however, it will be difficult to determine exactly the position of the sensor. Therefore, further investigations should be undertaken to study how the influence of tissue properties on reflectance pulse oximetry can be restricted so that fetal arterial oxygen saturation can be more accurately determined by reflectance pulse oximetry.

References

- Johnson N, Johnson VA, Fisher J, Jobbins B, Bannister J, Lilford RJ. Fetal monitoring with pulse oximetry. *Br J Obstet Gynaecol* 1991; 98: 36-41.
- Mendelson Y, Solomita MV. The feasibility of spectrophotometric measurements of arterial oxygen saturation from the fetal scalp utilizing noninvasive skin-reflectance pulse oximetry. *Biomed Instrum Technol* 1992; 26: 215-224.
- Severinghaus JW, Kelleher JF. Recent developments in pulse oximetry. *Anesthesiology* 1992; 76: 1018-1038.
- Graaff R, Dassel ACM, Zijlstra WG, de Mul FFM, Aarnoudse JG. How tissue optics influences reflectance pulse oximetry. In: Ince C, Kesecioglu J, Telci L, Akpir K, editors. *Oxygen Transport to Tissue XVII*. New York: Plenum Press, 1996: 117-132.
- Lindberg LG, Lennmarken C, Vegfors M. Pulse oximetry—clinical implications and recent technical developments. *Acta Anaesthesiol Scand* 1995; 39: 279-287.
- Johnson N. Development and potential of fetal pulse oximetry. *Contemp Rev Obstet Gynaecol* 1991; 3: 193-200.
- Buschmann J, Rall G, Knitza R. Fetal oxygen saturation measurement by transmission pulse oximetry. *Lancet* 1992; 339: 615.
- Decker MJ, Dickensheets D, Arnold JL, Cheung PW. A comparison of a new reflectance oximeter with the Hewlett-Packard ear oximeter. *Biomed Instrum Technol* 1990; 24: 122-126.
- Schram CMH, Gardosi JO. Artifacts in fetal pulse oximetry: nonarterial pulsatile signals. *Am J Obstet Gynecol* 1994; 170: 1174-1177.
- Nijland R, Jongsma HW, van den Berg PP, Nijhuis JG, Oeseburg B. The effect of pulsating arteries on reflectance pulse oximetry: measurements in adults and neonates. *J Clin Monit* 1995; 11: 118-122.
- Johnson N, Johnson VA, Bannister J, Lilford RJ. The effect of caput succedaneum on oxygen saturation measurements. *Br J Obstet Gynaecol* 1990; 97: 493-498.
- Schram CMH, Gardosi J. The effect of caput succedaneum on oxygen saturation measurements. *Br J Obstet Gynaecol* 1991; 98: 113-114.
- Dildy GA, Clark SL, Loucks CA. Preliminary experience with intrapartum fetal pulse oximetry in humans. *Obstet Gynecol* 1993; 81: 630-635.
- Graaff R, Dassel ACM, Koelink MH, Aarnoudse JG, de Mul FFM, Zijlstra WG, Greve J. Condensed Monte Carlo simulations applied to reflectance pulse oximetry. *Proc SPIE* 1993; 1888: 201-212.
- Doyle M. Near infrared spectroscopy used for intrapartum surveillance. *J R Soc Med* 1994; 87: 315-316.
- Dassel ACM, Graaff R, Aarnoudse JG, Elstrodt JM, Heida P, Koelink MH, de Mul FFM, Greve J. Reflectance pulse oximetry in fetal lambs. *Pediatr Res* 1992; 31: 266-269.
- Faris F, Thornley M, Wickramasinghe Y, Rolfe P, Livera N, Spencer A. Near infrared spectroscopy: in-vivo measurements of effective penetration depths and absorption coefficients. *Ann Int Conf IEEE Eng Med & Biol Soc* 1990; 12: 1542-1543.
- Benaron DA, Gwiazdowski S, Kurth CD, Steven J, Delivoria-Papadopoulos M, Chance B. Optical path length of 754 nm and 816 nm light emitted into the heads of newborns. *Ann Int Conf IEEE Eng Med & Biol Soc* 1990; 12: 1117-1119.
- Cormack GC, Lamberty BGH. Head and neck. In: *The Arterial Anatomy of Skin Flaps*. London: Churchill Livingstone, 1986: 114-130.
- Giacometti L. The anatomy of the human scalp. Chapter VI. In: Montagna W, editor. *Advances in the Biology of Skin*. Oxford: Pergamon Press, 1965: 97-120.
- Moretti G, Ellis RA, Mescon H. Vascular patterns in the skin of the face. *J Invest Dermatol* 1959; 33: 103-112.
- Mark JB. Systolic venous waves cause spurious signs of arterial hemoglobin desaturation. *Anesthesiology* 1989; 71: 158-160.
- Graaff R, Dassel ACM, Aarnoudse JG, Zijlstra WG, Heida P, de Mul FFM, Koelink MH, Greve J. Biophysical aspects of reflection pulse oximetry. In: Lafeber HN, Aarnoudse JG, Jongsma HW, editors. *Fetal and Neonatal Physiological Measurements*. Amsterdam: Elsevier, 1991: 129-134.
- Sami HM, Kleimann BS, Lonchina VA. Central venous pulsations associated with falsely low oxygen saturation measured by pulse oximetry. *J Clin Monit* 1991; 7: 309-312.
- Jorgensen JS, Schmid ER, König V, Faisst K, Huch A, Huch R. Limitations of forehead pulse oximetry. *J Clin Monit* 1995; 11: 253-256.
- Koch G, Wendel H. Adjustment of arterial blood gases and acid base balance in the normal newborn infant during the first week of life. *Biol Neonat* 1968; 12: 136-161.
- Suichies HE, Brouwer C, Aarnoudse JG, Jentink JW, de Mul FFM, Greve J. Skin blood flow changes, measured by laser Doppler flowmetry, in the first week after birth. *Early Hum Dev* 1990; 23: 1-8.

Received 13 June 1996

Returned for revision 24 October 1996

Revised version received 21 January 1997

Accepted 12 February 1997

Guerkan M. Arikan
Martin C.H. Haeusler
Josef Haas
Heinz Scholz

Department of Obstetrics and Gynecology,
University of Graz, Austria

Does the Hemoglobin Concentration in Fetal Blood Interfere with the Accuracy of Fetal Reflection Pulse Oximetry?

Key Words

Fetal surveillance
Reflection pulse oximetry
Hemoglobin concentration

Abstract

Objective: Our goal was to investigate the influence of the fetal hemoglobin (Hb) concentration on the accuracy of reflection pulse oximetry. **Methods:** 179 fetuses were monitored by a reflection pulse oximetry system (RPOX MK2). Pulse oximetry measurements (SO_{2POX}) were compared with the oxygen saturation and pH of umbilical artery and vein (UA-, UV-SaO₂) immediately after delivery. Correlation and linear regression analyses were performed. Because it is unknown whether low or high Hb concentrations might interfere with the SO_{2POX} measurements, the influence of the Hb level on the correlations was evaluated by weighting the linear regression in both ways; by Hb concentrations as weighting factor and as an inverse weighting factor (1/Hb). **Results:** There was a significant correlation between SO_{2POX} and UV-SaO₂ (for the last 10 min of delivery, $r = 0.45$, $p < 0.0005$) but not with pH or UA-SaO₂. Linear regression analysis between SO_{2POX} and UV-SaO₂ showed a multiple R of 0.45. Hb concentration in fetal blood ranged from 9.2 to 20.5 mg/dl. The weighted regression indicated a multiple R_{Hb} of 0.49, which did not differ by the inverse weighting (multiple $R_{inverse\ Hb}$: 0.49). **Conclusions:** Pulse oximetry measurements seem to reflect oxygen saturation in fetal blood, however further improvement is necessary. The Hb concentration in fetal blood does not interfere with the accuracy of fetal pulse oximetry and need not be taken into consideration in calibration curves.

Introduction

Persistent fetal hypoxemia can lead to acidosis and neurologic injury and current methods to detect fetal compromise are indirect and nonspecific. Theoretically, direct continuous noninvasive measurement of fetal oxy-

genation is desirable to improve intrapartum fetal assessment and, the specificity and detecting fetal compromise. The development of reflectance pulse oximetry has made it possible to measure fetal oxygen saturation during labor [1, 2].

The hemoglobin (Hb) concentration in fetal blood has a wide range (postpartum 1-13 days; 19.5 ± 5.0 g/dl) [3] and anemia or hemoconcentration could present a physi-

Supported by the Austrian Science Foundation (Grant 9344-Med).

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

© 1998 S. Karger AG, Basel
1015-3837/98/0134-0236\$15.00/0

Accessible online at:
<http://BioMedNet.com/karger>

M.G. Arikan, MD
Department of Obstetrics and Gynecology, Karl Franzens University
Auenbruggerplatz 14
A-8036 Graz (Austria)
Tel. +43 316 385 2201, Fax +43 316 385 3199, E-Mail arikan@email.kfunigraz.ac.at

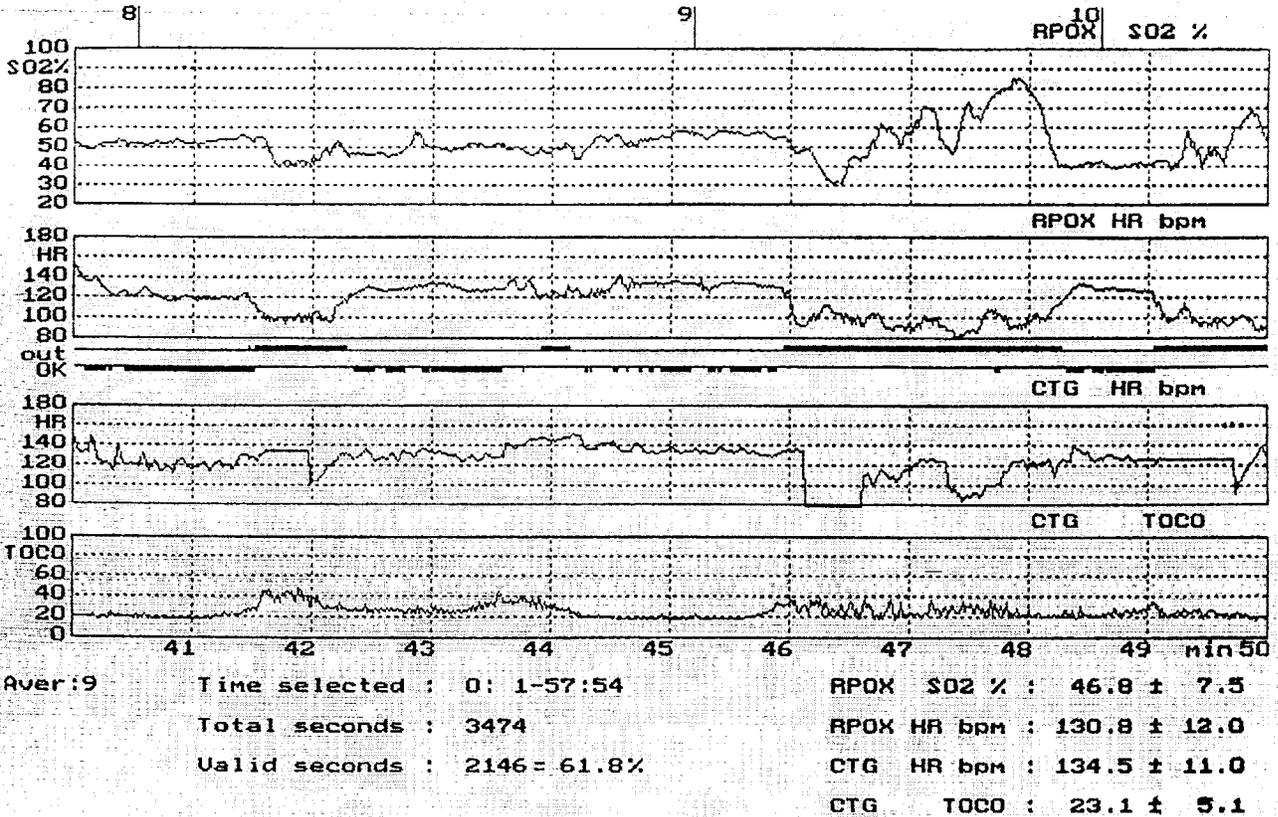


Fig. 1. Online display of reflection pulse oximeter RPOX MK2 in a surveillance period of 10 min. The oxygen saturation (RPOX SO₂), heart rate calculated by RPOX MK2 (RPOX HR) and CTG signals (CTG HR and CTG TOCO), infrared and red light reflection signals (IFR and RED respectively) are shown.

ologic limitation of fetal reflection pulse oximetry. The objective of this study was to investigate the influence of Hb concentrations in fetal blood on the accuracy of fetal reflection pulse oximetry measurements.

Material and Methods

179 term fetuses in vertex presentation were monitored after rupture of membranes by a reflection pulse oximetry system (RPOX MK2, Unit of Perinatal Research, University Hospital of Zürich, Switzerland). The study was approved by the Ethics Committee of the University of Graz, Austria, and all women gave informed written consent.

The RPOX MK2 allows visual evaluation of signal validity by online display of the red (660 nm) and infrared (920 nm) reflection signals [4, 5] (fig. 1). The signals are fed through filters into an ADC board. A Pascal program reads the data into an IBM computer and

calculates the average oxygen saturation (SO₂P_{OX}) over periods of nine heart beats, which provides a high sensitivity to artifacts and real changes in oxygen saturation. Flexible, slightly concave, silicone sensors (21 mm in diameter) were applied to the fetal head during a vaginal examination after rupture of the membranes and kept in place by suction (maximum negative pressure -300 mbar). Cardiocography was used as standard intraparturial surveillance method. Immediately after delivery, the umbilical cord was clamped on both ends and blood samples were taken. Umbilical vein and artery oxygen saturation (UV-, UA-SaO₂) were measured by a spectrophotometer (AVL CO-Oxylite 912, Graz, Austria) and pH by an IL 1306 pH/blood-gas analyzer (Milan, Italy).

The accuracy of fetal pulse oximetry was evaluated by comparing the pulse oximetry measurements (SO₂P_{OX}) within different time intervals before delivery (overall time, 60, 30, 10 min before delivery) with SaO₂ and pH in cord blood samples obtained immediately after delivery. Correlation and linear regression analyses between pulse oximetry measurements and umbilical cord blood values were performed with the Pearson and Spearman correlation coefficients,

Fig. 2. Standard linear regression analysis for the pulse oximetry measurements showed a multiple R of 0.45. The weighted analyses did not indicate differences in multiple R and equation (multiple R_{Hb} : 0.49; multiple $R_{inverse Hb}$: 0.49). The equations of the weighted regressions: (standard) UV-SaO₂ = 0.50*SO_{2POX} + 26.5; (w. factor: Hb) UV-SaO₂ = 0.532*SO_{2POX} + 24.8; (w. factor: 1/Hb) UV SaO₂ = 0.529*SO_{2POX} + 25.1.

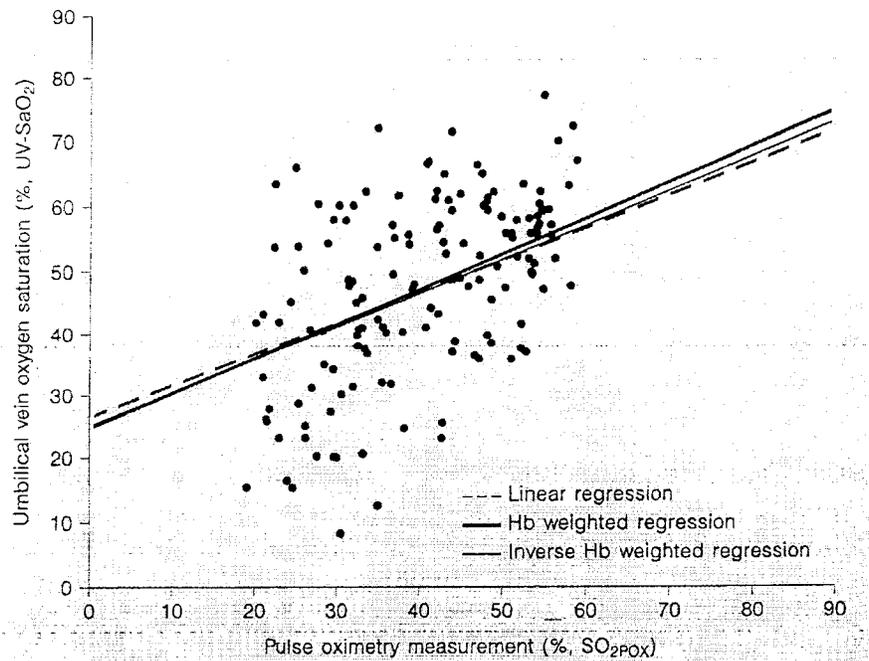


Table 1. Correlations between SO_{2POX} (mean ± SD, %) and SaO₂ according to time before delivery

Time	SO _{2POX}	r	p ¹
Overall time	49.3 ± 13.1		>0.05
Last 60 min	46.8 ± 13.1	0.28	<0.005
Last 30 min	45.4 ± 13.8	0.27	<0.002
Last 10 min	44.1 ± 13.9	0.45	<0.0005

¹ Spearman test.

ANOVA and regression analysis. A p value of 0.05 was considered as statistically significant.

Because it is unknown whether low or high Hb concentrations might interfere with the SO_{2POX} measurements, the influence of the Hb level on the accuracy of pulse oximetry measurements regarding SaO₂ values was evaluated by weighting the linear regression both ways; by Hb concentration as weighting factor and as an inverse weighting factor (1/Hb). The weighted regression analysis and the inversely weighted regression analysis were compared.

Results

There were 148 spontaneous vaginal deliveries, 20 forceps deliveries, and 11 cesarean sections. 26 women had epidural analgesia. The average duration of pulse oximetry was 84 min.

Pulse oximetry measurements (SO_{2POX}) correlated significantly with UV-SaO₂ (range 19–76%, mean ± SD, 48 ± 14.8%) (table 1) but not with pH or UA-SaO₂. UV-pH (range 7.06–7.48, mean ± SD, 7.31 ± 0.07) correlated with UV-SaO₂ (r = 0.42, p = 0.0001). UA-pH (range 7.03–7.42, mean ± SD, 7.24 ± 0.07) did not correlate with UA-SaO₂ (range 0.2–59%, mean ± SD, 19 ± 13%). In 11 cases UA-pH and in 17 cases UV-pH were below usually accepted limits for acidosis: <7.15 [6] and <7.20 [7], respectively.

Standard linear regression analysis for the pulse oximetry measurements in the last 10 min before delivery regarding UV-SaO₂ showed a multiple R of 0.45. The Hb concentration in fetal blood ranged from 9.2 to 20.5 mg/dl (16.3 ± 1.7 mg/dl). The weighted regression equation and multiple R (weighting factor: Hb concentration) did not differ by inverse weighting (multiple R_{Hb} : 0.49, multiple $R_{inverse Hb}$: 0.49) (fig. 2).

Discussion

These data showed significant correlations between reflection pulse oximetry measurements and oxygen saturation in fetal blood. The Hb concentration in fetal blood had a wide range, but this did not affect the accuracy of reflection pulse oximetry.

Ideally, fetal pulse oximetry measurements should be correlated with preductal oxygen saturation, but the access to the fetal preductal circulation is not feasible. Similar to previous clinical studies, we used the umbilical cord blood oxygen saturation for correlation analyses [2]. The preductal oxygen saturation lies somewhere between UV-SaO₂ and UA-SaO₂. The difference between UV-SaO₂ and UA-SaO₂ (Δ SaO₂) negatively affects the correlation between pulse oximetry measurements and umbilical cord blood SaO₂ [4, 8, 9]. Which reference value (UA or UV) to use to estimate preductal oxygen saturation is undefined. Although most authors tried to analyze the diagnostic value of SO₂POX related to UA values (pH or SaO₂), in several reports [4, 10, 11]. UV values seem to better represent the preductal values.

Our results confirm previously published significant correlations between pulse oximetry measurements and oxygen saturation in umbilical vein in the last stage of labor [2, 4, 12].

The available data do not permit evaluation of the changes of oxygen saturation in fetal blood during labor. However, higher correlations were found in the periods of measurements closer to delivery. This confirms that blood oxygenation can change rapidly during labor [13]. In some cases with lower average SO₂POX (e.g., <40%) during the last 10 min, UV-SaO₂ were discrepantly high (about twice SO₂POX) (fig. 2). This can be explained by the effect of Δ SaO₂ or by insufficient calibration of the pulse oximeter, showing further improvement is necessary.

A rigorous definition of severe birth asphyxia includes cord blood acidemia, neonatal depression (i.e., low Apgar scores), and evidence of neonatal end-organ damage such as early seizures and cardiac or renal dysfunction. However, acidemia is the most sensitive reflection of birth asphyxia; the absence of acidemia excludes asphyxia. Review of the literature sets the lower limit of normal UA-pH at 7.04–7.10 and normal UV-pH at 7.14–7.20 [7]. Several papers have dealt with the predictive value of SO₂POX for acidemia. Seelbach-Goebel et al. [14] observed that a fall of SO₂POX below 30% for >10 min resulted in an UA-pH of <7.2 in more than 50% of cases. Carbonne et al. [6] reported that SO₂POX <30% had a PPV of 43%, a NPV of 87%, a sensitivity of 30%, and a speci-

ficity of 92% for UA-pH \leq 7.15 and that these values were comparable to those of fetal blood analysis in cases with abnormal fetal heart rate. Alshimmiri et al. [10] observed poor correlations ($r = 0.30$, $p < 0.05$); McNamara et al. [12] found significant correlations between SO₂POX and UA-pH ($r = 0.66$, $p = 0.007$) but UV as reference showed a similar statistical power and there was no complicated pregnancy outcome; Langer et al. [11] reported significant correlations ($r = 0.55$ and $r = 0.63$ for UA- and UV-pH respectively, $p = 0.0001$), with only 1 of 40 newborns acidotic as defined above. On the contrary, others found no correlations between SO₂POX and fetal blood sample pH [15] or umbilical pH [4, 16]. Our study group differs from most previous studies by a higher rate of fetuses with acidosis and the lack of correlations can be explained by the fact that hypoxia and acidosis do not have a linear relation. Our study addressed the linear correlations between SO₂POX and SaO₂, but not the predictive value of SO₂POX related to acidosis.

Reflection pulse oximetry is currently used experimentally to study fetal oxygenation during labor [8, 9, 15, 17–21] and potentially may be introduced into clinical practice [2]. Technical problems such as motion artifacts, poor sensor-skin contact [16, 22–25] and physiologic conditions such as anatomic alterations in the vascular bed [13, 26], the relative rapidity of changes in oxygen saturation [13], venous pulsations [27] and altered Hb species [28, 29] may limit the clinical applicability of the technique.

Changes in the Hb concentration could affect the accuracy of pulse oximetry measurements due to changes of absorption and amplitudes of reflected light. Only a few reports have addressed the effect of Hb concentrations on pulse oximetry measurements in vitro [30, 31]. Flaig et al. [31] reported that reflection pulse oximetry could underestimate actual oxygen saturation due to low Hb concentrations. In our study, the first to evaluate the effect of Hb concentrations on the results of fetal reflection pulse oximetry in vivo, neither low nor high concentrations of Hb had an impact on the accuracy of pulse oximetry measurements. This contradictory result might be explained by the different spectrum of Hb concentrations (5.2–15.2 mg/dl) and different sensors and software used in the in vitro model. Larger clinical studies with reflection pulse oximetry will be required to evaluate the impact of Hb concentration in fetal blood.

We did not evaluate the interference that might be caused by fetal Hb. Rajadurai et al. [32] studied possible interferences in pulse oximetry by fetal Hb in 22 preterm infants between 1 h to 73 days of age whose Hb ranged between 0 and 100%. The authors concluded that fetal

Hb, even with this wide range, did not affect the correlations between the pulse oximetry measurements and arterial oxygen saturation. Most fetuses have red cells that contain over 80% Hb, which has not been shown to interfere significantly with most currently designed pulse oximeters [13].

In conclusion, oxygen saturation measurements by reflection pulse oximetry seem to reflect oxygen saturation in fetal blood. The wide range of the Hb concentration in

fetal blood neither interferes with the accuracy of reflection pulse oximetry measurements nor needs to be taken into consideration in calibration curves.

Acknowledgements

We thank Profs R. and A. Huch and Drs V. Koenig, C. Burry and F. Hug for their support, and Dr. K. Tamussino for editing the manuscript.

References

- 1 Peat S, Booker M, Ponte J: Continuous intrapartum measurement of oxygen saturation (letter). *Lancet* 1988;i:213.
- 2 Dildy GA, Clark SL, Loucks CA: Intrapartum fetal pulse oximetry: Past, present, and future. *Am J Obstet Gynecol* 1996;175:1-9.
- 3 Braunwald E, Isselbacher KJ, Petersdorf RG, Wilson JD, Martin JB, Fauci AS (eds): *Harrison's Principles of Medicine*. New York, McGraw-Hill, 1987, A-10.
- 4 Haeusler MCH, Arikan G, Haas J, Kainer F: Fetal pulse oximetry and visual online signal identification in the second stage of labor. *Am J Obstet Gynecol* 1996;175:1071-1074.
- 5 Arikan G, Haeusler MCH, Kainer F, Haas J: Visual online signal identification and the accuracy of fetal pulse oximetry in second stage of labor. *Am J Obstet Gynecol* 1996;174:491.
- 6 Carbonne B, Langer B, Goffinet F, Audibert F, Tardif D, Le Gueff F, Laville M, Maillard F, and French Study Group on Fetal Pulse Oximetry: Multicenter study on the clinical value of fetal pulse oximetry. *Am J Obstet Gynecol* 1997;177:593-598.
- 7 Boylan PC, Parisi V: Fetal acid-base balance; in Creasy RK, Resnik R (eds): *Maternal Fetal Medicine*. Philadelphia, Saunders, 1994, pp 349-358.
- 8 Dildy GA, Loucks CA, Clark SL: Intrapartum fetal pulse oximetry in the presence of fetal cardiac arrhythmia. *Am J Obstet Gynecol* 1993;169:1609-1611.
- 9 Arikan G, Etschmaier S, Schöll W, Kainer F, Stein M, Haeusler MCH: Vergleich von Reflexionspulsoximetrie und von Kardiotokographie zur intrapartalen Überwachung bei fetaler Arrhythmie und kardialem Vitium - ein Fallbericht. *Geburtshilfe Frauenheilkd* 1997;57:581-584.
- 10 Alshimmiri M, Bocking AD, Gagnon R, Natale R, Richardson BS: Prediction of umbilical artery base excess by intrapartum fetal oxygen saturation monitoring. *Am J Obstet Gynecol* 1997;177:775-779.
- 11 Langer B, Boudier E, Hadad J, Pain L, Schlacker G: Fetal pulse oximetry during labor of 62 patients. *Fetal Diagn Ther* 1996;11:37-45.
- 12 McNamara H, Cung CD, Lilford R, Johnson N: Do fetal pulse oximetry readings at delivery correlate with cord blood oxygenation and acidemia? *Br J Obstet Gynaecol* 1992;99:735-738.
- 13 Yount JE: Practical aspects of calibrating fetal pulse oximetry; in Knitza R, Rall G, Mainz S (eds): *Hypoxische Gefährdung des Fetus sub partu*. Darmstadt, Steinkopf, 1994, pp 17-21.
- 14 Seelbach-Goebel B, Butterwege M, Kuhnert M, Heupel M: Fetale Pulsoximetrie sub partu. Erfahrungen - Prognostische Bedeutung und Konsequenz-Ziele. *Z Geburtshilfe Perinatol* 1994;198:67-71.
- 15 Luttkus A, Fengler TW, Friedmann W, Dudenhausen JW: Continuous monitoring of fetal oxygen saturation by pulse oximetry. *Obstet Gynecol* 1995;85:183-186.
- 16 Johnson N, Johnson VA, Bannister J, Lilford RJ: The accuracy of fetal pulse oximetry in the second stage of labor. *Neonatal Intensive Care* 1992;5:46-49.
- 17 Dildy GA, Clark SL, Loucks CA: Intrapartum fetal pulse oximetry: The effects of maternal hyperoxia on fetal arterial oxygen saturation. *Am J Obstet Gynecol* 1994;171:1120-1124.
- 18 Van den Berg PP, Jongsma JW: Effects of maternal inhalation of 40% oxygen on fetal oxygen saturation. *Am J Obstet Gynecol* 1994;171:1120-1124.
- 19 McNamara H, Johnson N: The effect of uterine contractions on fetal oxygen saturation. *Br J Obstet Gynaecol* 1995;102:644-647.
- 20 Carbonne B, Benachi A, Leveque ML, Cabrol D, Papiernik E: Maternal position during labor: Effects on fetal oxygen saturation measured by pulse oximetry. *Am J Obstet Gynecol* 1996;88:797-800.
- 21 Johnson N, Oudgaarden VE, Montague IA, McNamara H: The effect of epidural analgesia on fetal oxygen saturation. *Br J Obstet Gynaecol* 1996;103:776-778.
- 22 Huch R, Ullrich G, König V, Huch A: Reflectance pulse oximetry potential and problems; in Ehryl AM (ed): *Clinical Oxygen Pressure Measurement*. III. Oxford, Blackwell, 1992, pp 24-31.
- 23 Rall G, Mainz S: Basic principles and general problems of pulse oximetry at low oxygen saturations; in Knitza R, Rall G, Mainz S (eds): *Hypoxische Gefährdung des Fetus sub partu*. Darmstadt, Steinkopf, 1994, pp 31-37.
- 24 Gardosi JO, Damianou D, Schram CMH: Artifacts in fetal pulse oximetry: Incomplete sensor-to-skin contact. *Am J Obstet Gynecol* 1994;170:1169-1173.
- 25 Schram CMH, Gardosi JO: Artifacts in fetal pulse oximetry: Nonarterial pulsatile signals. *Am J Obstet Gynecol* 1994;170:1174-1177.
- 26 Lawson D, Norley I, Korbon G, Loeb R, Ellis J: Blood flow limits and pulse oximeter signal detection. *Anesthesiology* 1987;67:864-865.
- 27 Faisst K, Koenig V, Jorgensen JS, Huch A, Huch R: Erfahrungen bei der Messung der Sauerstoffsättigung mittels eines eigenen Reflexions-Pulsoximetrie-Systems bei Erwachsenen und Neugeborenen sowie bei ersten Messungen während der Geburt; in Knitza R, Rall G, Mainz S (eds): *Hypoxische Gefährdung des Fetus sub partu*. Darmstadt, Steinkopf, 1994, pp 117-121.
- 28 Sidi A, Paulus DA, Rush W, Ravenstein N, Davis RF: Methylene blue and indocyanine green artifactually lower pulse oximetry readings of oxygen saturation. *Studies in dogs*. *J Clin Monit* 1987;3:249-256.
- 29 Temper KK, Parker SJ: Pulse oximetry. *Anesthesiology* 1989;70:98-108.
- 30 Vegfors M, Lindberg LG, Oberg PA, Lennmarken C: Accuracy of pulse oximetry at various hematocrits and during hemolysis in an in vitro model. *Med Biol Eng Comp* 1993;31:135-141.
- 31 Flaig M, Rall G, Mainz S, Knitza R, Edrich T: Experimental in vitro calibration of a pulse oximeter at low oxygen saturations; in Knitza R, Rall G, Mainz S (eds): *Hypoxische Gefährdung des Fetus sub partu*. Darmstadt, Steinkopf, 1994, pp 117-121.
- 32 Rajadurai VS, Walker AM, Yu VY, Oates A: Effect of fetal hemoglobin on the accuracy of pulse oximetry in preterm infants. *J Paediatr Child Health* 1992;28:43-46.

FR
R
Z
a De
Co
Ne
b Di

...
Ke
De
Gl
Va
Int
Pr

anc
mo
cor
ma
bec
gly
hav
inc
gen
gly
blo
tha
Qu

KA
Fax +
E-Mail
www

Accuracy of fetal pulse oximetry and pitfalls in measurements

Roel Nijland^{a*}, Henk W. Jongsma^a, Jan G. Nijhuis^a, Berend Oeseburg^b

^aPerinatal Research Group Nijmegen, Department of Obstetrics and Gynaecology, Faculty of Medical Sciences, University Hospital Nijmegen #15 GYN, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands

^bPerinatal Research Group Nijmegen, Department of Physiology, Faculty of Medical Sciences, University Hospital Nijmegen, 415 GYN, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands

Abstract

Pulse oximetry is a technique for estimating arterial oxygen saturation continuously and non-invasively. Reflectance pulse oximetry might become useful for monitoring the fetus during labour but it is much more susceptible to all kinds of physiological variations than the well-established transmission pulse oximetry for neonatal or adult monitoring. This review focuses on the accuracy of reflectance pulse oximetry. Results of human, animal, in vitro and theoretical models indicate that factors such as; blood volume fraction differences, haematocrit, and blood flow differences are major sources for inaccurate pulse oximetry readings in the fetal arterial oxygen saturation range of 10–80%. These factors cannot be overcome by systems using two wavelengths sensors with the 660/890 or 940 nm combination. Reported precision values (S.D. of difference between pulse oximeter and blood sample saturation) range between 2.5 and 12.9% for various 660 nm sensors. Most sensors were tested only once with a limited number of animals. A new 735/890 nm sensor (Nellcor Puritan Bennett) demonstrates a promising accuracy (precision around 5%) in two studies. Various other sensors have also been developed, but are not or scarcely evaluated. Without thorough establishment of the reliability of this technique, clinical fetal oxygen saturation data are still of limited value. © 1997 Elsevier Science Ireland Ltd.

Keywords: Accuracy; Animal; Arterial oxygen saturation; Fetal; In vitro; Pulse oximetry

1. Introduction

Accurate assessment of the fetal condition during labour is a major problem in clinical obstetrical practice. The most commonly used method of intrapartum fetal surveillance is the continuous recording of the fetal heart rate combined with the uterine activity (cardiotocogram, CTG). Unfortunately, this technique is limited and additional techniques are needed.

Pulse oximetry measures the arterial oxygen saturation (SaO₂) continuously and non-invasively, and has become a standard technique to monitor critically ill patients during anaesthesia and intensive care. With the development of a reflectance sensor this tech-

nique might be useful during labour. The first experimental reflectance sensors were built from the components of commercial transmission sensors [1–3]. Optimism rose when it appeared possible to obtain signals from the fetal scalp during labour for prolonged periods [1–3]. Since then other reflectance sensors have been developed and experiences during labour have been reported [4–7].

However, before reflectance pulse oximetry can be introduced into clinical practice, careful validation is required. In the human fetus validation is hampered because arterial blood samples cannot be obtained. The human adult is not a suitable subject because normal fetal SaO₂ values are mainly below 70% and it is unsafe to subject adults to such low saturation levels. The evaluation is therefore mostly done in animal models and in vitro models, and by simulations in theoretical models.

*Corresponding author. Tel.: +31 24 3616801; fax: +31 24 3541194.

The purpose of this paper is to give an overview of the accuracy of reflectance pulse oximetry for fetal use. Various factors which may influence the reliability of this technique will be discussed. The factors are divided in four groups: haemoglobin, tissue compartment, sensor-to-skin contact, and technical problems. Where possible, we will give an estimation of the magnitude of its effect for the fetal SaO_2 range (10–80%). Finally, alternative approaches in sensor design for intrapartum use will be discussed. It is beyond the scope of this survey to review all articles in which pulse oximetry is used (approx. 1000). Most articles are based on transmission pulse oximetry for an SaO_2 range of 70–100%, and have been extensively reviewed elsewhere [8–12].

2. Basic concept of reflectance pulse oximetry

Pulse oximetry relies on light absorption differences by oxyhaemoglobin (HbO_2) and deoxyhaemoglobin (Hb). Fig. 1 shows the absorption spectra of HbO_2 and Hb as measured by Zijlstra et al. [13]. In the red region of the spectrum (approx. 660 nm), Hb absorbs more light than HbO_2 , and vice versa in the infrared region (850–1000 nm). This explains why, in general, the colour of arterial blood is a more bright red than venous blood.

Reflectance pulse oximetry sensors are mostly equipped with two light emitting diodes (LEDs) which transilluminate tissue, one red and one infrared light. A photodetector receives the fluctuating back-scattered light intensities caused by the pulsating blood volume in the tissue. Pulse oximeters use a fixed empirically derived calibration curve for the relation between the SaO_2 and the ratio of the rela-

tive pulse sizes (fluctuating light intensities) for red and infrared light. As a consequence, variations in the relationship caused by differences in light propagation between subjects or locations, cannot be taken into account.

2.1. Haemoglobin

Human fetal (HbF) and human adult haemoglobin (HbA) differ slightly in their spectra in the visible range [13]. Since most commercial pulse oximeters are programmed with a calibration curve derived from studies in healthy adults, this curve might not be applicable to the fetus with high concentrations of HbF. Based on the Lambert–Beer model Zijlstra et al. [13] concluded that these differences in spectra do not affect the accuracy of pulse oximetry in the SaO_2 range of 70–100%. They used the extinction coefficients at 660 nm and 940 nm in their model [13]. An evaluation in neonates, in which arterial values were compared to pulse oximetry saturation readings (SpO_2) over a range of 80–100%, revealed similar results [14]. However, at an SaO_2 level of 25%, Nijland et al. [15] calculated that such commercial pulse oximeters will underestimate the SaO_2 by 5%. These calculations were made with the same wavelengths as Zijlstra et al. [13], using the Lambert–Beer model as well as a more complex model as described by Schmitt [15,16].

Being a two-wavelength device, a pulse oximeter can only measure the ratio of concentrations of HbO_2 and Hb, which makes it specifically sensitive to changes in SaO_2 . However, other haemoglobin derivatives, like carboxyhaemoglobin (COHb) and methaemoglobin (MetHb) also absorb light in the visible

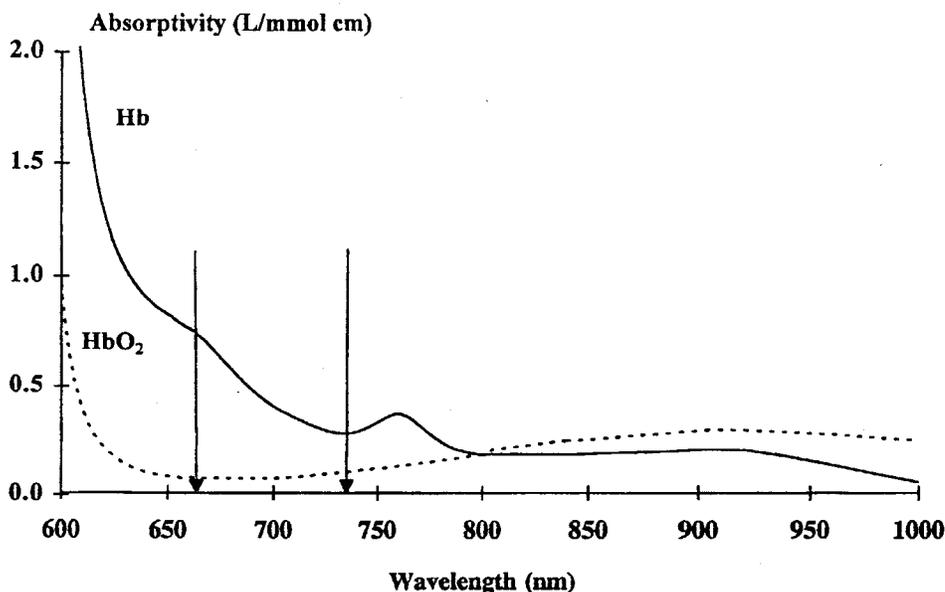


Fig. 1. Absorbance spectrum, HbO_2 : oxyhaemoglobin, Hb: deoxyhaemoglobin. Arrows indicate 660 nm and 735 nm wavelengths.

range and might therefore lead to errors in the SpO_2 . The error caused by the presence of 10% COHb appeared to be insubstantial over the whole SaO_2 range, for the wavelengths 660 nm and 940 nm, based on calculations with the Lambert–Beer model [13,15]. Barker et al. [17] and Reynolds et al. [18] reported that pulse oximeters provided erroneous readings in the presence of high levels of COHb. However, this was based on a misunderstanding of pulse oximetry, comparing the SpO_2 with the fraction of oxyhaemoglobin instead of the oxygen saturation [19]. In the presence of 10% MetHb, the Lambert–Beer model predicts an underestimation at $>70\%$ and an overestimation at $<70\%$ SaO_2 [13,15]. Similar findings were also reported by Reynolds et al. [18] using an in vitro model and by Barker et al. in dogs [20]. However, concentrations of 10% COHb and 10% MetHb are not expected in the human fetus during labour. In non-smoking pregnant women and their newborns, COHb concentrations are reported to be $<0.5\%$. COHb concentrations in blood of newborns of cigarette smoking mothers were 1.9% (S.D. 1.2%) [21].

The calibration of reflectance pulse oximetry for fetal use is more complicated than the calibration of transmission pulse oximetry for adult or neonatal use, as sample SaO_2 values cannot be obtained in the human fetus. In critically ill neonates, SaO_2 values may become as low as 60% [22], an SaO_2 value still not low enough for a fetal calibration. Therefore, animal models are used to calibrate reflectance pulse oximetry. Differences in the light absorption characteristics of haemoglobin of other species in the spectral range might lead to a different calibration line for the human fetus. Although, no differences were found at 660 nm and 940 nm for dogs and rabbits [23,24]. Presumably, haemoglobin light absorption characteristics of other mammals will not differ substantially from humans.

2.2. Tissue compartment

The attenuation of the light received at the photodetector is not only caused by absorption, but by scattering of light in tissue. The scattering of light by erythrocytes (e.g. velocity, size and shape) is of special importance, because it causes most of the fundamental problems in pulse oximetry at low saturation values. The scattering is largely determined by the haematocrit, blood flow conditions, and blood volume changes. Erythrocyte differences between human subjects and between animals might have an effect on the accuracy of pulse oximetry but this factor has not been studied yet.

The effect of various levels of haematocrit (Ht), using 660/940 or 950 nm transmission pulse oximetry,

was studied by De Kock and Tarassenko [25], and Vegfors et al. [26] with in vitro models, and by Lee et al. [27] in dogs. De Kock and Tarassenko found that the pulse oximeter was not affected by Ht differences (20, 39 and 60%) at SaO_2 levels $>50\%$, while $SaO_2 <50\%$ higher Ht levels resulted in lower red/infrared ratio's and thus in higher SpO_2 values [25]. However, Vegfors et al. found no correlation between SpO_2 readings and blood sample SaO_2 values over an SaO_2 range of 60–100% at Ht levels of 41–44%. Only after hemodilution to Ht levels of 10–11% a good agreement was found between pulse oximetry readings and sample SaO_2 values [26]. The contrasting results are probably caused by differences between the in vitro models. Lee et al. found that Ht changes did not seriously influence the accuracy of pulse oximetry when diluting the blood from 40 to 10% Ht. Below 10% Ht, pulse oximetry became inaccurate [27]. Fetal Ht levels in major blood vessels are mostly $>40\%$. In rabbit muscle capillaries Ht levels were found to be 10–15% [28]. The vascular distribution and which vascular tissue contributes to the received light is not known. It remains therefore to be seen how important Ht differences are for fetal reflectance pulse oximetry.

The effect of blood flow differences was studied with in vitro models, by De Kock and Tarassenko [25], and Lindberg et al. [29]. Above 40% SaO_2 , no effects were found on 660/950 nm transmission pulse oximetry values with different flow rates by De Kock and Tarassenko. Below 40% SaO_2 , lower flow rates resulted in lower red/infrared ratio's and higher SpO_2 values [25]. In contrast with these results, Lindberg et al. found lower SpO_2 values at low blood flow conditions at an SaO_2 of around 99%, with 660/940 nm transmission pulse oximetry [29]. It is not known how accurately the in vitro models represent the human fetal responses at low SaO_2 values.

The effect of blood volume fraction differences was studied with theoretical models [16,30] and in vitro models [25]. The theoretical models predicted that the influence of blood volume is of minor importance for the accuracy of 660/940 nm reflectance pulse oximetry if the $SaO_2 >70\%$ [16,30]. However, at an SaO_2 of 25% an overestimation of around 25% is predicted, when the blood volume was changed from 1 to 5% [16,30]. By changing the depth of the blood film in their in vitro model, De Kock and Tarassenko found similar results for 660/950 transmission pulse oximetry using an in vitro model [25]. By placing a prototype 660/890 nm reflectance sensor with the photodetector above the superficial temporal artery, Nijland et al. observed an underestimation with 5.8% for adults and 7.5% for neonates compared to the forehead location [31]. Placing the sensor with the LEDs over the artery did result in larger plethysmographic sig-

nals, but no difference in the SpO_2 values were observed [31]. An underestimation was also observed, when the same sensor was placed with the photodetector above a subcutaneous vein on the fetal lamb head [32]. The underestimation ranged from -16 to -28% in four fetal lambs, at an SaO_2 range of $20-50\%$. After coagulation of the vein, the difference between the intravascular SaO_2 and the SpO_2 was abolished [32]. The underestimation is in contradiction with the theoretical models [16,30] which predicted an overestimation as a result of increased blood volume. However, one must consider that in those models homogenous media of absorbers and scatters were used, which may not be applicable for the heterogeneity of in vivo tissue. Administration of adrenaline resulted in a vasoconstriction, and in an overestimation of $6-37\%$ in five fetal lambs, at an SaO_2 range of $20-50\%$ [32].

Using transmission pulse oximetry, venous pulsations are reported to give an underestimation of the SaO_2 , for normal adult SaO_2 values [33].

2.3. Sensor-to-skin contact

Scattering of light occurs in all situations whenever there are variations of the refractive index i.e. at cross-sections of different tissue layers, at the boundaries of blood vessels and even within the cells themselves (e.g. by the mitochondria). It is therefore likely that differences in skin structure between animals and humans will influence the calibration of reflectance pulse oximetry. For none of the animal models the magnitude of this effect is known. The piglet has histologically a skin structure most alike to humans [34].

Several circumstances at the level of sensor-to-skin contact may lead to a reduced accuracy. Johnson et al. showed that meconium stained skin caused an inaccurate oxygen saturation reading in a neonate. Their explanation for this inaccuracy was that red light was more absorbed by meconium than infrared light [35]. Optical shunting through hair is also mentioned as a possible cause for inaccuracy. However, Nijland [36] did not observe differences between measurements on wet hair or shaved skin in three fetal lambs, with a prototype $660/890$ nm Nellcor sensor. Gardosi et al. [37] showed that improper contact of the sensor to the skin can lead to erroneous pulse oximeter readings, if the light is directly shunted towards the photodetector.

Two studies have addressed the point of pressure to the back of the sensor [38,39]. Köning et al. [38] showed that pulsatility improved markedly at the forehead of adults if pressure was increased, but no consistent effect was observed in neonates. Dassel et al. [39] showed that red/infrared variability decreased with pressures between 80 and 120 mmHg applied on

the back of the sensor, at the forehead of adults. Increasing the pressure on the sensor probably decreases the venous blood in the tissue [39]. However, a lower pressure on the $660/940$ nm sensor gave inconsistent results in the red/infrared ratio. The red/infrared ratio decreased or increased to a stable level or remained unchanged [39]. The effect of most of the factors mentioned in this paragraph have not been studied in the fetal SaO_2 range.

2.4. Technical problems

Certain technical situations may interfere with a reliable estimation of the SaO_2 . Some problems related to the use of fetal reflectance pulse oximetry will be discussed in this paragraph: i.e. small pulses and signal analysis, the choice of the LED wavelengths, and motion artifacts.

The fetal plethysmographic signals obtained with reflectance pulse oximetry are typically one-tenth of the adult transmission pulse oximetry signals. The amplitude of the pulsatile component of the signal is often below 0.2% of the total signal, which is at the lower limit of signal acceptance for some commercial transmission pulse oximeters [8,40]. These small pulses lead to a lower signal to noise ratio and as a consequence a less accurate device. To optimize signal quality, fetal plethysmographic signals should be maximized while the noise is minimized. Pulse oximeters use several ways to enhance the signal processing. The fetal electrocardiogram is used to cardiosynchronize the red and infrared pulses. A high pass filter is used to detect the red and infrared peak and trough and the pulse oximeter verifies if the red and infrared peak and trough are in phase with each other. A weighted moving average of red to infrared ratio's is calculated over several heart beats [41] and the average value is converted into an SpO_2 value. If the red and infrared pulses are not properly synchronized to the fetal electrocardiogram or not in phase with each other, inaccurate SaO_2 estimations may be the result [42]. Such phase shifts of the red and infrared pulses with the heart rate was observed by placing a $660/940$ sensor on a caput succedaneum [42].

The LEDs used in commercial transmission sensors are not ideal light sources. The LEDs emit light in a narrow spectral range. However, the center wavelength of the emitted light varies between diodes of the same type of sensor, by up to 15 nm [43]. A shift in the wavelength results in a different extinction coefficient (Fig. 1) and hence in an error in the estimated SaO_2 . The effect of variation in the center wavelength will be greater for the red (660 nm) than for the infrared wavelength because its absorption spectrum shows a steeper slope. This problem can be solved in two ways. First, LEDs with center wavelengths which fall outside a specified range may be

reje
grar
wav
corr
A
that
ofte
[43].
not
migl

3. A

Fo
flect
side
stan
satu
tion
ters
devi
phot
satu
be
spec
over
subj

For
same
diffe
calcu
and
of a
stan
sion
syste
of t
stan
anal
prec
tion
racy.
eval
sens
no a

Th
syste
studi
calib
660 :
tect
plac
[46],
5.5%
Jong
SaO₂
Nell

rejected. Second, the pulse oximeter may be programmed to accept several ranges of LED center wavelength for both the red and infrared, and to correct for these different wavelengths internally [8].

Another problem related to the 660 nm LED is that a small amount of light in the infrared region is often emitted in addition to the center wavelength [43]. Although this so called 'secondary emission' does not influence the accuracy at high SaO_2 values, it might influence the accuracy at low fetal SaO_2 values.

3. Accuracy studies

For a proper evaluation of the accuracy of reflectance pulse oximetry, several issues should be considered. SpO_2 values should be compared to a reliable standard which measures the intra-arterial oxygen saturation. In general, arterial blood sample saturation values measured by multi-wavelength photometers are used. According to the manuals of these devices, the accuracy of various multi-wavelength photometers is $\pm 1\%$ absolute over the total oxygen saturation range of 0–100%. Sufficient subjects should be used and exclusion criteria for data should be specified beforehand. SpO_2 values should be obtained over the total fetal SaO_2 range, preferably for all subjects.

For the comparison of two methods measuring the same quantity, it is recommended that the mean difference and standard deviation of differences is calculated [44]. The mean difference is called the bias and may show a systematic over- or underestimation of a method relative to the standard method. The standard deviation of differences is called the precision and represents the random 'variability' of the system. Another measure for the random 'variability' of the system can be obtained by calculating the standard deviation of residuals with linear regression analysis. The standard deviation of residuals and the precision will be equal if the bias is zero. The correlation coefficient is not a sufficient measure of accuracy. If the accuracy of a reflectance pulse oximetry is evaluated in the same study in which the reflectance sensor is calibrated, the bias will be zero and will give no additional information.

The accuracy of various reflectance pulse oximetry systems has been reported in animal models. In two studies, a prototype sensor supplied by Nellcor was calibrated with either 660 and 925 nm LEDs [45], or 660 and 890 nm LEDs [46], and with a single photodetector placed 10 mm from both LEDs. The sensor was placed on the scalp of three [45], and two fetal lambs [46], respectively. Harris et al. found a precision of 5.5% over an oxyhemoglobin range of 6–81% [45] and Jongsma et al. found a precision of 3.5% above 30% SaO_2 and 6.6% below 30% SaO_2 [46]. Using the Nellcor 660/890 nm sensor Nijland et al. [36] found a

bias \pm precision of $4.7 \pm 7.3\%$ by placing the Nellcor 660/890 nm sensor on the neck of six fetal lambs over an SaO_2 range of 16–81%. In six piglets the precision was even less, using the same Nellcor 660/890 nm sensor, with a reported value of 12.9% over an SaO_2 range of 18–100% [47]. Mendelson et al. [48] developed a sensor with two pairs of 660/930 nm LEDs and a concentric row of six photodetectors and found a precision of 3.5, 4.1 and 4.8% for piglet scalp, neck and thigh measurements, respectively. The SaO_2 range was 30–100% [48]. Unfortunately, the number of animals is not stated [48]. Dassel et al. [49] also used a sensor of their own design with two LEDs for 660 and 940 nm and one photodetector at a distance of 7.5 mm from both LEDs on the fetal lamb scalp. They found a precision of 4.7% over an SaO_2 range of 17–82% in four fetal lambs [49]. Takatani et al. used a sensor with eight LEDs (four at 665 nm and four at 820 nm) placed in a circle around a single photodetector. Tissue was simultaneously warmed by additional 940 nm LEDs. The standard deviation of residuals was 2.5% for an SaO_2 range of 40–100% in five dogs [50].

4. New developments

From the reviewed studies it is clear that reflectance pulse oximetry is much more susceptible for all kind of physiological variables in the fetal SaO_2 range of 10–80% than transmission pulse oximetry in an SaO_2 range of 70–100%. Alternative approaches in sensor design must therefore be considered for intrapartum use. One theoretical suggestion is using three photodetectors at different distances of the LEDs [30].

Changing the red wavelength from 660 nm to 735 nm (Fig. 1) leads to less attenuation of the red light at low SaO_2 levels. In a theoretical Monte-Carlo model based on both absorption and scattering of light, Mannheimer [see Mannheimer P in this volume] predicted a significantly better similarity of light propagation for a 735/890 nm combination of LEDs than for a 660/890 nm combination of LEDs. A prototype reflectance sensor with a combination of 735 and 890 nm LEDs, and with a photodetector at a distance of 10 mm from both LEDs, developed by Nellcor, yielded much better results in six piglets compared with the 660/890 nm sensor [47], with a precision of 5.4%. A new version of this prototype sensor developed for intrapartum use, in which the LED-photodetector distance was changed from 10 to 14 mm was evaluated in two independent laboratories [36]. In seven piglets the sensor was calibrated. The precision was 4.7%. In a second series of four piglets this calibration was evaluated. The bias was -1.6% and the precision 5.4%. Measurements were made over an

SaO₂ range of 17–100%, with various sensors at several positions on each animal [36].

5. Conclusion

The aim of fetal surveillance during labour is straightforward: to identify fetal distress which may, if uncorrected, cause short-term morbidity, death, or possibly long-term morbidity. Undeniably, improved obstetrical care, together with cardiotocography, has led to a decrease in perinatal mortality in Western countries since 1940. The expected decrease in perinatal morbidity and long-term morbidity however was not observed, and due to a poor predictive value of cardiotocography, operative interventions during labour increased dramatically. In an effort to improve this unfortunate clinical situation it is tempting to rush for a new technique, like reflectance pulse oximetry.

Before reflectance pulse oximetry is used in obstetrical practice, it should be evaluated properly. First it should be evaluated in animal models, supported by quantitative support of in vitro models and theoretical models, and double sensor studies during labour. Several animal studies are needed in which the experimental set-up is varied. Second, if the accuracy has proven to be acceptable, clinical studies are needed to study the SaO₂ as a parameter for the fetal condition. Finally, if a clear understanding of the fetal SaO₂ monitoring together with cardiotocography has been established, a prospective randomized clinical trial can be performed.

From this review it is clear that reflectance pulse oximetry for fetal monitoring is susceptible for all kinds of physiological variables. Differences in blood volume, haematocrit and blood flow are major sources for inaccurate pulse oximetry readings with 660 nm sensors and cannot be overcome yet. Factors in the groups sensor-to-skin contact and technical problems can cause erroneous pulse oximeter values but may or have been solved. A new 735/890 nm Nellcor sensor demonstrated a promising accuracy but studies are limited.

References

- [1] Peat S, Booker M, Lanigan C, Ponte J. Continuous intrapartum measurement of fetal oxygen saturation *Lancet* 1988; ii: 213.
- [2] Johnson N, Lilford RJ. Continuous intrapartum measurement of fetal oxygen saturation. *Lancet* 1988; 2: 517.
- [3] Gardosi J, Carter M, Becket T. Continuous intrapartum monitoring of fetal oxygen saturation. *Lancet* 1989; 2: 692–693.
- [4] Gardosi JO, Schram CM, Symonds EM. Adaptation of pulse oximetry for fetal monitoring during labour. *Lancet* 1991; 337: 1265–1267.
- [5] Johnson N, Johnson VA, Fisher J, Jobbings B, Bannister J, Lilford RJ. Fetal monitoring with pulse oximetry. *Br J Obstet Gynaecol* 1991; 98: 36–41.
- [6] Knitza. Erfahrungen und Ergebnisse mit der Oxykardioto-kographie. In: Knitza R, editor. *Hypoxische Gefährdung des Fetus sub partu. Klinik und neue Überwachungsverfahren*. Darmstadt: Steinkopff, 1994; 211–218.
- [7] Dildy GA, van den Berg PP, Katz M et al. Intrapartum fetal pulse oximetry: fetal oxygen saturation trends during labor and relation to delivery outcome. *Am J Obstet Gynecol* 1994; 171: 679–684.
- [8] Tremper KK, Barker SJ. Pulse oximetry. *Anesthesiology* 1989; 70: 98–108.
- [9] Kelleher JF. Pulse oximetry. *J Clin Monit* 1989; 5: 37–62.
- [10] Mendelson Y. Pulse oximetry: theory and applications for non-invasive monitoring. *Clin Chem* 1992; 38: 1601–1607.
- [11] Severinghaus JW, Kelleher JF. Recent developments in pulse oximetry. *Anesthesiology* 1992; 76: 1018–1038.
- [12] Lindberg L-G, Lenmarken C, Vegfors M. Pulse oximetry. Clinical implications and recent technical developments. *Acta Anaesthesiol Scand* 1995; 39: 279–287.
- [13] Zijlstra WG, Buursma A, Meeuwse-van der Roest WP. Absorption spectra of human fetal and adult oxyhemoglobin, de-oxyhemoglobin, carboxyhemoglobin, and methemoglobin. *Clin Chem* 1991; 37: 1633–1638.
- [14] Rajadurai VS, Walker AM, Yu VYH, Oates A. Effect of fetal haemoglobin on the accuracy of pulse oximetry in preterm infants. *J Paediatr Child Health* 1992; 47: 1084–1085.
- [15] Nijland R, Jongsma HW, Nijhuis JG, Oeseburg B, Zijlstra WG. Notes on the apparent discordance of pulse oximetry and multiwavelength hemoglobin photometry. *Acta Anaesthesiol Scand* 1995; 39: Suppl 107: 49–52.
- [16] Schmitt JM. Simple photon diffusion analysis of the effects of multiple scattering on pulse oximetry. *IEEE Trans Biomed Eng* 1991; 38: 1194–1203.
- [17] Barker SJ, Tremper KK. The effect of carbon monoxide inhalation on pulse oximetry and transcutaneous PO₂. *Anesthesiology* 1987; 66: 677–679.
- [18] Reynolds KJ, Palayiwa E, Moyle JTB, Sykes MK, Hahn CEW. The effect of dyshemoglobins on pulse oximetry: part 1, theoretical approach and part 2, experimental results using an in vitro test system. *J Clin Monit* 1993; 9: 81–90.
- [19] Oeseburg B, Rolfe P, Siggaard Andersen O, Zijlstra WG. Definition and measurement of quantities pertaining to oxygen in blood. *Adv Exp Med Biol* 1994; 345: 925–930.
- [20] Barker SJ, Tremper KK, Hyatt J. Effect of methemoglobinemia on pulse oximetry and mixed venous oximetry. *Anesthesiology* 1989; 70: 112–117.
- [21] Fogh-Andersen N, Sindberg Eriksen P, Grinsted J, Siggaard-Andersen O. HbCO in mothers and newborns. *Scand J Clin Lab Invest* 1988; 48: Suppl 189: 27–32.
- [22] Boxer RA, Gottesfeld I, Singh S, LaCorte MA, Parnell A Jr, Walker P. Non-invasive pulse oximetry in children with cyanotic congenital heart disease. *Crit Care Med* 1987; 15: 1062–1064.
- [23] Sendak MJ, Harris AP, Donham RT. Accuracy of pulse oximetry during arterial oxyhemoglobin desaturation in dogs. *Anesthesiology* 1988; 68: 111–114.
- [24] Vegfors M, Sjöberg F, Linberg L-G, Gustafsson U, Lenmarken C. Basic studies of pulse oximetry in a rabbit model. *Acta Anaesthesiol* 1991; 35: 596–599.
- [25] Kock JP de, Tarassenko L. In vitro investigation of the factors affecting pulse oximetry. *J Biomed Eng* 1991; 13: 61–66.
- [26] Vegfors M, Lindberg-L, Öberg PÅ. Accuracy of pulse oximetry at various hematocrits and during hemolysis in an in vitro model. *Med Biol Eng Comp* 1993; 31: 135–141.

- [27] Lee S, Tremper KK, Barker SJ. Effects of anemia on pulse oximetry and continuous mixed venous haemoglobin saturation in dogs. *Anesthesiol* 1991; 75: 118-122.
- [28] Ley K, Lindbom L, Arfors KE. Haematocrit distribution in rabbit tenuissimus muscle. *Acta Physiol Scand* 1988; 132: 373-383.
- [29] Lindberg L-G, Vegfors M, Lennmarken C, Öberg PÅ. Pulse oximeter signal at various blood flow conditions in an in vitro model. *Med Biol Eng Comput* 1995; 33: 87-91.
- [30] Graaff R. Tissue optics applied to reflectance pulse oximetry. Thesis 1993, Groningen, The Netherlands.
- [31] Nijland R, Jongsma HW, van den Berg PP, Nijhuis JG, Oeschburg B. The effect of pulsating arteries on reflectance pulse oximetry: measurements in adults and neonates. *J Clin Monit* 1995; 11: 118-122.
- [32] Nijland R, Jongsma HW, Verbruggen IM, Nijhuis JG. Reflectance pulse oximetry in fetal lambs: subcutaneous vessels and vasoconstriction affects its reliability. *J Clin Monit* 1996; 12: 225-230.
- [33] Kim JM, Arakawa K, Benson KT, Fox DK. Pulse oximetry and circulatory kinetics associated with pulse volume amplitude measured by photoelectric plethysmography. *Anesth Analg* 1986; 65: 1333-1339.
- [34] Meyer W, Schwarz, Neurad K. The skin of domestic mammals as a model for the human skin, with special reference to the domestic pig. *Curr Probl Dermatol* 1978; 7: 39-52.
- [35] Johnson N, Johnson VA, Bannister J, McNamara H. The effect of meconium on neonatal and fetal reflectance pulse oximetry. *J Perinat Med* 1990; 18: 351-355.
- [36] Nijland R. Arterial oxygen saturation in the fetus: an experimental animal study with pulse oximetry. Thesis 1995, Nijmegen, The Netherlands.
- [37] Gardosi JO, Damianou D, Schram CMH. Artifacts in fetal pulse oximetry: Incomplete sensor-to-skin contact. *Am J Obstet Gynecol* 1994; 170: 1169-1173.
- [38] Köng V, Ullrich GJ, Huch A, Huch R. Reflection pulse oximetry — experiences in Zürich. In: Lafeber HN, Aarnoudse JG, Jongsma HW, eds. *Fetal and neonatal physiological measurements*. Amsterdam: Elsevier, 1991; 111-117.
- [39] Dassel ACM, Graaff R, Sikkema M, Meijer A, Zijlstra WG, Aarnoudse JG. Reflectance pulse oximetry at the forehead improves by pressure on the probe. *J Clin Monit* 1995; 11: 237-244.
- [40] Wukitsch MW, Petterson MT, Tobler DR, Pologe JA. Pulse oximetry: analysis of theory, technology, and practice. *J Clin Monit* 1988; 4: 290-301.
- [41] Technical issues of non-invasive fetal oxygen saturation monitoring using the Nellcor N-400. Pleasanton CA: Nellcor Puritan Bennett 1995; 1-13.
- [42] Schram CMH, Gardosi JO. Artifacts in fetal pulse oximetry: Non-arterial pulsatile signals. *Am J Obstet Gynecol* 1994; 170: 1174-1177.
- [43] Pologe JA. Pulse oximetry; Technical aspects of machine design. *Int Anesthesiol Clin* 1987; 25: 137-153.
- [44] Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; 1: 307-310.
- [45] Harris AP, Sendak MJ, Chung DC, Richardson CA. Validation of arterial oxygen saturation measurements in utero using pulse oximetry. *Am J Perinat* 1993; 10: 250-254.
- [46] Jongsma HW, Crevels J, Menssen JJM et al. Application of transmission and reflection pulse oximetry in fetal lambs. In: Lafeber HN, Aarnoudse JG, Jongsma HW, editors. *Fetal and Neonatal Physiological Measurements*. Amsterdam: Elsevier, 1991; 123-128.
- [47] Nijland R, Jongsma HW, Nijhuis JG. Reflectance pulse oximetry (RPOX): two sensors compared. *Am J Obstet Gynecol* 1995; 172, part 2, 365.
- [48] Mendelson Y, Yocum BL. Non-invasive measurement of arterial oxyhemoglobin saturation with a heated and non-heated skin reflectance pulse oximeter sensor. *Biomed Instrum Technol* 1991; 25: 472-480.
- [49] Dassel AC, Graaff R, Aarnoudse JG et al. Reflectance pulse oximetry in fetal lambs. *Pediatr Res* 1992; 31: 266-269.
- [50] Takatani S, Davies C, Sakakibara N. Experimental and clinical evaluation of a non-invasive reflectance pulse oximeter sensor. *J Clin Monit* 1992; 8: 257-266.

Pulse Oximetry: An Alternative Method for the Assessment of Oxygenation in Newborn Infants

Michael S. Jennis, MD, and Joyce L. Peabody, MD

From the Department of Pediatrics, Children's Hospital of San Francisco and the Cardiovascular Research Institute, University of California, San Francisco

ABSTRACT. Continuous monitoring of oxygenation in sick newborns is vitally important. However, transcutaneous PO₂ measurements have a number of limitations. Therefore, we report the use of the pulse oximeter for arterial oxygen saturation (SaO₂) determination in 26 infants (birth weights 725 to 4,000 g, gestational ages 24 to 40 weeks, and postnatal ages one to 49 days). Fetal hemoglobin determinations were made on all infants and were repeated following transfusion. SaO₂ readings from the pulse oximeter were compared with the SaO₂ measured in vitro on simultaneously obtained arterial blood samples. The linear regression equation for 177 paired measurements was: $y = 0.7x + 27.2$; $r = .9$. However, the differences between measured SaO₂ and the pulse oximeter SaO₂ were significantly greater in samples with >50% fetal hemoglobin when compared with samples with <25% fetal hemoglobin ($P < .001$). The pulse oximeter was easy to use, recorded trends in oxygenation instantaneously, and was not associated with skin injury. We conclude that pulse oximetry is a reliable technique for the continuous, noninvasive monitoring of oxygenation in newborn infants. *Pediatrics* 1987;79:524-528; *oximetry, monitoring, newborn, oxygen saturation*.

The continuous monitoring of oxygenation in sick newborn infants is routine in neonatal intensive care units. Transcutaneous PO₂ monitoring, the most widely used method, demonstrates wide fluctuations in PO₂ that cannot be detected by intermittent sampling of arterial blood.¹ Transcutaneous PO₂ permits rapid detection of hypoxemia associated with apnea, hypoventilation, or procedures.^{2,3} However, transcutaneous monitoring has

serious limitations including frequent calibration periods and a heated electrode, which causes first- and, occasionally, second-degree burns.⁴ Furthermore, unpredictable gradients have been reported between skin and arterial PO₂ values in older infants and in infants with bronchopulmonary dysplasia.^{5,6} The idea of an alternative noninvasive method for assessment of oxygenation is attractive.

The pulse oximeter, a newly available monitor, continuously and noninvasively measures the oxygen saturation (SaO₂) of arterial hemoglobin.^{7,8} This device uses spectrophotometric principles to determine SaO₂ with each arterial pulsation. Its accuracy in adults and children has been reported.⁸⁻¹⁰ However, several characteristics of newborn infants raise concerns regarding the applicability of this technique in neonatal medicine: (1) fetal hemoglobin is known to affect in vitro spectrophotometric methods of SaO₂ determination;¹¹⁻¹³ (2) the rapid heart rate may exceed the response time of the oximeter; and (3) the smaller, more fragile monitoring surfaces may limit the use of the sensor. Whereas some studies have included newborns,^{9,10,14,15} the effects of the newborn's characteristics have not been adequately studied. Therefore, we designed a study to test the reliability, accuracy, and practicality of the pulse oximeter for the assessment of oxygenation in sick newborn infants.

PATIENTS AND METHODS

Twenty-six infants with umbilical or peripheral arterial catheters in place for clinical management were entered into the study after written informed consent from the parents was obtained. This procedure was approved by the Human Experimentation Committee of Children's Hospital of San Francisco. Mean birth weight was 1,710 g (range 725 to

Received for publication Dec 2, 1985; accepted July 9, 1986.
Presented, in part, at the Western Society for Pediatric Research meeting, Feb 7, 1985, Carmel, CA.
Reprint requests to (M.S.J.) Department of Pediatrics, Kaiser-Permanente Medical Center, 280 W MacArthur Blvd, Oakland, CA 94611.
PEDIATRICS (ISSN 0031 4005). Copyright © 1987 by the American Academy of Pediatrics.

4,000 g), mean gestational age was 30.6 weeks (range 24 to 40 weeks), and postnatal age at the time of study ranged from one to 49 days. Three infants were studied when they were more than a month old. The percentage of fetal hemoglobin present was determined by electrophoresis at the time an infant was entered into the study and was repeated following each transfusion.

The Nellcor N-100 pulse oximeter (Hayward, CA) used for this study is composed of a disposable optical sensor connected to a microprocessor for calculation of SaO_2 . Heart rate and SaO_2 are displayed digitally. Calibration is not required.

The sensor was placed around the foot if an umbilical catheter was in place or on the ipsilateral hand if a radial catheter was in place. It was shielded if phototherapy lights or radiant warmers were in use. When in the correct position, the heart rate displayed on the pulse oximeter was the same as that observed on the infant's bedside monitor. A pulse oximeter reading was recorded when an arterial blood sample was obtained for clinical management. SaO_2 of the blood sample was measured on an Instrumentation Laboratory 282 CO-Oximeter (IL 282). In addition to SaO_2 , the IL 282 determined the percentages of carboxyhemoglobin and methemoglobin. Because of the known error in SaO_2 measurements when fetal hemoglobin is present,¹¹⁻¹³ the method of Cornelissen and co-workers¹⁶ was used to correct the falsely elevated carboxyhemoglobin levels reported by the IL 282. The fractions of oxyhemoglobin, methemoglobin, and corrected carboxyhemoglobin were used to calculate the functional saturation. Arterial PO_2 was measured on a Corning 170 blood gas analyzer.

In addition, heart rate, arterial BP measured from a Gould-Statham transducer (Hato Rey, Puerto Rico), axillary temperature, and serum bilirubin were measured. The use of vasopressor agents, muscle relaxants, and sedatives was recorded.

Linear regression analysis was performed to compare the pulse oximeter SaO_2 with the blood SaO_2 for all paired measurements. Data were also analyzed according to percentage of fetal hemoglobin present, grouped as 0% to 24%, 25% to 49%, 50% to 74%, and 75% to 100%. Analysis of variance was used to compare the differences between blood SaO_2 and pulse oximeter SaO_2 among the four groups.

RESULTS

From the 26 infants 177 paired arterial blood and pulse oximeter SaO_2 measurements were obtained (the number of measurements per infant was one to 35). The sensor was easily applied to the hand

or foot in all instances, even in the smallest infant who weighed 725 g. Readings could be obtained from all infants despite heart rates as high as 220 beats per minute.

The linear regression equation comparing pulse oximeter SaO_2 value to measured SaO_2 was $y = 0.7x + 27.2$ ($N = 177$; $r = .9$; SE of the estimate = 1.87%) (Figure). Blood SaO_2 values ranged from 70.1% to 100%, and pulse oximeter SaO_2 values ranged from 71% to 100%.

Forty-nine fetal hemoglobin determinations were made. Values varied from 5% to 100%. The measured values of blood SaO_2 , arterial PO_2 , and difference between blood SaO_2 and pulse oximeter SaO_2 according to fetal hemoglobin range are shown in Table. There were comparable numbers of paired pulse oximeter readings and arterial saturation measurements in the four ranges. Although PaO_2 values were similar among the four groups, the higher affinity of fetal hemoglobin for oxygen resulted in higher SaO_2 measurements when a greater percentage of fetal hemoglobin was present. The values were almost identical when fetal hemoglobin was <50% but a 2.8% to 3.6% error was observed when it exceeded 50% ($P < .001$). However, 68 of the 82 arterial samples were greater than 95% saturated in the two high fetal hemoglobin groups. When the fetal hemoglobin value was greater than 50% and the blood SaO_2 result was greater than 95%, the pulse oximeter SaO_2 value was always less than the blood SaO_2 value.

Measurements of heart rate, BP, and serum bilirubin and use of vasopressor agents (two infants), muscle relaxants (nine infants), or sedatives (11

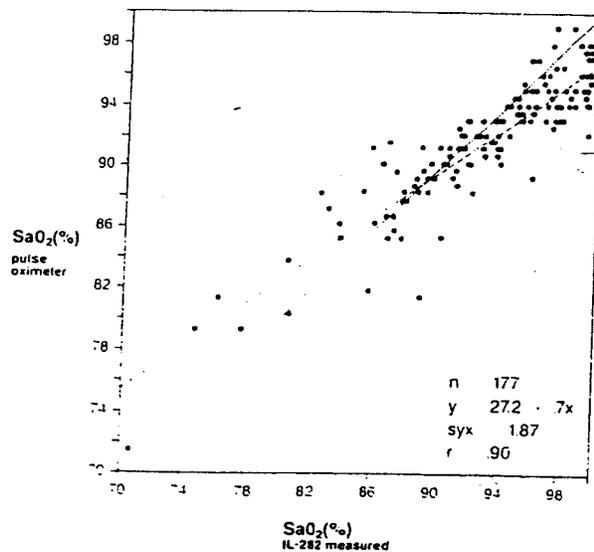


Figure. Pulse oximeter SaO_2 compared with blood SaO_2 (IL 282 CO-Oximeter) values. Solid line represents line of identity.

TABLE. Oxygenation Measurements According to Percentage of Fetal Hemoglobin*

Fetal Hb (%)	No. of Determinations	No. of Samples With SaO ₂ >95%	Blood SaO ₂ (IL 282) (%)	PaO ₂ (mm Hg)	ΔSaO ₂ (%)
75-100	40	35	97.4 ± 5.3	63.7 ± 19.5	3.6 ± 2.3†
50-74	42	33	96.4 ± 5.6	69.4 ± 20.5	2.8 ± 2.4†
25-49	45	14	92.8 ± 3.9	59.6 ± 10.3	0.5 ± 2.4
0-24	50	9	90.6 ± 4.9	61.9 ± 16.7	0.3 ± 1.9

* SaO₂, arterial oxygen saturation; ΔSaO₂, blood SaO₂ minus pulse oximeter SaO₂. Results are means ± SD.

† *P* < .001 compared to 0% to 24% fetal hemoglobin.

infants) were similar in the four fetal hemoglobin ranges and had no obvious effect on the results.

DISCUSSION

We found the Nellcor pulse oximeter to be a practical and accurate device for continuous assessment of oxygenation in newborn infants. Despite a wide range of birth weights, postnatal ages, and heart rates, monitoring was possible in all infants and no skin injuries were observed. Accuracy of pulse oximeter measurements varied among infants. Both the percentage of fetal hemoglobin present and the percentage saturation affected the difference between blood SaO₂ and pulse oximeter SaO₂ values. The greatest accuracy was observed when less than 50% fetal hemoglobin was present. The mean difference between measured SaO₂ and pulse oximeter SaO₂ values was 0.3% for 0% to 24% fetal hemoglobin and 0.5% for 25% to 49% fetal hemoglobin.

The reasons for the differences in pulse oximeter SaO₂ value seen with highly saturated fetal hemoglobin cannot be readily explained. The reliability of spectrophotometric techniques for the measurement of saturation in newborns has been questioned.¹¹⁻¹³ The IL 282 CO-Oximeter used for arterial saturation measurements in our study is a four-wavelength spectrophotometer. Zwart and co-workers¹¹ reported falsely low oxyhemoglobin and falsely elevated carboxyhemoglobin readings when the IL 282 was used for SaO₂ determinations on blood containing fetal hemoglobin. Zijlstra and co-workers¹³ suggested that this artifact was related to slight differences in the absorption characteristics of fetal and adult hemoglobin for the wavelengths used by the IL 282. These artifacts are most significant when SaO₂ is high and fetal hemoglobin predominates. However, Cornelissen and co-workers¹⁶ reported a practical correction for these errors. The correction enables the IL 282 to be used for SaO₂ determinations when fetal hemoglobin is present and was applied to all IL 282 measurements in our study.

The wavelengths used by the pulse oximeter are

in the red (660 nm) and infrared (920 nm) regions of the spectrum and are different from those used by the IL 282. Studies are in progress to evaluate whether significant differences exist between the light absorptions of adult and fetal hemoglobins for the wavelengths used by the pulse oximeter (B. Boesterling, personal communication, 1985). When fetal hemoglobin was greater than 50%, most SaO₂ measurements were greater than 95%; it is, therefore, not possible to eliminate the influence of high saturation on pulse oximeter measurements.

We were unable to identify any physiologic factors to explain our findings. Heart rate, BP, or use of drugs did not appear to affect the correlation. Adult hemoglobin was the predominant hemoglobin when infants were older and had had more complicated hospital courses. More transfusions were required in the clinical management of these infants. However, the accuracy of the pulse oximeter was greater in these sicker infants.

Environmental factors may affect pulse oximeter function. Heat lamps have been reported to interfere with the pulse oximeter because of the high intensity of the light that they emit.¹⁷ Saturation cannot be calculated because the small changes in light transmission detected by the pulse oximeter are masked by the strong ambient light. In preliminary studies, we found similar interference with pulse oximeter measurements when infants were on open tables under radiant warmers. This problem was avoided by shielding the sensor.

The pulse oximeter requires adequate perfusion of the underlying tissues. It must detect adequate arterial pulsations to differentiate arterial from venous and capillary SaO₂. Mihm and Halperin¹⁸ reported signal loss when adult patients were receiving dopamine infusions. We were able to successfully monitor two infants who were receiving dopamine.

Despite the observed, and as yet unexplained, effect of high fetal hemoglobin and high SaO₂ on pulse oximeter determination, our data suggest an acceptable accuracy for clinical use in all newborn infants. Furthermore, the use of the pulse oximeter

has a number of advantages over transcutaneous PO₂ monitoring. The pulse oximeter displays changes in oxygenation instantaneously. It is practical and easy to use, particularly during high-risk periods such as transport and surgery. Calibration is not required, and readings are available within seconds of application.

A major goal of continuous oxygen monitoring is to limit the number of episodes of hypoxemia and hyperoxemia that would otherwise go undetected. SaO₂ is more indicative of the total oxygen content of the blood than is PaO₂ and is most sensitive to hypoxemia when the steep portion of the oxygen dissociation curve is reached. With hyperoxemia, large increases in PaO₂ values may be associated with only a small change in SaO₂. To avoid hypoxemia and hyperoxemia, Wilkinson and co-workers¹⁹ have recommended that the goal for SaO₂ in newborns should be approximately 90%. The pulse oximeter is a practical means of adjusting inspired oxygen so that the desired SaO₂ can be achieved. A saturation monitor should not be used alone for the assessment of oxygenation when hyperoxemia is a concern. The periodic measurement of arterial blood gases is necessary to ensure that the PaO₂ value is in an acceptable range. This is particularly important for the immature infant with high fetal hemoglobin and high SaO₂ who may be at risk for retrolental fibroplasia.

Two groups of infants who may uniquely benefit from pulse oximeter monitoring were identified in our study. The very premature infant is particularly sensitive to skin injury caused by the heated transcutaneous PO₂ electrode and fixation ring. As the pulse oximeter sensor is not heated, thermal injury does not occur. The only potential source for skin injury is the adhesive on the sensor. However, we found no such injury in the four infants who weighed less than 1,000 g. Although the manufacturer recommends daily inspection of the sensor and site, we have monitored infants for as many as three days without changing sensor location.

Older infants and infants with bronchopulmonary dysplasia are known to have increased and unpredictable gradients between arterial and transcutaneous PO₂ values.^{5,6} Also, because it is often difficult to obtain arterial blood from these infants, the PaO₂ result reported may not be an accurate reflection of the infant's oxygenation. We have found the pulse oximeter SaO₂ to be a reliable measurement of SaO₂ in infants with greater than 50% adult hemoglobin. In addition, our observations in three infants with bronchopulmonary dysplasia suggest that the pulse oximeter is useful for both inpatient and outpatient management.

In summary, the pulse oximeter provides a reli-

able, continuous assessment of oxygenation in newborn infants. Its rapid response time and ease of use make it a practical device for use on all sick newborns. To avoid hyperoxemia, it should be used in conjunction with arterial blood gas measurements. It is a better way of monitoring oxygenation in immature infants and in infants with bronchopulmonary dysplasia.

ACKNOWLEDGMENTS

Dr. Jennis was supported, in part, by the American Lung Association of California.

The authors thank Sandi Feaster for assistance in the study, Dr June P. Brady and Marcia Allen for review of the manuscript, and Myrna Pantango for preparation of the manuscript.

REFERENCES

1. Peabody JL, Willis MM, Gregory GA, et al: Clinical limitations and advantages of transcutaneous oxygen electrodes. *Acta Anaesthesiol Scand* 1978;68(suppl):76-82
2. Peabody JL, Gregory GA, Willis MM, et al: Failure of conventional monitoring to detect apnea resulting in hypoxia. *Birth Defects* 1979;15:274-284
3. Long JG, Philip AGS, Lucey JF: Excessive handling as a cause of hypoxemia. *Pediatrics* 1980;65:203-207
4. Golden SM: Skin craters—A complication of transcutaneous oxygen monitoring. *Pediatrics* 1981;67:514-516
5. Rome ES, Stork EK, Carlo WA, et al: Limitations of transcutaneous PO₂ and PCO₂ monitoring in infants with bronchopulmonary dysplasia. *Pediatrics* 1984;74:217-220
6. Emery JR, Peabody JL: Are we misusing transcutaneous PO₂ and PCO₂ measurements in infants with bronchopulmonary dysplasia? abstracted. *Pediatr Res* 1983;17:374A
7. Yoshiya I, Shimada Y, Tanaka K: Spectrophotometric monitoring of arterial oxygen saturation in the finger tip. *Med Biol Eng Comput* 1980;18:27-32
8. Yelderman M, New W: Evaluation of pulse oximetry. *Anesthesiology* 1983;59:349-351
9. Swedlow DB, Stern S: Continuous non-invasive oxygen saturation monitoring in children with a new pulse oximeter; abstracted. *Crit Care Med* 1983;11:228
10. Fanconi S, Doherty P, Edmonds JF, et al: Pulse oximetry in pediatric intensive care: Comparison with measured saturations and transcutaneous oxygen tension. *J Pediatr* 1985;107:362-366
11. Zwart A, Buursma A, Oeseburg B, et al: Determination of hemoglobin derivatives with the IL 282 CO-Oximeter as compared with a manual spectrophotometric five-wave-length method. *Clin Chem* 1981;27:1903-1907
12. Huch R, Huch A, Tuchschnid P, et al: Carboxyhemoglobin concentration in fetal cord blood, letter. *Pediatrics* 1983; 71:461-462
13. Zijlstra WG, Buursma A, Koek JN, et al: Problems in the spectrophotometric determination of HbO₂ and HbCO in fetal blood, in Maas AHJ, Kofstad J, Siggard-Andersen O, et al (eds): *Proceedings of the 9th Meeting of the IFCC Expert Panel on pH and Blood Gases*. Oslo, Private Press 1984, pp 45-55
14. Monaco F, Feaster WW, McQuitty JC, et al: Continuous noninvasive oxygen saturation monitoring in sick newborns. *Respir Care* 1983;28:1362
15. Deckardt R, Seward DJ: Noninvasive arterial hemoglobin oxygen saturation versus transcutaneous oxygen tension monitoring in the preterm infant. *Crit Care Med* 1984; 12:935-939

16. Cornelissen PJH, van Woensel CLM, van Oel WC, et al: Correction factors for hemoglobin derivatives in fetal blood, as measured with the IL 282 CO-Oximeter. *Clin Chem* 1983;29:1555-1556
 17. Brooks TD, Paulus DA, Winkle WE: Infrared heat lamps interfere with pulse oximeters. *Anesthesiology* 1984;61:630
 18. Mihm FG, Halperin BD: Noninvasive detection of profound arterial desaturations using a pulse oximetry device. *Anesthesiology* 1985;62:85-87
 19. Wilkinson AR, Phibbs RH, Gregory GA: Continuous measurement of oxygen saturation in sick newborn infants. *J Pediatr* 1978;93:1016-1019
-

The Accuracy of Pulse Oximetry in Neonates: Effects of Fetal Hemoglobin and Bilirubin

JOHN V. ANDERSON, MD

The influence of bilirubin (total, indirect, and unbound) and fetal hemoglobin (HbF) on the accuracy of the Ohmeda-Biox 3700 (Boulder, CO) and the Nellcor N100 (Hayward, CA) pulse oximeters was evaluated. Eighteen ill infants (gestational age, 33.1 ± 4.5 [SD] weeks; weight, 2.039 ± 868 g; chronologic age, 6–149 hours) with indwelling umbilical arterial catheters were studied. Samples from the umbilical arterial catheter were measured on a Radiometer OSM-2 Hemoximeter, which was corrected for the effect of bilirubin using Radiometer's methodology. Accuracy of the oximeters was defined as the difference between the corrected value of the OSM-2 and the pulse oximeter reading. Unbound bilirubin was measured on 15 of the 18 infants with a UB Analyzer UA-1 (Labo Science USA, Inc., New York, NY). HgbF was determined with alkaline denaturation. The OB3700 and N100 had values of 90.6 ± 7.2 and 90.8 ± 8.7 , respectively. Analysis of variance showed no difference among the OB3700, N100, and OSM-2. The correlation coefficient of the OB3700 and N100 to the OSM-2 were 0.92 and 0.95, respectively. The standard error of the estimate for the two oximeters was 3.0. The relationship between bilirubin and HbF on the pulse oximeters' accuracies is listed in Table I.

The table shows that changes in bilirubin and HbF fail to account for variability in pulse oximeter accuracy. We conclude that both the OB3700 and N100 accurately reflect measured oxyhemoglobin independent of bilirubin and HbF levels.

Staff Neonatologist, Section of Neonatal/Perinatal Medicine, The Children's Mercy Hospital, Kansas City, Missouri.

Address correspondence and reprint requests to Dr. Anderson: Section of Neonatal/Perinatal Medicine, The Children's Mercy Hospital, 24th at Gilham Road, Kansas City, MO 64108.

0743-8346/87 \$0.00 + .25

	Range	Mean \pm SD	r^2	
			OB3700	N100
Total bilirubin mg/dl	2.9–12.8	6.7 \pm 2.8	0.22	0.06
Indirect bilirubin mg/dl	2.6–12.5	6.4 \pm 2.8	0.23	0.07
Unbound bilirubin μ g/dl	0.09–0.65	0.27 \pm 0.15	0.08	0.001
Fetal hemoglobin %	17–82	59.6 \pm 19.0	0.005	0.22

The Uses, Benefits, and Limitations of Pulse Oximetry in Neonatal Medicine: Consensus on Key Issues

WILLIAM W. HAY, Jr., MD, *Moderator*

The main goal of the meeting was to address issues surrounding the safe use of pulse oximetry in neonatal medicine. Fifty per cent of the symposium time was devoted to discussion of, and efforts to draw conclusions on, the issues identified by the participants. This article presents the group's consensus on these key topics, each of which was discussed during the course of the symposium as well as during the consensus session held on the final afternoon.

The key issues addressed are listed in the following section. The appendix at the end of this article lists the findings on a quick reference card.

1. What are the nomenclature and abbreviations for pulse oximetry readings?
2. What is the effect of "interfering substances and conditions" on the accuracy of pulse oximetry readings?
 - a. Fetal hemoglobin
 - b. Carboxyhemoglobin
 - c. Methemoglobin
 - d. Bilirubin
 - e. Skin pigmentation
 - f. Motion
3. What is the gold standard for correlation of pulse oximetry saturations?
4. How can you ensure that the correlating sample was drawn correctly and the most correct saturation number noted?
5. What are the safe saturation limits and alarm settings for infants? Are these different for different populations?

Nomenclature and Abbreviation

Pulse Oximetry

The terminology used to describe pulse oximetry should distinguish it from indwelling arterial oximetry, oximetry with the Hewlett-Packard ear oximeter, co-oximetry and hemoximetry, and transcutaneous oxygen monitoring.

It was agreed that the use of the word *transcutaneous* was not desirable with pulse oximetry. Though the light passes through the skin, the pulse oximeter has no interaction with the skin. Eliminating the word *transcutaneous* from discussions on pulse oximetry also will eliminate confusion between pulse oximetry and transcutaneous oxygen measurements with a Clarke electrode-type device.

The abbreviation to be used with pulse oximetry is SpO₂. This means arterial oxygen saturation as measured with a pulse oximeter. SpO₂ has been used previously in the literature.¹ (Other abbrevia-

Associate Professor of Pediatrics, Head, Section of Neonatology, University of Colorado Health Sciences Center, Denver, Colorado.

Address correspondence and reprint requests to Dr. Hay: University of Colorado Health Sciences Center, Department of Pediatrics, Box B-195, Denver, CO 80262.

0743-8346/87 \$0.00 + .25

tions suggested were SaO₂, SoxO₂, SpoO₂, Pox, oxSo₂, pSO₂.)

Interfering Substances and Conditions

These items are classified as to their theoretical significance, their clinical significance, and their need for further research.

Fetal Hemoglobin

Theoretically Significant? Yes—The chemical makeup and the extinction curve for fetal hemoglobin (HbF) are slightly altered from those for adult hemoglobin (HbA).

Clinically Significant? No—The pulse oximeter would read accurately because it is reading the per cent of hemoglobin that is saturated. Note, though, that the critical issue is to obtain a baseline PO₂ in premature infants with a left-shifted oxyhemoglobin dissociation curve; a baseline PO₂ needs to be obtained to correlate the existing PO₂ to the SaO₂.

Carboxyhemoglobin

Theoretically Significant? Yes—Pulse oximetry can only differentiate between bound hemoglobin and "reduced" (unbound) hemoglobin. Two wavelengths cannot do this, and to date, research has not been able to do it with three. The extinction curve for carboxyhemoglobin essentially mimics the oxyhemoglobin curve in the red-light range and falls off the useful chart in the 800-nm and beyond range.

Clinically Significant? Yes—Because it can differentiate only between bound and unbound hemoglobin, the readings may be falsely high. Clinical research has shown that if the carboxyhemoglobin is less than 3 per cent, it will not affect the readings. This is primarily because the relationship is not exactly one to one and under 3 per cent will fall within the accuracy specifications of a pulse oximeter. An approximate rule of thumb, however, is that for every 1 per cent of carboxyhemoglobin, you would have an additional per cent reading on your pulse oximeter. For example, the SaO₂ is 86 per cent and the carboxyhemoglobin is 7 per cent. The pulse oximeter would read 93 per cent. An even closer approximation would be that 80 per cent of the carboxyhemoglobin added to the SaO₂ would equal the SpO₂.

Methemoglobin/Sulfhemoglobin

Needs further research.

Bilirubin

Theoretically Significant? No—It depends on the wavelengths used in the oximeter. Bilirubin's extinction

curve is out of the wavelength range of 660 and 940 nm, those used in pulse oximetry. It does not affect the pulse oximeter's readings. It may affect co-oximeters, however, if they use wavelengths that are in that spectrum, that is, the shorter wavelengths.

Clinically Significant?—Not to pulse oximetry

Skin Pigmentation

Theoretically Significant? Yes and no—If the intensity of the light-emitting diodes (LEDs) is not bright enough, darkly pigmented skins may absorb enough light to give poor readings. Some oximeters will give a message such as "insufficient light detected" if a valid signal cannot be obtained.

Clinically Significant? Yes and no—Under the conditions just described, it is a problem if the oximeter cannot provide some alert to the problem with a message or symbol.

Motion Artifact

Theoretically or Clinically Significant: Yes—This is only a problem if you have no way to identify the motion artifact. A waveform can distinguish motion artifact from a good pulsatile flow. Motion artifact was acknowledged by most of the participants as something that should be eliminated to improve the usefulness of pulse oximeters. At this time, the technology of using two LEDs in a probe prohibits the complete elimination of motion artifact. Clinicians must demand of the manufacturers that they keep working on this issue. For example, a change in probe design could result in a decrease in the number of false alarms caused by motion.

The Gold Standard

"Gold standard" in this context refers to another existing technology against which the accuracy and/or reliability of the pulse oximeter is compared. At this time, the commonly used gold standards are 1) measured oxygen saturations from a co-oximeter/hemoximeter, and 2) calculated oxygen saturations from basic blood gas analyzers.

Measured Oxygen Saturations: Co-oximetry/Hemoximetry

This technology is accepted as the best gold standard at this time. However, co-oximeters use different wavelengths and, in fact, have shown erroneously elevated CO levels due to the effect of fetal hemoglobin. The Cornelissen correction factor has been used with some co-oximeters to attain closer correlations. The two-wavelength Radiometer OSM-2 hemoximeter has been shown to correlate very well with pulse oximetry without a correction factor.

Calculated O₂
 Calculated O₂
 machines are
 error reading:
 additional e
 clinician wil
 when, in fac
 that there a
 gas analysis
 assumptions o
 generate, an
 the algorithm
 analysis inst
 Sampling T
 Many factor:
 oxian to fal
 pO₂ readin
 when do yo

Terminology
 Abbreviations
 Gold Standard
 Interfering S
 HbF
 COHb
 MethHb
 SulfHb
 Bilirubin
 Skin pigm

Set Saturation
 Low
 High

Calculated Oxygen Saturations

Calculated oxygen saturations from standard blood gas machines are not acceptable for validating pulse oximeter readings, because the value calculated has its own additional error built in. The hazard here is that the clinician will judge the oximeter reading to be incorrect when, in fact, it might be correct. The group realizes that there are institutions that rely on standard blood gas analysis. The participants cautioned that the assumptions of normal adult hemoglobin, 2,3-diphosphoglycerate, and, in some cases, PCO₂ can lead to errors in the algorithm to calculate SaO₂ with some blood gas analysis instruments.

Sampling Techniques When Doing Correlations

Many factors in the sampling technique can lead the clinician to false conclusions regarding the accuracy of an SpO₂ reading. The key point raised in this meeting was, when do you look at the oximeter and take a reading:

before, during, or after the blood gas has been drawn? The suggestion is to read the oximeter while the blood is going into the syringe; the numbers should be allowed to stabilize for 5 to 10 seconds before and after you note the SpO₂.

Safe Upper and Lower Saturation Limits for Neonates

The discussion on this topic was long and complex. It was decided that this topic warranted further research. The following high and low saturations were agreed on by consensus: low SpO₂, 87 to 89 per cent; high SpO₂, 94 to 95 per cent. Further research will be needed. Pulse oximetry has made us reexamine how much oxygen/PO₂ babies need.

Reference

1. Payne JP, Severinghaus JW: Pulse Oximetry. New York, Springer-Verlag, 1986

Appendix: Reference Card for Pulse Oximetry in Neonatal Medicine

Terminology		Pulse Oximetry			Explanation
Abbreviation		SpO ₂			
Gold Standard		Co-oximetry/Hemoximetry			
Interfering Substances	Theoretically Significant	Clinically Significant	Needs More Research		
HbF	Yes	No	—		
COHb	Yes	Yes	—		Causes false-high values if <3% COHb
MechHb	—	—	Yes		
SulfHb	—	—	Yes		
Bilirubin	No	No	—		
Skin pigmentation	Yes/no	Yes/no	—		Device dependent; poor or no reading if LEDS insufficiently bright
Safe Saturation Limits for Neonates/Infants					
Low		87-89%			
High		94-95%			

before
tation,
approve
ion.

dilated

Gynecol

cerclage

Obster

cerclage

al. Clin

niocen-

neonatal

J Med

multiple

coming

Pulse Oximetry in Newborn Infants with Birth Weights of 620 to 4285 Grams Receiving Dopamine and Dobutamine

Smeeta Sardesai, MD

Manuel Durand, MD

Cindy McEvoy, MD

Cage Johnson, MD

Jean-Michel Maarek, PhD

The reliability of pulse oximetry in neonates receiving inotropic drugs because of hypotension and microcirculatory perfusion failure has not been well documented. Signal loss of the pulse oximeter in adult patients receiving dopamine infusions has been reported. To evaluate the relationship between pulse oximeter oxygen saturation (SaO₂) and co-oximeter directly measured oxygen saturation, we studied 30 infants in the first 4 days of life (birth weight 620 to 4285 gm, gestational age 26 to 43 weeks) receiving dopamine (30 patients) and dobutamine (10 infants). Infants had normal blood pressures at the time of the study. To minimize motion artifact a Nellcor N-200 (Nellcor Incorporated, Hayward, Calif.) oximeter with electrocardiographic synchronization was used. We compared pulse oximeter values with simultaneous arterial samples analyzed for oxygen saturation with an IL 282 co-oximeter (Instrumentation Laboratory, Inc., Lexington, Mass.). The values were corrected for spuriously elevated carboxyhemoglobin levels and fetal hemoglobin level was quantitatively measured. The partial pressure of oxygen at 90% hemoglobin saturation for each patient was calculated. The dosage of dopamine ranged from 4 to 28 µg/kg per minute and the dosage of dobutamine varied from 4 to 24 µg/kg per minute. Over a wide range of values for mean blood pressure (23 to 66 mm Hg), partial pressure of oxygen at 90% hemoglobin saturation (43.1 to 70.2 mm Hg), and oxygen saturation (SaO₂ 80% to 100%), linear regression analysis revealed a close correlation between pulse oximeter SaO₂ and co-oximeter SaO₂ values ($r = 0.83$, standard error of the estimate 2.2%, $p < 0.0001$). Our findings indicate that pulse oximetry can be used reliably for continuous oxygen monitoring in normotensive neonates with an SaO₂ of 80% to 100% who are receiving dopamine and dobutamine. (*J PERINATOL* 1996;16:31-4)

Division of Neonatal-Perinatal Medicine, Los Angeles County and University of Southern California Medical Center, and Departments of Pediatrics and Medicine, University of Southern California School of Medicine, Los Angeles.

Address correspondence and reprint requests to Manuel Durand, MD, LAC and USC Medical Center, Women's Hospital, Room L-919, 1240 N. Mission Rd., Los Angeles, CA 90033.

Copyright © 1996 by the National Perinatal Association and the California Perinatal Association.

0743-8346/96 \$5.00 + 0 381/162279

Critically ill neonates require close monitoring of oxygenation to avoid hypoxic and hyperoxic episodes. In addition to measurement of transcutaneous oxygen tension, pulse oximetry has been used for noninvasive oxygen saturation monitoring in pediatric patients¹ and, more recently, in neonates.²⁻⁶ Earlier studies on the reliability of pulse oximetry have focused on patients with respiratory distress and arterial oxygen saturation (SaO₂) greater than 75%.^{2,3,6}

As with any equipment, several limitations of pulse oximetry have been reported, such as motion artifact,^{4,5,7} inability to detect an adequate pulsation in cases of extreme hypotension,^{2,8} and overestimation of blood oxygen saturation⁹ with increasing hypoxia (SaO₂ less than 70%). Another concern among clinicians is the accuracy of pulse oximetry during the administration of vasoactive (vasoconstricting) drugs. A signal loss of the pulse oximeter in adult patients receiving dopamine infusions has been reported¹⁰; however, there is no detailed information in an exclusive population of neonates who are receiving dopamine and dobutamine because of hypotension and microcirculatory perfusion failure.

The objective of this study was to evaluate the relationship between co-oximeter directly measured oxygen saturation and pulse oximeter oxygen saturation in neonates with normal blood pressure values who require dopamine and dobutamine because of a compromised cardiovascular state. Only patients with an SaO₂ of 80% to 100% were enrolled in the study, to eliminate the confounding effects of severe hypoxia.⁹

SUBJECTS AND METHODS

We prospectively studied 30 newborn infants admitted to the newborn intensive care unit at the Los Angeles County and University of Southern California Medical Center; all patients were receiving vasopressors because of hypotension and microcirculatory perfusion failure. Diagnoses included meconium aspiration, nine patients; respiratory distress syndrome, 14; perinatal depression with pulmonary hypertension, four; chylothorax, two; and hydrops, one. Inclusion criteria included (1) age younger than 7 days, (2) SaO₂ 80% or higher, (3) normotensive condition at the time of the study,^{11,12} and (4) requirement of dopamine 4 µg/kg per minute or higher. All patients initially had hypotension necessitating dopamine or dopamine and dobutamine administration to improve their cardiovascular status.

Simultaneous measurements of pulse oximeter SaO₂,

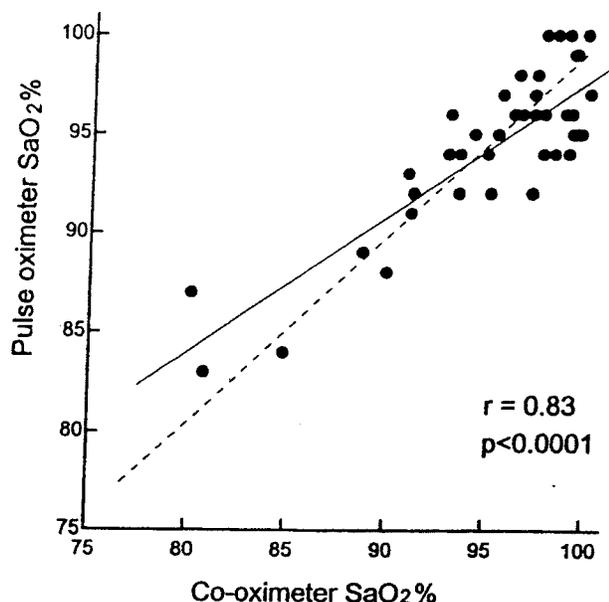


Figure 1 – Relationship between co-oximeter measured SaO_2 and pulse oximeter SaO_2 ($Y = 29.43 + 0.68X$, $\text{SEE} = 2.2\%$) in 30 patients receiving dopamine and dobutamine. Solid line, Regression line; dashed line, line of identity.

co-oximeter saturation, arterial blood gas values, and fetal hemoglobin level were obtained. Pulse oximeter SaO_2 was measured with a Nellcor N-200 monitor (Nellcor Incorporated, Hayward, Calif.). SaO_2 values were considered only if the pulse oximeter pulse rate did not differ more than five beats from the heart rate on the independent bedside monitor^{2,9} before electrocardiographic synchronization, which was used to minimize motion artifact at the time of blood sampling. The SaO_2 probe was placed according to the position of the arterial catheter (preductal or postductal) to avoid discrepancies resulting from shunting through a patent ductus arteriosus. In patients receiving phototherapy, the lights were temporarily turned off during sampling. A blood specimen was drawn for arterial blood gas analysis and for direct oxygen saturation measurements (co-oximetry) in 16 patients, and two sets of blood specimens were drawn at a 1- to 2-hour interval in 14 patients. All samples were obtained from indwelling arterial lines placed for routine clinical management. Arterial oxygen tension, arterial carbon dioxide tension, and pH were measured with a Radiometer BMS3 Mark II blood gas analyzer (Radiometer America, Westlake, Ohio) and SaO_2 with an IL 282¹³ co-oximeter (Instrumentation Laboratory, Inc., Lexington, Mass.). Blood SaO_2 (percent oxyhemoglobin) was measured for the total hemoglobin content, and values were corrected for spuriously elevated carboxyhemoglobin levels as previously described.^{2,14} Fetal hemoglobin (HbF) level was quantita-

Table 1 – Clinical Data in 30 Newborn Infants Receiving Dopamine and Dobutamine

	Mean \pm SD	Range
Birth weight (gm)	2270 \pm 1140	620-4285
Study weight (gm)	2256 \pm 1141	570-4240
Gestational age (wk)	34.8 \pm 6.0	26-43
Postnatal age (days)	2.3 \pm 1.0	1-4
Mean airway pressure (cm H_2O)*	7.8 \pm 2.7	3.4-13.3
Fraction of inspired oxygen	0.70 \pm 0.29	0.24-1.0

*Proximal mean airway pressure; 29 patients were receiving assisted ventilation at the time of the study.

tively measured by the alkaline denaturation method^{15,16} in 25 patients.

Heart rate and arterial blood pressure were monitored continuously. Because the maximal accuracy of pulse oximeters is for values greater than 80%, values for partial pressure of oxygen at 90% hemoglobin saturation (P90) were also calculated with use of an IBM computer.^{17,18} This study was approved by the Institutional Review Board at Los Angeles County and University of Southern California Medical Center and informed consent from the parents was obtained. Statistical significance of the differences was assessed by linear regression analysis and two-tailed *t* tests.

RESULTS

Clinical Features

The birth weight of infants in our study population ranged from 620 to 4285 gm and gestational age from 26 to 43 weeks. Nine patients had a birth weight < 1500 gm and eight infants had a gestational age of 30 weeks or less. All patients were 4 or fewer days old at the time of the study (Table 1). Thirty patients received a continuous infusion of dopamine (4 to 28 $\mu\text{g}/\text{kg}$ per minute) and 10 of these patients also received dobutamine simultaneously (4 to 24 $\mu\text{g}/\text{kg}$ per minute). The pH values ranged from 7.21 to 7.68 at the time of the study and mean blood pressure values from 23 to 66 mm Hg (Table 2).

Co-oximeter SaO_2 Versus Pulse Oximeter SaO_2

Forty-four data pairs were analyzed from the 30 patients. There was a close correlation in 44 paired values between co-oximeter measured SaO_2 and pulse oximeter SaO_2 ($r = 0.83$, $Y = 29.43 + 0.68X$, $p < 0.0001$). The standard error of the estimate (SEE) was 2.2% (Figure 1). The mean of the differences (bias) between pulse oximeter SaO_2 and co-oximeter SaO_2 was -0.9% , with a precision (standard deviation of the difference) of $\pm 2.7\%$ (range -5.2% to $+6.9\%$).

Fetal Hemoglobin and P90 Values

In our study population the HbF varied from 32.5% to 80.7%, whereas the calculated P90 ranged from 43.1 to 70.2 mm Hg (Table 2).

DISCUSSION

Pulse oximetry has been increasingly used for noninvasive monitoring of oxygen saturation in newborn infants. Despite the popularity of this technique, there is no detailed information on the accuracy of pulse oximetry in neonates with cardiovascular compromise necessitating the administration of dopamine, dobutamine, or both. Mihm and Halperin¹⁰ demonstrated that noninvasive oxygen monitoring of critically ill adult patients with respiratory distress or respiratory failure is feasible and can accurately detect potentially life-threatening arterial oxygen desaturations. They studied 18 elderly patients (age 67 ± 10 years, mean \pm SD) with an in vitro SaO_2 ranging from 56.2% to 99.9%. However, they also reported a signal loss of the pulse oximeter in two out of eight adult patients receiving dopamine infusions.

Conversely, Jennis and Peabody³ studied 26 neonates (1 to 49 days old) with blood SaO_2 values ranging from 70.1% to 100%; they reported a good function of the pulse oximeter in their two patients who were receiving dopamine. Dzedzic and Vidyasagar¹⁹ studied a total of 12 preterm infants with normal blood pressures and found a lower correlation between co-oximeter SaO_2 and pulse oximeter SaO_2 in infants receiving dopamine (SaO_2 $85.4\% \pm 7.6$) versus the correlation in infants not receiving dopamine infusions (SaO_2 $94\% \pm 6.1$).

In our study we were able to obtain reliable pulse oximeter SaO_2 data in infants who were receiving dopamine and dobutamine infusions to maintain an adequate blood pressure. The blood SaO_2 values in our patients also ranged from 80% to 100% to avoid the confounding effects of severe hypoxia.⁹ We found that there was an adequate correlation ($r = 0.83$) between pulse oximetry and co-oximetry oxygen hemoglobin saturations. This degree of correlation is comparable with that of earlier reports^{2,5,6} that used the Nellcor N-100 oximeter in neonates with acute disease ($r = 0.86, 0.90, \text{ and } 0.91$, respectively). The SEE is also comparable among these studies (range 1.87% to 2.2%).

It has been reported that carboxyhemoglobin values are elevated in the presence of HbF and this may affect oxyhemoglobin readings.¹⁴ In our patients we measured both carboxyhemoglobin and HbF, and SaO_2 values were corrected for spuriously elevated carboxyhemoglobin level as suggested by Cornelissen et al.¹¹ After birth the proportion of HbF that is structurally different from adult hemoglobin gradually decreases and the proportion of adult hemoglobin correspondingly increases. Sick newborn infants also receive frequent blood transfusions

Table 2—Clinical and Laboratory Findings in 30 Neonates Receiving Vasopressors

	Mean \pm SD	Range
Dopamine ($\mu\text{g}/\text{kg}/\text{min}$)	11 ± 6	4-28
Dobutamine ($\mu\text{g}/\text{kg}/\text{min}$)	14 ± 8	4-24
Heart rate (beats/min)	156 ± 17	119-190
Mean blood pressure (mm Hg)	42 ± 10	23-66
PaO_2 (mm Hg)	67 ± 19	38-114
PaCO_2 (mm Hg)	42 ± 12	23-64
Pulse oximeter SaO_2 (%)	94.6 ± 3.9	83-100
Co-oximeter SaO_2 (%)	95.5 ± 4.8	80.1-100
Hematocrit (%)	46 ± 7	34-61
HbF (%)	51.8 ± 14.1	32.5-80.7
P90 (mm Hg)	59.6 ± 8.0	43.1-70.2

PaO_2 , Arterial oxygen tension; PaCO_2 , arterial carbon dioxide tension.

as part of their clinical treatment. The changes in HbF and in hemoglobin oxygen affinity after birth have been characterized for term and preterm infants in previous studies.^{2,20} Pulse oximetry was a reliable method to monitor oxygen saturation in our patients, despite the wide range of HbF levels in the first 4 days of life (32.5% to 80.7%). Assessment of P90 has been suggested by previous investigators¹⁷ as a clinically relevant landmark on the oxyhemoglobin dissociation curve and as an alternative to the use of the partial pressure of oxygen at 50% hemoglobin saturation. We calculated the P90 in our patients (range 43.1 to 70.2 mm Hg); because P90 values are within the area of maximal accuracy of in vivo oximetric monitoring devices, such as pulse oximeters, these measurements may be useful in the care of newborn infants. The wide range of P90 values in our infants may be related to the concentrations of HbF.

Pulse oximetry requires adequate peripheral perfusion to operate accurately. Peripheral perfusion in turn is affected by hypothermia, decreased cardiac output, decreased mean arterial blood pressure, vasopressor drugs, and sympathetic tone.^{8,10,21} Vasoactive drugs, such as dopamine, could potentially affect the accuracy of pulse oximetry¹⁹ by altering the strength of pulsation of the peripheral vascular bed (peripheral vasoconstriction). Our patients had normal blood pressure values while receiving dopamine and dobutamine. Five patients from our study population received a dosage of 20 $\mu\text{g}/\text{kg}$ per minute or higher of these vasopressors. The apparent lack of adverse effects during administration of large dosages of dopamine and dobutamine in these infants is consistent with findings in previous reports in newborn infants.^{22,23} During hypotension the pulse oximeter continues to reflect arterial oxygen saturation as long as a true pulse is detected,^{8,10} that is, signal failure could be present in patients with extreme hypotension.

Our findings indicate that in neonates with an SaO₂ of 80% to 100% receiving dopamine and dobutamine in the first 4 days of life the pulse oximeter SaO₂ accurately reflects oxygenation. Further expanded evaluations are needed to clarify the role of vasoactive drugs and severe hypoxia on the reliability of pulse oximetry⁹ in neonates with hypotension.

Acknowledgments

We thank the Newborn Fellows and staff of the newborn intensive care unit for their cooperation during the study. We also thank the staff of the blood gas laboratory for their continued support.

References

1. Fanconi S, Doherty P, Edmonds JF, Barker GA, Bohn DJ. Pulse oximetry in pediatric intensive care: comparison with measured saturations and transcutaneous oxygen tension. *J Pediatr* 1985;107:362-6.
2. Durand M, Ramanathan R. Pulse oximetry for continuous oxygen monitoring in sick newborn infants. *J Pediatr* 1986;109:1052-6.
3. Solimano AJ, Smyth JA, Mann TK, Albersheim SG, Lockitch G. Pulse oximetry advantages in infants with bronchopulmonary dysplasia. *Pediatrics* 1986;78:844-9.
4. Durand M, McEvoy C, MacDonald K. Spontaneous desaturations in intubated very low birth weight infants with acute and chronic lung disease. *Pediatr Pulmonol* 1992;13:136-42.
5. Jennis MS, Peabody JL. Pulse oximetry: an alternative method for the assessment of oxygenation in newborn infants. *Pediatrics* 1987;79:524-8.
6. Walsh MC, Noble LM, Carlo WA, Martin RJ. Relationship of pulse oximetry to arterial oxygen tension in infants. *Crit Care Med* 1987;15:1102-6.
7. McEvoy C, Durand M, Hewlett V. Episodes of spontaneous desaturations in infants with chronic lung disease at two different levels of oxygenation. *Pediatr Pulmonol* 1993;15:140-4.
8. Barrington KJ, Ryan CA, Finer NN. Pulse oximetry during hemorrhagic hypotension and cardiopulmonary resuscitation in the rabbit. *J Crit Care* 1986;1:241-6.
9. Fanconi S. Reliability of pulse oximetry in hypoxic infants. *J Pediatr* 1988;112:424-7.
10. Mihm FG, Halperin BD. Noninvasive detection of profound arterial desaturations using a pulse oximetry device. *Anesthesiology* 1985;62:85-8.
11. Versmold HT, Kitterman JA, Phibbs RH, Gregory GA, Tooley WH. Aortic blood pressure during the first 12 hours of life in infants with birth weight 610 to 4220 grams. *Pediatrics* 1981;67:607-13.
12. Tan KL. Blood pressure in very low birth weight infants in the first 70 days of life. *J Pediatr* 1988;112:266-70.
13. Zwart A, Buursma A, Oeseburg B, Zijlstra WG. Determination of hemoglobin derivatives with the IL 282 co-oximeter as compared with a manual spectrophotometric five-wavelength method. *Clin Chem* 1981;27:1903-7.
14. Cornelissen PJH, van Woensel CLM, van Oel WC, de Jong PA. Correction factors for hemoglobin derivatives in fetal blood, as measured with the IL 282 co-oximeter. *Clin Chem* 1983;29:1555-6.
15. Jonxis JHP, Huisman THJ. The detection and estimation of fetal hemoglobin by means of the alkali denaturation test. *Blood* 1956;11:1009-13.
16. Betke K, Marti HR, Schlicht I. Estimation of small percentages of fetal hemoglobin. *Nature* 1959;184:1877-8.
17. Rebeck AS, Chapman KR. The-P90 as a clinically relevant landmark on the oxyhemoglobin dissociation curve. *Am Rev Respir Dis* 1988;137:962-3.
18. Kelman GR. Computer program for the production of O₂-CO₂ diagrams. *Respir Physiol* 1968;4:260-9.
19. Dziedzic K, Vidyasagar D. Pulse oximetry in neonatal intensive care. *Clin Perinatol* 1989;16:177-97.
20. Brown MS, Phibbs RH, Dallman PR. Postnatal changes in fetal hemoglobin, oxygen affinity and 2,3-diphosphoglycerate in previously transfused preterm infants. *Biol Neonate* 1985;48:70-6.
21. Palve H, Vuori A. Pulse oximetry during low cardiac output and hypothermia states immediately after open heart surgery. *Crit Care Med* 1989;17:66-9.
22. Perez CA, Reimer JM, Schreiber MD, Warburton D, Gregory GA. Effect of high-dose dopamine on urine output in newborn infants. *Crit Care Med* 1986;14:1045-9.
23. Durand M, Snyder JR, Gangitano E, Wu PYK. Oxygenation index in patients with meconium aspiration: conventional and extracorporeal membrane oxygenation therapy. *Crit Care Med* 1990;18:373-7.

Neonatal Pulse Oximetry: Accuracy and Reliability

William W. Hay, Jr, MD, Julia M. Brockway, BA, and Mario Eyzaguirre, MD

From the Neonatal Clinical Research Center, Department of Pediatrics, University of Colorado School of Medicine, Denver

ABSTRACT. Pulse oximetry has gained widespread use in neonatal oxygen monitoring. However, because specific morbidity in neonates has been related to abnormal levels of oxygen partial pressure (PaO_2), it is essential to demonstrate that pulse oxygen saturation values (SpO_2) are highly accurate and reflect with precision the simultaneous PaO_2 . In this report, data is presented that describe the accuracy of the Ohmeda Biox 3700 pulse oximeter. SpO_2 was highly correlated with arterial blood oxygen saturation ($r = .99$) measured on arterial (catheter) blood using a two-wavelength Radiometer OSM2 Hemoximeter. When compared with PaO_2 , SpO_2 values of $92\% \pm 3\%$ (mean \pm range) excluded all of the measured PaO_2 values less than 45 mm Hg and greater than 100 mm Hg. SpO_2 - tcPO_2 (transcutaneous PO_2) and SpO_2 - PaO_2 (catheter or percutaneous arterial PO_2) correlations showed that bronchopulmonary dysplasia, percutaneous arterial sampling, and nipple feeding skewed the tcPO_2 but not the PaO_2 correlations with SpO_2 , indicating that SpO_2 is not sensitive to peripheral factors that affect tcPO_2 . SpO_2 - PaO_2 correlation was not affected by gestational age. A high degree of accuracy of SpO_2 values and SpO_2 prediction of normal appearing PaO_2 values are defined by these results. *Pediatrics* 1989;83:717-722; *neonate, oxygen, pulse oximetry.*

ABBREVIATIONS. SpO_2 , pulse oxygen saturation; SaO_2 , arterial blood oxygen saturation determined by in vitro hemoximeter-spectrophotometer, oxyhemoglobin as percentage of $\text{Hb} + \text{HbO}_2$; HbO_2 , oxygenated (saturated) hemoglobin, or oxyhemoglobin; PaO_2 , arterial oxygen partial pressure in millimeters of Hg; tcPO_2 , transcutaneous oxygen partial pressure in millimeters of Hg; P_{50} , PO_2 at 50% oxygen saturation of hemoglobin.

Received for publication Oct 9, 1987; accepted June 20, 1988. Preliminary aspects of this study were presented at the Continuous Oxygen Monitoring Meeting, Zurich, Oct 1 to 4, 1986, and the Topics in Neonatology Meeting, Washington, DC, Dec 7 to 9, 1986.

Reprint requests to (W.W.H.) University of Colorado School of Medicine, Department of Pediatrics, B-195, 4200 E 9th Ave, Denver, CO 80262.

PEDIATRICS (ISSN 0031 4005). Copyright © 1989 by the American Academy of Pediatrics.

During the past several years, pulse oximetry has gained widespread use in neonatal oxygen monitoring. In several reports, pulse oxygen saturation (SpO_2) values have been documented in a variety of clinical conditions in newborn infants, and pulse oxygen saturation has been compared with arterial blood oxygen saturation (SaO_2) and both arterial (PaO_2) and transcutaneous (tcPO_2) oxygen partial pressure.¹⁻⁷ In general, these reports have been favorable regarding the application of pulse oximetry to neonatal oxygen monitoring, emphasizing the easy application of SpO_2 probes, lack of instrument calibration requirement, infrequency of cutaneous injury, rapid response of SpO_2 to changes in blood oxygenation, and significant correlation of SpO_2 with SaO_2 .

Recently, several questions have emerged regarding the accuracy and reliability of pulse oximetry in neonatal oxygen monitoring: (1) What is the accuracy of the pulse oximeter v a reference laboratory hemoximeter? (2) How accurately does the pulse oximeter detect unacceptably lower or higher levels of PaO_2 ? (3) How well does the pulse oximeter compare with currently available noninvasive, continuous tcPO_2 instruments to determine the effect on blood oxygenation of advancing gestational age, chronic lung disease, and nursing and medical procedures? Answers to these questions are important to help clinicians select the optimal form of oxygen monitoring in patients requiring oxygen therapy and for selecting the optimal SpO_2 values for securing and maintaining appropriate blood oxygenation in patients monitored by pulse oximetry. The present study was conducted to answer these questions by investigating the measurement of pulse oxygen saturation in preterm and full-term infants who required oxygen therapy.

MATERIALS AND METHODS

Study Design

The present investigations were performed in the newborn intensive care unit at University Hospital, University of Colorado Health Sciences Center between June 1985 and June 1987. The investigations were approved by and conducted with the support of the Pediatric/Neonatal Clinical Research Center. Approval was obtained from the University of Colorado Health Science Center Human Subjects Research Committee. No study was conducted without approval and consent of each infant's parents or guardians, attending neonatologist(s), and primary nurse. Inspired oxygen concentration and blood or transcutaneous oxygen levels were not manipulated or sampled solely for the purposes of these investigations. However, all data were reported immediately to each infant's nurse and physician.

Infants

Subjects were preterm and full-term infants in the newborn intensive care unit for whom a physician had ordered a catheter arterial blood gas, a percutaneous arterial blood gas, and/or a transcutaneous PO₂ study, either to measure the blood oxygenation or to determine how a particular medical, surgical, or nursing procedure affected blood oxygenation. At the time of study, each infant was judged to be physiologically stable based on evidence during the preceding 24 hours of normal range temperature, pulse rate, BP, hematocrit, urine flow rate, skin perfusion ("capillary refill" after gentle pressure), degree of physical activity, and absence of signs of systemic infection.

Equipment

The pulse oximeter used in these investigations was the Ohmeda Biox 3700 (Ohmeda, Boulder, CO). All tcPO₂ values were recorded with a Hewlett-Packard model 78850A oxygen monitor. Arterial blood gas values were measured on a Corning model 168 pH/blood gas analyzer. SaO₂ values were measured on the arterial blood gas samples using a Radiometer OSM2 Hemoximeter. The Hemoximeter was calibrated three times per week using fresh placental blood obtained from a doubly clamped cord segment obtained from an elective cesarean section or vaginal delivery.

The pulse oximeter probe was applied to the left hand or either foot. tcPO₂ and pulse oximeter recordings did not include the flow distribution of preductal blood. Pulse saturation values were recorded only when the pulse rate was equal to the

electrical monitor heart rate for at least 20 seconds. Pulse oximeter and tcPO₂ recordings were made for at least three minutes before, during, and at least three minutes after a blood sample was drawn or a procedure performed. For blood sample comparisons, the simultaneous pulse oxygen saturation value and the 30 second postsampling tcPO₂ value were used. Before and during nursing and medical procedures, five-minute average pulse oxygen saturation and tcPO₂ values were compared.

Arterial blood samples (0.3 mL) for PaO₂ and SaO₂ were drawn into plastic 1.0-mL syringes lined with dried or liquid heparin. Air bubbles were expressed immediately without drawing any air into the syringe, the syringe was capped with a rubber stopper and placed on ice, and the blood was analyzed within three minutes of sampling.

Statistical Analyses

Linear regression (standard least squares method) and paired and unpaired Student's *t* test with analysis of variance were used to compare SpO₂ with simultaneously measured tcPO₂, PaO₂, and SaO₂. Best fit correlations were made using a Sigma Plot 3 computer program. Data analysis was based on the number of measurements, which averaged approximately 1.9 per subject.

RESULTS

Comparison of SpO₂ with SaO₂

SpO₂ was highly significantly correlated with simultaneous arterial (catheter) SaO₂ ($y = 0.938x + 5.413$, $r = .99$, $P < .0001$, $n = 117$ separate data points in 58 infants of <1 week postnatal age, gestational age of 27 to 39 weeks, mean of 1.9 studies each) (Fig 1).

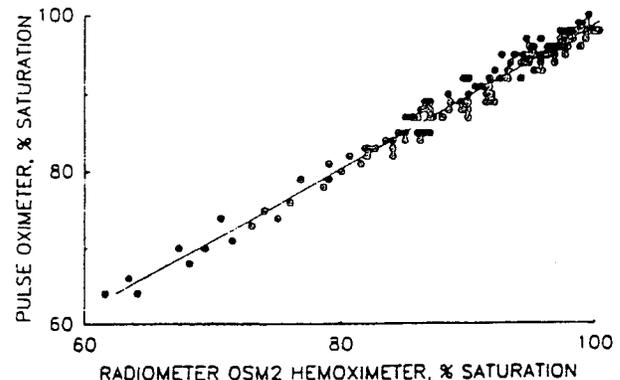


Fig 1. Comparison of pulse oxygen saturation with arterial blood oxygen saturation in infants <1 week postnatal age; $n = 111$, $y = 0.938x + 5.413$, $r = .987$, $P < .0001$.

Comparison of SpO₂ with PaO₂ and tcPO₂

Infants With Chronic O₂ Requirement. SpO₂ was compared with simultaneously measured PaO₂ (n = 111) and tcPO₂ (n = 56) in 56 infants with a clinically defined chronic oxygen requirement (FIO₂ > 0.30, age > 28 days postnatal, 30 to 38 weeks' gestational age at study) (Fig 2). Greater than PaO₂ or tcPO₂ of 40 mm Hg, there was no difference between the SpO₂-PaO₂ and SpO₂-tcPO₂ relationships ($P > .5$ for both mean and mean ± 2 SD). Less than PO₂ of 40 mm Hg, a given SpO₂ value was correlated with a simultaneous tcPO₂ value that was significantly less than the simultaneous PaO₂ value ($P < .05$ for mean difference of 10 ± 2.3 (SD) mm Hg between tcPO₂ and PaO₂ at PO₂ (40 mm Hg). The predicted PO₂ at 50% oxygen saturation of hemoglobin (P₅₀) with the SpO₂-tcPO₂ relationship was 8 mm Hg; the predicted P₅₀ with the SpO₂-PaO₂ relationship was 25 mm Hg; these predicted values were significantly different ($P < .01$).

Newly Born Infants With Acute O₂ Requirement. In infants of less than 1 week postnatal age (n = 73, gestational age 27 to 38 weeks), the entire SpO₂-PaO₂ relationship (n = 110 data points) was not different from the entire SpO₂-tcPO₂ relationship (n = 56 data points) when the PaO₂ was measured

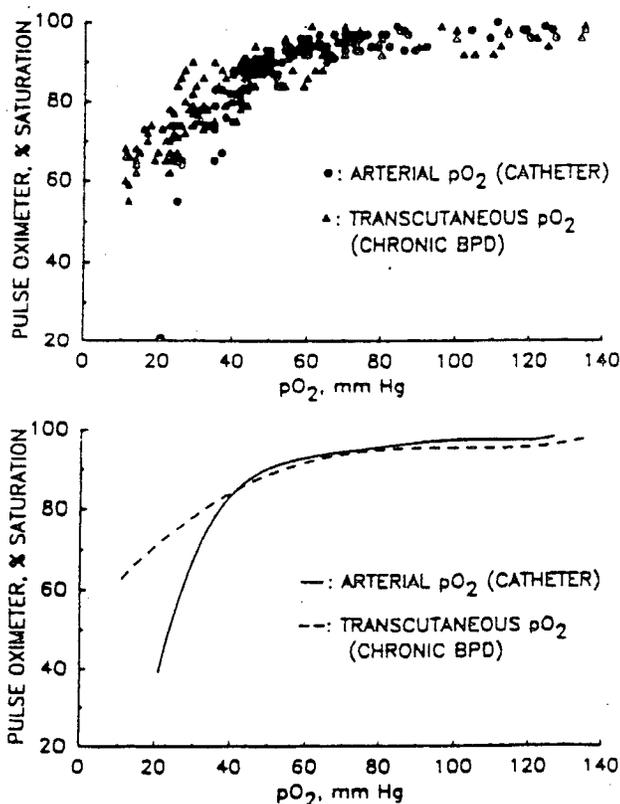


Fig 2. Top, comparison of data points for pulse oxygen saturation-transcutaneous PO₂ and pulse oxygen saturation-PaO₂ in infants with chronic bronchopulmonary dysplasia (BPD). Bottom, mean regression lines.

on blood sampled from an indwelling catheter (Fig 3). However, when the PaO₂ was sampled by percutaneous arterial puncture (n = 46, nonanesthetized, 40 of 46 infants crying and/or struggling), a given SpO₂ value was correlated with a tcPO₂ value that was significantly less than the simultaneous PaO₂ value (mean difference of 8.8 ± 2.8 mm Hg at PO₂ values less than 40 mm Hg) (Fig 4).

Comparison of SpO₂-PaO₂ (Catheter) at Different Gestational Ages in Infants Less Than 1 Week Postnatal Age

The SpO₂-PaO₂ relationship was not different ($P > .5$) in infants of <1 week postnatal age (PO₂, range 30 to 122 mm Hg) who were ≤ 28 weeks' gestational age (n = 61) compared with infants who were ≥ 38 weeks' gestational age (n = 57) (Fig 5).

Pulse Saturation Detection of PaO₂

Higher PO₂ Range. In the infants in whom SpO₂ and PaO₂ (catheter) measurements were made, SpO₂ averaged 96.7% (± 0.2 % SEM, n = 29) greater than the PaO₂ range of 60 to 80 mm Hg (Fig 6). At greater than the PO₂ range of 80 to 100 mm Hg,

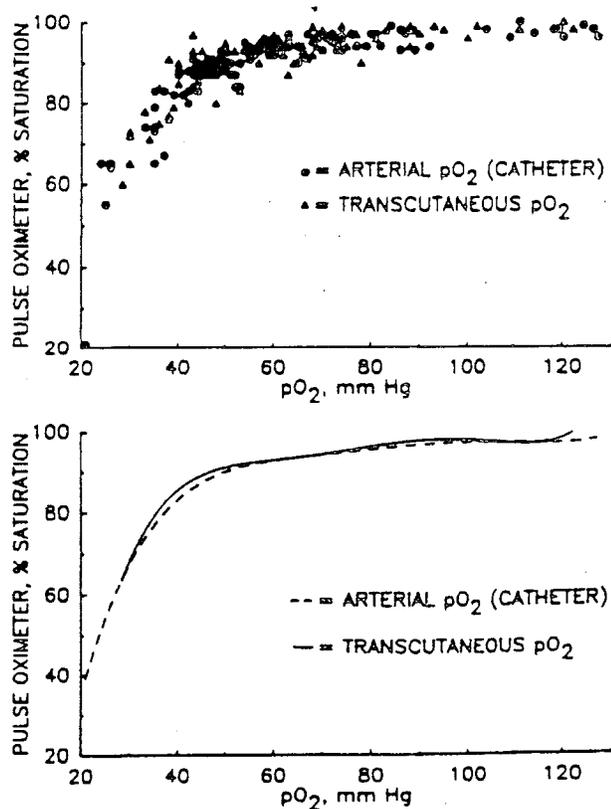


Fig 3. Top, comparison of data points for pulse oxygen saturation-transcutaneous PO₂ and pulse oxygen saturation-PaO₂ (catheter) in infants in first week of life. Bottom, mean regression lines.

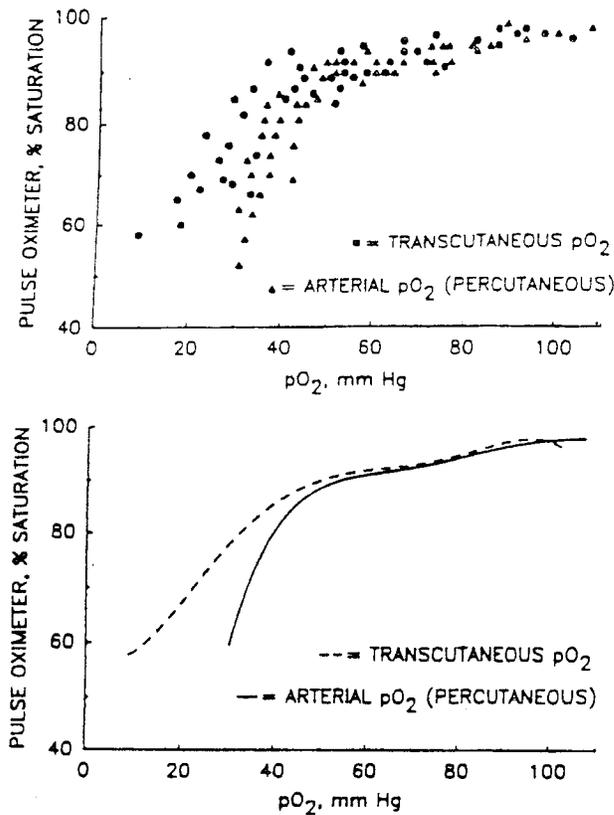


Fig 4. Top, comparison of data points for pulse oxygen saturation-transcutaneous PO_2 and pulse oxygen saturation- PaO_2 (percutaneous) in infants in first week of life. Bottom, mean regression lines.

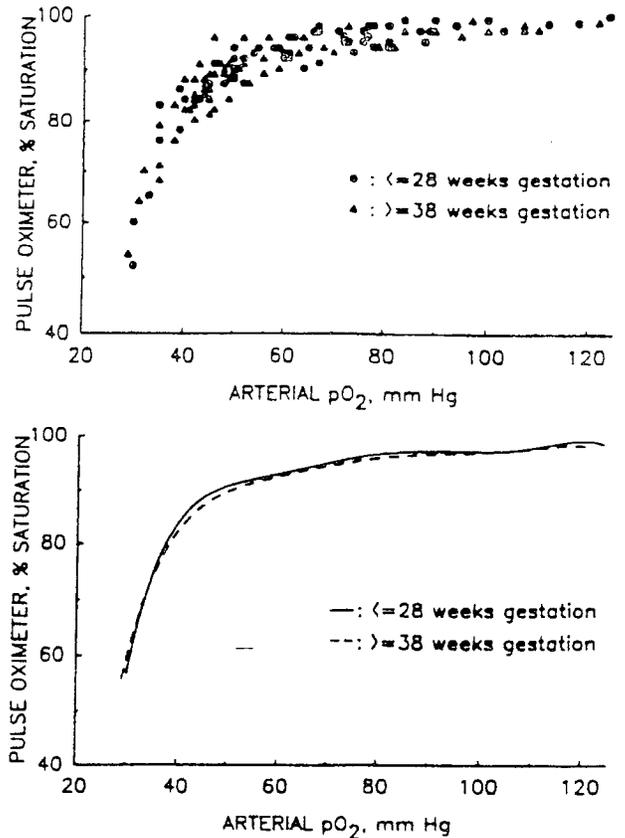


Fig 5. Top, comparison of data points for pulse oxygen saturation PaO_2 (catheter) in infants in first week of life who are ≤ 28 weeks' gestation or ≥ 38 weeks' gestation. Bottom, mean regression lines.

SpO_2 averaged 98.3% ($\pm 0.3\%$ SEM, $n = 8$, and greater than the PO_2 range of 100 to 120 mm Hg, SpO_2 averaged 98.6% ($\pm 0.4\%$ SEM, $n = 10$). Of the ten infants with PaO_2 of >100 mm Hg, not one had an SpO_2 value of 100%.

Among the 32 infants with SpO_2 , $\geq 97\%$, nine (28%) had $PaO_2 \geq 100$ mm Hg, whereas among the 23 infants with SpO_2 of $\geq 94\%$ and $\leq 97\%$, only one (4%) had $PaO_2 \geq 100$ mm Hg and only two (9%) had $PaO_2 \geq 80$ mm Hg.

Lower PO_2 Range. Among the 19 infants with SpO_2 and $\geq 90\%$ $< 94\%$, eight (42%) had $PaO_2 < 50$ mm Hg; not one of these 19 infants had PaO_2 of < 45 mm Hg and none had $PaO_2 > 65$ mm Hg. Nine infants had SpO_2 of $\geq 85\%$ and $< 90\%$, all but one of these infants had $PaO_2 < 50$ mm Hg, and four (44%) of these infants had $PaO_2 \geq 39 < 45$ mm Hg.

For the PaO_2 range of 45 to 100 mm Hg, the highest SpO_2 value with 100% sensitivity (included only $PaO_2 > 100$ mm Hg) and 100% specificity (included only $PaO_2 < 100$ mm Hg) was 95%. The lowest SpO_2 value that had 100% sensitivity (included only $PaO_2 < 45$ mm Hg) and 100% specificity (included only $PaO_2 > 45$ mm Hg) was 89%.

Effect of Nursing and Medical Procedures on SpO_2 and $tcPO_2$

Pulse oxygen saturation and $tcPO_2$ values were recorded simultaneously for at least five minutes before and for at least five minutes during several medical and nursing procedures (Fig 7). In comparison with the pulse saturation values, greater variability was observed for the $tcPO_2$ values, both for the mean values in each period and for the percent change from the before to the during period. Significant decreases of $tcPO_2$ were observed for nipple feeding and endotracheal tube suctioning. A significant decrease of pulse oxygen saturation was observed only for endotracheal tube suctioning.

DISCUSSION

Adverse effects of abnormal levels of blood oxygenation in newborn infants have been documented in extensive clinical experience and research. PaO_2 values less than 45 to 50 mm Hg are associated with direct vasoconstriction of the pulmonary vasculature⁸ and vasodilation of the ductus arteriosus⁹ leading to pulmonary hypertension, reduced pulmonary blood flow, right to left shunt,

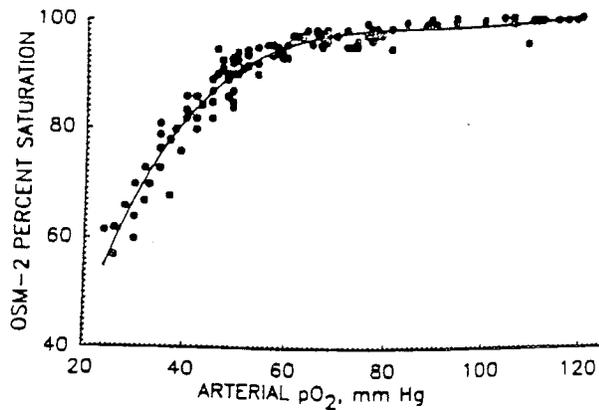


Fig 6. Comparison of pulse oxygen saturation with PaO_2 (catheter) in infants in first week of life. OSM, osmolality.

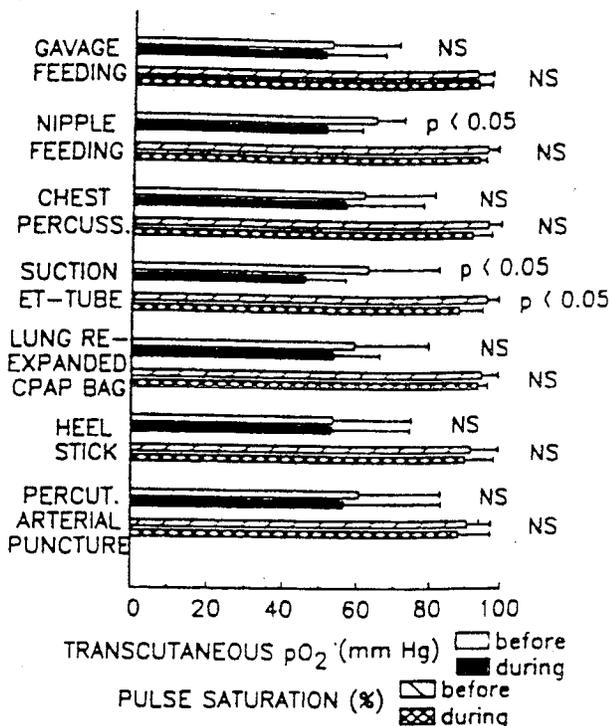


Fig 7. Mean \pm SD values and statistical comparisons of transcutaneous PO_2 and pulse oxygen saturation in infants undergoing various nursing and medical procedures. ET, endotracheal tube; CPAP, continuous positive airway pressure.

and systemic hypoxia and acidosis. Additionally, PO_2 values greater than 100 mm Hg have been associated with retinal vascular injury and other forms of oxygen toxicity.¹⁰⁻¹³ Furthermore, reduction in blood O_2 content leads to direct changes in the distribution of peripheral blood flow favoring the brain, myocardium, and adrenal glands at the expense of the skin, gut, skeletal muscle, and abdominal viscera.^{13,14} Because of such deleterious effects of abnormal blood oxygenation, it is imperative that instruments used to measure blood oxygenation are highly accurate and sensitive to even minor changes in blood oxygenation.

With respect to the accuracy of the pulse oximeter compared with an in vitro reference instrument, the methods and results of the present study show an extremely strong correlation between SpO_2 and SaO_2 ($r = .9875$, SEM correlation = 1.31). In addition to the inherent accuracy of the pulse oximeter, this strong correlation may have been due, in part, to strict attention to preparing and handling of the blood samples (particularly avoiding drawing a small amount of air into the blood gas syringe to help coalesce trapped air bubbles prior to expelling the trapped air and sealing the syringe) and, in part, to using in vitro conditions for the Hemoximeter that more closely approximate the in vivo conditions of the pulse oximeter. For example, placental blood containing largely HbF was used for calibration of the Hemoximeter based on the theoretical concern that HbF and HbA will yield slightly but significantly different saturation values.¹⁵

The comparison of SpO_2 values with PaO_2 values was done to test the capacity of SpO_2 to accurately predict PaO_2 . A sensitivity-specificity analysis showed that the SpO_2 range of $92 \pm 3\%$ (89% to 95%) indicated the PaO_2 range of 45 to 100 mm Hg with 100% sensitivity and 100% specificity at both ends of the PaO_2 range. Although similar estimates can be derived from other published data,¹⁻⁷ the present analysis is important in defining quantitatively the SpO_2 prediction of PaO_2 .

At lower SpO_2 - PaO_2 levels, there is more variability in the SpO_2 - PaO_2 relationship. The reasons for this increased variability are not known but may include SaO_2 sample contamination with air, less accuracy in the manufacturer's instrument calibration, and differences in the oxygen dissociation curve due to different values of PCO_2 , pH, temperature, and the influence of different proportions of HbA and HbF. Saturation differences due to PCO_2 , pH, and temperature were not corrected for in the present study because these corrections are seldom made clinically and because significant derangements in these values did not occur in the infants studied. Nevertheless, unacceptably low PaO_2 levels (arbitrarily defined as a $\text{PaO}_2 < 45$ mm Hg) were not missed using a lower limit SpO_2 of 89%.

Several important differences between these two forms of PO_2 measurement were apparent from comparison of SpO_2 with simultaneous PaO_2 and tcPO_2 . First, there were no differences between the SpO_2 - PaO_2 and SpO_2 - tcPO_2 relationships greater than a PO_2 of 40 mm Hg. This observation is reasonable based on the much greater tissue and skin PO_2 at more than PO_2 levels¹⁶ and the likelihood that skin blood flow was greater in such infants compared with those who were relatively hypoxic.^{13,14} Second, at PO_2 values less than 40 mm

Hg in infants with chronic lung disease, a given SpO₂ value was associated with a tcPO₂ value significantly less than the simultaneous PaO₂. Relatively lower tcPO₂ values for a given SpO₂ or SaO₂ in the lower PO₂ range in such infants have been observed before¹⁷⁻¹⁹ and have been ascribed hypothetically to factors such as decreased skin vascularity, decreased skin blood flow, increased skin and subcutaneous tissue thickness, and increased skin and subcutaneous water content.²⁰ It is important to note that SpO₂ is comparatively insensitive to such tcPO₂ discrepancies, indicating that SpO₂ might reflect blood oxygenation more accurately than does tcPO₂, particularly in infants with bronchopulmonary dysplasia.²¹ On the other hand, this tcPO₂-PaO₂ discrepancy may prove important with respect to cutaneous developmental and pathogenetic problems specific to the infant with chronic lung disease; thus, the use of oxygen monitoring in which this problem is exclusively ignored may be short-sighted.

Similarly, the significantly lower tcPO₂ than PaO₂ values (at the lower PO₂ range) in the percutaneously sampled infants with chronic lung disease and the greater variability and percentage of change of tcPO₂ compared with SpO₂ during various nursing and medical procedures both suggest that such infants may have an increased peripheral vasomotor response to painful stimuli, perhaps mediated by an increased vascular sensitivity or an increased neural-vascular responsiveness. As with the tcPO₂-PaO₂ discrepancy in the older infants with chronic lung disease, this possible increase in peripheral vasomotor response deserves investigation in its own right. The increase also validates the use of the pulse oximeter as a noninvasive instrument to assess systemic oxygenation when skin oxygenation may not be normal.

In summary, the data presented in this article document a great degree of accuracy of the Ohmeda Biox 3700 pulse oximeter when compared with an in vitro reference SaO₂ instrument, the Radiometer OSM2 Hemoximeter. The great degree of accuracy of the pulse oximeter provides considerable reliability in using SpO₂ as a measure of SaO₂ to predict PaO₂, and many of the problems associated with the use of tcPO₂ instrumentation are avoided (particularly in the lower PO₂ range). Restriction of an infant's oxygen supply to produce SpO₂ values of 92% ± 3% (range) seems prudent and safe. However, this conclusion is arbitrary and not tested. Based on the present data there is sufficient variation at greater and lower SpO₂ levels that SpO₂ should not be used exclusive of PaO₂ when high or low PaO₂ levels are likely (ie, at SpO₂ values <89% or >95%).

ACKNOWLEDGMENTS

We thank Jonas A. Pologe, Research Manager, Ohmeda, Boulder, CO, for assistance with data analysis and for a critical review of this article.

REFERENCES

1. Ramanathan R, Durand M, Larrazabel C: Pulse oximetry in very low birth weight infants with acute and chronic lung disease. *Pediatrics* 1987;79:612-617
2. Jennis MS, Peabody JL: Pulse oximetry: An alternative method for the assessment of oxygenation in newborn infants. *Pediatrics* 1987;79:524-528
3. Fanconi S, Doherty P, Edmonds JF, et al: Pulse oximetry in pediatric intensive care: Comparison with measured saturations and transcutaneous oxygen tension. *J Pediatr* 1985;107:362-366
4. Mok JYQ, McLaughlin FJ, Pintar M, et al: Transcutaneous monitoring of oxygenation: What is normal? *J Pediatr* 1986;108:365-371
5. Deckardt R, Steward DJ: Non-invasive arterial hemoglobin oxygenation saturation versus transcutaneous oxygen tension monitoring in the preterm infant. *Crit Care Med* 1984;12:935-939
6. Monaco F, Feaster WW, McQuitty JC, et al: Continuous noninvasive oxygen saturation monitoring in sick newborns. *Respir Care* 1983;28:1362
7. Hay WW Jr: *Application of Pulse Oximetry in Neonatal Medicine: Technical Report*, Ohmeda. Boulder, CO, BOC Group, Inc, 1986
8. Fishman AP: Respiratory gases in the regulation of the pulmonary circulation. *Physiol Rev* 1961;41:241
9. Moss AF, Emmanouilides GC, Adams FH, et al: Response of ductus arteriosus and pulmonary and systemic arterial pressures to changes in oxygen environment in the newborn infant. *Pediatrics* 1964;33:937-944
10. Frank L, Bucher JR, Roberts RJ: Oxygen toxicity in neonatal and adult animals of various species. *J Appl Physiol* 1978;45:699-704
11. Kinsey VE, Jacobus JT, Hemphill FM, et al: Cooperative study of retrolental fibroplasia and the use of oxygen. *Arch Ophthalmol* 1956;56:481-543
12. Lucey JF, Dangman B: A reexamination of the role of oxygen in retrolental fibroplasia. *Pediatrics* 1984;73:82-96
13. Peeters LLH, Sheldon RE, Jones MD Jr, et al: Blood flow to fetal organs as a function of arterial content. *Am J Obstet Gynecol* 1979;135:637-646
14. Sheldon R, Peeters LLH, Jones MD Jr, et al: Redistribution of cardiac output and oxygen delivery in the hypoxemic fetal lamb. *Am J Obstet Gynecol* 1979;135:1071-1078
15. Pologe JA: The technology of pulse oximetry: Theory and principles. Presented at the Broadmoor Symposium: The Uses, Benefits and Limitation of Pulse Oximetry in Neonatal Medicine, Colorado Springs, CO, Nov 12-14, 1986
16. Huch R, Lübbers DW, Huch A: Quantitative continuous measurement of partial oxygen pressure on the skin of adults and newborn babies. *Pflugers Arch* 1972;337:185-198
17. Peabody JL, Gregory GA, Willis MM: Transcutaneous oxygen tension in sick newborns. *Am Rev Resp Dis* 1978;118:83-87
18. Rome ES, Stork EK, Carlo WA, et al: Limitations of transcutaneous PO₂ and PCO₂ monitoring in infants with bronchopulmonary dysplasia. *Pediatrics* 1984;74:217-220
19. Hamilton PA, Whitehead MD, Reynolds EOR: Underestimation of arterial oxygen tension by transcutaneous electrode with increasing age in infants. *Arch Dis Child* 1985;60:1162-1165
20. Peabody JL, Willis MM, Gregory GA, et al: Clinical limitations and advantages of transcutaneous oxygen electrodes. *Acta Anaesthesiol Scand* 1978;68(suppl):76-82
21. Solimano AJ, Smyth JA, Mann TK, et al: Pulse oximetry advantages in infants with bronchopulmonary dysplasia. *Pediatrics* 1986;78:844-849

THE EFFECT OF PULSATING ARTERIES ON REFLECTANCE PULSE OXIMETRY: MEASUREMENTS IN ADULTS AND NEONATES

Roel Nijland, MD,* Henk W. Jongsma, PhD,*
Paul P. van den Berg, MD,*
Jan G. Nijhuis, MD, PhD,*
and Berend Oeseburg, MD, PhD†

Nijland R, Jongsma HW, van den Berg PP, Nijhuis JG, Oeseburg B.
The effect of pulsating arteries on reflectance pulse oximetry: measurements in adults and neonates.

J Clin Monit 1995;11:118-122

ABSTRACT. Objective. The objective of our study was to describe the results from human experiments during normoxia that demonstrate the effect of pulsating arteries on the measured arterial oxygen saturation (SpO₂) using a reflectance pulse oximeter sensor. **Methods.** In 6 healthy adults and 7 healthy neonates, a Nellcor reflection sensor (FS-10 oxisensor, Nellcor, Inc., Pleasanton, CA) was placed in three different positions: (1) on the forehead, (2) on the temporal area, with the photodiode placed over the superficial temporal artery, and (3) on the temporal area, with the light-emitting diodes (LEDs) placed over the superficial temporal artery. **Results.** Placement of the sensor in position 2 resulted in a significantly lower SpO₂ reading, compared to sensor position 1: 5.8% ($p < 0.01$) lower for adults and 7.5% ($p < 0.01$) lower for neonates. Placement of the sensor in position 3 resulted in significantly larger plethysmographic signals, compared to sensor position 1; but, the SpO₂ readings were alike. **Conclusions.** Pulsating arteries can affect the reliability of reflection pulse oximetry. Depending on the position of the sensor, a falsely low SpO₂ value can be observed.

KEY WORDS. Measurement techniques, pulse oximetry: accuracy. Monitoring: hemoglobin oxygen saturation.

INTRODUCTION

Transmission pulse oximetry has become a standard method for monitoring the arterial oxygen saturation (SaO₂) continuously and noninvasively in anesthesia and intensive care units. Tissue is transilluminated by red (R) and infrared (IR) light; from the alternating forward-scattered light intensities caused by the pulsating blood volume in the tissue, a red to infrared ratio is calculated [1,2]. This red to infrared ratio is empirically calibrated with sample SaO₂ values [1,2]. Sensor application with transmission pulse oximetry is possible in limited areas of the body, such as in the finger tip, earlobe or toe, and in the foot or palm in neonates.

With the development of reflectance pulse oximetry, SaO₂ can also be estimated from the backscattered light [3]. The skin is transilluminated by the light source and the pulsatile signals are obtained by a photodetector, which is sited adjacent to the light source. These reflection sensors can be placed on almost all parts of the body where sufficient signals can be detected and can be placed on a central position, such as the forehead or the temple, when the peripheral circulation is diminished. The reflection sensor can also be used for intrapartum fetal monitoring, placing the sensor on the cheek or temporal area of the fetus during labor [4].

When the sensor is placed coincidentally over an artery, large plethysmographic waveforms can be expected. In studies with fetal lambs with the reflection

From the *Department of Obstetrics and Gynaecology, and the †Department of Physiology, Perinatal Research Group, University Hospital Nijmegen, Nijmegen, The Netherlands.

Received Apr 19, 1994, and in revised form Jul 25, 1994. Accepted for publication Jul 28, 1994.

Address correspondence to Dr Jongsma, Department of Obstetrics and Gynaecology, University Hospital Nijmegen 415 GYN, PO Box 9101, 6500 HB Nijmegen, The Netherlands.

sensor placed over a visible subcutaneous artery or vein, we observed that the oxygen saturation estimated by pulse oximetry (SpO_2) was lower than the sample SaO_2 value (unpublished data). However, the physiologic SaO_2 values in the fetus are below 70%; it is not known whether superficial vascular structures also affect the reliability of pulse oximeter readings after birth, when normal SaO_2 values are near 100%. The purpose of this study was to investigate whether pulsating arteries can affect reflectance pulse oximetry in healthy human adults and neonates.

METHODS AND MATERIALS

After informed consent had been obtained, 6 healthy volunteers (aged 25 to 40 years; 4 women, 2 men) took part in the study, as well as 7 healthy neonates (aged 1 to 13 days postpartum; 3 boys, 4 girls).^{*} An FS-10 reflection sensor and a prototype N-400 oximeter were used in this study (Nellcor, Inc., Hayward, California). The FS-10 reflection sensor was developed for fetal monitoring. The sensor consists of two LEDs, one for red (660 nm) and one for infrared light (890 nm), and one photodetector, which is placed 10 mm from the LEDs [4]. The N-400 oximeter is provided with an algorithm derived from measurements made on healthy adults for an SaO_2 range of 51% to 100% and for a range of 10% to 50% with measurements on fetal sheep, compared to SaO_2 values measured with a CO-Oximeter (IL282^R/IL482^R, Instrumentation Laboratories, Lexington, MA).

The sensor was placed and fixed by an elastic band, without applying excessive pressure to prevent compression of circulation. The sensor made appropriate contact with the skin, preventing direct shunting from red and infrared light to the photodetector. The sensor was placed in three different positions: (1) on the forehead above the right or left eye; (2) on the temporal area, with the photodetector over the superficial temporal artery (or the frontal branch of the superficial temporal artery); and (3) on the temporal area, with the LEDs over the superficial temporal artery. The temporal artery was located by palpation and the LED-detector axis of the sensor was placed perpendicular to the artery, in front of the ear.

In the adults, measurements were performed in a resting position. The neonates were measured while in a quiet sleep state, after nourishment between 10:00 and 11:30 am or between 2:00 and 3:00 pm. All measurements were made at room temperature of around 22°C. After a control period of 2 min, 2 min of signals were

collected, after which the sensor was removed. The reflection sensor was connected to the N-400 pulse oximeter and a personal computer. Signals were analyzed off line. The plethysmographic waveforms were visually verified to ascertain that red and infrared peak and trough were adequate and in phase with each other. Red and infrared signals were sometimes shortly disturbed by movement artifacts, resulting in incorrect red and infrared values. Therefore, a 10-sec period without such artifacts was selected from the collected 2 min, and these 10 sec were used for further analysis. For each heartbeat, the minimum and maximum value of the red and infrared signals were used to calculate percentage ac/dc of red and infrared (where ac is amplitude and dc is level) and red to infrared ratio $[(ac_R/dc_R)/(ac_{IR}/dc_{IR})]$. All calculations were performed for each heartbeat separately, after which the data were averaged over 10 sec. SpO_2 output of the N-400 was averaged over the same period.

The N-400 pulse oximeter uses a scoring system for signal quality, based on multiple factors, such as pulse synchrony and pulse amplitude. For this study, the quality of the recordings is expressed as a percentage of the maximum obtainable score.

The results were analyzed using the Student's paired *t* test for SpO_2 and ratio red to infrared. For the other parameters, the Wilcoxon's signed rank test was used. Placement of the sensor on the forehead was compared with placement of the sensor with photodiode over the temporal artery or placement of the sensor with LEDs over the temporal artery. The measurements are displayed as mean (SD); $p < 0.05$ was considered significant.

RESULTS

Adults

After a few seconds a reliable signal could be obtained in all three positions. In each position, the intraindividual range of the SpO_2 during the 4-min period was 2%. In all recordings, a 10-sec period could be analyzed with a signal quality near the maximum score. Heart rate did not change during the measurements in the 6 subjects.

When the photodiode was placed over the artery, the pulse oximeter measured a significantly higher red to infrared ratio and, hence, a significantly lower SpO_2 ($p < 0.01$, Student's paired *t* test). The oximeter read 5.8% (1.0) lower, compared with placement of the sensor on the forehead (Table 1). The percentages ac/dc-R and ac/dc-IR light showed no significant change.

Placement of the LEDs over the artery led to a significant rise in percentages ac/dc-R and ac/dc-IR light ($p < 0.05$, Wilcoxon's signed rank test), compared to placement of the sensor on the forehead. However, the

^{*}This study was approved by the head of the department.

Table 1. Mean (SD) of SpO_2 and Quality Output of N-400 Pulse Oximeter: Calculated Values of Percentages ac/dc and R to IR Ratio of 6 Adults in Three Positions

	Forehead	Photodiode on Temporal Artery	LEDs on Temporal Artery
SpO_2 N-400 oximeter (%)	99.8 (0.4)	94.0 (1.3) ^a	99.2 (1.0)
Mean difference (%)		5.8 (1.0) ^a	0.7 (1.2)
Quality (%)	99.8 (0.4)	99.3 (1.6)	99.6 (1.1)
Percentage ac/dc-R	0.75 (0.41)	0.94 (0.43)	1.61 (0.29) ^b
Percentage ac/dc-IR	1.49 (0.83)	1.38 (0.69)	3.02 (0.50) ^b
R to IR ratio	0.50 (0.03)	0.68 (0.04) ^a	0.53 (0.05)

^a $p < 0.01$, Student's paired t test.

^b $p < 0.05$, Wilcoxon's signed rank test.

Table 2. Mean (SD) of SpO_2 and Quality Output of N-400 Pulse Oximeter: Calculated Values of Percentages ac/dc and R to IR Ratio of 6 Neonates in Three Positions

	Forehead	Photodiode on Temporal Artery	LEDs on Temporal Artery
SpO_2 N-400 oximeter (%)	99.7 (0.8)	92.2 (1.9) ^a	98.5 (1.4)
Mean difference (%)		7.5 (1.9) ^a	1.2 (0.8) ^b
Quality (%)	100.0 (0.0)	98.0 (4.9)	96.5 (8.6)
Percentage ac/dc-R	0.30 (0.13)	0.77 (0.57) ^c	0.59 (0.46) ^c
Percentage ac/dc-IR	0.57 (0.28)	1.07 (0.85)	1.10 (0.87) ^c
R to IR ratio	0.53 (0.04)	0.74 (0.06) ^{a*}	0.54 (0.06)

^a $p < 0.01$, Student's paired t test.

^b $p < 0.05$, Student's paired t test.

^c $p < 0.05$, Wilcoxon's signed rank test.

red to infrared ratio and the SpO_2 were not statistically different.

Neonates

In 1 neonate, it was not possible to obtain a reliable signal, because of its restless state. In the other 6 neonates, a reliable signal could be obtained within a few seconds. The intraindividual range of SpO_2 was 3%, during all measurements. Heart rate did not change. Placement of the sensor over the artery was slightly more difficult than in the adults because we did not want to disturb the sleep state.

When the photodiode was placed over the temporal artery, the red to infrared ratio was significantly higher and the measured SpO_2 was subsequently lower, compared with the forehead position (Table 2). SpO_2 decreased from 99.7% to 92.2% ($p < 0.01$, Student's paired t test). The percentage ac/dc-R was significantly larger ($p < 0.05$, Wilcoxon's signed rank test). For infrared light, it was larger in 5 subjects; but, this difference was not significant.

With the placement of the LEDs over the artery, the

percentages ac/dc-R and ac/dc-IR were significantly larger ($p < 0.05$, Wilcoxon's signed rank test), compared with placement on the forehead. The red to infrared ratio did not change significantly; but, the mean SpO_2 decreased from 99.7 to 98.5 when the LED was moved from the forehead to the temporal artery, respectively.

DISCUSSION

This study shows that pulsating arteries affect the reliability of reflection pulse oximetry during normoxia, depending on the position of the sensor over a superficial artery. The SpO_2 values measured on the forehead are in the expected normal range, as well for the adults as for the neonates. When the sensor was placed with the LEDs over the artery, we found that the SpO_2 was approximately 1% lower than when measured on the forehead; this is clinically not relevant. However, when the sensor was placed with the photodiode over the artery, the oximeter read 6% to 7% too low, which can be falsely interpreted as hypoxia.

Several factors may influence the SpO_2 display by the

pulse oximeter. First, a transient decrease in SaO_2 can occur during the experiment. However, the observed difference in SpO_2 cannot be expected to be due to a transient drop in SaO_2 , since all 12 subjects breathed steadily. Furthermore, the intraindividual range of the SpO_2 in the 4 min was within a range of 3%, and did not decrease or increase during this period. Second, malpositioning of the sensor can cause a falsely low SpO_2 reading by the pulse oximeter. Underestimations of the saturation in case of light shunting was shown by Gardosi et al [5] for reflection sensors. In this study, special attention was paid to proper contact of the sensor with the skin. It is, therefore, not likely that our results can be explained by shunting of light. Finally, the N-400 oximeter was developed as a possible monitoring device for the fetus during labor. The coefficients a and b of the relation

$$SaO_2 = a \cdot \text{ratio} + b$$

are usually experimentally derived for a saturation range of approximately 70% to 100%, by measuring blood sample SaO_2 with a CO-Oximeter and measuring the red to infrared ratio by a pulse oximeter. The coefficients used in the N-400 are based on measurements in adults and in fetal sheep over a much wider range (10% to 100%). The difference of 5% to 7% between SpO_2 on the forehead and with the photodiode over the temporal artery, as measured with the N-400 in its present form, would also have been measured if this oximeter was only calibrated for a 70% to 100% SaO_2 range.

Although other reflection pulse oximetry sensors have been developed, these sensors have not yet been widely tested for their accuracy. Mendelson et al [3,6] have developed a reflectance probe of their own design and have reported satisfactory monitoring. Severinghaus et al [7] evaluated three experimental reflectance pulse oximeters (Criticare, Datex, and Kontron) that were placed on the forehead. The accuracy of these oximeters was comparable or better than the transmission sensors with the same instruments during profound hypoxia in healthy adults. However, Cheng et al [8] reported that the Criticare reflectance sensor was less satisfactory than the transmission sensors in critically ill patients. Decker et al [9] used a Simed forehead sensor; they also found that it was less accurate and more prone to fail to detect a signal, compared to a transmission sensor.

Placement of the photodiode over the temporal artery increased the percentage ac/dc-R more than the percentage ac/dc-IR light. This results in a higher red to infrared ratio and, hence, a lower SpO_2 value. When the sensor was placed with the LEDs over the superficial

temporal artery, there were also significantly larger percentages ac/dc. However, the relative increase was equal for red and infrared light; the red to infrared ratio and the SpO_2 reading remained the same. It is not clear whether the increased ratio is due to the red light or to the infrared light. Not much is known about the paths of red and infrared light through tissue. As infrared light penetrates more deeply than red light [10], the paths of the two wavelengths transverse different tissue compartments, which can lead to a different absorbance. The fact that placement over the temporal artery in the two positions did not lead to the same results can possibly be explained if one assumes that the paths of red and/or infrared light from LEDs to photodiode are not the same for positions 2 and 3. The LEDs are much smaller (about 1 mm² placed under a window of 30 mm²) than the photodiode (30 mm²).

For the relation of SaO_2 and red to infrared ratio, a theoretical model, which incorporates the effects of multiple scattering [11], shows that factors such as flow rate, haematocrit, blood content, and pulsatility have only little effect (1% to 3.3%) in clinical situations for adults and neonates with an arterial SaO_2 of more than 70%. Scattering of photons due to a greater blood volume would result in a deviation of 1% or 2%, smaller than the difference we observed in our experiments. From the multiple scattering model, it can be seen that at SaO_2 values lower than 70%, which is normal for a fetus, deviations will be much larger. De Kock and Tarassenko [12] have shown, with in vitro measurements and using transmission pulse oximetry, that changing of the blood content had no influence above an SaO_2 of 50%; but, deviations increased below an SaO_2 of 50%.

In summary, placement of a reflection sensor with the photodiode above a superficial artery results in falsely low SpO_2 readings. Reflection pulse oximetry can be a possible alternative when conventional transmission pulse oximetry is hampered. More studies, however, have to be performed to gain insight into the light paths of red and infrared light in tissue and to determine the accuracy and reliability of reflectance pulse oximetry.

Financial support for this study was provided by Nellcor, Inc., Pleasanton, CA.

REFERENCES

1. Tremper KK, Barker SJ. Pulse oximetry. *Anesthesiology* 1989;70:98-108
2. Wukitsch MW, Petterson MT, Tobler DR, Pologe JA.

- Pulse oximetry: Analysis of theory, technology, and practice. *J Clin Monit* 1988;4:290-301
3. Mendelson Y, Ochs BD. Noninvasive pulse oximetry utilizing skin reflectance photoplethysmography. *IEEE Trans Biomed Eng* 1988;35:798-805
 4. Dildy GA, Clark SL, Loucks CA. Preliminary experience with intrapartum fetal pulse oximetry in humans. *Obstet Gynecol* 1993;81:630-635
 5. Gardosi JO, Damianou D, Schram CM. Inappropriate sensor application in pulse oximetry. *Lancet* 1992;340:920
 6. Mendelson Y, McGinn MJ. Skin reflectance pulse oximetry: In vivo measurements from the forearm and calf. *J Clin Monit* 1991;7:7-12
 7. Severinghaus JW, Naifeh KH, Koh SO. Errors in 14 pulse oximeters during profound hypoxia. *J Clin Monit* 1989;5:72-81
 8. Cheng EY, Hopwood MB, Kay J. Forehead pulse oximetry compared with finger pulse oximetry and arterial blood gas measurement. *J Clin Monit* 1988;4:223-226
 9. Decker MJ, Dickensheets D, Arnold JL, Cheung PW, Strohl KP. A comparison of a new reflectance oximeter with the Hewlett-Packard ear oximeter. *Biomed Instrum Technol* 1990;24:122-126
 10. Jöbsis-VanderVliet FF, Piantadosi CA, Sylvia AL, et al. Near-infrared monitoring of cerebral oxygen sufficiency. *Neurol Res* 1988;10:7-17
 11. Schmitt JM. Simple photon diffusion analysis of the effects of multiple scattering on pulse oximetry. *IEEE Trans Biomed Eng* 1991;38:1194-1203
 12. de Kock JP, Tarassenko L. In vitro investigation of the factors affecting pulse oximetry. *J Biomed Eng* 1991;13:61-66

Reflectance pulse oximetry in neonates

Karin Faisst^{*a}, Whitney Hannon^a, Jan S. Jørgensen^a, Volker König^a, Hans U. Bucher^b,
Albert Huch^a, Renate Huch^a

^aDepartment of Obstetrics, Unit of Perinatal Physiology, University Hospital of Zurich, Frauenklinikstrasse 10, CH-8091 Zurich, Switzerland

^bDepartment of Neonatology, University Hospital of Zurich, Frauenklinikstrasse 10, CH-8091 Zurich, Switzerland

Accepted 28 March 1995

Abstract

Objective: To test the feasibility and reliability in neonates of an in-house reflectance pulse oximetry (RPOX) system as an alternative method of non-invasive oxygen saturation monitoring when transmission pulse oximetry (TPOX) cannot be used, as in fetal scalp oxygen saturation monitoring during delivery. **Study Design:** The study population consisted of 31 intensive care neonates. The RPOX sensor was attached by suction to the forehead, cheek, occiput and back; recordings were under simultaneous TPOX control. **Results:** There was close agreement between RPOX and TPOX oxygen saturation and heart rate values, even in periodic breathing. RPOX signals from the back were unreliable because of breathing artifacts. Differences in mean absolute RPOX and TPOX oxygen saturation values were due to different calibrations. Both systems were equally sensitive to motion artifacts. **Conclusion:** As a feasible and reliable method of non-invasive oxygen saturation monitoring in neonates, RPOX has potential applications in fetal scalp monitoring.

Keywords: Reflectance pulse oximetry; Transmission pulse oximetry; Neonates; Oxygen saturation

1. Introduction

Pulse oximetry determines the arterial oxygen saturation (SO₂) and heart rate (HR) by a combination of optical plethysmography and spectrophotometry [1]. Transmission pulse oximetry (TPOX) is used routinely in neonatal intensive care and anaesthesia for continuous SO₂ monitoring. The fact that tissue must be placed between the light-emitting diodes (LEDs) and the light-receiving photo diodes limits the use of TPOX to peripheral sites, e.g. fingers, ears and toes. Under certain conditions in which non-invasive SO₂ monitoring would be highly desirable, such as on the presenting fetal part during labour, no peripheral sites are available and TPOX cannot be used.

Reflectance pulse oximetry (RPOX) was introduced on an experimental basis to overcome this problem [2–11], using the same basic concept as TPOX, with the

important difference that the light-emitting and -receiving diodes are located on the same side of the tissue, so that the light detected is back-scattered and not transmitted. Technical and physical limitations are however still greater than in TPOX because:

- RPOX works with weaker signals (reflected light is less intensive).
- Correct calculated saturation values require red and infra-red light to traverse the same tissue area. In RPOX, the different path lengths of red and infra-red light caused by different absorptions of the two wavelengths may lead to incorrect calculations of the saturation values.
- Reflectance saturation values can be altered by light travelling directly from the light emitters to the light detectors without passing through tissue.
- Currently available pulse oximeters are considerably less accurate at saturation values < 70%. Since RPOX is intended for fetal scalp SO₂ measurement during labour, with an expected satura-

* Corresponding author, Tel.: +41 1 255 5148; Fax: +41 1 255 4430.

tion < 70%, experimental calibration in this range is required.

So far, attempts to develop a reflectance sensor have been based on modifying commercial transmission sensors, while maintaining the standard transmission signal processing equipment. However, light intensities, sensor configuration and signal processing all have to be modified for the special requirements of RPOX. We therefore designed a dedicated RPOX system comprising sensors, electronics and computer programmes, which was successfully beta-tested in adults [12].

The purpose of the present study was to answer the following practical questions before performing measurements on the fetal scalp during labour: did the reflectance sensor match the shape of the baby's head; could it be fixed by vacuum in the presence of hair; and were the signals strong enough to give reliable SO_2 and HR values?

2. Materials and methods

2.1. Equipment

A RPOX system was developed in-house [13], and was comprised of a radially symmetric reflectance sensor and two central LEDs (red: 660 nm; infra-red: 920 nm), surrounded by six light-receiving diodes (Siemens BPX90). The computer uses a Pascal program to process

the directly transferred input data, plot the intensity and quality of the pulsatile red and infra-red signals, and display the SO_2 and HR values. Control and standard values were obtained using a transmission mode pulse oximeter (Nelcor N-100). The TPOX SO_2 and HR values were read into the computer programme and displayed simultaneously with the corresponding RPOX values.

2.2. Patients

Thirty-one infants from the neonatal intensive care unit of the University of Zurich Hospital were monitored. Body weights ranged from 1400 to 3980 g (mean: 2411 ± 592 g) on the day of measurement, and birth weights from 720 to 4160 g (mean: 2038 ± 903 g). They were in intensive care for a variety of reasons including prematurity, maternal diabetes or maternal drug abuse. During measurement the quiet or sleeping infants were clinically stable and receiving no vasoactive drugs.

2.3. Protocol

Parental permission was obtained before each measurement. The reflectance sensor was fixed at four different sites: mid-forehead ($n = 31$), temple ($n = 28$), occiput (through hair) ($n = 15$), and lower back ($n = 15$). The transmission sensor was wound around the hand, providing continuous simultaneous standard and control SO_2 and HR data (Fig. 1). Following sen-

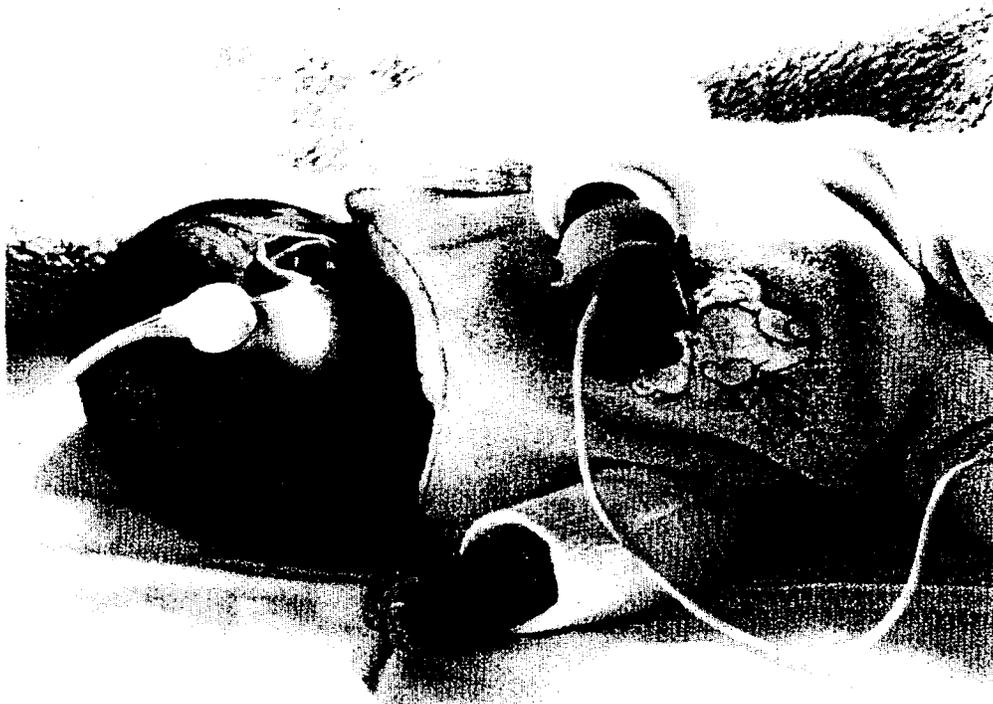


Fig. 1. Simultaneous measurement of SO_2 and HR with the reflectance sensor placed on the temple and the transmission sensor on the left hand.

sensor placement, data recording was initiated as soon as a suitable pulsatile signal was obtained. High frequency disturbances or movements were flagged in the computer file and noted in written records. A representative sample was obtained from each infant (2-10 min) before moving the reflectance sensor to a new site.

Individual SO_2 and HR values were expressed as the mean of the longest continuous artifact-free interval (30 s-4 min). Data were analysed using StatView 4.0 and Microsoft Excel 3.0.

3. Results

3.1. Sensor attachment and signal acquisition

The reflectance vacuum sensor fixed readily to the forehead, temple and occiput, and gave reliable pulsatile signals for the calculation of SO_2 and HR. Although fixation on the back was also easy, signals were unreliable due to breathing artifacts.

Ease of fixation differed with site. Fixation and signal reception were satisfactory on the forehead in 30/31 cases (97%) and on the temple in 26/28 cases (93%). Fixation was more difficult on the occiput, given a considerable amount of hair in 11/15 infants (73%) but was

facilitated by wetting the hair first. The infants were not disturbed by fixation or continuous use of the vacuum sensor and within a few minutes of removal all suction marks had disappeared.

3.2. Motion artifacts

Reflectance and transmission mode measurements were equally disrupted by motion artifacts, and particularly by breathing artifacts at various locations on the back.

3.3. Intra-individual RPOX vs. TPOX

Continuous TPOX vs. RPOX monitoring in a 6-day-old girl (2680 g, born at 36.14 weeks) from a reflectance sensor on the temple and a transmission sensor on the right hand showed good quality reflectance sensor AC and DC signals (Fig. 2). Reflectance SO_2 values were lower than the controls but the lines were parallel. HR values showed a similar parallelism.

Two infants exhibited periodic breathing. SO_2 and HR values in a 32-day-old 1660 g premature girl (gestational age 30.14 weeks), obtained from a mid-forehead reflectance sensor closely followed the SO_2 fluctuations shown by TPOX (Fig. 3). RPOX and TPOX SO_2 values

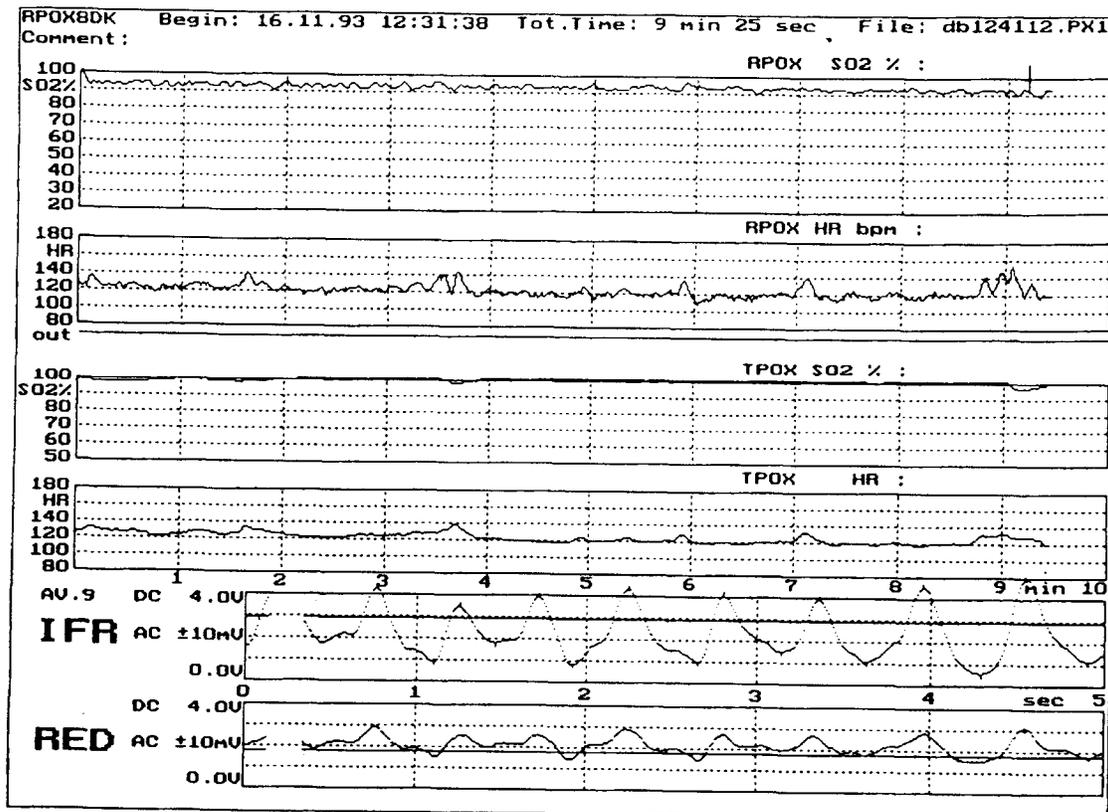


Fig. 2. Continuous 10-min print-out. Upper two lines, RPOX SO_2 and HR values; middle two lines, TPOX SO_2 and HR values; bottom, RPOX sensor AC and DC signals.

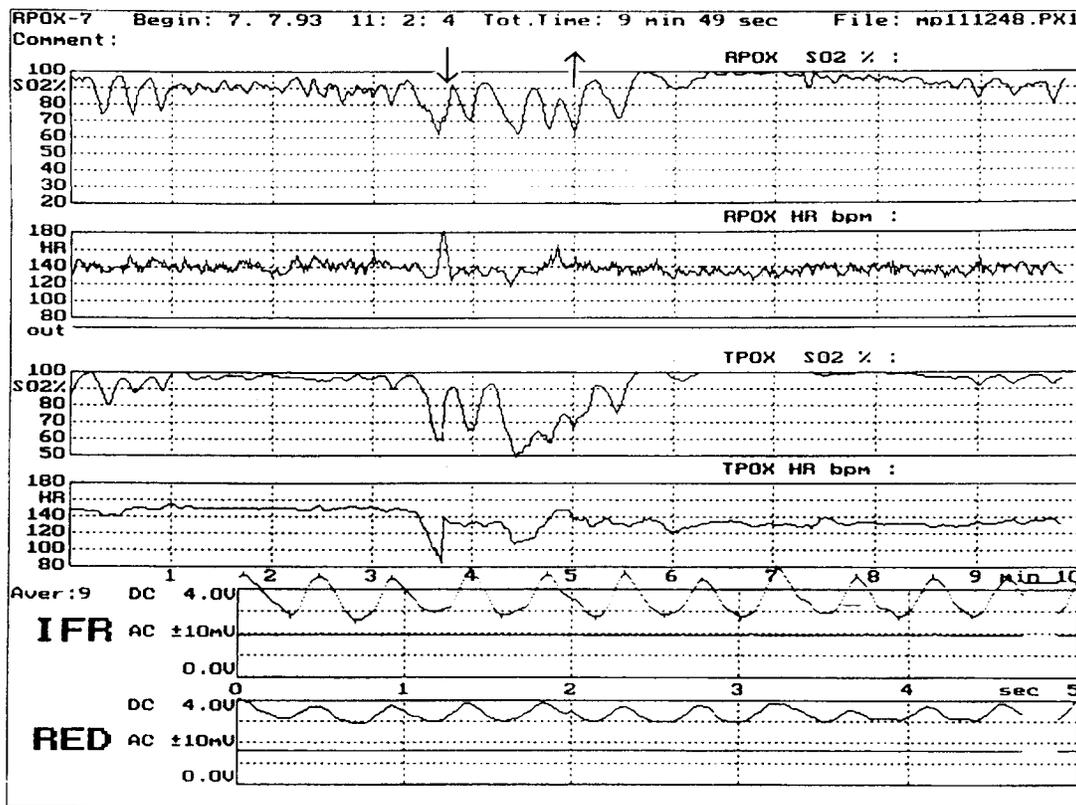


Fig. 3. Continuous simultaneous RPOX and TPOX measurement of SO₂ and HR in a neonate with periodic breathing. First arrow (1), onset of periodic breathing; second arrow (1), exogenous oxygen.

decreased and increased in parallel during episodes of apnea and following O₂ administration, respectively.

3.4. Inter-individual RPOX vs. TPOX

Reflectance SO₂ values were lower than the TPOX controls, while HR values were similar. The mean ΔSO₂[SO₂(TPOX) - SO₂(RPOX)] differed depending on the site of fixation, unlike the mean Δ(HR) = [HR(TPOX) - HR(RPOX)] (Table 1). ΔSO₂ also differed intra- and inter-individually depending on the fixation site.

Table 1
Comparison of ΔSO₂ and ΔHR with the corresponding standard deviations at different RPOX fixation sites

Site	n	ΔSO ₂ ± S.D.	ΔHR ± S.D.
Forehead	30	5.9 ± 2.8	0.6 ± 9.4
Temple	26	4.3 ± 2.9	0.9 ± 9.1
Occiput	11	2.4 ± 3.4	1.2 ± 5.8

ΔSO₂ = SO₂(TPOX) - SO₂(RPOX);
 ΔHR = HR(TPOX) - HR(RPOX).

4. Discussion

RPOX has obvious advantages over TPOX, opening new perspectives in clinical situations where TPOX is limited by the requirement for tissue between the sensors. In addition to non-invasive monitoring of the fetal scalp SO₂ during labour, these situations include measurement from the forehead or chest in the presence of low peripheral perfusion, burns or peripheral edema.

Although several reflectance pulse oximeters have been described, no routine clinical application has yet been reported. This study was designed to evaluate the feasibility of RPOX in neonates and compare the SO₂ and HR results with those obtained by TPOX. The results show that fluctuations in neonatal SO₂ can be monitored equally well by RPOX and TPOX, even in the presence of the dramatic fluctuations seen in periodic breathing.

The ideal sensor should be easy to attach and detach, yet should remain in position during movements while having no adverse effect at the fixation site. These requirements are even more stringent regarding measurements from the fetal scalp during labour. Johnson [8] used several different methods of sensor application in-

cluding glue, suction and clip fixation, while Mendelson and Solomita [14] used adhesive tape in combination with a suction cup.

The sensor used in the present study was similarly non-invasive and applied by suction. The soft flexible surface of the sensor casing adapted easily to each body part and yielded reliable signals even through a considerable amount of hair. In an earlier study comparing suction vs. adhesive fixation in adults, pulsatility was not reduced when suction was applied for longer periods of time, and the mean SO_2 values did not differ [12]. The present study confirmed the absence of suction induced changes in signal quality or SO_2 values over the measurement period.

Mendelson and Solomita [14] postulated that the tighter attachment of the vacuum sensor to the skin accounts for the significantly fewer motion artifacts produced by normal respiration and sensor movement. Movement is the most common cause of pulse oximeter failure and false alarm when subjects are awake [15]. Our experience confirms Dear's finding [16] that pulse oximetry in neonates is reliable only during quiet periods. The fact that movement disrupted both RPOX and TPOX measurements indicates that, contrary to speculation, RPOX has no advantage over TPOX in this regard. Signal processing by commercial transmission pulse oximeters excludes some motion noise, but no such filter has yet been incorporated into our system. A major obstacle is that the closer the approximation between movement frequency and HR, the more difficult it is to discriminate between the real pulse signal and motion artifacts.

Due to the rapid neonatal respiration rate, it was extremely difficult to obtain pulsatile signals from the back for reliable SO_2 data. This site cannot be recommended for RPOX monitoring purposes.

Mean absolute RPOX SO_2 values were consistently lower than their TPOX counterparts in all individuals. Our adult data showed a similar TPOX-RPOX discrepancy of 4.5% and is due to a difference in the calibration of our system [12]. It can be easily corrected by adjusting the algorithm software. HR values, on the other hand, were similar in the two systems.

Fixation site dependency of SO_2 values, in contrast to HR values, has also been noted with TPOX [17,18]. Proposed causes include low blood flow causing desaturation of the pulsating blood due to local tissue oxygen consumption, light leakage around instead of through the tissue, venous pulsation associated with venous congestion, and variations of tissue thickness [17,19]. As fixation site differences were not consistent between individuals, intra- and inter-individual characteristics of the fixation site must influence absolute RPOX SO_2 values.

5. Conclusions

RPOX is feasible in neonates, and provides reliable (TPOX-controlled) SO_2 and HR data, even in the presence of considerable occiput hair. The greatest challenge to its projected application to the fetus in labour is likely to come from motion artifacts. We are therefore now planning to start clinical trial measurements on the fetus during labour.

Acknowledgements

We thank the nursing staff at the neonatal intensive care unit for their help with this study.

References

- [1] Bowes III WA, Corke BC, Hulka J. Pulse oximetry: A review of the theory, accuracy, and clinical applications. *Obstet Gynecol* 1989; 74: 541–6.
- [2] Mendelson Y, Cheung PW, Neuman MR. Spectrophotometric investigation of pulsatile blood flow for transcutaneous reflectance oximetry. *Adv Exp Med Biol* 1983; 159: 93–102.
- [3] Mendelson Y, Kent JC, Yocum BL, Birle MJ. Design and evaluation of a new reflectance pulse oximeter sensor. *Med Instrum* 1988; 22: 167–73.
- [4] Mendelson Y, Ochs BD. Non-invasive pulse oximetry utilizing skin reflectance photoplethysmography. *IEEE Trans Biomed Eng* 1988; 35: 798–805.
- [5] Cheng EY, Hopwood MB, Kay J. Forehead pulse oximetry compared with finger pulse oximetry and arterial blood gas measurement. *J Clin Monit* 1988; 4: 223–6.
- [6] Shimada Y, Nakashima K, Fujiwara Y, Komatsu T, Kawanishi M. Evaluation of a new reflectance pulse oximeter for clinical applications. *Med Biol Eng Comput* 1991; 29: 557–61.
- [7] Decker MJ, Dickensheets D, Arnold JL, Cheung PW, Strohl KP. A comparison of a new reflectance oximeter with the Hewlett-Packard ear oximeter. *Biomed Instrum Technol* 1990; 24: 122–6.
- [8] Gardosi JO, Schram CM, Symonds EM. Adaptation of pulse oximetry for fetal monitoring during labour. *Lancet* 1991; 337: 1265–7.
- [9] Johnson N, Johnson VA, Fisher J, Jobbings B, Bannister J, Lilford RJ. Fetal monitoring with pulse oximetry. *Br J Obstet Gynaecol* 1991; 98: 36–41.
- [10] Takatani S, Davies C, Sakakibara N et al. Experimental and clinical evaluation of a non-invasive reflectance pulse oximeter sensor. *J Clin Monit* 1992; 8: 257–66.
- [11] Dildy GA, Clark SL, Loucks CA. Preliminary experience with intra-partum fetal pulse oximetry in humans. *Obstet Gynecol* 1993; 81: 630–5.
- [12] König V, Ullrich GJ, Faisst K, Jørgensen JS, Huch R, Huch A. Reflexions-Pulsoximetrie — Untersuchungen mit eigenem Mess-System. *Biomed Tech* 1992; 37: 39–40.
- [13] Lafeber HN, ed. Fetal and neonatal physiological measurements. *Proceedings of the 4th International Conference on Fetal and Neonatal Physiological Measurements*. Amsterdam: Excerpt Medica, 1991.
- [14] Mendelson Y, Solomita M. The feasibility of spectrophotometric measurements of arterial oxygen saturation from the fetal scalp utilizing non-invasive skin-reflectance pulse oximetry. *Biomed Instrum Technol* 1992; 26: 215–24.

- [15] Wilson S. Conscious sedation and pulse oximetry: False alarms? *Pediatr Dent* 1990; 12: 228–32.
- [16] Dear PRF. Monitoring oxygen in the newborn: saturation or partial pressure? *Arch Dis Child* 1987; 62: 879–81.
- [17] Severinghaus JW, Naifeh KH. Accuracy of response of six pulse oximeters to profound hypoxia. *Anesthesiology* 1987; 67: 551–8.
- [18] Clayton DG, Webb RK, Ralston AC, Duthie D, Runciman WB. A comparison of the performance of 20 pulse oximeters under conditions of poor perfusion. *Anaesthesia* 1991; 46: 3–10.
- [19] Broome IJ, Reilly CS. Explanation for the over-estimation of oxygen. *Anaesthesia* 1991; 46: 424.

Wavelength Selection for Low-Saturation Pulse Oximetry

Paul D. Mannheim,* James R. Casciani, Michael E. Fein, *Member, IEEE*, and Steven L. Nierlich

Abstract—Conventional pulse oximeters are accurate at high oxygen saturation under a variety of physiological conditions but show worsening accuracy at lower saturation (below 70%). Numerical modeling suggests that sensors fabricated with 735 and 890 nm emitters should read more accurately at low saturation under a variety of conditions than sensors made with conventionally used 660 and 900 nm band emitters. Recent animal testing confirms this expectation. It is postulated that the most repeatable and stable accuracy of the pulse oximeter occurs when the fractional change in photon path lengths due to perturbations in the tissue (relative to the conditions present during system calibration) is equivalent at the two wavelengths. Additionally, the penetration depth (and/or breadth) of the probing light needs to be well matched at the two wavelengths in order to minimize the effects of tissue heterogeneity. At high saturation these conditions are optimally met with 660 and 900 nm band emitters, while at low saturation 735 and 890 nm provide better performance.

Index Terms—Emitter wavelengths, low saturation, medical optics, pulse oximetry, tissue optics.

I. INTRODUCTION

PULSE oximetry is used to monitor continuously the arterial blood oxygen saturation of adults, children, and neonates in the operating room, recovery room, intensive care units, and increasingly on the hospital's general floor. Patients encountered in these environments typically have saturation greater than 90% and rarely below 70%. When saturation does fall below the normal range, an unhealthy clinical condition is indicated and some form of intervention generally occurs. Here, limited accuracy at low saturation does not affect the clinical utility of the system.

Recently, the use of pulse oximetry has been expanded into the obstetrical delivery room where it is being used for monitoring the oxygen status of the fetus during labor and delivery [1]. The range of normal saturations in the fetus is much lower, typically 20–75% [2], [3], and accuracy in the low saturation range takes on additional importance in assessing fetal well being [4], [5]. As conventional oximeters tend to read less accurately at very low saturations [6]–[8], there is a need to determine what causes such errors and, if possible, to redesign the system accordingly.

Manuscript received May 17, 1995; revised September 13, 1996. *Asterisk indicates corresponding author.*

*P. D. Mannheim is with Nellcor Puritan Bennett, 4280 Hacienda Drive, Pleasanton, CA 94588 USA (e-mail: paul.mannheimer@nellcorpb.com).

J. R. Casciani, M. E. Fein, and S. L. Nierlich are with Nellcor Puritan Bennett, Pleasanton, CA 94588 USA.

Publisher Item Identifier S 0018-9294(97)01467-5.

Typical pulse oximetry sensors employ a photodetector and red (660 nm) and near IR (900 nm band)¹ Light emitting diodes (LED's) to measure the light that scatters through blood perfused tissues. Wavelength selection traditionally emphasizes sensitivity to changes in arterial oxygen saturation (SaO₂), with at least one of the emitter wavelengths chosen from a spectral region where the absorption coefficient of oxygenated hemoglobin, O₂Hb, is markedly different from that of deoxygenated hemoglobin, HHb [9], [10]. Although others have considered the effect of wavelength choice on the performance of pulse oximetry [11], [12], the published literature has not attempted to optimize accuracy at very low oxygen saturations under a variety of "physio-optical" conditions.

This paper presents an analysis of the effect emitter wavelengths have on the accuracy of the pulse oximeter when the system is subjected to changes in the bulk tissue optical properties relative to the conditions present during the oximeter's calibration. To incorporate the scattering nature of light in tissues, the Monte Carlo modeling method of Bonner *et al.* [13] and photon diffusion theory of Schmitt [14] are utilized. Estimated optical characteristics of blood-perfused tissues are used in numerical models based on these works to compute the effect of changes in tissue hemoglobin content upon the oximeter response function for a variety of emitter wavelength pairs. Optimum performance is predicted to result when emitter wavelengths are chosen so that perturbations in the tissue optics result in balanced changes to the red and infrared (IR) light paths.

II. BACKGROUND

The typical pulse oximetry sensor contains two LED's that emit red and IR light into a pulsatile tissue bed. The scattered light is collected with a photodiode positioned on an opposite surface (transmission pulse oximetry) or an adjacent surface (reflectance pulse oximetry). The "pulse" comes from the time-varying amount of arterial blood in the tissue during the cardiac cycle. Signals collected by the photodetector create a plethysmographic waveform due to the resulting cycling light attenuation. The relative modulation of the collected red and IR light signals, referred to as the modulation ratio "R," is used to estimate arterial oxygen saturation, SpO₂, based on an empirical calibration relationship expressed within the oximeter [15] (the lower case "p" indicates that the value comes from

¹Pulse oximeters described in the literature or sold commercially typically choose a near IR LED in the wavelength range of 880–905 nm or further out near 940 nm. We will refer to all of these wavelengths as the "900 nm band."

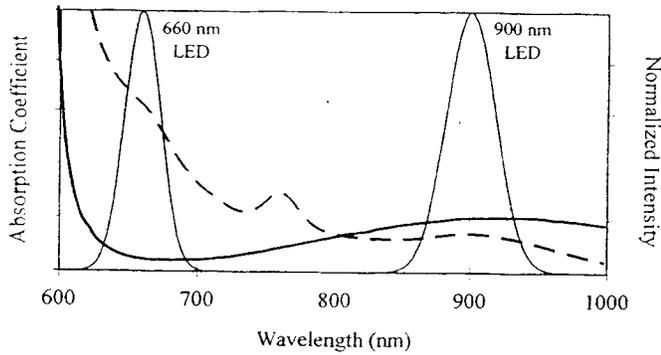


Fig. 1. Absorption coefficient versus wavelength for oxygenated (solid) and deoxygenated (dashed) hemoglobin. The normalized spectral distributions of conventionally chosen LED's are overlaid on the same wavelength scale for comparison.

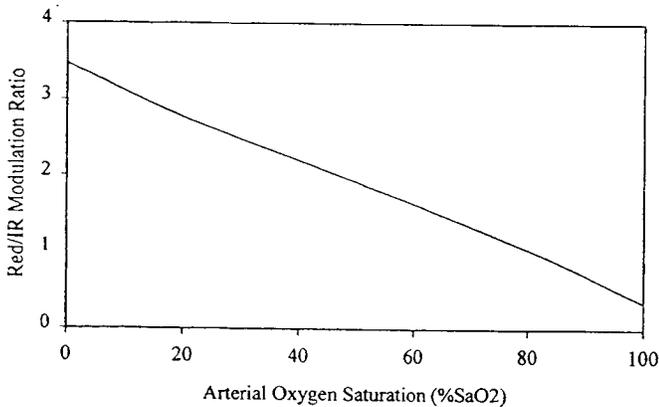


Fig. 2. Theoretically predicted relationship between red/IR modulation ratio [defined in (1)] and arterial oxygen saturation.

pulse oximetry). Fig. 1 shows the spectra of conventionally chosen LED's overlaid on the relative absorption coefficients of oxygenated and deoxygenated hemoglobin. Fig. 2 shows the resulting modulation ratio (R) versus SaO₂ for this set of conventional wavelengths.

Calibration and sensitivity of the pulse oximeter are influenced strongly by light absorption due to the pulsing arterial blood. However, absorption and light scattering characteristics of the entire tissue bed, beyond that of just the arterial blood component, affect the actual behavior of the system's ratio versus saturation response [14], [16]. Using photon diffusion theory, Schmitt [14] evaluates the sensitivity of the calibration to normal variations in parameters such as tissue blood volume, venous blood saturation, hemoglobin concentration, and source-detector placement. For arterial oxygen saturations above 70%, normal physiological variations are found to affect minimally the accuracy of the conventional pulse oximeter. SpO₂ measurement variations due to changes in variables other than SaO₂ increase significantly at lower saturations. Schmitt attributes this behavior to the effect of multiple scattering of light in the tissue and concludes that reduced accuracy at lower arterial oxygen saturation is an inherent limitation in pulse oximetry. For applications of pulse oximetry where the typical and/or critical range of arterial

TABLE I
TISSUE ABSORPTION AND SCATTERING CONSTANTS USED

Coefficient (mm ⁻¹)	Wavelength					
	660 nm	735 nm	760 nm	805 nm	890 nm	940 nm
μ_a bloodless tissue	0.010	0.008	0.008	0.008	0.007	0.007
HHb	1.676	0.616	0.798	0.373	0.393	0.318
O ₂ Hb	0.126	0.178	0.245	0.380	0.549	0.561
μ'_s	1.43	1.22	1.16	1.05	0.89	0.82

All units are mm⁻¹, and assume base e logarithms. Translation of $\mu_{a\text{HHb}}$ and $\mu_{a\text{O}_2\text{Hb}}$ from values given by Zijlstra [17] assumes a hemoglobin molecular weight of 16 000 and a blood hemoglobin concentration of 15 g/dl.

oxygen saturation is below 70%, such as fetal saturation monitoring, such inherent limitations could restrict the utility of the technology.

III. METHOD

Two different models are used to explore numerically the effect of using different emitter wavelength pairs. The first model is based on the Monte Carlo method of Bonner *et al.* [13] and will be referred to as the MC model. The second utilizes the equations derived by Schmitt [14] using photon diffusion theory (PD model). Both models consider reflectance pulse oximetry geometry and assume isotropic scattering within a semi-infinite homogeneous tissue bed. Although a simplification of the true optical nature of the tissue, which is heterogeneous with irregular boundaries, these models are useful for predicting behaviors of pulse oximetry and the sensitivity to many design parameters. In both MC and PD models the bulk tissue absorption ($\mu_{a\text{total}}$) is calculated as a sum of contributions from the arterial and venous blood and the background tissue absorption. The reduced scattering coefficient (μ'_s) is considered to be determined exclusively by the bloodless tissue (unaffected by the small percentage of blood volume in the tissue) [16]. Spectral widths of the LED's are not considered in either of the models in this analysis. Hemoglobin extinction coefficients are taken from Zijlstra [17] and tissue absorption and scattering coefficients are estimated from Schmitt [14] using spline interpolation. A summary of the scattering and absorption coefficients used is shown in Table I.

The MC model utilizes (12) of the Bonner reference [13] to calculate the probability (Γ) of a photon re-emerging at the surface of a semi-infinite medium. The probability is solely a function of the separation from the point of entry (r) and of the reduced scattering and absorption coefficients of the bulk tissue. For the model of pulse oximetry presented here, this probability is used to calculate signal intensities, Γ_{dias} and Γ_{sys} , using diastolic and systolic values for the bulk tissue absorption coefficient. Modulation ratio (R) is calculated as

$$R = \frac{\log \left(\frac{\Gamma_{\text{sys}}}{\Gamma_{\text{dias}}} \right)_{\text{red}}}{\log \left(\frac{\Gamma_{\text{sys}}}{\Gamma_{\text{dias}}} \right)_{\text{IR}}} \approx \frac{\left(\frac{ac}{dc} \right)_{\text{red}}}{\left(\frac{ac}{dc} \right)_{\text{IR}}} \quad (1)$$

TABLE II
EXAMPLE OF MODELED SIGNALS AND RATIO VERSUS SATURATION

SaO ₂	MC Model				PD Model	
	660 nm red		890 nm IR		Ratio	Ratio
	Γ_{sys}	Γ_{dias}	Γ_{sys}	Γ_{dias}	(R)	(R)
100	1.2476x10 ⁻⁵	1.2526x10 ⁻⁵	5.6584 x10 ⁻⁵	5.7234 x10 ⁻⁵	0.35	0.35
80	6.1817x10 ⁻⁶	6.2520x10 ⁻⁶	5.9655x10 ⁻⁵	6.0311x10 ⁻⁵	1.03	1.06
60	3.3749x10 ⁻⁶	3.4329x10 ⁻⁶	6.2944x10 ⁻⁵	6.3606x10 ⁻⁵	1.63	1.66
40	1.9627x10 ⁻⁶	2.0061x10 ⁻⁶	6.6474x10 ⁻⁵	6.7138x10 ⁻⁵	2.20	2.23
20	1.1947x10 ⁻⁶	1.2263x10 ⁻⁶	7.0266x10 ⁻⁵	7.0932x10 ⁻⁵	2.77	2.79
0	8.9031x10 ⁻⁷	9.1801x10 ⁻⁷	7.2801x10 ⁻⁵	7.3447x10 ⁻⁵	3.47	3.49

MC model signal levels for 660 nm red and 890 nm infrared light at systolic and diastolic blood concentrations in the tissue are shown, as well as the resulting modulation ratio [using (1)]. Ratio determined from the PD model is shown in the last column. All values correspond to the baseline tissue characteristics described in the text. Arterial blood volume is considered to increase between diastole and systole by 5%.

The "ac/dc" approximation on the right-hand side is an adequate approximation for small pulse amplitudes and is sometimes used in the literature [18]. Modulation ratio as a function of saturation is calculated by varying numerically the arterial and venous blood oxygen saturations and reapplying (1). Baseline tissue and sensor characteristics are considered to be: 5% tissue blood volume; 10 g/dl hemoglobin concentration; 3:1 venous-to-arterial blood volume ratio within the tissue (compartmentalization); 10% arterio-venous saturation difference; an emitter-detector spacing of 12 mm. These baseline conditions serve to simulate a nominal environment, and the calculated R versus SaO₂ response serves as the SpO₂ calibration function for subsequent calculations.

Schmitt [14] solves for the intensity of the signal available at the detector as a function of the three values r , μ'_s , and $\mu_{a,\text{total}}$ as well. He derives an equation for the modulation ratio, again using systolic and diastolic blood volumes, and utilizes the ratio of peak-to-peak ac amplitudes to dc signal levels at the two wavelengths as shown on the right-hand side of (1). Solutions are offered for both transmissive and reflectance geometries. For the purpose of comparing results between the PD and MC models, Schmitt's equations for the reflectance geometry have been used in the PD model. An example of the calculated signals from the MC model, and the corresponding modulation ratios from both models, are shown in Table II.

System stability after a change in tissue characteristics from those considered during the baseline "calibration" was evaluated for several pairings of red and infrared emitter wavelengths. For each of the pairings considered, the theoretical relationship of red to infrared modulation ratio (R) was calculated using both models for the baseline set of tissue characteristics. To evaluate the sensitivity of this response (R versus SaO₂) to potential changes in physiological conditions, one or more of the baseline conditions may be varied. A simple change in tissue blood volume simulates multiple tissue perturbations, such as anemia, placing the sensor over a region of low vascularization, or local exsanguination caused by force applied to the skin, since each of these reduces

the amount of hemoglobin present in the local tissue (tissue hemoglobin content equals the product of tissue blood volume and blood hemoglobin concentration). Furthermore, changing blood volume has been found previously to have a greater impact on reading stability than the other parameters of the model [14]. Accordingly, for the stability analysis presented here, tissue blood volume was decreased to one-fourth its nominal value, or 1.25%. Revised SpO₂ values were calculated from the resulting new modulation ratio using the baseline response curve as the calibration function. The difference between revised and baseline SpO₂ values indicate how much measurement error would result from using a high-blood-volume calibration curve in a low-blood-volume tissue bed.

IV. MODELING RESULTS

Results from the two models were in qualitative agreement with one another. Fig. 3 presents the results of the MC model when using a conventional 660 and 890 nm wavelength emitter pair. As can be seen in the figure, a drop in tissue blood volume from 5% to 1.25% is predicted to have minimal influence on SpO₂ readings for saturations above approximately 70%. The effect is increasingly significant, however, as the saturation drops below this level. Fig. 4 shows the similar behavior predicted by the PD model for these emitter wavelengths. The magnitude of the error and the saturation where the error vanishes ("cross-over point") are similar in the two models.

Figs. 5 and 6 show the predicted behavior of a 735 and 890 nm wavelength emitter pair when subjected to the same change in tissue blood volume. As can be seen in the figures, the saturation region where the error becomes minimum shifts to lower values of SaO₂. Additionally, the worst case errors, now at the extremes of the saturation range, are smaller in magnitude than with the 660/890 nm wavelength pair. Sensitivity of the modulation ratio to changes in arterial oxygen saturation (slope of the curves in the left-hand figures) becomes reduced with the 735/890 nm pair (this is why, despite the apparent match between the perturbed and baseline curves in the left-hand figures, there are significant deviations

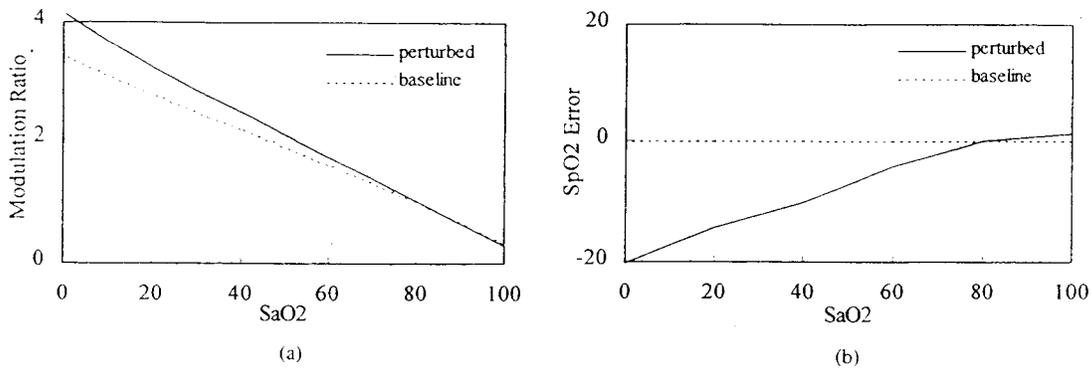


Fig. 3. MC model results. (a) Modulation ratio and (b) SpO2 error due to changing the tissue blood volume from 5% (baseline) to 1.25% for a 660 and 890 nm emitter pair according to the MC model are shown. This perturbation simulates the effects of tissue hemoglobin concentration variations within the patient population due to, for example, anemia, ischemia, or localized exsanguination of blood in the tissue. The left-hand curves show the modulation ratio versus saturation for baseline and perturbed conditions. The resulting error in estimated SpO2 is shown in (b) in units of percent saturation. This value is equivalent to the horizontal separation between the perturbed and baseline curves in (a).

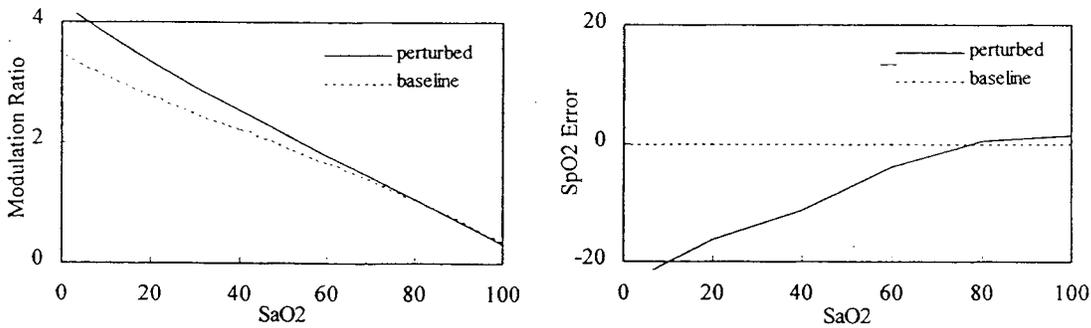


Fig. 4. PD model results. The effect of changing tissue blood volume from 5% to 1.25% with 660 and 890 nm emitters is shown according to the PD model. These curves are similar to the findings of Schmitt [14], who considers a different IR emitter wavelength.

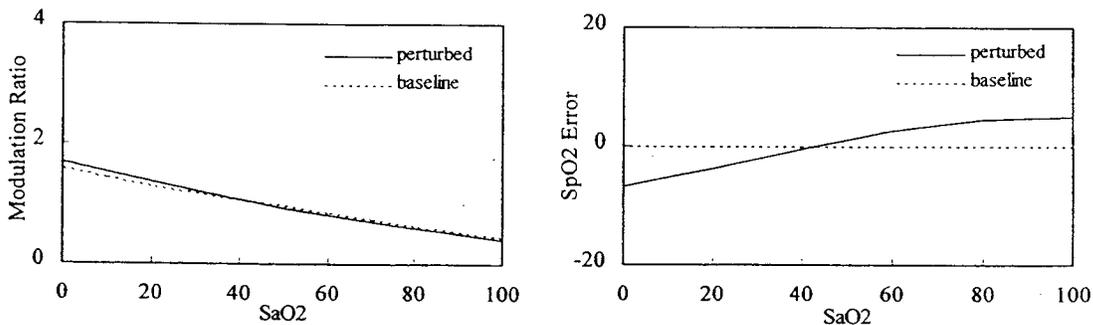


Fig. 5. MC Model results for 735/890 nm. Shown here is the same analysis as in Fig. 3, but considering a 735 and 890 nm emitter pair. Notice that the crossover point where the error is zero has shifted to a lower saturation, and the worst case errors are smaller.

shown in the right-hand figures). As was found with the 660/890 nm pair, the magnitude of the error and the crossover point are similar in the MC and PD models.

MC model results of other wavelength combinations taken from the red and IR portions of the spectrum are shown in Figs. 7–10. PD model results, not shown, are similar. The following wavelength pairs are presented: 660/805, 660/940, 760/890, and 805/940 nm. These figures again reflect the change in predicted SpO2 reading due to a change in tissue blood volume from the “calibration” condition of 5% nominal to 1.25%. Sensitivity of the measured modulation ratio R to changes in arterial oxygen saturation varies depending on the wavelength pairing used. The cross-over point also varies with

wavelength choice, spanning the range 45–95% for the pairs considered.

V. DISCUSSION

The results of both numerical models are very similar to the conclusions of Schmitt [14] and the clinical observations of Severinghaus [8]. When conventional emitter wavelengths are used, typically 660 nm and 880–905 or 940 nm, the accuracy of the pulse oximetry measurement is dependent on the amount of hemoglobin present in the tissue. For a homogeneous tissue bed, the tendency is to read erroneously low values of SpO2 at low saturations when there is less hemoglobin in the tissue

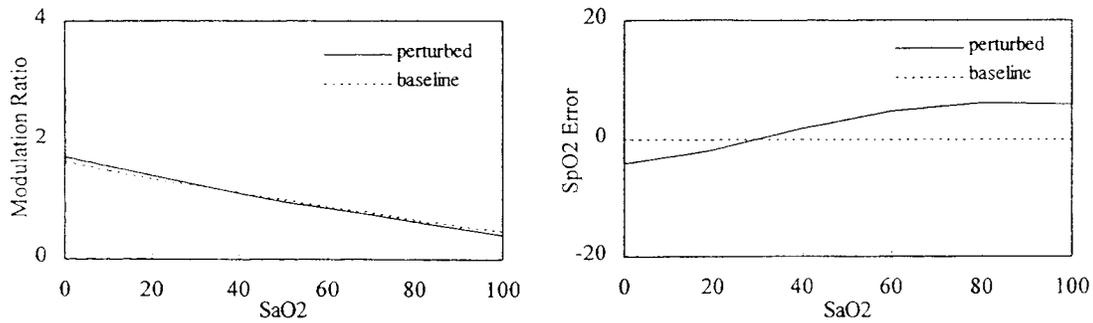


Fig. 6. PD model results for 735/890 nm. These results are very similar to the MC model, although the crossover point is predicted to be at a slightly lower saturation.

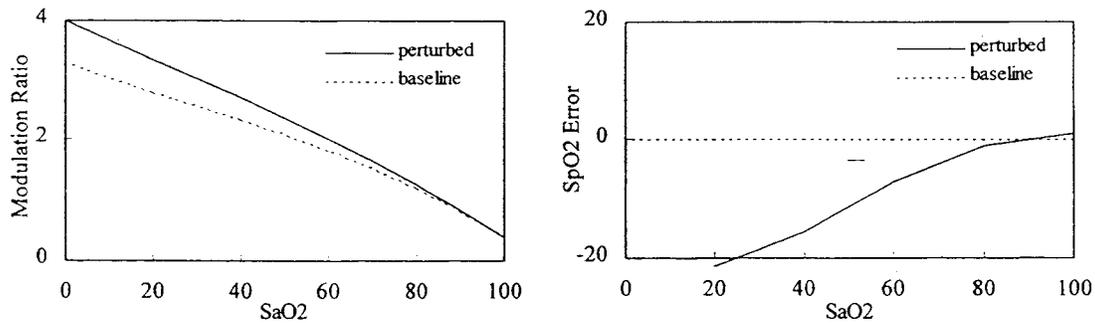


Fig. 7. 660 and 805 nm emitter pair (MC model).

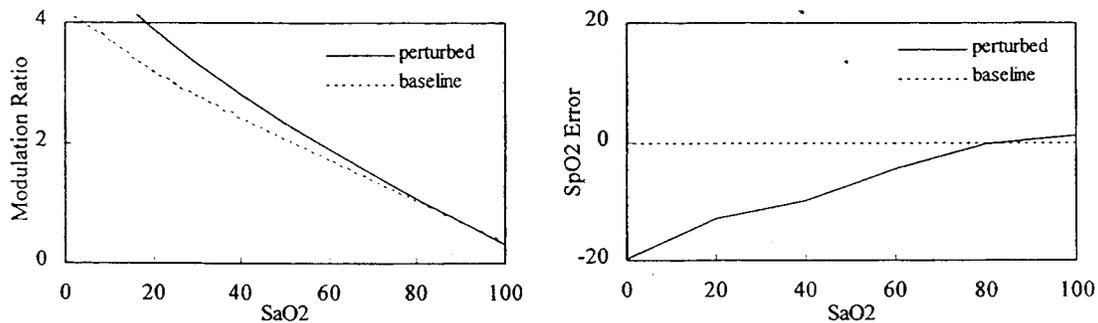


Fig. 8. 660 and 940 nm emitter pair (MC model).

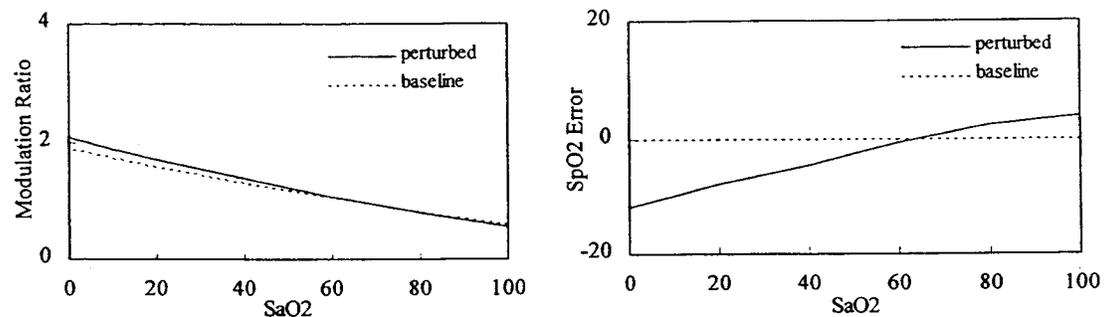


Fig. 9. 760 and 890 nm emitter pair (MC model).

relative to when the system was initially calibrated, e.g., in anemic or ischemic conditions relative to a healthy population. Schmitt predicts this type of behavior for both reflectance and transmittance pulse oximetry geometries.

The left-hand curves in Figs. 3–10 show the varying slopes of the R versus SaO_2 relationship as a function of emitter wavelength pair. The difference in light absorption by oxygenated and deoxygenated hemoglobin is greatest near 660

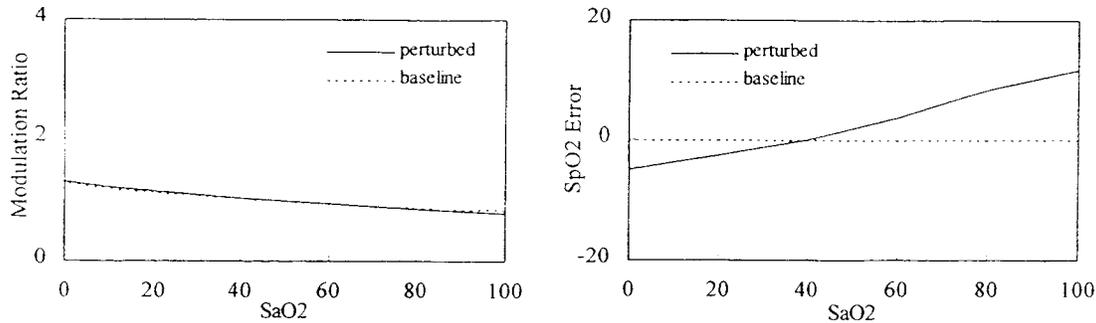


Fig. 10. 805 and 940 nm emitter pair (MC model).

nm, and relatively constant in the near IR beyond 840 nm (Fig. 1). Thus the *sensitivity* of the measured modulation ratio to changes in arterial oxygen saturation is optimum when using 660 nm red and an IR wavelength in the 840–940 nm range. With this choice of wavelengths, however, slope of the ratio versus SaO₂ relationship changes as the amount of hemoglobin in the tissue varies, “pivoting” around a point somewhere near 80–90% saturation (left-hand curves in Figs. 3 and 8). Although not presented here, similar changes occur when other “physio-optical” parameters are varied, such as arterio-venous saturation difference or compartmentalization.

When the red wavelength is moved to the far red, in the range of 700–800 nm, the slope of the *R* versus SaO₂ response becomes smaller. This is because there is less difference in the absorption coefficients of O₂Hb and HHb. However, both models suggest that the oximeter’s accuracy at low saturation becomes more robust in the face of changes in “physio-optical” conditions such as blood volume changes or variations in compartmentalization. As will be discussed below, the reason for this improved stability likely relates to the similarity of certain tissue optical properties at the two sensor wavelengths, and to the extent to which the resulting detected photon paths overlap one another within the tissue bed.

Although it is difficult to create these specific physio-optical tissue characteristics *in vivo* in order to test the modeled predictions, animal studies have been conducted which confirm the improved low saturation accuracy using the 735/890 nm system. We have observed, in studies conducted on lambs at low saturations, less dependence of SpO₂ reading on sensor placement (for example, head versus rump or neck), and less sensitivity to the force used in applying the sensor (unpublished data), with the 735 nm system. Figs. 11 and 12 show the results of a sensor-placement study comparing readings obtained on the lamb’s head versus the neck. Sensors were fabricated using either 660/895 or 735/895 nm emitter pairs, with an emitter-detector spacing of 14 mm center-to-center. The optical components were molded into black silicone housings with clear windows over the emitter and detector apertures. Animal preparation and test protocol followed the same procedure described elsewhere [19]. After shaving the sites to be free of hair, two sensors were held in place on the crown of the lamb’s head and two on the side of the neck, each sensor held down with approximately 50 gram force using a circumferential band and a small leaf-spring force gauge. Optical cross-talk among

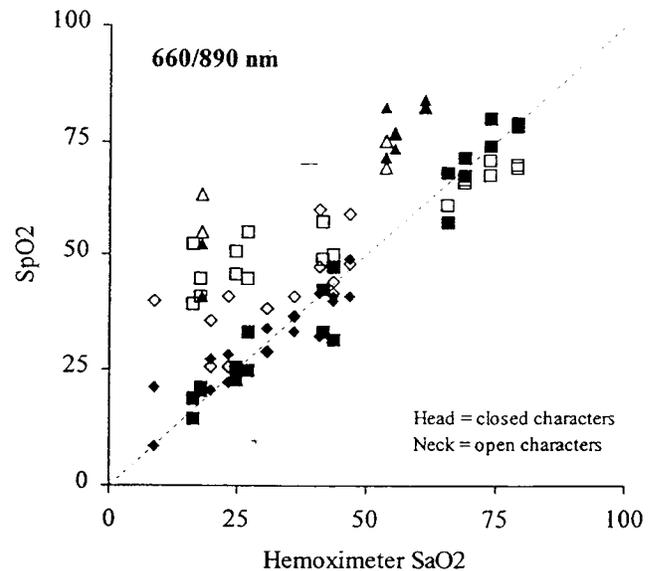


Fig. 11. Head versus neck reading comparison of the 660 nm system in a series of three lambs ($n = 44$ head, $n = 43$ neck). Each animal is represented by a different symbol, with open and closed symbols referring to the neck and head, respectively.

the adjacent sensors was verified to be absent during the study. Preductal arterial sampling was accomplished with an indwelling catheter threaded through the axillary artery and located outside the left ventricle. Samples were analyzed with a laboratory hemoximeter (Radiometer OSM2 or OSM3, Copenhagen, Denmark). Hypoxia was induced by varying FiO₂ in a stepwise fashion, with blood sampling and oximeter readings occurring after at least a one minute period of stability. As can be seen in Figs. 11 and 12, the 660/890 nm sensor (three lambs) shows significantly more head-neck variability at saturations less than 75% than the 735/890 nm sensors (four lambs). Presumably, the underlying tissues of the neck have different optical properties than the head and affect the calibration of the sensor in a different manner.

The observation of enhanced low saturation stability has also been confirmed in studies conducted in The Netherlands. Nijland [20], [21], in a series of pig studies evaluated the performance of sensors fabricated in our facilities with 660/890 nm and 735/890 nm LED pairs. Placing sensors over the left and right groin of the animal, he found more intra- and interanimal reproducibility when using the 735 nm system.

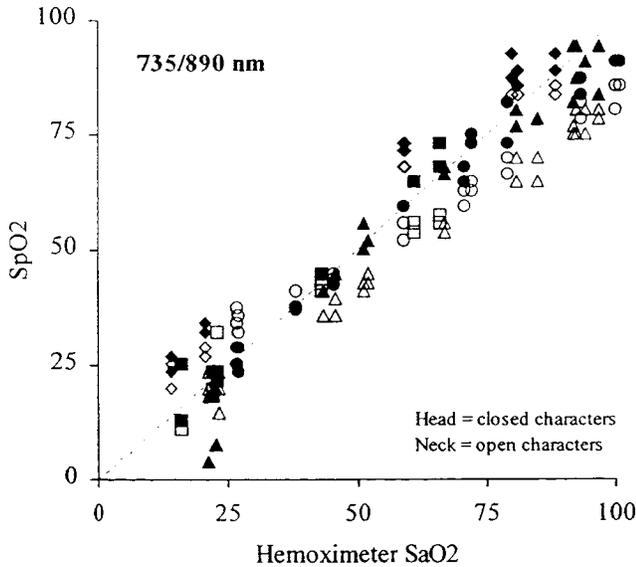


Fig. 12. Head versus neck reading comparison of the 735 nm system in a series of four lambs ($n = 76$, each). Each animal is represented by a different symbol, with open and closed symbols referring to the neck and head, respectively.

The 660 nm system overestimated the saturation in two of the six piglets by 30 and 50% at an SaO₂ of 25%, while similar observations were not seen with the 735 nm system. The standard deviation of the residuals of the 660/890 nm sensors around the calibration line was 11.5% ($n = 199$), while the same statistic for the 735/890 sensors was 5.4% ($n = 176$). These observations again suggest that local variations in tissue properties affect the 660 nm system to a greater extent than they do with the 735 nm system.

An explanation for these behaviors may come from considering how the detected light travels within the tissue bed as a result of scattering and absorption. Because the optical properties of the tissue are a function of wavelength, photon paths are not necessarily the same at the two emitter wavelengths. The simple Lambert-Beer law description of pulse oximetry is known to be inaccurate when photon path lengths and concentrations are assumed to be equal at the two wavelengths. This simple model becomes more accurate in describing oximeter performance, however, when the light scattering-affected path length and concentration terms are retained. Consider the intensity of light exiting the tissue bed (I) to be related to the incident intensity (I_0) as

$$I = I_0 \cdot e^{-\left(\sum \beta_i [c_i]\right) \langle \bar{\ell} \rangle} \quad (2)$$

where β_i and $[c_i]$ refer to the various absorbers' respective extinction coefficients and concentrations in the tissue, and $\langle \bar{\ell} \rangle$ refers to the effective mean path length traveled by the detected light. The time derivative of the signal intensity divided by the signal intensity results in isolating the arterial blood contribution in the summation, as the tissue concentration of the other absorbers are assumed to be constant during the cardiac cycle

$$\frac{\dot{I}}{I} = -\beta_a \langle \bar{\ell} \rangle [\dot{c}_a] \quad (3)$$

$[\dot{c}_a]$ reflects the time derivative of arterial blood concentration within the tissue and is considered to be small enough so as to not significantly affect $\langle \bar{\ell} \rangle$ during the pulse. Making the approximation that $\Delta I \approx \dot{I} \cdot \Delta t$ and $\Delta [c_a] \approx [\dot{c}_a] \cdot \Delta t$, (3) may be replaced with

$$\frac{\Delta I}{I} = -\beta_a \langle \bar{\ell} \rangle \Delta [c_a] \quad (4)$$

Given an arterial saturation S , we may substitute for β_a a linear combination of the extinction coefficients for oxygenated (β_{O_2Hb}) and deoxygenated hemoglobin (β_{HHb})

$$\beta_a = [S\beta_{O_2Hb} + (1-S)\beta_{HHb}] \quad (5)$$

Recognizing that the modulation ratio, R , is given by the ratio of red to infrared signal modulations (4), we find

$$R = \frac{\left(\frac{\Delta I}{I}\right)_{\text{red}}}{\left(\frac{\Delta I}{I}\right)_{\text{IR}}} = \frac{[S\beta_{O_2Hb} + (1-S)\beta_{HHb}]_{\text{red}} \cdot \frac{\Delta [c_a]_{\text{red}}}{\Delta [c_a]_{\text{IR}}} \cdot \frac{\langle \bar{\ell} \rangle_{\text{red}}}{\langle \bar{\ell} \rangle_{\text{IR}}}}{[S\beta_{O_2Hb} + (1-S)\beta_{HHb}]_{\text{IR}}} \quad (6)$$

where the subscripts "red" and "IR" have been retained for each term to reflect that the concentration values and path length values are not necessarily the same for the detected light at the two wavelengths.

In standard commercial pulse oximeters, the embedded mathematical model typically assumes the concentrations and path lengths to be equal at the two wavelengths. Empirical calibration of the oximeter then accounts for the intrinsic difference in photon paths. Subsequent changes in optical properties of the bulk tissue, however, may cause this calibration to become erroneous [14] since the mean path lengths are affected [13]–[16], [22]. Equation (6) indicates that if the pulsatile component of the blood concentration is uniform within the tissue bed, as is assumed in the homogeneous-tissue models reported in this work, the calibration will be unchanged by tissue perturbations if the ratio $\langle \bar{\ell} \rangle_{\text{red}} / \langle \bar{\ell} \rangle_{\text{IR}}$ is maintained. Stated otherwise, if

$$\frac{\langle \bar{\ell} \rangle_{\text{red}}^{\text{baseline}}}{\langle \bar{\ell} \rangle_{\text{IR}}^{\text{baseline}}} = \frac{\langle \bar{\ell} \rangle_{\text{red}}^{\text{perturbed}}}{\langle \bar{\ell} \rangle_{\text{IR}}^{\text{perturbed}}}$$

or equivalently

$$\frac{\langle \bar{\ell} \rangle_{\text{red}}^{\text{perturbed}}}{\langle \bar{\ell} \rangle_{\text{red}}^{\text{baseline}}} = \frac{\langle \bar{\ell} \rangle_{\text{IR}}^{\text{perturbed}}}{\langle \bar{\ell} \rangle_{\text{IR}}^{\text{baseline}}} \quad (7)$$

then the relationship of modulation ratio to the arterial oxygen saturation is largely unaffected by changes in the optical properties of the tissue.

Bonner [13] offers a solution in the Monte Carlo model for the mean path length traveled by the detected light as a function of emitter-detector spacing and tissue scattering and absorption. Using the same baseline and perturbed tissue optical characteristics described earlier, Fig. 13 shows the ratio of $\langle \bar{\ell} \rangle_{\text{red}}^{\text{perturbed}} / \langle \bar{\ell} \rangle_{\text{red}}^{\text{baseline}}$ as a function of wavelength, as predicted by Bonner's (16). As can be seen, the ratiometric change

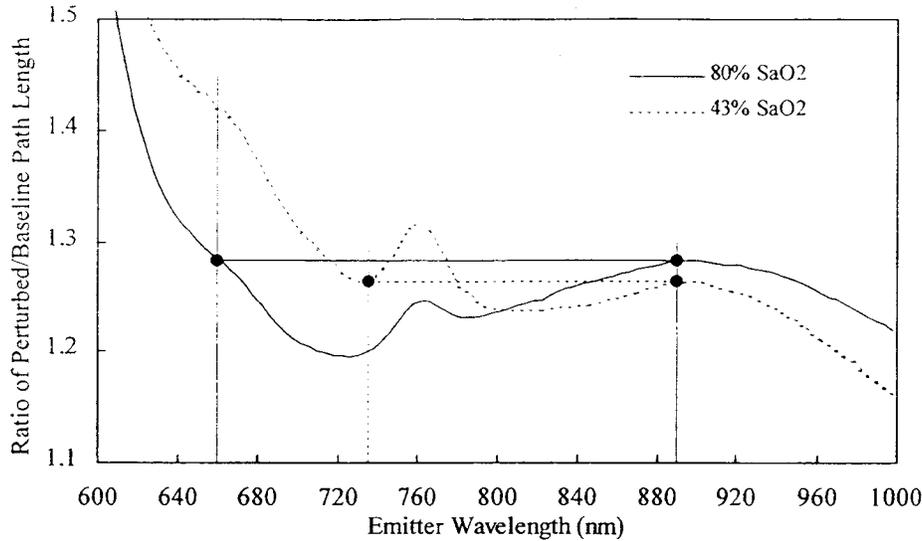


Fig. 13. Ratio of mean perturbed-to-baseline path lengths versus wavelength, with saturation as a parameter. The solid curve represents 80% SaO₂, while the dotted curve shows the ratio at 43% SaO₂. The emitter wavelengths of 660, 735, and 890 nm are highlighted to show the precise matching that occurs between the red and IR pairings at high and low saturation. These wavelengths and saturations correspond to the crossover points depicted in Figs. 3 and 5.

in mean path length due to a change in tissue hemoglobin content is perfectly matched at 80% saturation for 660 and 890 nm, and at 43% saturation for 735 and 890 nm. These are precisely the saturations of the crossover points in Figs. 3 and 5, respectively. The significant mismatch between 660 nm and 805–940 nm values at 43% saturation corresponds to the large errors seen at low saturation in Figs. 3, 4, 7, and 8. The fact that the crossover saturations predicted by Fig. 13 are consistent with *both* the MC and PD models (Figs. 3–6) suggests that this result is not specific to the Monte Carlo model.

So far the discussion has focused on homogeneous tissues. Equation (6), however, suggests a second issue to be considered in the design of a pulse oximetry system that is not considered in the models so far discussed: the assumption that detected light has been exposed to equal concentrations of pulsatile blood. Living tissues are not physiologically or optically homogeneous. Skin, fat, muscle, bone, etc., all have differing absorption and scattering characteristics, and all contain different percentages of arterial blood and degrees of pulsation. As is apparent especially in reflectance pulse oximetry, if the red and IR light do not penetrate to similar depths within the tissue, the ratio $\Delta[c_a]_{\text{red}}/\Delta[c_a]_{\text{IR}}$ in (6) may vary with physiological condition or sensor placement. Thus a second appropriate design goal in choosing emitters for pulse oximetry is to match closely the depths, or regions, of penetration for the two wavelengths.

Weiss *et al.* [23] offer solutions for the distribution and mean penetration depths of detected light based on the same Monte Carlo model developed in the Bonner reference. Utilizing the tissue constants described earlier, Figs. 14 and 15 show the distribution of penetration depths calculated according to the methods of Weiss. At high arterial saturation, the penetration depths for detected 660 and 890 nm light are remarkably similar. At lower saturations, however, these penetration depths diverge, with the detected red light becoming more confined

to the surface. The 735 nm far red light shows a better match in penetration depths at all saturations never becoming as different from the 890 nm light as does the 660 nm red.

Following the premise that matching penetration depth further contributes to a more stable pulse oximetry system, calculations can be made to optimize wavelength selection by using the approximation for mean depth offered in [23]. Defining ρ as the dimensionless separation between emitter and detector on the surface, and μ as the ratio of absorption and scattering coefficients, Weiss estimates the dimensionless mean penetration depth (ζ) of detected light as

$$\langle \zeta | \rho \rangle \approx \frac{0.400\rho^{1/2}}{\mu^{1/4}}. \quad (8)$$

Weiss found a similar relationship with a different proportionality constant for the standard deviation of the depth of penetration (“breadth” of penetration). Replacing Weiss’ dimensionless variables with their physical counterparts, the mean penetration depth of detected light for an emitter-detector separation r becomes

$$\langle z | r \rangle \approx \frac{0.476r^{1/2}}{(\mu_{a,\text{total}}\mu'_s)^{1/4}}. \quad (9)$$

(The following transformations were used: $\rho = r\mu'_s/\sqrt{2}$, $\zeta = z\mu'_s/\sqrt{2}$, $\mu = \mu_{a,\text{total}}/\mu'_s$, where the variables and coefficients are the same as defined earlier, and z is the depth in mm.)

Equation (9) suggests that the best overlap of penetration (in both mean depth and breadth) occurs when wavelengths are chosen with similar products of their associated tissue scattering and absorption coefficients. Fig. 16 shows the estimated mean penetration depth versus wavelength for an emitter-detector separation of 12 mm, according to (9) and considering the same assumptions of baseline tissue optical characteristics noted earlier. As was seen in Fig. 14, there is similarity in mean penetration depth at 100% SaO₂ when conventional wavelengths are used (calculated depths are 4.1

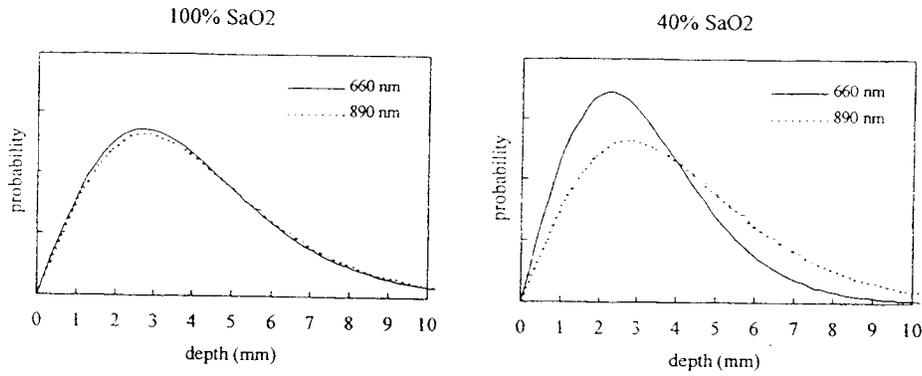


Fig. 14. Distribution of penetration depths of detected photons for 660 and 890 nm light. Plotted is the probability of light penetration versus depth in mm, normalized for total probability (area), according to the modeling of Weiss [23] and using the constants considered in this work (Table I). Red light is depicted with solid lines, while the dashed lines show the IR light. Notice the discrepancy in penetration depths between the red and IR light at 40% SaO₂.

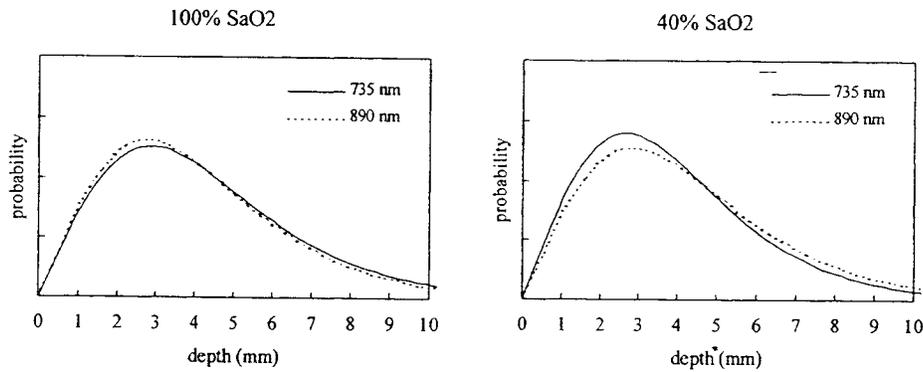


Fig. 15. Distribution of penetration depths of detected photons for 735 and 890 nm light. Plotted is the probability of light penetration versus depth as in Fig. 14. A better match in light penetration is seen at these wavelengths at both high and low saturations.

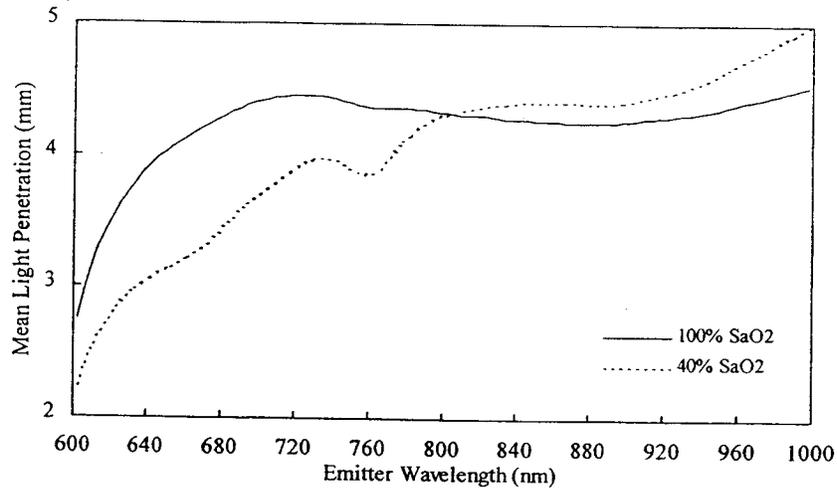


Fig. 16. Plot of mean penetration depth versus wavelength, according to (9). Similarity in depths is evident at 100% SaO₂ (solid line) for the conventional 660 and 880–940 nm wavelength pair. At 40% arterial saturation (dotted line), depth matching with the conventional wavelength choice becomes very poor, while improvement is found using far red wavelengths coupled with 890 nm IR.

and 4.3 mm at 660 and 890 nm, respectively). As the saturation drops, the detected red light penetrates less deeply due to increased absorption by deoxygenated hemoglobin at shorter wavelengths (Fig. 1). At 40% SaO₂, the mean depths at these wavelengths become 3.2 and 4.3 mm. The dotted curve in Fig. 16 indicates that replacing the 660 nm emitter with

one chosen from the far red region (700–800 nm) results in significant improvement in matching of penetration depths at low saturations.

The work described here suggests that at high oxygen saturation, the conventional choice of emitter wavelengths is optimum—resulting in *both* penetration depth matching and

matching of fractional photon path length changes caused by tissue perturbation. As the saturation drops below 70%, neither of these two conditions are met with the conventional wavelengths, yielding SpO₂ readings that are more dependent on the specific tissues being measured. Changing the red wavelength to one in the far red significantly improves the low saturation match in both of these parameters, producing a more robust pulse oximeter system for the low saturation region. The relative importance of the two parameters (depth and fractional path length changes) is difficult to assess. The animal studies conducted comparing head and neck SpO₂, or left rump and right rump, were incapable of distinguishing the cause of the observed improvement. It could only be observed that the 735/890 nm system performed considerably better at low saturation than the 660/890 nm system. The improvement at low saturation, however, does not come without cost. The analysis presented here suggests that a tradeoff exists in the design of a fetal pulse oximeter: *saturation accuracy* over a variety of physiological conditions, versus SpO₂ measurement *sensitivity*. By using a far red and IR wavelength pair, the stability of the calibration at low saturation can be engineered to be less sensitive to potentially changing tissue optical properties caused by a variety of physiological stresses. However, the lower slope of the ratio versus SaO₂ response places additional burden on design of the hardware and software of the pulse oximeter. Accurate measurements of the modulation ratio become more critical as small errors in *R* correspond to larger errors in SpO₂.

Figs. 13 and 16 suggest that a wavelength pair chosen in the 800–950 nm range will result in good low-saturation matching for fractional path length changes and detected light penetration, but the measurement sensitivity becomes exceedingly small (see for example Fig. 10, pairing 805 and 940 nm). Optimum sensitivity results when the wavelengths utilized have the greatest difference in the two oxy- and deoxyhemoglobin absorption differences, such as in the visible red and 900 nm regions (Fig. 1). Unfortunately for all such pairings, there are no simultaneous matches of the two emitters' photon-path parameters. Although additional analysis may offer further refinement in determining a true optimum, the 735 and 900 nm band pairing affords a clinically useful compromise of accuracy and sensitivity for a practical instrument. Conveniently, commercial LED emitters are available in these two wavelength regions. For oximeters designed to function best at high saturation, no tradeoff is necessary. Here, the conventional choice of 660 and 900 nm band emitters results in excellent sensitivity *and* good matching of the detected light photon paths. The effects of other perturbations, such as the presence of dysfunctional hemoglobins, fetal hemoglobin, or potential shunting of light through hair, have not been analyzed at these new wavelengths, but are not expected to alter significantly the results presented here. Further research will be necessary to explore these effects.

It should be noted that the tables and figures presented here are a result of theoretical modeling only and do not reflect the actual empirical calibration found in commercial pulse oximeters. Several approximations and assumptions have been made in the generation of these predicted response curves.

The heterogeneous nature of living tissues, and interactions with the specific details of the sensor's optical design, make theoretically derived calibrations inappropriate for systems to be used in clinical management.

VI. CONCLUSIONS

In summary, the nature of the correlation between the red to IR modulation ratio and the arterial oxygen saturation is related to the bulk tissue's optical properties. The sensitivity to varying physiological parameters, other than the arterial oxygen saturation, is affected by choice of emitter wavelengths. For high oxygen saturations, the choice of 660 and 900 nm band emitters appears optimal for stable pulse oximetry estimates, while 735 and 900 nm band emitters perform better at low saturations. Optimum performance of the oximeter is believed to occur when the fractional change in photon path lengths due to perturbations in the tissue is equivalent at the two emitter wavelengths. Additionally, matching penetration depth and/or breadth at the two wavelengths minimizes the effects of tissue heterogeneity.

ACKNOWLEDGMENT

The authors wish to extend their appreciation to Dr. D. Swedlow, MD for his critical comments in the development of this work, and for his help in the preparation of this manuscript. They extend special thanks to K. Springer, to Dr. A. Harris, MD, of The Johns Hopkins University School of Medicine, and to Dr. F. Vega, VMD and Dr. J. L. Garcia, DVM, of BABCO for their assistance in obtaining the animal study data that has contributed to this research.

REFERENCES

- [1] H. McNamera and N. Johnson, "Fetal monitoring by pulse oximetry and CTG," *J. Perinat. Med.*, vol. 22, pp. 475–480, 1994.
- [2] G. Dildy, P. van den Berg, M. Katz, S. Clark, H. Jongsma, J. Nijhuis, and C. Loucks, "Intrapartum fetal pulse oximetry: Fetal oxygen saturation trends during labor and relation to delivery outcome," *Amer. J. OB/GYN*, vol. 171, pp. 679–84, 1994.
- [3] T. Eskes, H. Jongsma, and P. Houx, "Percentiles for gas values in human umbilical cord blood," *Eur. J. OB Repro. Biol.*, vol. 14, pp. 341–346, 1983.
- [4] B. Oeseburg, B. Ringnalda, J. Crevels, H. Jongsma, P. Mannheimer, J. Menssen, and J. Nijhuis, "Fetal oxygenation in chronic maternal hypoxia: What's critical?," in *Oxygen Transport to Tissues XIV*, W. Erdmann and D. Bruley, Eds. New York: Plenum, 1992, pp. 499–502.
- [5] B. Richardson, L. Carmichael, J. Homan, and J. Patrick, "Electrocortical activity, electroocular activity and breathing movements in fetal sheep with prolonged and graded hypoxemia," *Amer. J. OB/GYN*, vol. 167, no. 2, pp. 553–558, Aug. 1992.
- [6] M. Sendak, A. Harris, and R. Donham, "Accuracy of pulse oximetry during arterial oxyhemoglobin desaturation in dogs," *Anesthesiol.*, vol. 68, pp. 111–114, Jan. 1988.
- [7] J. W. Severinghaus, K. Naifeh, and S. Koh, "Errors in 14 pulse oximeters during profound hypoxia," *J. Clin. Monit.*, vol. 5, pp. 72–81, Apr. 1989.
- [8] J. W. Severinghaus and S. O. Koh, "Effect of anemia on pulse oximeter accuracy at low saturation," *J. Clin. Monit.*, vol. 6, pp. 85–88, Apr. 1990.
- [9] A. P. Shepherd, J. W. Kiel, and G. L. Riedel, "Evaluation of light-emitting diodes for whole blood oximetry," *IEEE Trans. Biomed. Eng.*, vol. BME-31, no. 11, pp. 723–725, Nov. 1984.
- [10] Y. Mendelson, J. C. Kent, B. L. Yocum, and M. J. Birle, "Design and evaluation of a new reflectance pulse oximeter sensor," *Med. Instrum.*, vol. 22, pp. 167–173, Aug. 1988.
- [11] Y. Shimada, K. Nakashima, Y. Fujiwara, T. Komatsu, J. Takezawa, and S. Takatani, "A noninvasive reflectance oximeter as a useful monitor in the ICU," *Anesthesiol.*, vol. 71, no. 3A, p. A367, Sept. 1989.

- [12] S. Takatani, C. Davies, N. Sakakibara, A. Zurick, E. Kraenzler, L. R. Golding, G. P. Noon, and M. E. DeBakey, "Experimental and clinical evaluation of a noninvasive reflectance pulse oximeter sensor." *J. Clin. Monit.*, vol. 8, no. 4, pp. 257-266, Oct. 1992.
- [13] R. Bonner, R. Nossal, S. Havlin, and G. Weiss, "Model for photon migration in turbid biological media." *J. Opt. Soc. Amer. A*, vol. 4, pp. 423-432, Mar. 1987.
- [14] J. Schmitt, "Simple photon diffusion analysis of the effects of multiple scattering on pulse oximetry," *IEEE Trans. Biomed. Eng.*, vol. 38, no. 12, pp. 1194-1203, Dec. 1991.
- [15] M. Yelderman and J. Corenman, "Real time oximetry," in *Computing in Anesthesia and Intensive Care*, O. Prakash, Ed. Boston, MA: Martinus Nijhoff, 1983.
- [16] R. Graaf, "Tissue optics applied to reflectance pulse oximetry," doctoral thesis, Rijksuniversiteit Groningen, 1993.
- [17] W. Zijlstra, A. Buursma, and W. Meeuwesen-van der Roest, "Absorption spectra of human fetal and adult oxyhemoglobin, de-oxyhemoglobin, carboxyhemoglobin, and methemoglobin," *Clin. Chem.*, vol. 37, no. 9, pp. 1633-1638, 1991.
- [18] M. Wukitsch, M. Petterson, D. Tobler, and J. Pologe, "Pulse oximetry: Analysis of theory, technology, and practice," *J. Clin. Monit.*, vol. 4, pp. 290-301, 1988.
- [19] A. Harris, M. Sendak, D. Chung, and C. Richardson, "Validation of arterial oxygen saturation measurements in utero using pulse oximetry," *Amer. J. Perinatol.*, vol. 10, no. 3, pp. 250-254, May 1993.
- [20] R. Nijland, H. Jongsma, and J. Nijhuis, "Reflectance pulse oximetry (RPOX): Two sensors compared in piglets," *Amer. J. Gynecol.*, vol. 172, no. 1, part 2, p. 386, Jan. 1995.
- [21] R. Nijland, "Arterial oxygen saturation in the fetus," doctoral thesis, Katholieke Universiteit Nijmegen, The Netherlands, ch. 4.5, Dec. 1995.
- [22] M. Patterson, B. Chance, and B. Wilson, "Time resolved reflectance and transmittance for the noninvasive measurement of tissue optical properties," *Appl. Opt.*, vol. 28, no. 12, pp. 2331-2336, June 1989.
- [23] G. Weiss, R. Nossal, and R. Bonner, "Statistics of penetration depth of photons re-emitted from irradiated tissue," *J. Modern Opt.*, vol. 36, no. 3, pp. 349-359, 1989.



James R. Casciani received the B.S. degree in mechanical engineering from the Ohio State University, Columbus, OH, in 1979.

His past work has focused on the research and development of innovative products at Battelle Laboratories, Columbus, OH, Hewlett-Packard, Palo Alto, CA, and Nellcor Puritan Bennett, Pleasanton, CA, in the product areas of optoelectronic components, computer hardware, and medical devices. As Director of Product Development, he has spent the past five years leading the research and development

of the first commercial fetal pulse oximeter.



Michael E. Fein (S'64-M'69) received the B.S. degree in engineering from Harvard College, Cambridge, MA, in 1963, and the M.S. and Ph.D. degrees, both in electrical engineering, from the University of Illinois at Urbana-Champaign, in 1966 and 1969, respectively.

He has developed plasma display panels, lasers, and a variety of optical instruments, and holds 39 US Patents. Since 1991, he has worked in pulse oximetry at Nellcor Puritan Bennett, most recently as Manager of Sensor Research.



Paul D. Mannheimer received the B.A. degree in physics, from the University of California, Berkeley, in 1979, and the M.S. degree in applied physics from Stanford University, Stanford, CA, in 1984.

From 1979-1987, he was a Development Engineer at Hewlett-Packard Company, San Jose, CA, in the Optoelectronic and Optical Communications Divisions, where he contributed to the development of fatigue resistant optical fibers and various optoelectronic components. Since 1987, he has worked

in the field of adult and fetal pulse oximetry at Nellcor Puritan Bennett, most recently as a Senior Research Engineer in the Technology Development Department.



Steven L. Nierlich received the B.S. degree in mechanical engineering from Stanford University, Stanford, CA, in 1989, and the M.S. degree in mechanical engineering from the Massachusetts Institute of Technology, Cambridge, MA, in 1991.

From 1991 to the present, he has worked in Nellcor Puritan Bennett's Perinatal Division, Pleasanton, CA, currently as a Research and Development Engineer. The focus of his work has been the development of a commercially viable fetal pulse oximetry system.

LIMITATIONS OF FOREHEAD PULSE OXIMETRY

Jan S. Jørgensen, MD,* Edith R. Schmid, MD,†
Volker König, PhD,* Karin Faisst, MD,*
Albert Huch, MD,* and Renate Huch, MD*

Jørgensen JS, Schmid ER, König V, Faisst K, Huch A, Huch R.
Limitations of forehead pulse oximetry.

J Clin Monit 1995;11:253-256

ABSTRACT. During initial clinical tests to calibrate our reflectance pulse oximetry system, we observed serious physiologic limitations to the use of pulse oximetry in the forehead region. We present a case of simultaneous reflectance and transmission mode pulse oximetry monitoring in a child undergoing cardiac surgery for congenital cyanotic heart disease with a large intracardiac shunt. During general anesthesia, when the patient was endotracheally intubated and mechanically ventilated, the transmission mode saturation agreed well with arterial oxygen saturation measurements; but, our reflectance pulse oximeter, with the sensor applied to the forehead, displayed spuriously lower (-18%) oxygen saturations. Before and after anesthesia and surgery, there was fine agreement between reflectance and transmission mode saturation values. We suggest that the difference was caused by vasodilatation and pooling of venous blood due to compromised venous return to the heart, and a combination of arterial and venous pulsations in the forehead region. This means that the reflectance pulse oximeter measured a mixed arterial-venous oxygen saturation.

KEY WORDS. Monitoring: pulse oximetry. Measurement techniques: pulse oximetry.

INTRODUCTION

Pulse oximetry, a standard noninvasive technique used worldwide to monitor arterial hemoglobin oxygen saturation [1], combines the principles of optical plethysmography and spectrophotometry. The pulse oximeter emits red and infrared light into tissue and measures light intensity after absorption in the tissue and the vascular bed. Absorbance in bloodless tissue and blood in (normally) nonpulsating veins gives a signal constant in time (DC), while absorbance in blood in pulsating arteries and arterioles gives a periodically changing signal (AC). Arterial oxygen saturation is calculated on the assumption that arterial pulsation is the sole source of this periodic change [2]. Most modern commercial pulse oximeters work in the transmission mode, in which tissue is placed between emitting and receiving light diodes. This requires the sensor to be applied peripherally—e.g., on a finger. The theoretical advantages of a reflectance mode sensor, its instrumentation, and related technical problems have been discussed [3]. A notable advantage is that it can be applied centrally—e.g., on the head or chest—or even at the presenting part of the fetus during labor. Several attempts to design such reflectance sensors have been reported [4-6]. We have developed a clinically applicable reflectance mode system [7].

To assess the accuracy and calibration of our system, initial clinical testing of the system was planned where

From the *Department of Obstetrics, Unit of Perinatal Physiology, and the †Institute of Anesthesiology, University Hospital of Zurich, Zurich, Switzerland.

Received Aug 9, 1994, and in revised form Dec 27, 1994. Accepted for publication Jan 9, 1995.

Address correspondence to Dr Renate Huch, Department of Obstetrics, Unit of Perinatal Physiology, University Hospital of Zurich, Frauenklinikstr 10, CH-8091 Zurich, Switzerland.

low saturation ranges were expected. This testing included monitoring children before, during, and after surgical correction of congenital cyanotic heart disease. A case is presented where we observed serious limitations to the use of pulse oximetry in the forehead region.

METHODS AND MATERIALS

Equipment

Our reflectance mode pulse oximeter was developed in-house for special research purposes, and is not commercially available. The reflectance sensor (Fig 1) is radially symmetric, with an outer diameter of 21 mm. Two light-emitting diodes (LEDs; red at 600 nm and infrared at 920 nm) are centrally placed. Six receiving photodiodes (Siemens BPX90) surround the LEDs. The sensors can be applied by different fixation methods, such as double-adhesive transparent tape, or by suction. In either case, the housing is of metal or silicon-rubber; but, the optical arrangement is unchanged. After electronic amplification, filtering and ambient light subtraction, the signals are directly transferred through an analog-to-digital converter into an IBM 386 (IBM Corporation, Armonk, NY) computer. The computer processes the input data using a Pascal program and displays the calculated saturation, the heart (pulse) rate, and a graphic presentation of the ratio of red/infrared AC signals to evaluate their intensity and quality (Fig 2).

CASE HISTORY

An 8-year-old girl underwent open-heart surgery (Fontan's operation) for cyanotic heart disease with a bidirectional intracardiac shunt (right ventricular hypoplasia, subvalvular pulmonary stenosis, atrial and ventricular septal defects). The tricuspid valve was found to be competent by cardiac catheterization. Oxygen saturation in the ascending aorta was 79%. The patient was premedicated with midazolam. Saturation was monitored with a commercial transmission pulse oximeter (Ohmeda, Boulder, CO) at the right index finger. Our reflectance sensor was applied with double-adhesive tape on the midline of the forehead 2 to 3 cm below the hairline. General anesthesia was induced with nitrous oxide and halothane, and maintained with flunitrazepam and fentanyl. Neuromuscular blockade was induced by pancuronium bromide.

Mechanical ventilation was performed using a volume-controlled ventilator (Servo Ventilator 900D, Siemens-Hema). During the oxyhemoglobin saturation

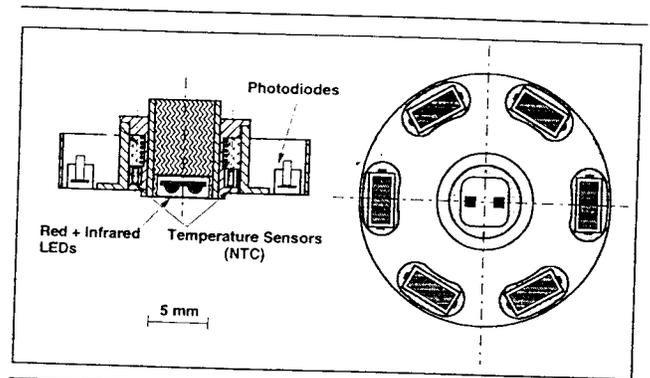


Fig 1. The reflectance sensor. Cross-section and a view of the optical components (skin surface).

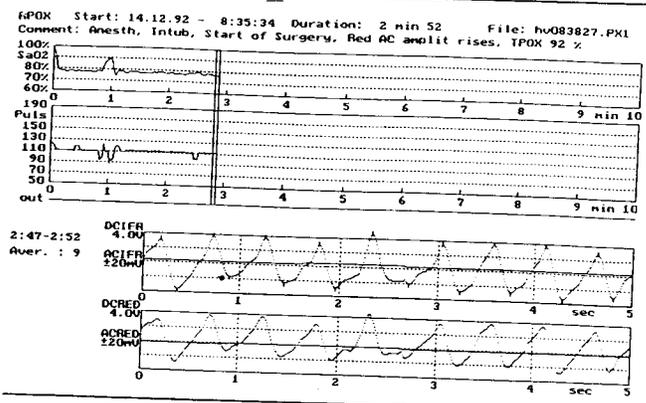


Fig 2. Reflectance mode pulse oximetry tracing of the monitoring period just after intubation. The computer displays the calculated saturation (SaO_2) and heart-rate (pulse) values in the upper part. The lower part shows the pulsatile plethysmographic red/infrared AC absorbance signals and the level of the DC signals. Note high amplitude of red AC signal.

measurements the patient was not in a head-down position and no positive end-expiratory pressure was applied. Arterial blood samples were taken from a left radial artery catheter, and analyzed directly in a CO-oximeter (OSM2 Hemoximeter, Radiometer Copenhagen).

Before induction of anesthesia, there was agreement between mean finger and forehead saturation readings (82% and 79%, respectively). The mean pulse rate was 110 beats/min at both fixation sites (Fig 3).

During induction of anesthesia, a constant increase in the transmission saturation was observed. During mechanical ventilation, the transmission mode and arterial values were in close agreement with saturations of 91% and 93%, respectively. Reflectance mode saturation from the forehead remained at 79% (see Fig 2). Calculated heart rates of the two systems and ECG heart rates were identical. During cardiopulmonary bypass, there

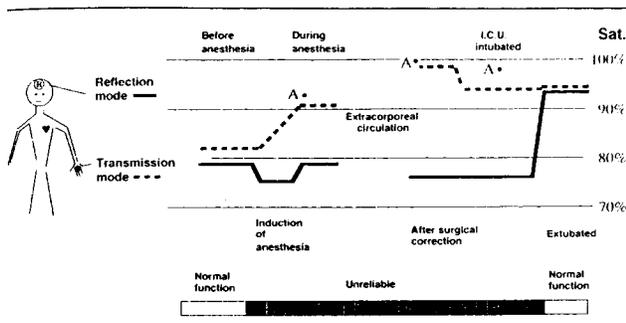


Fig 3. Oxygen saturation (Sat.) measured by the forehead sensor (bold line), the finger sensor (dashed line), and arterial blood samples (A●). Shaded period indicates unreliable function of the forehead sensor.

were no detectable AC signals and, therefore, no reasonable reflectance mode saturation or heart-rate values. The transmission mode pulse oximeter displayed "disturbed function," and neither saturation nor heart-rate values.

After a successful surgical repair and weaning from bypass, the forehead sensor continued to show low saturation values of 76% with correct heart-rate calculations. Transmission mode saturation and arterial values were high, around 99%. In the intensive care unit 6 hr later, the patient was still sedated and endotracheally intubated with stable vital signs. The same discrepancy between transmission mode and reflectance mode saturation was observed (94% vs 76%). Direct measured arterial oxygen saturation was 98%.

The next day, extubation was performed, and the patient was no longer sedated. Transmission mode saturation was now 94% and reflectance mode saturation was 95%.

To test whether the heart-lung machine or other theater and recovery room electronics were affecting the function of our equipment, one of the investigators was placed in the same rooms, with the same electronics working, and with the reflectance sensor applied to his forehead. The saturation was between 96% and 98%, and pulse oximeter heart rate corresponded to the radial pulse. Red and infrared AC signals were of normal pulsatile plethysmographic shape. No low- or high-frequency disturbances were observed.

DISCUSSION

In this case, our forehead reflectance mode pulse oximetry system failed to agree with both a finger transmission pulse oximetry system and oximeter saturation measurements during anesthesia with endotracheal intubation. The reflectance mode pulse oximetry readings were all approximately 18% lower. The pulsatile ple-

thysmographic shape of the AC signals and the agreement between the heart rate as measured by our equipment and the electrocardiographic values indicated that our system was functioning normally. Before and after anesthesia and surgery, the two pulse oximetry systems were in fine agreement.

Identical observations under analogous circumstances were observed when monitoring a 2½-year-old boy who also underwent a Fontan operation for a large intracardiac shunt. Unfortunately all transmission pulse oximetry data were lost in the data sampling process, so that neither data analysis nor comparison between the two pulse oximetry methods and the two cases was possible.

Electronic devices have been reported to affect pulse oximeter function [8]. Exclusion of the possibility of technical interference indicates physiologic reasons for the observed phenomenon, although this was only in a single patient with a large intracardiac shunt. These observations prompted a systematic study in endotracheally intubated and ventilated adults during surgery and general anesthesia, and in healthy adult subjects placed in the head-down tilt (Trendelenburg) position. With the reflectance sensor applied to the forehead, a similar phenomenon was observed, which was most pronounced in the head-down tilt position. Even transmission pulse oximetry with the sensor applied to the nose showed spuriously low saturation measurements when the subjects were kept in a head-down tilt with an angle of -30° (Jørgensen et al, unpublished data). Other investigators may have observed the same phenomena using commercially available reflectance sensors. The information insert for RS-10 Reflection SpO₂ Sensor (Nellcor, Germany) states under "Directions for Use" that it should not be used on patients connected to a mechanical ventilator or when the patient is in a head-down tilt (Trendelenburg) position. However, no scientific publications concerning these situations have been found.

We propose the following explanation. Vasodilatation is common during anesthesia and is compounded by mechanical ventilation, which reduces venous return to the heart. Since veins in the head and facial region are valveless, these factors combine to cause local pooling of venous blood, which is favored in the head-down tilt position. Venous pulsation—i.e., retrotransmitted heart movements—occurs in central veins under normal physiologic conditions [9–10] and has been reported to affect pulse oximeter function during cardiac surgery with observed abnormal systolic central venous pressure [11, 12]. When venous return is compromised, venous pulsation is transmitted even further backwards, due to the local absence of valves, resulting in a pool of

venous blood moving from a combination of arterial and venous pulsations [13].

This phenomenon was not seen using the finger transmission mode sensor, probably because the venous valves in the limbs, and the distance between the sensor and the heart, reduce the effect of the retrotransmitted venous pulsations. Thus, the oxygen saturation measured by the forehead sensor during anesthesia and surgery was not arterial, so much as arteriovenous, with average values of 75 to 80%. Others have reported spuriously low saturations measured in the tip and the base of a dependent finger with a transmission mode sensor and postulate that this is due to venous pulse volume generated by shunting of the arterial pulse via open arteriovenous anastomoses in the cutaneous circulation of the dependent finger [14]. This is a similar phenomenon, which we did not observe when our patient's finger with the sensor was kept horizontal. Central venous pressure (CVP) measurements cannot be used to support our hypothesis because the CVP line was inserted after induction of anesthesia and mechanical ventilation, and thus no baseline values for CVP were recorded. In the intensive care unit, only the mean CVP was measured. It was found to be slightly higher during mechanical ventilation than during spontaneous breathing following extubation (12–13 and 11–12 mm Hg, respectively). Mean CVP during mechanical ventilation, however, is influenced by the higher mean intrathoracic pressures during inspiration, and thus does not necessarily reflect effective transmural right atrial pressure.

We conclude that, in this case, forehead pulse oximetry was unreliable during anesthesia with endotracheal intubation and mechanical ventilation. Presumably, this conclusion applies generally. To clarify this, and to test our system in settings with expected low saturation, further studies are now underway in our respective departments.

This work was supported by a grant from the Desirée and Nils Yde Foundation, Zurich, Switzerland.

REFERENCES

1. Severinghaus JW, Kelleher JF. Recent developments in pulse oximetry. *Anesthesiology* 1992;76:1018–1038
2. Tremper KK, Barker SJ. Pulse oximetry. *Anesthesiology* 1989;70:98–108
3. Swedlow D. Future aspects of reflection pulse oximetry. In: *Fetal and neonatal physiological measurements*. Amsterdam: Elsevier Science Publishers BV, 1991:103–109
4. Mendelsohn Y, Yocum BL. Noninvasive measurement of arterial oxyhemoglobin saturation with a heated and a non-heated skin reflectance pulse oximeter sensor. *Bio-med Instr Technol* 1991;25:472–480
5. Takatani S, Sakakibara N, Zurick A, et al. Experimental and clinical evaluation of a noninvasive reflectance pulse oximeter sensor. *J Clin Monit* 1992;8:257–266
6. Gardosi JO, Schram CM, Symonds EM. Adaptation of pulse oximetry for fetal monitoring during labour. *Lancet* 1991;337:1265–1267
7. König V, Ullrich GJ, Faisst K, et al. Reflektions-Pulsoximetrie Untersuchungen mit eigenem Mess-System. *Biomedizinische Technik* 1992;37:39–40
8. Costarino AT, Davis DA, Keon TP. Falsely normal saturation readings with the pulse oximeter. *Anesthesiology* 1987;67:830–831
9. Abu-Yousef MM. Normal and respiratory variations of the hepatic and portal venous duplex Doppler waveforms with simultaneous electrocardiographic correlation. *J Ultrasound Med* 1992;11:263–268
10. Kurmanavicius J, Huch A, Huch R. Blood flow velocity waveforms in the maternal hepatic vein during pregnancy. *J Matern Fetal Invest* 1993;3:169–173
11. Sami HM, Kleimann BS, Lonchyna VA. Central venous pulsations associated with a falsely low oxygen saturation measured by pulse oximetry. *J Clin Monit* 1991;7:309–312
12. Mark JB. Systolic venous waves cause spurious signs of arterial hemoglobin desaturation. *Anesthesiology* 1989;71:158–160
13. Broome IJ, Mills GH, Spiers P, Reilly CS. An evaluation of the effect of vasodilatation on oxygen saturations measured by pulse oximetry and venous blood gas analysis. *Anesthesia* 1993;48:415–416
14. Kim JM, Arawaka K, Benson KT, Fox DK. Pulse oximetry and circulatory kinetics associated with pulse volume amplitude measured by photoelectric plethysmography. *Anesth Analg* 1986;65:1333–1339

Accuracy of Pulse Oximeters: The European Multi-Center Trial

Patrick F. Wouters, MD, PhD*, Hartmut Gehring†, Geert Meyfroidt*, Lorenzo Ponz‡, John Gil-Rodriguez§, Christoph Hornberger||, R. Bonk¶, H. Frankenberger¶, K. Benekos#, J. Valais#, J. Avgerinos#, and Ewald Konecny||

*Department of Anesthesiology, University Hospital Katholieke Universiteit Leuven, Belgium; †Department of Anesthesiology, Klinik für Anaesthesiologie, MU zu Lübeck, Germany; ‡Department of Anesthesiology, Instituto Oncologico, San Sebastian, Spain; §Department of Anesthesiology, St. Mary's Hospital, London, UK; ||Department of Anesthesiology, Institut für Medizintechnik, MU zu Lübeck, Germany; ¶Department of Anesthesiology, Labor für Biomedizintechnik, FH Lübeck, Germany; and #T.E.I., Athens, Greece

Pulse oximeters have become invaluable monitoring tools in the operating room and critical care unit (1,2). Despite considerable reliance placed on the information they provide, the underlying principles and limitations are not well understood by medical practitioners (3,4). Pulse oximetry is subject to several potential sources of error and requires a critical interpretation (5,6).

Recent reports have questioned the accuracy of pulse oximeters in clinical practice (7–9). These reports contrast with earlier studies and with most manufacturers' statements on accuracy (10–13). The controversy might be due to differences in population characteristics and in testing conditions between small sample studies. Furthermore, there is a lack of consistency on which type of error predominates in the reported variability of pulse oximeter performance among the different studies.

Most studies on accuracy have been performed in healthy volunteers (14) or in small groups of patients with particular clinical conditions (15). While such data provide invaluable information they may not be entirely representative for the heterogeneous clinical population. With the approval of a EU-funded project aiming at the development of a pulse oximeter calibrator, we recently had the opportunity to collect data from a large number of patients in the perioperative setting at four clinical centers. In this paper we report on the analysis of this database to validate the accuracy of pulse oximeters and to identify important sources of error in clinical pulse oximetry.

Address correspondence to Patrick Wouters, MD, PhD, Department of Anesthesiology, University Hospitals Katholieke Universiteit Leuven, Herestraat 49, B-3000 Leuven, Belgium. Address e-mail to Patrick.Wouters@uz.kuleuven.ac.be.

Methodology

The study was approved by the authors' institutional human investigation committees. Pulse oximetry recordings were obtained from patients who had radial arterial lines placed as indicated by their clinical condition. No further exclusion criteria were applied. For the purpose of this project, only Nellcor N3000 and Hewlett Packard CMS monitors were used. Corresponding standard adult finger clips were placed on the patients' index finger opposite the side of the arterial line. Skin temperature was measured at the same site and core temperature was measured with an esophageal thermometer. Clinical management was left to the discretion and judgement of the treating physician.

In most patients, three successive recordings of pulse oximetry data were obtained and stored in digital format: 1) immediately before induction of anesthesia, 2) during surgery and 3) postoperatively in the recovery room or intensive care unit. Recordings were made in steady state conditions for five minutes, while an arterial blood gas sample was drawn at the beginning and at the end of the pulse oximetry recording. For patients presenting with low oxygen saturation (< 92%) despite optimal clinical treatment, the recording time was limited to one minute. Recordings were considered valid only when the pulse oximeter readings did not change for more than 3% during the data acquisition period. Blood gas samples were analyzed using different commercially available multi-wavelength co-oximeters (Radiometer ABL 505 and 520, Ciba Corning 270 and 288). A number of demographic and clinical data (Table 1) were entered in the database and digitally stored. Finger thickness was measured along the direction of the pulse oximeter's light beam

Table 1. Demographic and Clinical Data Recorded During Evaluation of Pulse Oximetry

Demographics	Blood samples	Clinical variables
Age	Hemoglobin	Systolic Blood pressure
Gender	Hematocrit	Diastolic Blood pressure
Skin Color	Carboxyhemoglobin	Pulse Pressure
Finger thickness	Methemoglobin	Core temperature
	Bilirubin	Peripheral temperature
	Arterial PCO ₂	Mode of respiration
	Arterial PO ₂	Blood loss
	Arterial pH	Vasoactive drugs
		Anesthetics

using a micrometer device. Skin color was scored arbitrarily according to six categories with incremental skin pigmentation: Celtic, European light, European Dark, Mediterranean, Mediterranean dark and black.

All files with deliberately induced motion artifacts, electrocautery and light pollution (i.e., experimental conditions required by the main project's protocol on the development of a pulse oximeter calibrator) were removed from the database for the purpose of this analysis.

For each measurement point, the difference between pulse oximetry (SpO₂) and *in vitro* CO-oximetry values (SaO₂ = reference value) was calculated and entered as the dependent variable in a multivariate analysis (MANOVA -Statview 5.0, SAS Institute Inc). The accuracy of pulse oximetry as compared to bench CO-oximetry was studied using Bland-Altman analysis of bias and precision.

Results

A total of 2694 recordings, obtained from 1483 patients (40% female, 60% male) in four clinical centers were considered valid for analysis. This data set included 139 recordings of patients with oxygen saturations (bench oxymetry) below 93%.

Bland-Altman analysis showed a bias of pulse oxymetry versus multi-wavelength bench oxymetry of 0.19% and a precision of 2.22% over a range of hemoglobin saturation values between 60 and 100%. (Fig. 1) The limits of agreement (bias ± 2sd) extend from +4.63 to -4.25%.

Multivariate analysis identified four independent variables to have impact on the degree of error of pulse oximeters: 1) peripheral temperature (*P* = 0.0012), 2) finger thickness (*P* = 0.0019), 3) hemoglobin concentration (*P* = 0.0025) and 4) skin color (*P* =

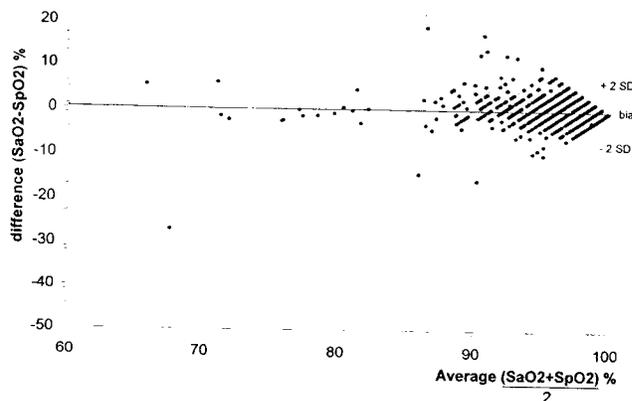


Figure 1. Analysis of bias and precision of pulse oximeters. Solid line indicates the bias of 0.19% and dashed lines show limits of agreement (± 2sd).

0.0253). The model based on the interaction of these four variables was significantly related to the inaccuracy of pulse oximeter readings (*P* = 0.008) with a calculated power of 0.89.

Other variables, including blood pressure, age, gender, core temperature, bilirubin concentration, carboxyhemoglobin and methemoglobin levels, use of vasoactive drugs, blood loss or type of anesthesia, failed to show a correlation with pulse oxymetry error in both univariate and multivariate analyses.

The incidence of dyshemoglobinemia was very low in this group of patients. Methemoglobin levels exceeding 2.5% were found in only 3 patients. Only one patient had a carboxyhemoglobin level higher than 5%.

Discussion

Our data show that the overall accuracy of contemporary pulse oximeters is within clinically acceptable limits. The bias of 0.19% is small and a precision of 2-3% agrees with most manufacturers' statements and with previous publications (10-13). To our knowledge, this is the first prospective study to include such an extensive number of patients in a variety of clinical conditions.

Multivariate analysis identified four variables to be associated with inaccuracy, which was defined as the difference between pulse oximeter readings and *in vitro* multi-wavelength oximetry values obtained from arterial blood: finger thickness, hemoglobin level, skin color and peripheral temperature. Although most of these variables have previously been identified as possible causes of scattering this has not been a consistent finding. It is generally accepted that the most important source of error in clinical pulse oximetry is related to a low signal-to-noise ratio caused by motion artifacts, peripheral hypoperfusion, electrocautery or venous pressure waves (16). Since pulse oximeters rely

on a solid photoplethysmographic waveform, any failure to discern between the AC and DC component of this waveform causes the device to produce an alarm message with no reading value. The major clinical concern on this type of error is the occurrence of false alarms and failure to record data (17-19). New developments are currently focusing on photoplethysmographic waveform interpretation and the design of new algorithms to address these issues (20-22). In our study, we chose to exclude files with non-reading values and only selected data with steady state pulse oximetry readings. Consequently, we believe that our data are not in contrast with previous studies, but focused more particularly on less obvious sources of inaccuracy that are more likely to go unattended by the device and/or its user.

Another well-known limitation of pulse oximetry is related to the use of only two wavelengths and the consequent failure to account for the presence of dyshemoglobins (23-25). In our study, we found very few cases with increased carboxyhemoglobin or methemoglobin levels. This explains while our analysis had insufficient power to indicate dyshemoglobinemia as an important source of error. Other rare types of hemoglobin with potentially confounding effect on pulse oximetry were not systematically investigated.

Yet, another important shortcoming of pulse oximetry which is most frequently overlooked relates to the assumptions made in applying photometric principles to biological tissue. The theory of pulse oximetry is simple and based on the different absorption spectra of oxygenated and deoxygenated hemoglobin. However, the dominant process in biological tissue is not absorption of light but scattering which is neglected by the Beer-Lambert law (26). The effect of scattering on the light spectrum, as received by a pulse oximeter's LED, depends on the composition of the transilluminated biological tissue (finger, earlobe, toe...) and "pollutes" the effect of absorption to a variable and almost unpredictable extent. For this reason, calibration of pulse oximeters is still an empirical procedure: healthy volunteers are deliberately desaturated and blood samples are taken to determine hemoglobin saturation with multi-wavelength CO-oximetry. Empirical algorithms are then constructed to convert the pulse oximetry signal to its readout value. Obviously, the calibration population plays an important role in the accuracy of each manufacturer's device. For example, a mismatch in dyshemoglobin levels between the calibration data and the patient population might be a source of systematic errors (27). Similarly, differences in the composition of transilluminated tissue between the calibration sample and patients would affect the accuracy of pulse oximeters (28). To our opinion, the results of the present study should be interpreted in

light of this knowledge. The determinants of inaccuracy that were identified in this study all to some extent affect the composition of transilluminated tissue. Skin temperature has previously been shown to affect accuracy of pulse oximeters (15,29,30) and shows an excellent correlation with fingertip bloodflow (31). Alterations in fingertip bloodflow may affect the accuracy by changing the AC/DC relationship of the photoplethysmographic signal but also by changing the blood volume in the transilluminated tissue (and therefore the absorption and scattering of light). In analogy with this, finger thickness also showed to be a determinant of accuracy. We used a single-size standard adult fingerclip for all patients and excluded children below the age of ten. Nevertheless, for smaller patients, size mismatching of the probe could have led to errors similar to those induced by malpositioning (32). Skin color has previously been shown to affect the accuracy of pulse oximeters (33-35). Highly pigmented skin was associated more frequently with an overestimation of oxygen saturation. Finally, hemoglobin content was also found to affect accuracy. Previous studies have demonstrated little effect of anemia at normal levels of saturation (36) but indicate an increased bias with desaturation (37). This emphasizes the importance of using multivariate statistical analysis as the only solid means to study the effect of several independent variables together. This technique studies the potential interaction of variables and allows the detection of covariance. However, large number of observations are required and most studies lack statistical power to perform multivariate analysis.

A limitation of this study is that it includes a relatively small number of severe desaturations. This was due to the fact that deliberate desaturations were not allowed for ethical reasons, and that clinical treatment was always optimized. It is known that pulse oximeters are not calibrated to saturation levels below 70% and a loss of accuracy has been reported in that range (38). Our database includes only two patients with bench oximetry values below 70% and the results reported here cannot be applied to this group of severely desaturated patients.

In summary, our results of a multicenter observational study on the accuracy of pulse oximeters support the conclusions of previous smaller scale studies in showing a small bias as compared to bench cooximetry and a precision of 2.22%. The main determinants of inaccuracy were skin color, peripheral temperature, hemoglobin levels and finger thickness. These findings are in concert with the conclusion of a previous theoretical analysis (39) and suggest that between-subject variability in the composition of transilluminated biological tissue plays an important role in the accuracy of pulse oximeters. Current calibration methods do not account for such large variability. It is

likely that optimization of calibration procedures could improve the performance of currently available devices.

References

1. Tremper KK, Barker SJ. Pulse oximetry. *Anesthesiology* 1989;70:98-108.
2. Eichhorn JH, Cooper JB, Cullen DJ, Maier WR, Philip JH, Seeman RG. Standards for patient monitoring during anesthesia at Harvard Medical School. *JAMA* 1986;256:1017-20.
3. Kruger PS, Longden PJ. A study of a hospital staff's knowledge of pulse oximetry. *Anaesth Intensive Care* 1997;25:38-41.
4. Stoneham MD, Saville GM, Wilson IH. Knowledge about pulse oximetry among medical and nursing staff. *Lancet* 1994;344:1339-42.
5. Sinex JE. Pulse oximetry: principles and limitations. *Am J Emerg Med* 1999;17:59-67.
6. Jubran A. Pulse oximetry. *Crit Care (Lond)* 1999;3:R11-R17.
7. Kelly AM, McAlpine R, Kyle E. How accurate are pulse oximeters in patients with acute exacerbations of chronic obstructive airways disease? *Respir Med* 2001;95:336-40.
8. Seguin P, Le Rouzo A, Tanguy M, Guillou YM, Feuillu A, Malledant Y. Evidence for the need of bedside accuracy of pulse oximetry in an intensive care unit. *Crit Care Med* 2000;28:703-6.
9. McGovern JP, Sasse SA, Stansbury DW, Causing LA, Light RW. Comparison of oxygen saturation by pulse oximetry and co-oximetry during exercise testing in patients with COPD. *Chest* 1996;109:1151-5.
10. Severinghaus JW. History and recent developments in pulse oximetry. *Scand J Clin Lab Invest Suppl* 1993;214:105-11.
11. Aughey K, Hess D, Eitel D, Bleecher K, Cooley M, Ogden C, Sabulsky N. An evaluation of pulse oximetry in prehospital care. *Ann Emerg Med* 1991;20:887-91.
12. Hannhart B, Michalski H, Delorme N, Chapparo G, Polu JM. Reliability of six pulse oximeters in chronic obstructive pulmonary disease. *Chest* 1991;99:842-6.
13. Jensen LA, Onyskiw JE, Prasad NG. Meta-analysis of arterial oxygen saturation monitoring by pulse oximetry in adults. *Heart Lung* 1998;27:387-408.
14. Trivedi NS, Ghouri AF, Lai E, Shah NK, Barker SJ. Pulse oximeter performance during desaturation and resaturation: a comparison of seven models. *J Clin Anesth* 1997;9:184-8.
15. Villanueva R, Bell C, Kain ZN, Colingo KA. Effect of peripheral perfusion on accuracy of pulse oximetry in children. *J Clin Anesth* 1999;11:317-22.
16. Severinghaus JW, Kelleher JF. Recent developments in pulse oximetry. *Anesthesiology* 1992;76:1018-38.
17. Reich DL, Timcenko A, Bodian CA, Kraidin J, Hofman J, DePerio M, Konstadt SN, Kurki T, Eisenkraft JB. Predictors of pulse oximetry data failure. *Anesthesiology* 1996;84:859-64.
18. Rheineck-Leyssius AT, Kalkman CJ. Influence of pulse oximeter settings on the frequency of alarms and detection of hypoxemia: theoretical effects of artifact rejection, alarm delay, averaging, median filtering or a lower setting of the alarm limit. *J Clin Monit Comput* 1998;14:151-6.
19. Rheineck-Leyssius AT, Kalkman CJ. Influence of pulse oximeter lower alarm limit on the incidence of hypoxaemia in the recovery room. *Br J Anaesth* 1997;79:460-4.
20. Barker SJ, Shah NK. The effects of motion on the performance of pulse oximeters in volunteers (revised publication). *Anesthesiology* 1997;86:101-8.
21. Belal SY, Taktak AF, Nevill AJ, Spencer SA. A fuzzy system for detecting distorted plethysmogram pulses in neonates and paediatric patients. *Physiol Meas* 2001;22:397-412.
22. Edrich T, Flaig M, Knitza R, Rall G. Pulse oximetry: an improved in vitro model that reduces blood flow-related artifacts. *IEEE Trans Biomed Engl* 2000;47:338-43.
23. Hampson NB. Pulse oximetry in severe carbon monoxide poisoning. *Chest* 1998;114:1036-41.
24. Nijland R, Jongsma HW, Nijhuis JG, Oeseburg B, Zijlstra WG. Notes on the apparent discordance of pulse oximetry and multi-wavelength haemoglobin photometry. *Acta Anaesthesiol Scand Suppl* 1995;107:49-52.
25. Lang SA, Chang PC, Laxdal VA, Huisman TH. Haemoglobin Hammersmith precludes monitoring with conventional pulse oximetry. *Can J Anaesth* 1994;41:965-8.
26. Fine I, Weinreb A. Multiple scattering effect in transmission pulse oximetry. *Med Biol Engl Comput* 1995;33:709-12.
27. Ralston AC, Webb RK, Runciman WB. Potential errors in pulse oximetry. I. Pulse oximeter evaluation. *Anaesthesia* 1991;46:202-6.
28. Hornberger C, Knoop P, Nahm W, Matz H, Konecny E, Gehring H, Bonk R, Frankenberger H, Meyfroidt G, Wouters P, Gil-Rodriguez J, Ponz L, Benekos K, Valais J, Avgerinos J, Karoutis A, Ikiades A, Weininger S. A Prototype Device for Standardized Calibration of Pulse Oximeters. *J Clin Monit* 2000;16:161-169.
29. Schramm WM, Bartunek A, Gilly H. Effect of local limb temperature on pulse oximetry and the plethysmographic pulse wave. *Int J Clin Monit Comput* 1997;14:17-22.
30. Iyer P, McDougall P, Loughnan P, Mee RB, Al-Tawil K, Carlin J. Accuracy of pulse oximetry in hypothermic neonates and infants undergoing cardiac surgery. *Crit Care Med* 1996;24:507-11.
31. Sessler DI, McGuire J, Hynson J, Moayeri A, Heier T. Thermoregulatory vasoconstriction during isoflurane anesthesia minimally decreases cutaneous heat loss. *Anesthesiology* 1992;76:670-5.
32. Barker SJ, Hyatt J, Shah NK, Kao YJ. The effect of sensor mal-positioning on pulse oximeter accuracy during hypoxemia. *Anesthesiology* 1993;79:248-54.
33. Lee KH, Hui KP, Tan WC, Lim TK. Factors influencing pulse oximetry as compared to functional arterial saturation in multi-ethnic Singapore. *Singapore Med J* 1993;34:385-7.
34. Ralston AC, Webb RK, Runciman WB. Potential errors in pulse oximetry. III: Effects of interferences, dyes, dyshaemoglobins and other pigments. *Anaesthesia* 1991;46:291-5.
35. Anonymous. Noninvasive blood gas monitoring. a review for use in the adult critical care unit. Technology Subcommittee of the Working Group on Critical Care, Ontario Ministry of Health CMAJ 1992;146:703-12.
36. Jay GD, Hughes L, Renzi FP. Pulse oximetry is accurate in acute anemia from hemorrhage. *Ann Emerg Med* 1994;24:32-5.
37. Severinghaus JW, Koh SO. Effect of anemia on pulse oximeter accuracy at low saturation. *J Clin Monit* 1990;6:85-8.
38. Schmitt HJ, Schuetz WH, Proeschel PA, Jaklin C. Accuracy of pulse oximetry in children with cyanotic congenital heart disease. *J Cardiothorac Vasc Anesth* 1993;7:61-5.
39. Schmitt JM. Simple photon diffusion analysis of the effects of multiple scattering on pulse oximetry. *IEEE Trans Biomed Engl* 1991;38:1194-203.

Accuracy of two pulse oximeters at low arterial hemoglobin-oxygen saturation

Bradley G. Carter, MAppSc; John B. Carlin, PhD; James Tibballs, MBBS, BMedSc, MEd, FFICANZCA; Helen Mead, MBBS, FRACP, FACEM; Mark Hochmann, BAppSc; Anthony Osborne

Objective: To evaluate the performance of two pulse oximeters in the measurement of arterial hemoglobin saturation in hypoxemic children.

Design: Prospective, repeated-measures observational study.

Setting: A 16-bed pediatric intensive care unit in a children's tertiary hospital.

Patients: Sixty-six patients with arterial saturation of <90%.

Interventions: Three arterial blood samples were taken from each subject during a 48-hr period. Pulse oximeter measurements of arterial saturation were compared with arterial saturation determined by cooximetry.

Measurements and Main Results: Arterial saturation was measured using one or both pulse oximeters (SpO_2) and compared with the arterial hemoglobin saturation determined by cooximetry (SaO_2). Sixty-two subjects were studied, using the Ohmeda pulse oximeter giving 185 data points (78 with saturations <75% [defined by the average of pulse oximeter and cooximeter]); 53 subjects were studied, using the Hewlett-Packard pulse oximeter yielding 155 data points (60 with saturations <75%). SpO_2 ranged from 24% to

94%. Bias and precision of the Ohmeda pulse oximeter were -2.8% and 4.8% >75% and -0.8% and 8.0% <75%. Bias and precision of the Hewlett-Packard pulse oximeter were -0.5% and 5.1% >75% and 0.4% and 4.6% <75%. Inpatient regression coefficient (r) for the differences between pulse oximeter and cooximeter was 0.58 for the Ohmeda and 0.59 for the Hewlett-Packard. Regression coefficients for predicting change in cooximeter value given a change in the Ohmeda pulse oximeter were 0.59 and 0.71 <75% and >75%, respectively. Similar coefficients for the Hewlett-Packard pulse oximeter were 0.50 and 0.70, respectively.

Conclusion: The performance of the Ohmeda pulse oximeter deteriorated below an SpO_2 of 75%. The Hewlett-Packard pulse oximeter performed consistently above and below an SpO_2 of 75%. The ability of both pulse oximeters to reliably predict change in SaO_2 based on change in pulse oximetry was limited. We recommend measurement of Pao_2 or SaO_2 for important clinical decisions. (Crit Care Med 1998; 26:1128-1133)

KEY WORDS: pulse oximetry; bias; precision; hypoxemia; fetal hemoglobin; within subject variation; predicting change

Pulse oximetry (SpO_2) was introduced for semiquantitative detection of hypoxemia, but is now used to titrate oxygen therapy in hypoxemic states and frequently replaces the use of repeated Pao_2 and arterial hemoglobin saturation (SaO_2) measurements.

Although the use of a noninvasive device is desirable, the accuracy of pulse oximeters at low saturations remains unclear. Their performance at low saturations (defined here as <75%) has not been adequately studied. Manufacturers do not provide performance specifications below ~75%, while most published studies examining the performance of pulse oximeters at low saturations are flawed in some

way. The aim of this study was to compare the performance of two pulse oximeters at saturations <75%, defined by $(SpO_2 + SaO_2)/2$.

MATERIAL AND METHODS

The study was conducted in the pediatric intensive care unit. Subjects were patients with arterial catheters *in situ* and who had SpO_2 concentrations <90%. Approval for the study was obtained from the hospital Ethics Committee and informed consent was obtained from the parents or guardians of each subject.

SpO_2 measurements were obtained from subjects using two commercially available pulse oximeters (Ohmeda Biox 3700, revision P, Ohmeda, Louisville, CO; and the M1020A pulse oximetry module, Hewlett-Packard Component Monitoring System, revision B, Hewlett Packard, North Hollywood, CA). The Ohmeda oximeter

specifies an accuracy (1 SD) of 1.5% in the range 90% to 100%, 2.1% in the range 80% to 89.9%, 2.4% in the range 60% to 100%, and is unspecified at <60%. Accuracy is unspecified for the Hewlett-Packard oximeter. Initially, only the Ohmeda pulse oximeter was studied. The Hewlett-Packard pulse oximeter was included a short time after. Subjects were studied using one or both pulse oximeters. The Ohmeda pulse oximeter was used in conjunction with a Flex II probe (PN 0380-1000-080, Ohmeda), while the Hewlett-Packard pulse oximeter was used in conjunction with a Nellcor probe (D-20, Nellcor Incorporated, Hayward, CA). The averaging times for the pulse oximeters were 6 secs and 8 beats, respectively. Probes were sited on the limb with the arterial catheter to avoid the confounding effects of a patent ductus arteriosus.

After the pulse oximeters had achieved an adequate signal, an arterial

From the Paediatric Intensive Care Unit (Mr. Carter, Drs. Tibballs and Mead, Mr. Hochmann, and Mr. Osborne), and the Clinical Epidemiology and Biostatistics Unit (Dr. Carlin), Royal Children's Hospital, Parkville, Melbourne, Victoria, Australia.
Copyright © 1998 by Williams & Wilkins

blood sample was drawn. At this time, SpO_2 was recorded from both pulse oximeters. The pulse rates measured by the oximeters and the heart rate determined from an electrocardiogram were also recorded. Subjects were excluded if the difference between the pulse rate and heart rate exceeded 5 beats/min as is common practice (1-5). Sao_2 was determined by cooximetry using the six wavelength Radiometer OSM3 cooximeter (Radiometer-Copenhagen, Copenhagen, Denmark). Fetal hemoglobin was measured and compensation made with the HbF% and HbF modes of the OSM3 cooximeter. All references to saturation measured by the cooximeter refer to fractional saturation unless otherwise indicated. Three arterial blood samples were taken from each subject during a 48-hr period at intervals varying from a few minutes to several hours.

The differences between pulse oximeter and cooximeter saturations were analyzed as recommended by Bland and Altman (6, 7). In this method, the agreement between two techniques purporting to measure the same parameter is examined by analyzing the mean difference (bias) between the two techniques (mean pulse oximeter value minus mean cooximeter value) and the standard deviation (precision) of the differences. The expected range of the difference between the two measurements (the limits of agreement) can then be calculated as the bias \pm 1.96 SD. The bias and precision were calculated for all subjects in this study and separately for subjects with saturation concentrations $>75\%$ and $<75\%$, as defined by the average of pulse oximetry and cooximetry. The cutoff value of 75% was based on the average value of pulse oximeter and cooximeter to avoid it being correlated with either value (7). As a result, a direct comparison of the two pulse oximeters' performance $>75\%$ and $<75\%$ was not practical due to the ambiguity of the cutoff point and the fact that the difference between the two was similar across the entire range of saturations. Thus, a single bias and precision were calculated for the difference between the Ohmeda and Hewlett-Packard across the entire range of saturations.

The bias and precision were estimated using a variance components model, which allows for inpatient correlation in repeated measurements.

These analyses were extended by mixed model linear regression to assess the dependence of the bias on patient characteristics, including saturation by cooximetry (at $>75\%$ or $<75\%$), and percentage fetal hemoglobin. These analyses were performed using the PROC MIXED procedure of the SAS package (SAS Technical report P-229, SAS/STAT Software, Release 6.07, SAS Institute, Cary, NC). Inpatient correlation was calculated as the ratio of between-subject variance to the sum of between and within-subject variance (with the variances estimated using the REML method in the PROC MIXED procedure).

The capability of the two pulse oximeters to reliably predict changes in arterial saturation as measured by the cooximeter was examined by plotting the changes in cooximeter saturations against the corresponding changes in the pulse oximeter values. Linear regression was used to quantify the predictive relationship with the regression line constrained to predict zero change in cooximeter saturation when there was no change in pulse oximeter saturation.

RESULTS

Sixty-six subjects were included in the study. One data point was excluded from the Merlin group because of an extreme value. Subject details are given in Table 1. Three subjects from both the Ohmeda and Hewlett-Packard analyses were included in the study after being tested on two separate occasions with time intervals of between 3 and 8 mos. In the Ohmeda analysis, one subject had only one measurement taken, two measurements were taken from each subject on five occasions, three measurements were taken from each subject on 54 occasions, and a set of five and seven repeat measurements were taken once each. In the Hewlett-Packard analysis, two measurements were taken on four occasions and three measurements were taken on 49 occasions. Sixty of the subjects in the Ohmeda analysis and 51 subjects in the Hewlett-Packard analysis had congenital cardiac defects. Other diagnoses included bronchiolitis, pneumonia, and bronchomalacia.

Figure 1 (top) shows the differences between the Ohmeda pulse oximeter and the cooximeter plotted against the

Table 1. Summary of patient data

	Ohmeda (n = 62)	Hewlett-Packard (n = 53)
Number of data points	185	155
SpO_2 (%) (range)	24-94	26-93
Age (mo) (median)	3.3	3.2
Age (range)	1 day- 11 yrs, 5 mos	1 day- 11 yrs, 5 mos
Weight (kg) (median)	4	4
Weight (kg) (range)	2-26	2-26

Ohmeda, Louisville, CO; Hewlett-Packard, North Hollywood, CA.

average value of the two. It appears from this figure that the performance of the Ohmeda pulse oximeter deteriorates at $<75\%$. No such effect was seen for the Hewlett-Packard pulse oximeter (Fig. 1, bottom). Table 2 provides the bias and precision for both pulse oximeters. At $>75\%$, the Ohmeda pulse oximeter underestimates the true saturation with a mean bias of -2.8 ± 4.8 (SD) %. At $<75\%$, the underestimation decreases to $-0.8 \pm 8.0\%$ and there is a marked increase in variability. The Hewlett-Packard pulse oximeter on the other hand showed a much smaller bias of $-0.5 \pm 5.1\%$ at $>75\%$, and $0.4 \pm 4.6\%$ at $<75\%$. The difference between the biases in the $\geq 75\%$ group and the $<75\%$ group was not statistically significant for either pulse oximeter ($p = .23$).

There was substantial inpatient correlation in saturation concentrations and in the differences between pulse oximeter and cooximeter values; this finding is illustrated by Figure 1, in which "typical" individuals (highlighted with open, cross-hatched symbols) exhibit less within-subject variability than the overall variability of points on the graph. Inpatient correlation in the differences of all saturation values (pulse oximetry minus cooximetry) was 0.58 for the Ohmeda and 0.59 for the Hewlett-Packard.

Fetal hemoglobin had a marginally statistically significant effect on the bias of the Ohmeda pulse oximeter ($p = .05$), with a regression coefficient of 0.035 (95% confidence interval, -0.001 to 0.070). This finding means that the bias of the Ohmeda pulse oximeter increased on average 0.35% for every 10% increase in fetal hemoglobin

concentration. The bias of the Hewlett-Packard pulse oximeter was not affected by fetal hemoglobin ($p = .5$).

In comparison with each other, the Ohmeda pulse oximeter underestimated the Hewlett-Packard pulse

oximeter with a bias of $2.1 \pm 5.7\%$, $n = 139$, $p = .002$) over the entire range of saturations studied.

Figure 2 illustrates the performance of the pulse oximeters in predicting a change in SaO_2 . Results of linear regression of a change in SaO_2 value vs. a change in SpO_2 value are shown in Table 3. In conjunction with Figure 2, these data demonstrate that changes in SpO_2 do not tightly predict changes in SaO_2 and that this effect is worse at $<75\%$. For example, a decrease of 10% in the Ohmeda SpO_2 in the range $<75\%$ predicts a change of -5.9% in SaO_2 with a 95% prediction interval of -15.3% to 3.5% . The same change at $>75\%$ predicts a decrease of 7.1% in SaO_2 with a 95% prediction interval of -12.8% to -1.4% .

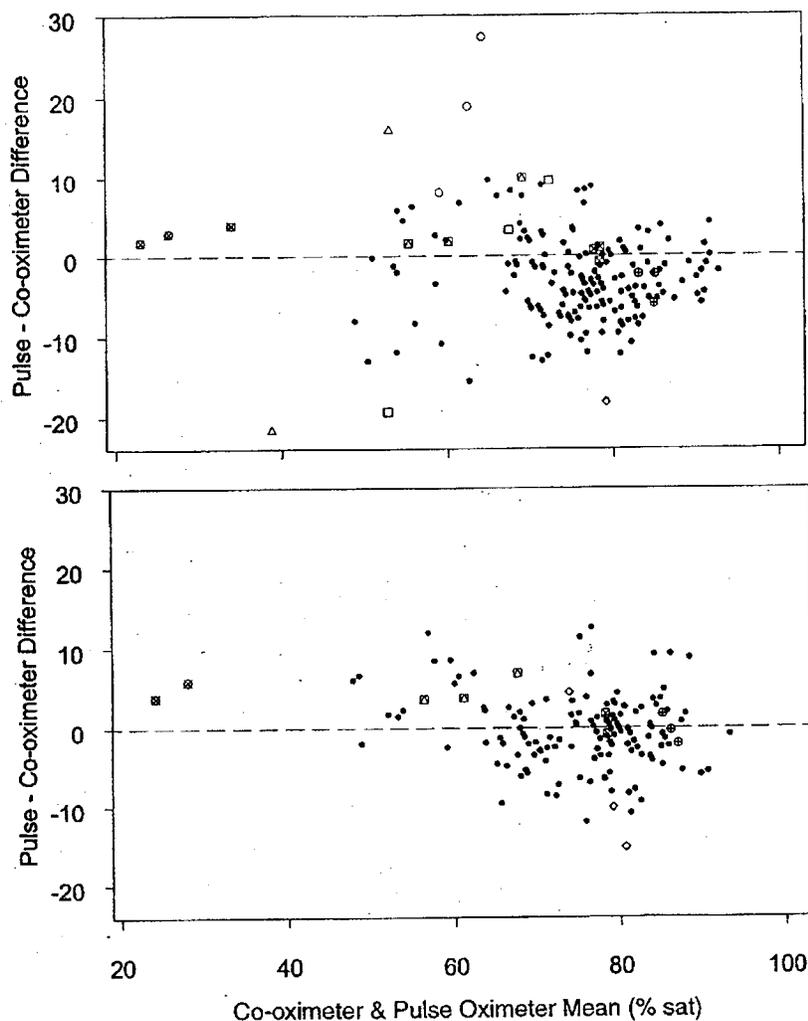


Figure 1. Differences between Ohmeda (top) and Hewlett-Packard (bottom) pulse oximeter and cooximeter measurements of arterial saturation. *Solid symbols*, all patients; *open symbols*, patients who showed large intrasubject variation; *cross-hatched symbols*, patients with small intrasubject variation. Ohmeda Biox 3700, revision P, Ohmeda, Louisville, CO; and the M1020A pulse oximetry module, Hewlett-Packard Component Monitoring System, revision B, Hewlett-Packard, North Hollywood, CA.

DISCUSSION

Low arterial saturations are often encountered in critically ill patients. Readings from pulse oximeters are regarded as a vital source of information. However, accurate measurements of saturation are required.

Many studies suggest that pulse oximeters are inaccurate at low saturations (1-3, 8-12), with bias increasing and precision decreasing as SaO_2 decreases; with SpO_2 increasingly overestimating SaO_2 . However, many studies contain methodologic problems which limit their utility. Studies that have used human volunteers as subjects are unable to evaluate the performance of pulse oximeters under clinical conditions of severe hypoxemia. Only three studies (8, 11, 13) have examined the performance of pulse oximeters at low saturations in patients under typical clinical

Table 2. Analysis of agreement results for the Ohmeda and Hewlett-Packard pulse oximeters

O ₂ Sat (%)	Ohmeda			Hewlett Packard		
	<75	≥75	All	<75	≥75	All
Patients (No.)	78	107	185	60	95	155
Mean ± sd bias	-0.8 ± 8.0	-2.8 ± 4.8	-2.1 ± 6.3	0.4 ± 4.6	-0.5 ± 5.1	0.0 ± 4.8
95% CI for mean bias	-3.2 to 1.5	-4.1 to -1.5	-3.4 to -0.8	-1.3 to 2.0	-2.1 to 1.1	-1.1 to 1.1
p Value*			.23			.23
95% range of agreement	-16.6 to 14.9	-12.2 to 6.6	-14.5 to 10.3	-8.6 to 9.4	-10.5 to 9.5	-9.4 to 9.4

O₂ Sat, oxygen saturation; CI, confidence interval; bias, $SpO_2 - SaO_2$. Bias and precision results are for the Ohmeda (Louisville, CO) and Hewlett-Packard (North Hollywood, CA) pulse oximeters. The 75% cut-off point is defined by the average of pulse oximetry and cooximetry.

*p value for comparison between $<75\%$ and $\geq 75\%$ groups for each device, using an unpaired t-test.

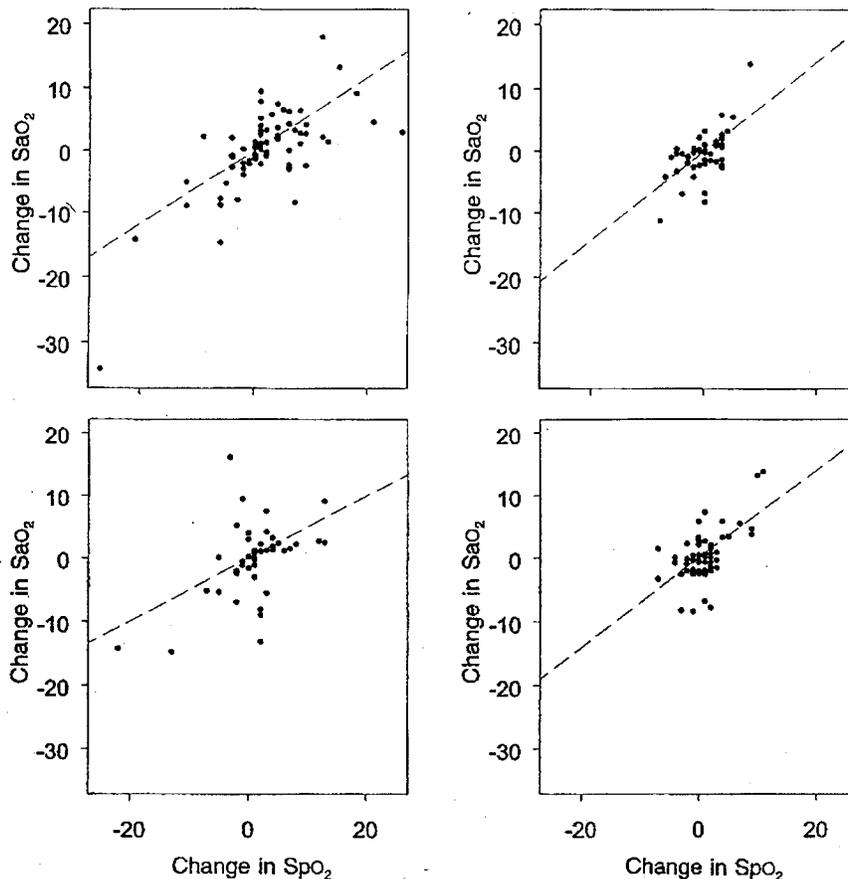


Figure 2. Change in arterial hemoglobin saturation (SaO_2) as predicted by the Ohmeda (top panels) and Hewlett-Packard (bottom panels) pulse oximeter. Left panels, data with saturation (measured by pulse oximeter) $<75\%$; right panels, data with saturation (measured by pulse oximeter) $>75\%$. Ohmeda Biox 3700, revision P, Ohmeda, Louisville, CO; and the M1020A pulse oximetry module, Hewlett-Packard Component Monitoring System, revision B, Hewlett-Packard, North Hollywood, CA.

conditions and have reported bias and precision.

Another limitation of many studies is the small number of data points with truly low saturations. Few studies (2, 3, 11) have $>30\%$ of data points with an $SpO_2 <75\%$. Moreover, some studies (14) used large numbers of repeated measurements from a small number of subjects. This practice confounds variation between subjects with variation within subjects. Lewallen et al. (14) for instance, recorded between one and 13 measurements from each subject.

In the current study, we addressed the shortcomings of other studies. We included a large number of data points with an $SpO_2 <75\%$ (78 and 60 data points for the Ohmeda and Hewlett-Packard oximeters, respectively). We examined bias and precision for both pulse oximeters separately at saturations $>75\%$ and $<75\%$. In doing this, however, it was important to define the groups on the basis of the average

of pulse oximeter and cooximeter values rather than simply on one or the other. The bias would change significantly in our study if the cutoffs for study were to be based on pulse oximeter values alone. We handled potential problems raised by the use of repeated measurements on the same subject in two ways. First, an (approximately) equal number of values was recorded from each subject; a method whereby a simple analysis based on pooled data would produce valid estimates of mean bias but incorrect variance estimates. Second, we used a mixed model analysis which explicitly allowed for separate components of variance at the between-subject and within-subject levels. Although the estimates of overall standard deviation (and so the Bland-Altman range of agreement) combine both components and differ little from what would be obtained by simply pooling all the data, the estimates of the precision of esti-

Table 3. Analysis of the pulse oximeter's ability to predict changes in true saturation.

	RC	RMSE	N
Ohmeda			
All	0.60	4.12	122
$<75\%$	0.59	4.80	72
$\geq 75\%$	0.71	2.92	50
Hewlett-Packard			
All	0.56	4.18	102
$<75\%$	0.50	5.13	44
$\geq 75\%$	0.70	3.28	58

RC, regression coefficient; RMSE, Root mean square error; N, number of patients.

Results of regression analysis for predicting change in cooximeter value given a change in pulse oximeter value.

Ohmeda, Louisville, CO; Hewlett-Packard, North Hollywood, CA.

mation of both mean (bias) and standard deviation are affected and would be underestimated if the data were pooled, given the substantial level of inpatient correlation.

The results of our study indicate some reduction in pulse oximeter performance at saturations of $<75\%$. Changes in bias were minor and not statistically significant. For the Ohmeda oximeter, bias changed little, from -2.8% at $>75\%$ to -0.8% at $<75\%$ ($p = .23$). However, at the same time, and more importantly, the precision decreased, with the standard deviation increasing from 4.8% to 8.0% . The limits of agreement between SaO_2 and SpO_2 for both instruments are relatively wide, especially for the Ohmeda at saturations $<75\%$ where the range required to cover 95% of differences extends from -16.6% to 14.9% .

No other study provides bias and precision information directly comparable with this study. Of the studies that do provide bias and precision at $<80\%$, all use different pulse oximeters. The Ohmeda 3700 pulse oximeter has been specifically examined in only one study using volunteer subjects (15). Of the six pulse oximeters examined in that study, all except the Ohmeda 3700 showed clear tendencies to increase bias with decreasing saturation. In the current study, the precision of both pulse oximeters is similar to others and the biases for the Ohmeda and Hewlett-Packard become more positive at low saturations, but we found negative biases for all but one (Hewlett-Packard $\geq 75\%$) group. It is more

common for the bias to be positive at low saturations where SpO_2 overestimates SaO_2 as SaO_2 decreases (1-4, 8, 12, 14-16). A number of explanations are possible. Definition of the cutoff value for saturation can have a significant effect on the calculated bias, as previously mentioned. Bias calculated in the range of saturations between 75% and 100% may be different to the bias from studies using a narrower range (i.e., 90% to 100%). Bias is known to decrease in magnitude as SpO_2 approaches 100% (8, 15). This study had only a few data points >90%. Negative biases were reported in two other studies (4, 17) with patients using a Nellcor pulse oximeter. However, the data in those studies were not restricted to an SpO_2 of <75%.

When directly compared, the Ohmeda and Hewlett-Packard pulse oximeters showed a statistically significant difference from each other with a mean bias of $-2.1 \pm 5.7\%$ ($n = 139, p = .002$) with the Hewlett-Packard reading higher than the Ohmeda. A similar comparison (18) using a Nellcor N100 instead of the Hewlett-Packard found a mean difference of $-1.61 \pm 2.69\%$ over the saturation range 50% to 100% with the Nellcor reading higher than the Ohmeda. This difference may be a consequence of design differences. Pulse oximeters may be programmed to measure closer to either functional or fractional saturation as a result of the manufacturer's calibration (19). Functional saturation is the proportion of oxygenated hemoglobin compared with the total amount of oxygenated and reduced hemoglobin, whereas fractional saturation is the proportion of oxygenated hemoglobin compared with all species of hemoglobin present, including methemoglobin and carboxyhemoglobin. Thilo et al. (18) showed that Ohmeda pulse oximeters measure closer to fractional saturation while Nellcor pulse oximeters measure closer to functional saturation. Nellcor literature supports this contention (20). Since the Hewlett-Packard oximeter uses Nellcor probes, it may be expected to behave similarly and be an additional reason to explain our bias findings.

Fetal hemoglobin concentrations showed a marginally statistically significant effect ($p = .05$) on the bias of the Ohmeda oximeter, (increasing by 0.35% for every .10% increase in fetal

hemoglobin) but not with the bias of the Hewlett-Packard oximeter. Other studies (16, 21) have also reported increased biases with fetal hemoglobin >50%. However, most studies (1, 3, 5, 22) have reported that fetal hemoglobin has no effect on the accuracy of pulse oximetry. The OSM3 cooximeter used in this study measures fetal hemoglobin levels satisfactorily (23), and accounts for it when comparing pulse oximetry with cooximetry values. Compensation for fetal hemoglobin by a cooximeter is important for accurate measurement of saturation (18, 23, 24).

Despite a lack of data, it is assumed that pulse oximeters provide accurate trend information. The absolute accuracy of pulse oximeters is less important if used to provide trend information. Some investigations (25, 26) have shown that SpO_2 closely follows SaO_2 for individual patients. Others (9, 15) have shown that regression lines for different patients are essentially parallel, indicating the consistent performance within individuals.

We examined the relationship between a change in SpO_2 and corresponding change in SaO_2 . Prediction of SaO_2 from SpO_2 was imperfect and deteriorated at <75%. The two pulse oximeters performed similarly in this regard. For every 10% decrease <75% in the Ohmeda and Hewlett-Packard SpO_2 , the SaO_2 decreased by an average of $5.9 \pm 4.8\%$ and $5.0 \pm 5.1\%$, respectively. These data suggest there is a considerable variability in true saturation changes which cannot be predicted by pulse oximetry. However, there is a high within-subject correlation with variation between subjects accounting for ~60% of all variation. This finding lends support to the view that pulse oximeters are more valuable as trend indicators than an absolute measure of arterial saturation. This fact is clearly demonstrated in Figure 1 where typical subjects can be seen to exhibit less variation than that of the entire group.

A number of explanations have been proposed for the limited performance of pulse oximeters at low saturations. One explanation is the use of software "look-up" tables to empirically determine saturation from the available data on light transmission and amplitude. "Look-up" tables are derived from volunteers under nonclinical conditions. Low saturations are obtained by in-

The performance of the older pulse oximeters, the Ohmeda deteriorates at low saturation as does the ability to predict changes in SaO_2 by both machines at <75%. We recommend measurement of Pao_2 or SaO_2 for low saturations for important clinical decisions.

ducing hypoxemia, but for ethical reasons this is limited to an SpO_2 of ~75%. Extrapolation is used below this level (22, 27, 28). Additional reasons for limited performance at low saturation are the slight variations in the output wavelength of the light-emitting diodes which generate proportionally larger errors at low saturations (29, 30), multiple light scattering effects (31), and the generation of proportionally larger errors in the measurement of transmitted red light than for infrared light at low saturations because of the large extinction coefficient of reduced hemoglobin (32). Clinical data should be used to determine the extent of any inaccuracy and utilized to improve performance. The newer machine, the Hewlett-Packard, performs better than the Ohmeda without deterioration of its performance at <75%. We speculate that one reason for this difference is the continual improvement of the "look-up" tables using clinical data such as this study to overcome inherent difficulties at low saturations.

Although the results of this study are not surprising based on the general findings of other studies, we have clearly quantified for the first time, the performance of two common pulse oximeters in hypoxic subjects. The performance of the older pulse oximeter, the Ohmeda, deteriorates at low saturation as does the ability to predict changes in SaO_2 by both machines at <75%. We recommend measurement

of Pao₂ or Sao₂ at low saturations for important clinical decisions.

REFERENCES

1. Lebecque P, Shango P, Stijns M, et al: Pulse oximetry versus measured arterial oxygen saturation: A comparison of the Nellcor N100 and the Biox III. *Pediatr Pulmonol* 1991; 10:132-135
2. Fanconi S: Reliability of pulse oximetry in hypoxic infants. *J Pediatr* 1988; 112:424-427
3. Fanconi S: Pulse oximetry and transcutaneous oxygen tension for detection of hypoxemia in critically ill infants and children. *Adv Exp Med Biol* 1987; 220:159-164
4. Mok J, Pintar M, Benson L, et al: Evaluation of noninvasive measurements of oxygenation in stable infants. *Crit Care Med* 1986; 14:960-963
5. Rajadurai VS, Walker AM, Yu VYH, et al: Effect of fetal hemoglobin on the accuracy of pulse oximetry in preterm infants. *J Paediatr Child Health* 1992; 28:43-46
6. Bland JM, Altman DG: Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; i:307-310
7. Bland JM, Altman DG: Comparing methods of measurement: Why plotting differences against standard method is misleading. *Lancet* 1995; 346:1085-1087
8. Schmitt HJ, Schuetz WH, Proeschel PA, et al: Accuracy of pulse oximetry in children with cyanotic congenital heart disease. *J Cardiothorac Vasc Anesth* 1993; 7:61-65
9. Hannhart B, Haberer J-P, Saunier C, et al: Accuracy and precision of fourteen pulse oximeters. *Eur Respir J* 1991; 4:115-119
10. Severinghaus JW, Naifeh KH, Koh SO: Errors in 14 pulse oximeters during profound hypoxia. *J Clin Monit* 1989; 5:72-81
11. Boxer RA, Gottesfeld I, Singh S, et al: Noninvasive pulse oximetry in children with cyanotic congenital heart disease. *Crit Care Med* 1987; 15:1062-1064
12. Chapman KR, Liu FLW, Watson RM, et al: Range of accuracy of two wavelength oximetry. *Chest* 1986; 89:540-542
13. Modica R, Rizzo A: Accuracy and response time of a portable pulse oximeter. *Respiration* 1991; 58:155-157
14. Lewallen PK, Mammel MC, Coleman JM, et al: Neonatal transcutaneous arterial oxygen saturation monitoring. *J Perinatol* 1987; 7:8-10
15. Hannhart B, Michalski H, Delorme N, et al: Reliability of six pulse oximeters in chronic obstructive pulmonary disease. *Chest* 1991; 99:842-846
16. Praud J-P, Carofilis A, Bridey F, et al: Accuracy of two wavelength pulse oximetry in neonates and infants. *Pediatr Pulmonol* 1989; 6:180-182
17. Ridley SA: A comparison of two pulse oximeters. Assessment of accuracy at low arterial saturation in pediatric surgical patients. *Anaesthesia* 1988; 43:136-140
18. Thilo EH, Andersen D, Wasserstein ML, et al: Saturation by pulse oximetry: Comparison of the results obtained by instruments of different brands. *J Pediatr* 1993; 122:620-626
19. Emergency Care Research Institute: Pulse Oximeters. *Health Devices* 1989; 18:185-230
20. Measurement of functional and fractional saturation. Pulse oximetry note number 2. Nellcor Incorporated, 1987
21. Jennis MS, Peabody JL: Pulse oximetry: An alternative method for the assessment of oxygenation in newborn infants. *Pediatrics* 1987; 79:524-528
22. Kelleher JF: Pulse Oximetry. *J Clin Monit* 1989; 5:37-62
23. Wimberley PD, Siggaard-Andersen O, Fogh-Andersen N: Accurate measurements of hemoglobin oxygen saturation, and fractions of carboxyhemoglobin and methemoglobin in fetal blood using Radiometer OSM3: Corrections for fetal hemoglobin fraction and pH. *Scand J Clin Lab Invest* 1990; 50(Suppl 203): 235-239
24. Krzeminski A: Why correct for fetal hemoglobin in blood oximetry measurement? Info No. 1992-3, OSM3 ABL510/520, Radiometer A/S, Denmark, May 1992
25. Mihm FG, Halperin BD: Noninvasive detection of profound arterial desaturations using a pulse oximetry device. *Anesthesiology* 1985; 62:85-87
26. Wimberley PD, Helledie NR, Friis-Hansen B, et al: Pulse oximetry versus transcutaneous Po₂ in sick newborn infants. *Scand J Clin Lab Invest* 1987; 47(Suppl 188):19-25
27. Wukitsch MW, Petterson MT, Tobler DR, et al: Pulse oximetry: Analysis of theory, technology and practice. *J Clin Monit* 1988; 4:290-301
28. Yelderman M, New W: Evaluation of pulse oximetry. *Anesthesiology* 1983; 59:349-352
29. Welch JP, DeCesare R, Hess D: Pulse oximetry: Instrumentation and clinical applications. *Respir Care* 1990; 35: 584-601
30. Wahr JA, Tremper KK: Noninvasive oxygen monitoring techniques. *Crit Care Clin* 1995; 11:199-217
31. Shimada Y, Yoshiya I, Oka N, et al: Effects of multiple scattering and peripheral circulation on arterial oxygen saturation measured with a pulse-type oximeter. *Med Biol Eng Comput* 1984; 22:475-478
32. Reynolds KJ, Moyle JTB, Sykes MK, et al: Response of 10 pulse oximeters to an *in vitro* test system. *Br J Anaesth* 1992; 68:365-369

Pulse oximetry – clinical implications and recent technical developments

L. G. LINDBERG¹, C. LENNMARKEN² and M. VEGFORS²

Departments of ¹Biomedical Engineering and ²Anaesthesiology, Linköping University, Linköping, Sweden

The pulse oximeter has been shown to be a reliable monitor of arterial oxygen saturation and has therefore been recommended as mandatory monitoring for patients during anaesthesia and intensive care. In 1989 two review articles on pulse oximetry were published (1, 2) and two years ago Severinghaus and Kelleher summarized the literature between 1989 and October 1991 (3). Our aim is to focus the discussion on technical aspects and applications of pulse oximetry with special attention centred on recent developments. This review is consequently an update on pulse oximetry since the end of 1991, and the first on technically-based publications in the two last decades.

TRANSMISSION PULSE OXIMETRY

Most pulse oximeters work in the transmission mode, where the light illuminates the tissue and is picked up by a photodetector positioned on the opposite side of the tissue, e.g. finger, earlobe and toe.

INTERACTION BETWEEN LIGHT AND TISSUE

The technique of pulse oximetry relies on absorption of light by oxyhaemoglobin (HbO₂) and reduced haemoglobin (Hb). Light of two different wavelengths is used. For red light (660 nm) Hb is the main absorber, whereas for near infrared light (940 nm) HbO₂ predominates (Fig. 1). In order to record arterial oxygen saturation, measurements are made with reference to the change in light transmission that occurs with each arterial pulse for 660 and 940 nm. The ratio of the red (R) to near infrared (IR) pulsatile signals (R/IR) is then used to compute the arterial oxygen saturation using an inbuilt algorithm in which the R/IR ratio corresponds to an empirically found saturation value (Fig. 2).

THE LAMBERT-BEER'S LAW

The relationship between R/IR and the arterial oxygen saturation has been explained by the Lambert-Beer's law. This law describes penetration of light in homogen-

ous tissue. In pulse oximetry the absorption of the red and near infrared light is influenced by the absorption and scattering properties of the various tissues the light passes. The scattering coefficient, μ_s , in units of mm^{-1} , is the rate of radiant energy loss due to scatter per unit pathlength in tissue. It should be noted that this coefficient varies widely for red light in various mammalian soft tissues and for different physiological conditions (4–6). In blood alone light scattering is a function of several factors such as haematocrit, blood flow, red cell de-

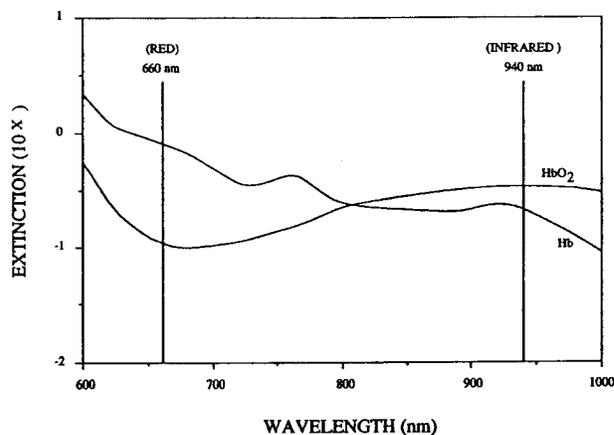


Fig. 1. Oxygenated haemoglobin (HbO₂) and reduced haemoglobin (Hb) exhibit different absorption (extinction) characteristics to red light 660 nm and near infrared light 940 nm.

formation, cell aggregation and orientation of the red blood cells (7, 8). In addition the Lambert-Beer's law is based on the assumption that the pathlength of light between the light source and the photodetector is constant and equal for both wavelengths used in pulse oximetry. Due to movements caused by the arterial pulse and varying light scattering these criteria for the Lambert-Beer's law are not fulfilled. Therefore, according to the circumstances mentioned above, the Lambert-Beer's law does not fully account for scattering in tissues and blood (9). This is probably the explanation why the empirical calibration curves, used in pulse oximetry, differ from the theoretical curves (6).

REFLECTION PULSE OXIMETRY

In reflection pulse oximetry the light source and the detector are placed adjacent to each other. One major advantage of reflection mode compared to transmission mode is that the probe can be used on a number of surfaces such as forearm, thigh, chest, forehead and cheeks.

However, the accuracy of reflection pulse oximeters may sometimes be insufficient. This may be due to low signal to noise ratio, small heart-related pulsations and the lack of a reliable signal analysis (10). Similar to transmission pulse oximetry it is the ratio R/IR that is used to estimate the arterial oxygen saturation (6, 10–17). The R/IR ratio varies with light propagation in tissue, which in turn varies with the distance between the light source and the photodetector and the type of tissue (18). It is therefore likely that the theoretical modelling for describing the basis of pulse oximetry is different for transmission and reflection modes. In reflection pulse oximetry the enhanced degree of multiple scattering must be accounted for (6, 10).

Compared to transmission pulse oximetry, a smaller

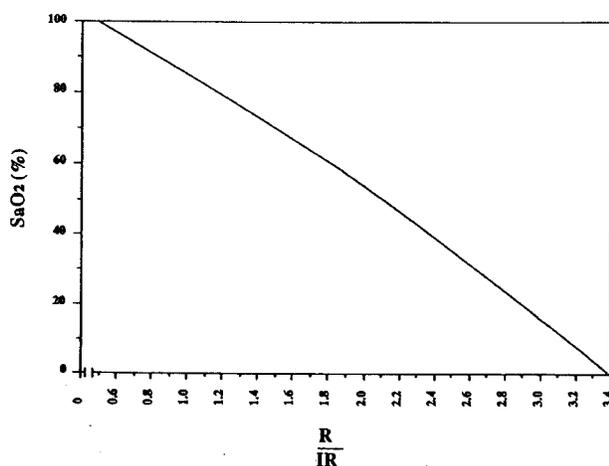


Fig. 2. A typical pulse calibration curve.

fraction of illuminated light reaches the photodetector. Due to weaker pulse signals, probe configuration, light intensity, number of optical components and signal processing are very important in the design of reflection pulse oximeters. There are different solutions to these problems in sensor design, e.g. light sources surrounding the detector (10, 15), the opposite configuration (12, 14) and also lining of the LED and the photodetectors (6). In the latter solution (Fig. 3) several photodetectors are utilized in processing to achieve a more accurate measurement of oxygen saturation. The light sources used are basically the same as for transmission pulse oximetry, but also wavelengths near the isobestic point (805 nm = insensitive for oxygen saturation) are used as reference (10). Some probes also incorporate a heating assembly to increase the pulse wave (10, 14).

The Ciba-Corning instrument is one example of a commercially available reflection pulse oximeter. This device has an unacceptable signal failure rate of 59% with its probe on the forehead and 27% failure rate when used on the finger (3). However, in patients gradually warming up from heart surgery, with compromised peripheral perfusion and low peripheral skin temperature, the Criticare 504 US monitor (Criticare Systems, Milwaukee, WI) placed on the forehead gives reliable saturation and regains signal earlier than a probe placed on the ear lobe (19, 20). Watney et al. have also found reflection pulse oximetry accurate and practically useful in anaesthetized horses with the pulse oximeter probe attached to the mucosa of the mandible (21).

ACCURACY IN ANIMAL STUDIES

Accuracy of pulse oximetry has been evaluated in two animal studies using a Biox 3700, (Ohmeda, USA, Revision P). Jacobson et al. showed in dogs that SpO_2 tended to underestimate at high SpO_2 values and to overestimate at low SpO_2 values (22). In another study using rabbits and an OXI pulse oximeter (Radiometer, Copenhagen), with identical algorithm as the Biox pulse

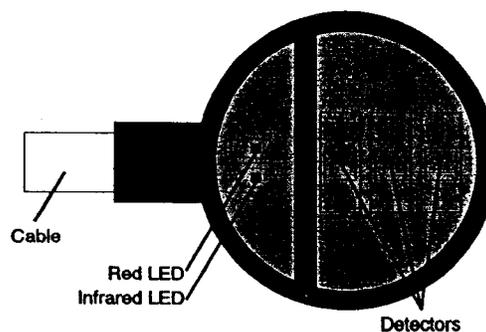


Fig. 3. Example of probe for reflection pulse oximetry. (By the courtesy of R. Graaff, University of Groningen, The Netherlands).

oximeter, similar results were found with an overread in SpO_2 at low saturation values (23).

PULSE OXIMETRY DURING ANAEMIA

The experience with pulse oximetry during severe anaemia is limited. In studies using an *in vitro* model and in animal experiments it has been demonstrated that the pulse oximeter readings are dependent on haemoglobin content (23, 24). At a "normal" haemoglobin level a good correlation was found comparing invasive (So_2) and noninvasive (SpO_2) measurements in a wide range of oxygen haemoglobin saturation. After haemodilution the correlation was improved in the SpO_2 range exceeding 85% (23). In two patients suffering from severe anaemia the SpO_2 differed by less than 4% from blood gas analyses (So_2) (25). In a patient with haemoglobin-H, and suffering from profound anaemia and poor clinical condition, the pulse oximeter continued to demonstrate a high saturation value. However, arterial blood gas analysis was not performed (26).

PULSE OXIMETRY DURING HYPOVENTILATION

When the concentration of inspired oxygen is high, respiratory depression may result in hypercapnia and normal oxygen saturation as measured by a pulse oximeter (27, 28). A pulse oximeter is therefore a poor indicator of hypoventilation when patients receive high fractional oxygen concentrations which result in a decrease in saturation that appears late. As the pulse oximeter does not warn of hypercapnia the SpO_2 may give a totally wrong impression to the clinician of a very dangerous situation. Although this is not a failure of the pulse oximeter technique itself, knowledge and awareness of this possibility is of the utmost importance.

MOVEMENT ARTIFACTS AND PROBE POSITION

It is well known that pulse oximeter data are confounded by movement artefacts. To determine the incidence of true and false pulse oximeter alarms in a clinical setting, 123 surgical patients in a postanaesthesia unit were studied using pulse oximetry and air flow monitoring. A high incidence of pulse oximeter alarms was found and 77% of the alarms were "false" and caused by sensor displacement, motion artifacts and/or perfusion (29). One way to reduce this unacceptable high incidence of "false" alarm is the method of using two pulse oximeters, whereas a desaturation occurring in only one of the monitors was classified as artefactual. Another way is to identify the changes in the photoplethysmographic

waveform, preceding a desaturation event, and retrospectively reject saturation data whenever applicable (30).

During induced hypoxaemia in volunteers, the calibration curves of the pulse oximeters were greatly altered by various positions of the sensor (31). Compared to invasive arterial oxygen saturation, buccal pulse oximeter measurements were more accurate than readings from sensors placed on a finger (32). Tongue oximetry functioned during peripheral vasoconstriction in children when the peripheral sensor failed. This application is, however, limited to paralyzed, intubated patients (33). Sensors placed centrally on the human body seem to detect both desaturation and resaturation earlier than peripheral located sensors (34).

LOW PERFUSION

Signal failure may occur due to low perfusion. To restore blood flow it has been suggested to give vasodilators (35) or perform digital nerve blocks (36). Another solution is to place a disposable hand glove filled with warm water in the patient's hand (37).

SpO_2 AND DYES

Intravenous dyes can cause false saturation readings on a pulse oximeter. Intradermal injection of patent blue dye is a surgical technique for intraoperative mapping of the lymphatic drainage of a malignant melanoma. After injection of dye a marked decrease in oxygen saturation as monitored by a pulse oximeter could be registered (38).

Injection of indocyanine green also resulted in transient false desaturation. Böhrer et al. have therefore suggested injecting the dye into a central venous line to confirm intravascular placement (39).

METHAEMOGLOBINAEMIA, FOETAL HAEMOGLOBIN AND SICKLE CELL ANAEMIA

Trillo & Aukburg described a case where a sulfonamide induced methaemoglobinaemia. The injection of the antibiotic was followed by a decrease in the pulse oximetry readings (40). Pulse oximetry may also be of value in making the diagnosis of methaemoglobinaemia induced by prilocaine (41).

To evaluate the effect of foetal haemoglobin in pre-term infants, oxygen saturation from a Nellcor N-200 pulse oximeter (Hayward, CA, USA) was compared with simultaneous arterial values measured by a Radiometer OSM 3 apparatus (Radiometer, Copenhagen) over a SpO_2 range of 83–99%. It was concluded that the pulse oximeter was unaffected by foetal haemoglobin (42).

In patients with sickle cell disease SpO_2 was similar to invasively measured saturations. However, both overestimates and underestimates were sometimes observed (43).

COMPLICATIONS

A few cases of skin injury due to pulse oximeter probes have been reported in children. A skin injury on the pulp of the toes appeared on an 11-month-old girl. This was believed to be due to thermal (44) and/or pressure-related factors (45). A 4-month-old baby suffered burns to its big toe related to the site of application of a Nellcor N25 oxisensor after 14 days use. The reason was a short circuit between the wires in the pulse oximeter probe. The author suggested that the probe application should be regularly inspected, the position of the probe changed at regular time intervals and disposable probes restrictively re-used (46). Sobel also reported a case of burn due to a presumed shorting of the nondisposable probe cables when used on the foot of a neonate born prematurely (47).

BLOOD PRESSURE MEASUREMENTS

Pulse oximetry can be used to indirectly measure systolic blood pressure. A good agreement was found when comparing the return of the pulse wave on the pulse oximeter and the Korotokoff sounds with oscillometric noninvasive blood pressure equipment (48).

BLOOD FLOW AND PULSE OXIMETRY

By measuring the time interval between the beginning of the QRS complex on ECG and the upstroke of the pulse oximeter measured on the pulse oximeter plethysmogram, the peripheral circulatory status of a neonate can be evaluated (49).

During reactive hyperaemia in ten volunteers the oxygen saturation was significantly lower compared to the other arm (50). The authors claimed that this was partly due to pulsatile venous blood flow.

Leg elevation causes reduced blood flow in the foot. The pulse oximeter reading also decreased significantly as measured on a toe during leg elevation. This altered reading was mainly a result of reduced amplitude of the transmitted infrared pulsatile light (51). The influence of blood flow on the accuracy of pulse oximetry was also confirmed in an *in vitro* model (52) showing that reduced blood flow affected the displayed oxygen saturation. Ding et al. demonstrated that increased blood-flow after brachial plexus block in the upper limb reduced the time taken for a change in finger pulse oximeter value after increasing the F_{iO_2} (53).

Early detection of an epidural block may be observed

as an increase in the amplitude of the pulse oximeter waveform when the sensor is placed on the toe. In addition, more reliable pulse oximeter signals can be obtained from the toe compared to the finger during lumbar epidural anaesthesia (54).

Palmar collateral circulation was evaluated using a pulse oximeter. The results indicated that the pulse oximeter cannot be used to demonstrate palmar collateral circulation. However, a plethysmographic signal, extracted from the pulse oximeter, can be used (55).

It is suggested that pulse oximetry can be used to assess the adequacy of peripheral perfusion when impairment of regional blood flow is suspected. However, Mars & Hadley have reported two cases of hand surgery where pulse oximetry was inadequate as an indicator of limb perfusion (56).

Pulse oximetry was of undoubted benefit in the management of primary respiratory arrest, but of equivocal value in cardiac arrest in twenty patients requiring cardiopulmonary resuscitation. During external chest compressions, pulse oximeter data were displayed, but were unreliable (57). Dawalibi et al. studied two pulseless patients, one after cardiectomy and one with visually observed asystole during operation. In both cases the pulse oximeter continued to display normal or subnormal saturation values (58).

In eight patients who underwent cardiac surgery Haessler et al. evaluated catheter oximetry versus pulse oximetry. Pulse oximetry was, under these circumstances, an insufficient method compared to catheter oximetry. The latter method was superior in obtaining readings, and also in the reliability of the obtained readings. Of course, invasiveness and high costs would influence the decision whether to use catheter oximetry (59).

Pulse oximetry has been used to provide a useful and rapid method of monitoring changes of blood flow. After spinal anaesthesia, pulse volume and heart rate were changed following Valsalva manoeuvre (60). In both pregnant patients and nonpregnant volunteers Woods et al. showed that Valsalva manoeuvre is associated with abrupt haemodynamic changes. These changes interface with predetermined criteria for the pulse wave identification during pulse oximetry. There were consistent interruptions in the transmitted oxygen saturation data during the Valsalva manoeuvre (61).

In a patient with cardiomyopathy requiring intra-aortic balloon counterpulsation, venous pulsations were demonstrated to result in underestimation of oxygen saturation measured by a pulse oximeter (62). In addition, erroneous measurements of pulse oximeter readings have been described after blood transfusion in a 26 month old girl. After the blood transfusion, the pulse oximeter probe began to show a decrease in SpO_2 from 100% to 65%. The authors suggest that a combination

of l
cell

EV.

An
flow
scri
Do
pro
cor
me
unc

EV

PU

Pul
int
pul
tio
int

PU

Th
ear
cor
(68
da
in

Sp

Se
go
80
ox
to
sci
the
at
tes
we
brto
su
fo
is
ra
su
in
ni

of hypovolaemia and rapid injection of stored red blood cells can cause low SpO_2 (63).

EVALUATION OF MICROCIRCULATION

An instrument that measures microcirculatory blood flow and oxygen saturation simultaneously has been described (64). This instrument is a combination of a laser Doppler flowmeter and a reflection pulse oximeter. A prototype of the instrument was compared with a Nellcor N-100 transmission pulse oximeter. The new instrument showed a variability of readings of $\pm 4\%$ and underestimations of 5–10% (65).

EVALUATION OF INTESTINAL VIABILITY BY PULSE OXIMETRY

Pulse oximetry has the potential to be of value in the intraoperative assessment of intestinal blood flow (66). A pulse oximeter was used to detect safe margins for resection of a strangulated stomach, by placing the sensor intraoperatively on various portions of the stomach (67).

PULSE OXIMETRY DURING EXERCISE

The accuracy of pulse oximetry, when measuring on the earlobe, during intense exercise may be reduced due to compromised peripheral blood flow or motion artefacts (68). However, the saturations measured with an Ohmeda 3740 oximeter was found to be valid during exercise in normoxia and acute hypoxia (69).

SpO_2 MONITORING DURING SLEEP

Several clinical studies have been published reporting good experiences using pulse oximetry during sleep (70–80). Williams & Stein concluded, however, that pulse oximetry is not sufficiently sensitive as the only screening tool in obstructive sleep apnoea (80). Issa et al. has described a digital recorder (SNORESAT) that monitors the sound of snoring and SpO_2 and compared this apparatus with standard polysomnography. The laboratory testing of SNORESAT indicated that the device can well estimate the presence or absence of nocturnal breathing abnormalities (77).

Pulse oximetry has been described to be a useful tool to detect postoperative hypoxaemia (79). Twenty-nine surgical patients have been studied using pulse oximetry for up to 3 nights after the operation. Several mechanisms are thought to be responsible for oxygen desaturation and these mechanisms differ before and after surgery (70). In another study, pulse oximetry monitoring has been performed two nights before and three nights after abdominal surgery under general anaes-

thetia in 10 patients. The episodic hypoxaemic events were increased after surgery (71). In patients with cystic fibrosis and severe airway obstruction Braggion et al. found limited agreement between pulse oximeter readings and invasively obtained saturation values during sleep. However, the authors concluded that overnight oximetry provided useful clinical information (72). Smith et al. concluded, in children, that overnight studies can be reduced to 4 hours without loss of clinical significance (73).

SpO_2 DURING INTRAVENOUS SEDATION OR ANALGESIA

During oral surgery under local analgesia a fall in oxygen saturation as measured by pulse oximetry was found following midazolam administration (81). During sedation with benzodiazepines the oxygen saturation measured with pulse oximetry was lower to begin with and tended to fall further with sedation in older age groups (82). With midazolam sedation some instances of a brief fall in the oxygen saturation were found during dental surgery and in the immediate postoperative period (83). Kluger et al. found that the duration of desaturation increased postoperatively compared to preoperative values in patients receiving analgesia (84).

SENSORS FOR MONITORING THE FOETUS

Several sensors have been developed to work on the principle of reflection pulse oximetry on the foetus (17, 85–88). A highly significant correlation has been reported between the pulse oximeter reading and cord blood Ph (85), and an increase in foetal arteriolar oxygen saturation when oxygen was administered to the mother (86). It is suggested that a foetal pulse oximeter has the potential to be used as a foetal monitoring tool (86). One should, however, be cautious about using sensors with an irregular surface on the foetus due to the possible risk of scalp ulceration (89).

Harris and coworkers have designed a foetal sensor which was evaluated in acutely instrumented foetal sheep. The measurements correlated well with *in vitro* measurements over the oxyhaemoglobin range of 6–81% suggesting that this technique appears useful and merits further evaluation (87). Mendelson & Solomita have also demonstrated the feasibility of measuring arterial oxyhaemoglobin saturation on the foetal scalp using an optical reflection sensor. Two prototype sensor assemblies were studied, also incorporating different means of attachment to the scalp (88).

Finally, Takatani and coworkers have evaluated a new reflection pulse oximeter sensor. This prototype consists of 8 light-emitting diode (LED) chips and photodiode

chip mounted on a single substrate. Both an animal study and a clinical study were performed. The authors concluded that the reflection pulse oximeter sensor may yield accurate measurements of oxygen saturation (10).

PULSE OXIMETRY AND CHILDREN

Pulse oximetry is a valuable tool when studying neonates (90, 91), intubated, very low birth weight infants (92) or asymptomatic premature infants (93).

It is difficult to apply adhesive-backed oximeter probes to the extremities of small children. A study was performed with the clip-on probe for adults placed on either part of the infant's hand including some fingers or part of the foot including some toes. The authors concluded this to be a simple alternative technique and saturation readings were within 1% of those obtained by the conventional procedure (94).

One hundred neonates were studied with the pulse oximeter probes placed on the hand and on the Achilles tendon. One and 5 minutes after partus, SpO_2 recorded from the hand was higher than recorded from the lower extremities. After 24 hours these differences had disappeared. These results can be explained by the presence of shunting at the ductus arteriosus level (90).

OTHER USES OF PULSE OXIMETERS

There is a lack of reference data on oxygen saturation data of children. Pulse oximetry can therefore be used to achieve data at high altitudes (95, 96) and is also useful when evaluating oxygen saturation in patients with pulmonary oedema due to high altitude (97).

Pulse oximetry application in the labour and delivery unit shows that the degree of arterial desaturation appears to be greater during pregnancy (98).

Monitoring with pulse oximetry did not reduce post-operative cognitive impairment in a study including 736 patients (99).

Various peroxygenation techniques were assessed using pulse oximetry. To be able to prevent hypoxaemia defined as $SpO_2 < 90\%$ the authors found that preoxygenation with $FiO_2 = 0.5$ is just as effective as preoxygenation with $FiO_2 1.0$ (100).

IN VITRO TESTS

Several *in vitro* models have been developed and described during the last few years (6, 52, 94, 101-106). Some of these models account only for blood volume changes simulating the pulsations (101, 102, 104-106). Other models account both for blood volume changes and red cell orientations during the pulse wave (6, 52, 94, 103). There were, however, differences in results

when comparing the *in vitro* models mentioned above. This could be due to the type of finger model used and by the routines of handling the blood.

Severe hypoxaemia and anaemia were studied in an *in vitro* model with circulating human blood (94). At a haematocrit level of 41-44% there was no correlation between SaO_2 and SpO_2 readings. After diluting the blood with normal saline to a haematocrit of 10-11% a good correlation between SaO_2 and SpO_2 was found. This suggests an influence of the haematocrit value on the pulse oximeter saturation.

Reynolds and coworkers have developed an *in vitro* test system for pulse oximeters. Ten different pulse oximeters were tested and compared with invasive measurements over a range of SaO_2 for 50 to 100%. The oximeters tested varied widely in their accuracy and linearity (104). In addition, studies of theoretical relationships between pulse oximeter readings and functional and fractional actual readings were performed. Theoretical predictions and experimental results were found to agree well in the presence of carboxyhaemoglobin, but not so well in the case of methaemoglobin (105).

FIBRE OPTIC PULSE OXIMETRY

The conventional pulse oximeter probe may cause problems during MR investigations in two ways, firstly by causing burns on the skin due to induced currents and secondly by producing artifacts on the MR-images (107,108). These drawbacks can be overcome by using optical fibres to guide the light to and from the skin surface. Optical fibre technology is therefore suitable for use in environments with electromagnetic disturbances. A newly developed portable fiberoptic pulse oximeter has been found not to produce artifacts (109).

FUTURE PROSPECTS

The pulse oximeter utilizes the photoplethysmographic (PPG) signal to calculate oxygen saturation. However, the PPG signal contains not only heart synchronous variations, but also reflects a number of physiological parameters, among them slow ventilation-dependent features. By choosing suitable band-pass filter characteristics it is possible to identify the respiratory signal using a new sensor (110). This new sensor utilizes fibreoptics in the reflection mode and correlates well with the more traditional methods like capnography and transthoracic impedance plethysmography for respiratory rate monitoring (111).

The potential of pulse oximetry to detect vascular integrity within the human tooth is described. Both Schnettler et al. and Mills support the need for further

worl
and
R
sels
beca
in vitro
requ
A
the
an
eter
ebra
thro
chyl
ligh
also
potl
(115
vali
bull
(116

REL

1.

2.

3.

4.

5.

6.

7.

8.

9.

10.

11.

12.

13.

14.

above.
ed and

work to determine how reliable this technique may be and in what situations it can be used (112, 113).

Reflection pulse oximetry of blood in the retinal vessels offers advantages over conventional pulse oximetry because it reflects cerebral oxygenation. Preliminary *in vivo* results are encouraging but further investigations are required to validate the technique (114).

A brain oximeter which uses multiple wavelengths in the range 650 to 1100 nm, and which does not require an arterial pulse, is commercially available. This oximeter is designed for use on adult patients at risk of cerebral hypoxaemia (115–117). Infrared light propagates through the scalp, skull, and into the cerebral parenchyma and returns to receivers placed adjacent to the light source on the head (118). McCormick et al. have also described the use of the technique during deep hypothermic circulatory arrest for giant aneurysm repair (115). In addition, the same research group confirms the validity of the new technique compared with jugular bulb venous blood samples analyzed by a co-oximeter (116).

REFERENCES

1. Tremper K, Barker S. Pulse oximetry. *Anesthesiology* 1989; **70**: 98–108.
2. Kelleher J F. Pulse Oximetry. *J Clin Monit* 1989; **5**: 37–62.
3. Severinghaus J W, Kelleher J F. Recent developments in pulse oximetry. *Anesthesiology* 1992; **76**: 1018–1038.
4. Wilson B C, Jacques S L. Optical reflectance and transmittance of tissue: principles and applications. *IEEE J Quantum Electron* 1990; **26**: 2186–2199.
5. Arnfield M R, Tulip J, McPhee M S. Optical propagation in tissue with anisotropic scattering. *IEEE Trans Biomed Eng* 1988; **35**: 372–381.
6. Graaff R. Tissue optics applied to reflectance pulse oximetry. Thesis, University of Groningen, the Netherlands 1993.
7. Graaff R, Dassel A C M, Koelink M H, deMul F F M, Aarnoudse J G, Zijlstra W G. Optical properties of human dermis *in vitro* and *in vivo*. *Appl Opt* 1993; **32**: 435–447.
8. Lindberg L-G, Öberg P Å. Optical properties of blood in motion. *Optical Engineering* 1993; **32**: 253–257.
9. Cejnar M, Kobler H, Hunyor S N. Quantitative photoplethysmography: Lambert-Beer law or inverse function incorporating light scatter. *J Biomed Eng* 1993; **15**: 151–154.
10. Takatani S, Davies C, Sakakibara N et al. Experimental and clinical evaluation of a noninvasive reflectance pulse oximeter sensor. *J Clin Monit* 1992; **8**: 257–266.
11. Mendelson Y, Ochs B D. Noninvasive pulse oximetry utilizing skin reflectance photoplethysmography. *IEEE Trans Biomed Eng* 1988; **35**: 798–805.
12. Mendelson Y, Kent J C, Yocum B L, Birtle M J. Design and evaluation of a new reflectance pulse oximeter sensor. *Med Instr* 1988; **22**: 167–173.
13. Decker M J, Dickensheets D, Arnold J L, Cheung P W, Strohl K P. A comparison of a new reflectance oximeter with the Hewlett-Packard ear oximeter. *Biomed Instrum Technol* 1990; **24**: 122–126.
14. Mendelson Y, McGinn M J. Skin reflectance pulse oximetry: *in vivo* measurements from the forearm and calf. *J Clin Monit* 1991; **7**: 7–12.
15. Shimada Y, Nakashima K, Fujiwara Y et al. Evaluation of a new reflectance pulse oximeter for clinical applications. *Med & Biol Eng & Comput* 1991; **29**: 557–561.
16. Johnson N, Johnson V A, Fisher J, Jobbings B, Bannister J, Lilford R J. Fetal monitoring with pulse oximetry. *Br J Obstet Gynaecol* 1991; **98**: 36–41.
17. Dassel A C, Graaff R, Aarnoudse J G et al. Reflectance pulse oximetry in fetal lambs. *Pediatr Res* 1992; **31**: 266–269.
18. Takatani S, Graham M D. Theoretical analysis of diffuse reflectance from a two-layer tissue model. *IEEE Trans Biomed Eng* 1979; **26**: 656–664.
19. Palve H. Reflection and transmission pulse oximetry during compromised peripheral perfusion. *J Clin Monit* 1992; **8**: 12–15.
20. Palve H. Comparison of reflection and transmission pulse oximetry after open-heart surgery. *Crit Care Med* 1992; **20**: 48–51.
21. Watney G C G, Norman W M, Schumacher J P. Accuracy of a reflectance pulse oximeter in anesthetized horses. *Am J Vet Res* 1993; **54**: 497–501.
22. Jacobson J D, Miller M W, Matthews N S, Hartfield S M, Knauer K W. Evaluation of accuracy of pulse oximetry in dogs. *Am J Vet Res* 1992; **53**: 537–540.
23. Vegfors M, Lindberg L-G, Öberg P Å, Lennmarken C. The accuracy of pulse oximetry at two haematocrit levels. *Acta Anaesthesiol Scand* 1992; **36**: 454–459.
24. Vegfors M, Lindberg L-G, Öberg P Å, Lennmarken C. Accuracy of pulse oximetry at various haematocrits and during haemolysis in an *in vitro* model. *Med & Biol Eng & Comput* 1993; **31**: 135–141.
25. Ramsing Th, Rosenberg J. Pulse oximetry in severe anaemia. *Intensive Care Med* 1992; **18**: 125–126.
26. Jay G D, Renzi F P. Evaluation of pulse oximetry in anemia from hemoglobin-H disease. *Ann Emerg Med* 1992; **21**: 572–574.
27. Davidson J A H, Hösie H E. Limitations of pulse oximetry: respiratory insufficiency—a failure of detection. *BMJ* 1993; **307**: 372–373.
28. Hutton P, Clutton-Brock T. The benefits and pitfalls of pulse oximetry. *BMJ* 1993; **307**: 457–458.
29. Wiklund L, Hök B, Ståhl K, Jordeby-Jönsson A. Post-Anesthesia monitoring revisited: Incidence of true and false alarms from different monitoring devices. *J Clin Anaesth* 1994; **6**: xx.
30. Visram A R, Jones R D M, Irwin M G, Bacon-Shone J. Use of two oximeters to investigate a method of movement artefact rejection using photoplethysmographic signals. *Br J Anaesth* 1994; **72**: 388–392.
31. Barker S J, Hyatt J, Shah N K, Kao J. The effect of sensor malpositioning on pulse oximeter accuracy during hypoxaemia. *Anesthesiology* 1993; **79**: 248–254.
32. O'Leary R J, Landon M, Benumof J L. Buccal pulse oximeter is more accurate than finger pulse oximeter in measuring oxygen saturation. *Anesth Analg* 1992; **75**: 495–498.
33. Coté C J, Daniels A L, Connolly M, Szyfelbein S K, Wickens C D. Tongue oximetry in children with extensive thermal injury: comparison with peripheral oximetry. *Can J Anaesth* 1992; **39**: 454–457.
34. Reynolds L M, Nicolson S C, Steven J M, Escobar A, McGonigle M E, Jobses D R. Influence of sensor site location on pulse oximetry kinetics in children. *Anesth Analg* 1993; **76**: 751–754.
35. Holroyd K, Lui M, Beattie C. Intraarterial vasodilator administration to restore pulse oximeter function. *Anesthesiology* 1993; **79**: 388–390.
36. Bourke D L, Grayson R F. Digital nerve blocks can restore pulse oximeter signal detection. *Anesth Analg* 1991; **73**: 815–817.
37. Gupta A, Vegfors M. A simple solution. *Anaesthesia* 1992; **47**: 822 (letter).
38. Morell R C, Heyneker T, Kashtan H I, Ruppe C. False desaturation due to intradermal patent blue dye. *Anesthesiology* 1993; **78**: 363–364.

39. Böhrer H, Schmidt H, Bach A. Confirmation of intravascular catheter placement by pulse oximetry following indocyanine green injection (letter). *Anaesthesia* 1993; **48**: 647-648.
40. Trillo R A, Aukburg S. Dapsone-induced methemoglobinemia and pulse oximetry. *Anesthesiology* 1992; **77**: 594-596.
41. Bellamy M C, Hopkins P M, Halsall P J, Ellis F R. A study into the incidence of methaemoglobinaemia after "three-in-one" block with prilocaine. *Anaesthesia* 1992; **47**: 1084-1085.
42. Rajadurai V S, Walker A M, Yu V Y H, Oates A. Effect of fetal haemoglobin on the accuracy of pulse oximetry in preterm infants. *J Paediatr Child Health* 1992; **28**: 43-46.
43. Pianosi P, Charge T D, Esseltine D W, Coates A L. Pulse oximetry in sickle cell disease. *Arch Dis Child* 1993; **68**: 735-738.
44. Pettersen B, Kongsgaard U, Aune H. Skin injury in an infant with pulse oximetry. *Br J Anaesth* 1992; **69**: 204-205.
45. Bethune D W, Baliga N. Skin injury with a pulse oximeter (letter). *Br J Anaesth* 1992; **69**: 665.
46. Mills G H, Ralph S J. Burns due to pulse oximetry (letter). *Anaesthesia* 1992; **47**: 276-277.
47. Sobel D B. Burning of a neonate due to a pulse oximeter: arterial saturation monitoring. *Pediatrics* 1992; **89**: 154-155.
48. Chawla R, Kumarvel V, Girdhar K K, Sethi A K. Can pulse oximetry be used to measure systolic blood pressure? *Anesth Analg* 1992; **74**: 196-200.
49. Oishi M, Nishida H, Kabe K, Hoshi J. Monitoring neonatal peripheral circulation by electrocardiogram-to-oximeter pulse velocity. *Pediatr Res* 1993; **33**: 653-657.
50. Broome I J, Mills G H, Spiers P, Reilly C S. An evaluation of the effect of vasodilatation on oxygen saturations measured by pulse oximetry and venous blood gas analysis. *Anaesthesia* 1993; **48**: 415-416.
51. Vegfors M, Lindberg L-G, Lennmarken C. The influence of changes in blood flow on the accuracy of pulse oximetry in humans. *Acta Anaesthesiol* 1992; **36**: 346-349.
52. Lindberg L-G, Vegfors M, Lennmarken C, Öberg P Å. The pulse oximetry signal at various blood flow conditions in an in vitro model *Med & Biol Eng & Comput*, in press 1995.
53. Ding Z-N, Shibata K, Yamamoto K, Kobayashi T, Murakami S. Decreased circulation time in the upper limb reduces the lag time of the finger pulse oximeter response. *Can J Anaesth* 1992; **39**: 87-89.
54. Mineo R, Sharrock N E. Pulse oximeter waveforms from the finger and toe during lumbar epidural anesthesia. *Reg Anesth* 1993; **18**: 106-109.
55. Fuhrman T M, Pippin W D, Talmage L A, Reilley T E. Evaluation of collateral circulation of the hand. *J Clin Monit* 1992; **8**: 28-32.
56. Mars M, Hadley G P. Pulse oximetry in the assessment of limb perfusion. *S Afr Med J* 1992; **82**: 486.
57. Spittal M J. Evaluation of pulse oximetry during cardiopulmonary resuscitation. *Anaesthesia* 1993; **48**: 701-703.
58. Dawalibi L, Rozario C, van den Bergh A A. Pulse oximetry in pulseless patients. *Anaesthesia* 1991; **46**: 990-991.
59. Haessler R, Brandl F, Zeller M, Briegel J, Peter K. Continuous intra-arterial oximetry, pulse oximetry, and co-oximetry during cardiac surgery. *J Cardiothorac Vasc Anesth* 1992; **6**: 668-673.
60. Macfie A G, Brimacombe J. Response to the valsalva manoeuvre after spinal anaesthesia. *Anaesthesia* 1992; **47**: 13-16.
61. Woods A M, Queen J S, Lawson D. Valsalva maneuver in obstetrics: the influence of peripheral circulatory changes on function of the pulse oximeter. *Anesth Analg* 1991; **73**: 765-771.
62. Sami H M, Kleinman B S, Lonchyna V A. Central venous pulsations associated with a falsely low oxygen saturation measured by pulse oximetry. *J Clin Monit* 1991; **7**: 309-312.
63. Nachman J A, Schwartz R E. Erroneous measurement of arterial oxygen saturation. *J Paediatr Child Health* 1993; **29**: 396-397.
64. Dougherty G, Lowry J. Design and evaluation of an instrument to measure microcirculatory blood flow and oxygen saturation simultaneously. *J Med Eng Technol* 1992; **16**: 123-128.
65. Dougherty G, Barnett N J, Pettinger S J. A prototype instrument combining laser doppler flowmetry and reflection pulse oximetry. *Clin Phys Physiol Meas* 1992; **13**: 105-114.
66. MacDonald P H, Dinda P K, Beck I T, Mercer C D. The use of oximetry in determining intestinal blood flow. *Surg Gynecol Obstet* 1993; **176**: 451-458.
67. Katz Y, Shoshani G. Intraoperative assessment of blood flow to strangulated stomach by pulse oximetry. *J Ped Surg* 1992; **27**: 509-510.
68. Norton L H, Squires B, Craig N P, McLeay G, McGrath P, Norton K I. Accuracy of pulse oximetry during exercise stress testing. *Int J Sports Med* 1992; **13**: 523-527.
69. Martin D, Powers S, Cicale M, Collop N, Haung D, Criswell D. Validity of pulse oximetry during exercise in elite endurance athletes. *J Appl Physiol* 1992; **72**: 455-458.
70. Beydon L, Hassapopoulos J, Quera M A et al. Risk factors for oxygen desaturation during sleep, after abdominal surgery. *Br J Anaesth* 1992; **69**: 137-142.
71. Rosenberg J, Wildschödtz G, Pedersen M H, von Jessen F, Kehlet H. Late postoperative nocturnal episodic hypoxaemia and associated sleep pattern. *Br J Anaesth* 1994; **72**: 145-150.
72. Braggion C, Pradal U, Mastella G. Hemoglobin desaturation during sleep and daytime in patients with cystic fibrosis and severe airway obstruction. *Acta Paediatr* 1992; **81**: 1002-1006.
73. Smith T C, Proops D W, Pearman K, Hutton P. Hypoxia in sleeping children: overnight studies can be reduced to 4 hours without loss of clinical significance. *Clin Otolaryngol* 1992; **17**: 243-245.
74. Hedner J A, Wilcox I, Laks L, Grunstein R R, Sullivan C E. A specific and potent pressor effect of hypoxia in patients with sleep apnea. *Am Rev Respir Dis* 1992; **146**: 1240-1245.
75. Sériès F, Pierre S St, Carrier G. Effect of surgical correction of nasal obstruction on the treatment of obstructive sleep apnea. *Am Rev Respir Dis* 1992; **146**: 1261-1265.
76. Pack A I. Simplifying the diagnosis of obstructive sleep apnea. *Ann Intern Med* 1993; **119**: 528-529.
77. Issa F G, Morrison D, Hadjuk E, Iyer A, Feroah T, Remmers J E. Digital monitoring of sleep-disordered breathing using snoring sound and arterial oxygen saturation. *Am Rev Respir Dis* 1993; **148**: 1023-1029.
78. Johannessen N, Jensen P F, Kristensen S, Juul A. Nasal packing and nocturnal oxygen desaturation. *Acta Otolaryngol* 1992; Suppl: **492**: 6-8.
79. Reeder M K, Goldman M D, Loh L, Muir A D, Casey K R, Lehane J R. Late postoperative nocturnal dips in oxygen saturation in patients undergoing major abdominal vascular surgery. *Anaesthesia* 1992; **47**: 110-115.
80. Williams A J, Stein M. Screening for obstructive sleep apnea using pulse oximetry. *West J Med* 1992; **157**: 175-176.
81. Matthews R W, Malkawi Z, Griffiths M J, Scully C. Pulse oximetry during minor oral surgery with and without intravenous sedation. *Oral Surg Oral Med Oral Pathol* 1992; **74**: 537-543.
82. Kitagawa E, Iida A, Kimura Y et al. Responses to intravenous sedation by elderly patients at the Hokkaido University Dental Hospital. *Anesth Prog* 1992; **39**: 73-78.
83. Zacharias M, Luyk N H, Parkinson R T. Oxygen saturation during intravenous sedation using midazolam. *N Z Dent J* 1992; **88**: 94-96.
84. Kluger M T, Owen H, Watson D et al. Oxyhaemoglobin saturation following elective abdominal surgery in patients receiving continuous intravenous infusion or intramuscular morphine analgesia. *Anaesthesia* 1992; **47**: 256-260.
85. McNamara H, Chung C, Lilford R, Johnson N. Do fetal pulse

- oximetry readings at delivery correlate with cord blood oxygenation and acidemia. *Br J Obstet Gynaecol* 1992; **99**: 735-738.
86. McNamara H, Johnson N, Lilford R. The effect on fetal arterial oxygen saturation resulting from giving oxygen to the mother measured by pulse oximetry. *Br J Obstet Gynaecol* 1993; **100**: 446-449.
 87. Harris A P, Sendak M J, Chung D C, Richardson C A. Validation of arterial oxygen saturation measurements in utero using pulse oximetry. *Am J Perinatol* 1993; **10**: 250-254.
 88. Mendelson Y, Solomita M V. The feasibility of spectrophotometric measurements of arterial oxygen saturation from the fetal scalp utilizing noninvasive skinreflectance pulse oximetry. *Biomed Instrum Technol* 1992; **26**: 215-224.
 89. Johnson N, McNamara H. Monitoring the fetus with a sensor covered with an irregular surface can cause scalp ulceration. *Br J Obstet Gynaecol* 1993; **100**: 961-963.
 90. Dimich I, Singh P P, Adell A, Hendler M, Sonnenklar N, Jhaveri M. Evaluation of oxygen saturation monitoring by pulse oximetry in neonates in the delivery system. *Can J Anaesth* 1991; **38**: 985-988.
 91. Samuels M P, Poets C F, Stebbens V A, Alexander J A, Southall D P. Oxygen saturation and breathing pattern in preterm infants with cyanotic episodes. *Acta Paediatr* 1992; **81**: 875-880.
 92. Durand M, McEvoy C, MacDonald K. Spontaneous desaturations in intubated very low birth weight infants with acute and chronic lung disease. *Pediatr Pulmonol* 1992; **13**: 136-142.
 93. Spear M L, Stefano J L, Spitzer A R. Prolonged apnea and oxymoglobin desaturation in asymptomatic premature infants. *Pediatr Pulmonol* 1992; **13**: 151-154.
 94. Mikawa K, Maekawa N. A simple alternate technique for the application of the pulse oximeter probe to infants (letter). *Anesthesiology* 1992; **77**: 400-401.
 95. Lozano J M, Duque O R, Buitrago T, Behaine S. Pulse oximetry reference values at high altitude. *Arch Dis Child* 1992; **67**: 299-301.
 96. Bergqvist G. Oxygen saturation in newborns at altitude (letter). *Am J Dis Child* 1992; **146**: 1134.
 97. Bachman J J, Beatty T, Levene D E. Oxygen saturation in high-altitude pulmonary edema. *J Am Board Fam Pract* 1992; **5**: 429-431.
 98. Pope L L, Hankins G D. Pulse oximetry. Applications in the labor-and-delivery unit of a tertiary care center. *J Reprod Med* 1991; **36**: 853-856.
 99. Moller J T, Svernild I, Johannessen N W et al. Perioperative monitoring with pulse oximetry and late postoperative cognitive dysfunction. *Br J Anaesth* 1993; **71**: 340-347.
 100. Khoo S T, Woo M, Kumar A. An assessment of preoxygenation techniques using the pulse oximeter. *Ann Acad Med Singapore* 1992; **21**: 705-707.
 101. de Kock J P, Tarassenko L. In vitro investigation of the factors affecting pulse oximetry. *J Biomed Eng* 1991; **13**: 61-66.
 102. Shimada Y, Yoshiya I, Oka N, Hamaguri K. Effects of multiple scattering and peripheral circulation on arterial oxygen saturation measured with a pulse-type oximeter. *Med & Biol Eng & Comput* 1984; **22**: 475-478.
 103. Mendelson Y, Kent J C. An in vitro tissue model for evaluating the effect of carboxyhemoglobin concentration on pulse oximetry. *IEEE Trans Biomed Eng* 1989; **36**: 625-627.
 104. Reynolds K J, Moyle J T B, Sykes M K, Hahn C E W. Response of 10 pulse oximeters to an in vitro test system. *Br J Anaesth* 1992; **68**: 365-369.
 105. Reynolds K J, Palayiwa E, Moyle J T B, Sykes M K, Hahn C E W. The effect of dyshemoglobins on pulse oximetry: part I, theoretical approach and part II, experimental results using an in vitro test system. *J Clin Monit* 1993; **9**: 81-90.
 106. de Kock J P, Tarassenko L. Pulse oximetry: theoretical and experimental methods. *Med & Biol Eng & Comput* 1993; **31**: 291-300.
 107. Shellock F G, Slimp G. Severe burn of the finger caused by using a pulse oximeter during MR imaging (letter). *AJR* 1989; **153**: 1105.
 108. Holshouser B A, Hinshaw D B, Shellock F G. Sedation, anesthesia, and physiological monitoring during MRI. In: ARRS Syllabus. Reston, VA: American Roentgen Ray Society; 1991: 9-15.
 109. Shellock F G, Myers S M, Kimble K J. Monitoring heart rate and oxygen saturation with a fiber-optic pulse oximeter during MR imaging. *AJR Am J Roentgenol* 1992; **158**: 663-664.
 110. Lindberg L-G, Ugnell H and Öberg P. Monitoring of respiratory- and heart rates using a fibre optic sensor. *Med & Biol Eng & Comput* 1992; **30**: 533-537.
 111. Vegfors M, Ugnell H, Hök B, Öberg P Å, Lennmarken C. Experimental evaluation of two new sensors for respiratory rate monitoring. *Physiological Measurement* 1993; **14**: 171-181.
 112. Schnettler J M, Wallace J A. Pulse oximetry as a diagnostic tool of pupal vitality. *J Endod* 1991; **17**: 488-490.
 113. Mills R W. Pulse oximetry - a method of vitality testing for teeth. *Br Dent J* 1992; **9**: 334-335.
 114. de Kock J P, Tarassenko L, Glynn C J, Hill A R. Reflectance pulse oximetry measurements from the retinal fundus. *IEEE Trans Biomed Eng* 1993; **40**: 817-823.
 115. McCormick P W, Balakrishnan G, Stewart M, Lewis G, Ausman J I. Cerebral oxygen metabolism measured during hypothermic circulatory arrest. A case report. *J Neuro Anest* 1991; **3**: 302-307.
 116. McCormick P W, Stewart M, Goetting M G, Balakrishnan G. Regional cerebrovascular oxygen saturation measured by optical spectroscopy in humans. *Stroke* 1991; **22**: 596-602.
 117. McCormick P W, Stewart M, Goetting M G, Dujovny M, Lewis G, Ausman J I. Noninvasive cerebral optical spectroscopy for monitoring cerebral oxygen delivery and hemodynamics. *Crit Care Med* 1991; **19**: 89-97.
 118. McCormick P W, Stewart M, Lewis G, Dujovny M, Ausman J I. Intracerebral penetration of infrared light. *J Neurosurg* 1992; **76**: 315-318.

Address:

Magnus Vegfors, M.D. Ph.D.
 Department of Anaesthesiology
 University Hospital
 S-581 85 Linköping
 Sweden

Title: ACCURACY OF PULSE OXIMETRY IN CYANOTIC CONGENITAL HEART DISEASE

Authors: V.A. Lazzell, M.D. and M.W. Jopling, M.D.

Affiliation: Department of Anesthesiology, West Virginia University
School of Medicine, Morgantown, West Virginia 26506

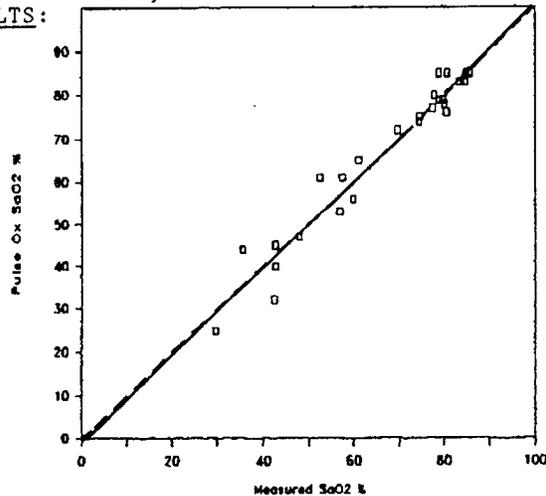
INTRODUCTION:

Children with cyanotic congenital heart disease (CCHD) during their perioperative course can undergo rapid changes in their physical status. Measurement of oxygen saturation (SaO₂) is an invaluable monitor to detect hypoxemia, as well as to optimize pulmonary and systemic blood flows during anesthesia and in the ICU (1). While several investigators have evaluated oximetry in the 90 % SaO₂ range (1,2,3), we have investigated the accuracy of SaO₂ values less than 85 % as derived from pulse oximetry.

METHODS:

Nine children, ages 4 days - 18 months with various CCHD defects were studied. This study was approved by the Institutional Review Board. Simultaneous routine measurements of SaO₂ by pulse oximetry and arterial blood gas co-oximetry in the same extremity were obtained perioperatively. Blood drawn from an indwelling arterial line was evaluated for pH, pO₂, pCO₂, HCO₃, SaO₂ and hemoglobin content. The co-oximeter, an Instrumentation Laboratories IL282, measured the arterial blood SaO₂ (% O₂ Hgb). Continuous SaO₂ was monitored using the Nellcor N-100 pulse oximeter. Co-oximeter and pulse oximeter SaO₂ values were compared by linear regression analysis.

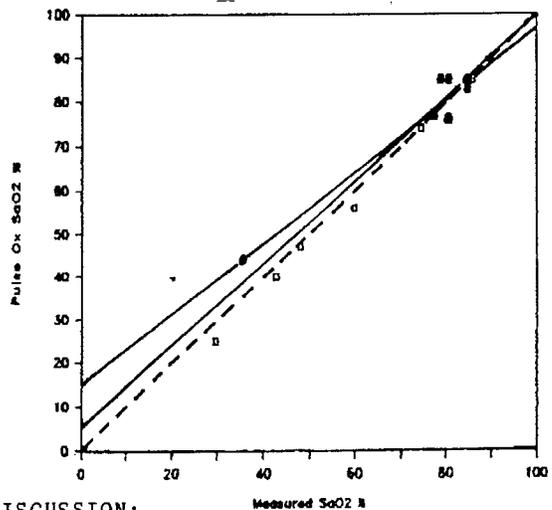
RESULTS:



Twenty-six paired measurements were made of pulse oximetry and co-oximetry SaO₂ of values less than or equal to 85%. Linear regression analysis of the paired arterial blood and pulse oximetry SaO₂ values revealed a correlation $Y = 1.01x - 0.71$, $r = 0.97$. The standard error of the esti-

mate (SEE) = 4.1, N = 26. The regression is demonstrated by the solid line and the dashed line is the line of identity in the figure above.

The question has been raised as to whether the regression analysis of such pooled patient data is valid.(4) Individual linear regression analysis was performed in two of our patients with N > 4. The regression equations were: $Y = 0.823x + 14.9$, $r = 1.0$, SEE = 3.2, N = 7 and $Y = 1.06x - 5.7$, $r = 1.0$, SEE = 1.2, N = 6. These are illustrated in the following figure:



DISCUSSION:

These results demonstrate a good correlation between pulse oximeter and arterial blood co-oximeter SaO₂ for values less than or equal to 85%. Pulse oximetry allows accurate continuous assessment of the patient's arterial oxygenation by means of a rapid noninvasive method of measurement.

REFERENCES:

1. Lynn AM, Bosenberg A: Pulse oximetry during cardiac catheterization in children with congenital heart disease. J Clin Monit 1(3):156-160, 1985.
2. Fanconi S, Doherty P, et al: Pulse oximetry in pediatric intensive care: comparison with measured saturations and transcutaneous oxygen tension. J Pediatr 107(3):362-366, 1985.
3. Yelderman M, New W Jr: Evaluation of pulse oximetry. Anesthesiology 59(4):349-352, 1983.
4. Lichtor JL: Regression lines using multiple measurements from multiple patients. Anes Anal 66(4):367-68, 1987.

brief report

Noninvasive pulse oximetry in children with cyanotic congenital heart disease

ROBERT A. BOXER, MD; ILENE GOTTESFELD, RN, MN; SHARANJEET SINGH, MD;
MICHAEL A. LACORTE, MD; VINCENT A. PARNELL, JR, MD; PETER WALKER, MD

Arterial oxygen saturation, determined noninvasively by pulse oximetry in 32 pediatric patients with cyanotic congenital heart disease (CHD), was compared with oxygen saturation measured by a cooximeter in simultaneously obtained arterial blood samples. The patients were studied in the cardiac catheterization laboratory, operating room, and ICU. Excellent correlation by linear regression ($n = 108$, $r = .95$) was observed between the two methods at oxygen saturations ranging from 35% to 95%. These observations show that in infants and children with cyanotic CHD, arterial oxygen saturations can be determined accurately and reliably by pulse oximetry at rest and during changing circulatory states.

(Crit Care Med 1987; 15:1062)

Oxygen delivery to tissues is of major clinical interest in patients with cyanotic congenital heart disease (CHD). Arterial blood gas analysis is used commonly to determine the adequacy of oxygenation in cyanotic patients. However, *in vitro* determinations of arterial oxygen saturation (SaO_2) and tension are invasive procedures requiring arterial entry with intermittent sampling. Continuous transcutaneous oxygen tension monitoring requires calibration, induces cutaneous hyperthermia necessitating frequent changes of sensor location, and may correlate poorly with actual PaO_2 during low cardiac output states (1). Pulse oximetry is an alternative, noninvasive method which provides rapid, continuous monitoring of SaO_2 (2).

The present study describes our initial experience with the use of pulse oximetry for the noninvasive determination of SaO_2 in children with moderate to severe cyanosis due to CHD. The accuracy of SaO_2 determined by pulse oximetry was evaluated by com-

paring it with direct measurement of SaO_2 by a cooximeter in simultaneously obtained blood samples.

PATIENTS AND METHODS

The study group was comprised of 32 infants and children with ages ranging from 3 months to 15 yr (mean 4.6 yr) and weights varying from 2.5 to 46 kg (mean 15). Cardiac diagnoses included tetralogy of Fallot ($n = 21$), transposition of the great arteries ($n = 5$), single ventricle ($n = 4$), pulmonary atresia ($n = 1$), and tricuspid atresia ($n = 1$).

SaO_2 measurements, noninvasive and by cooximeter, were determined during cardiac catheterization, in the ICU, or in the operating room during palliative shunt procedures. Arterial blood samples were obtained from indwelling arterial lines.

Noninvasive SaO_2 was determined by a pulse oximeter (N-100, Nellcor, Inc., Hayward, CA), consisting of an electro-optical sensor coupled to a microprocessor-based signal processor and light-emitting diode display. The sensor was applied to the finger in children over 2 yr of age; in younger patients, the site of application included the great toe, the dorsum of the foot, or the finger. Calculated SaO_2 results are displayed automatically along with the heart rate (HR) in a digital mode. The application of the skin sensor does not result in skin penetration, tissue constriction, electrical contact, or heat transfer. To ensure reliability of the pulse oximeter readings, the pulse readout on the oximeter had to agree within 10 beat/min with the HR determined by an ECG monitor.

In vitro analysis of SaO_2 was performed by a cooximeter (IL-282, Instrumentation Laboratories, Lexington, MA) using 0.5 ml of arterial blood. Arterial BP, monitored continuously using fluid-filled pressure transducers, was displayed along with the ECG.

Statistical Analysis

SaO_2 measurements determined by pulse oximetry and by cooximeter were compared using standard linear regression analysis and paired *t*-tests. To examine

From the Departments of Pediatrics (Drs. Boxer, Singh, and LaCorte and Ms. Gottesfeld), Surgery (Dr. Parnell), and Anesthesiology (Dr. Walker), North Shore University Hospital, and Cornell University Medical College, Manhasset, NY.

Address requests for reprints to: Robert A. Boxer, MD, Pediatric Cardiology, North Shore University Hospital, 300 Community Drive, Manhasset, NY 11030.

whether the relationship between SaO_2 determined by the two methods was consistent with respect to the patient's weight, age, hemoglobin (Hgb) concentration, HR, and mean arterial BP (MAP), the correlation between the paired differences of pulse oximeter minus measured SaO_2 values vs. each variable was calculated by linear regression analysis. In addition, the data were evaluated by computing the bias (mean difference of paired values of SaO_2 from the cooximeter minus the pulse oximeter) and the precision (the SD of these differences).

RESULTS

In the 32 patients, Hgb concentrations ranged from 12 to 19.9 g/dl (mean 16.4), MAP varied between 35 and 91 mm Hg (mean 64), and measured SaO_2 varied between 35% and 95% (mean 82.6).

One hundred and eight data pairs were available for comparing SaO_2 determined by the pulse oximeter and cooximeter methods. Linear regression analysis of SaO_2 from these two methods yielded a slope of 1.01, which is significantly ($p = .001$) different from zero; the intercept (0.15), however, was not different from zero. The resulting equation describing the relationship of pulse oximeter to cooximeter SaO_2 was $y = 1.01x + 0.15$ ($r = .95$; Fig. 1). Linear regression analysis of the paired differences between pulse oximeter and cooximeter SaO_2 showed that the discrepancy between SaO_2 determined by these two methods was unaffected by the patient's weight, age, Hgb concentration, MAP, or HR. For all 108 data pairs, the bias was -0.87 , with a

precision (SD) of 3.70. When the data pairs were divided into two groups on the basis of cooximeter $SaO_2 > 80\%$ ($n = 46$) and $SaO_2 \leq 80\%$ ($n = 62$), the bias and precision for each group were $-0.56, 2.33$ and $-1.09, 4.46$, respectively.

The accuracy of SaO_2 readouts from the pulse oximeter was, however, dependent on the proper application of the sensor. A large discrepancy between the HR determined by ECG monitoring and that measured by pulse oximeter was observed in five patients, requiring reapplication of the sensor so that the pulse rates coincided within 10 beat/min.

In eight children, the pulse oximetry provided valuable information concerning instantaneous changes in SaO_2 during rapidly changing hemodynamic states before any manifest clinical signs or symptoms. Four patients with tetralogy of Fallot had hypoxic spells; three patients had significant intraoperative changes in SaO_2 during placement of an aorto-pulmonary shunt; in one patient, changes in oxygenation were studied after balloon atrial septostomy.

DISCUSSION

The results of our study have demonstrated that pulse oximetry is a noninvasive, accurate method of determining SaO_2 in cyanotic patients under various clinical states. Other workers (3-6) have reported that pulse oximetry provides reliable evaluation of SaO_2 in adults with respiratory distress and in critically ill pediatric patients in the pediatric or neonatal ICU.

This study reports accurate measurements of SaO_2 by pulse oximetry obtained over a wide range of SaO_2 varying from 35% to 95% and MAP (31 to 91 mm Hg). There was close agreement between the two methods of SaO_2 determination, with a slight tendency for pulse oximetry to overestimate the in vitro SaO_2 . When cooximeter $SaO_2 > 80\%$, this overestimation is larger than when $SaO_2 \leq 80\%$. In the former group, the bias was -0.56 ± 2.33 (SD), and in the latter group, it was -1.09 ± 4.46 . Therefore, in more profound hypoxemic states, the pulse oximeter was slightly less precise; however, this difference was not clinically significant and did not substantially affect patient management or identification of arterial desaturation. In our patients, the relationship between the pulse oximeter and measured SaO_2 did not vary according to weight, age, Hgb concentration, or MAP. However, it is possible that the accuracy of pulse oximetry may vary under more extreme conditions of hypotension, hypoxemia, and anemia than exhibited by the patients in this study group.

The reliability of the pulse oximeter is dependent on proper application of the sensor probe, which can be verified by accurate tracking of the pulse of the oximeter. The sensor had to be reapplied in five patients due to excessive movement of the patient ($n = 3$), improper sensor application ($n = 1$), and sensor mal-

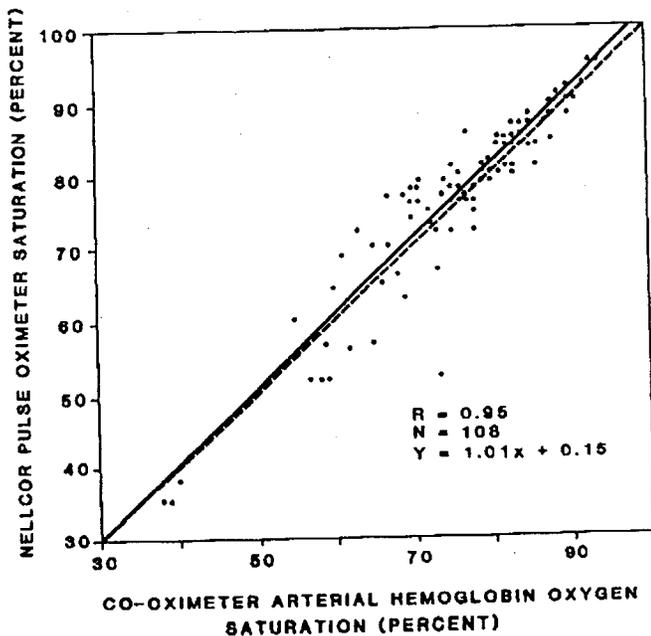


FIG. 1. Comparison of simultaneous pulse oximeter SaO_2 on the y-axis and in vitro SaO_2 determined by a cooximeter on the x-axis. The dashed line indicates the line of identity.

function ($n = 1$). Once the adjustments were made, accurate readings were obtained from all sites of application. The probe could be left in place indefinitely without any morbidity.

Since children with cyanotic CHD are hypoxemic, conditions causing further deterioration in SaO_2 may be life-threatening. Hypoxic spells or intraoperative manipulation of the airway or pulmonary vasculature result in rapid diminution of pulmonary blood flow and ventilation/perfusion inequalities. Recognition of these altered states of oxygenation by clinical variables is very difficult, especially when the patient is covered with sterile drapes in the catheterization laboratory or operating room. Measurement of arterial blood gases requires insertion of an indwelling arterial line and loss of blood. Loss of valuable time occurs in blood gas analysis, and prompt treatment is delayed. These problems can be obviated by the use of the noninvasive pulse oximeter, which provides a continuous and accurate readout of SaO_2 . Thus, appropriate changes in therapy can be made to improve SaO_2 .

In summary, in children with cyanotic CHD, the noninvasive measurement of SaO_2 by pulse oximetry was found to be accurate during conditions of cardiac

catheterization and cardiac surgery and in the ICU. When the sensor is applied properly, the oximeter reveals instantaneous readouts of SaO_2 , allowing immediate changes in clinical management to be made when alterations in oxygenation occur.

ACKNOWLEDGMENT

We gratefully acknowledge Martin Lesser, PhD, for assistance in the statistical analysis.

REFERENCES

1. Tremper KK, Shoemaker WC: Transcutaneous oxygen monitoring of critically ill adults, with and without low flow shock. *Crit Care Med* 1981; 9:706
2. Yelderman M, New W: Evaluation of pulse oximetry. *Anesthesiology* 1983; 59:349
3. Mimh FG, Halperin BD: Noninvasive detection of profound arterial desaturations using a pulse oximetry device. *Anesthesiology* 1985; 62:85
4. Swedlow DB, Stern S: Continuous noninvasive oxygen saturation monitoring in children with a new pulse oximeter. *Abstr. Crit Care Med* 1983; 11:228
5. Deckardt R, Steward DJ: Noninvasive arterial hemoglobin oxygen saturation versus transcutaneous oxygen tension monitoring in the preterm infant. *Crit Care Med* 1984; 12:935
6. Fanconi S, Doberty P, Edmonds JF, et al: Pulse oximetry in pediatric intensive care: Comparison with measured saturations and transcutaneous oxygen tension. *J Pediatr* 1985; 107:362

Original Article

Reflectance Pulse Oximetry from Core Body in Neonates and Infants: Comparison to Arterial Blood Oxygen Saturation and to Transmission Pulse Oximetry

Amir Kugelman, MD
Yoram Wasserman, PhD
Frida Mor, RN, BA
Leonid Goldinov, BSc
Yoav Geller
David Bader, MD

CONCLUSIONS: Reflectance pulse oximetry measured from core body of neonates and infants is accurate and reliable and is comparable to the transmission SpO₂ when compared to functional SaO₂. We speculate that the reflectance method might be advantageous in cases of poor peripheral perfusion in neonates and infants.

Journal of Perinatology (2004) **24**, 366–371. doi:10.1038/sj.jp.7211102
Published online 1 April 2004

OBJECTIVE: To compare pulse oximetry oxygen saturation (SpO₂) measured by a novel reflectance method from core body to arterial oxygen saturation (SaO₂) in neonates and infants. Transmission pulse oximetry (TPO) was measured for comparison.

STUDY DESIGN: We monitored 18 infants by the two pulse oximeters simultaneously. The reflectance pulse oximetry (RPO) (PRO2, ConMed, Utica, NY) was measured on the upper back or chest, while the TPO (N395-Nellcor, Pleasanton, CA) was measured from the finger of the infant on the left hand or feet. Data from the two methods were compared to functional SaO₂ derived from blood sample drawn from arterial line for patient care and measured by a Co-oximeter (Ilex, Instrument Lab, Lexington, MA). The potential advantage of the RPO is demonstrated in a case of a premature infant with hypovolemic shock, where SaO₂ or TPO could not be obtained but oximetry was available from the RPO.

RESULTS: We used for analysis 56 RPO and 32 TPO measurements. SpO₂ obtained from the RPO was 88.3±9.8%, from the TPO 84.2±10.1%, and functional SaO₂ was 88.2±11.7%, with correlation coefficient of 0.93 and 0.88, respectively ($p < 0.0001$). The mean difference (bias) and standard deviation of the differences (precision) between the RPO and the TPO compared to functional SaO₂ were $-0.09 \pm 4.5\%$ and $1.26 \pm 5.9\%$ and the absolute errors were $3.2 \pm 3.1\%$, and $4.4 \pm 4.0\%$, respectively. The accuracy of both RPO and TPO was diminished when SaO₂ was $< 85\%$, but only the RPO remained correlated with the functional SaO₂.

INTRODUCTION

Pulse oximetry arterial oxygen saturation (SpO₂) has become the “fifth vital sign” in the examination of every newborn and infant with respiratory system presentation.^{1–3} Pulse oximetry is not invasive, easy to use, has no side effects, is accurate and allows continuous monitoring and is the preferred method of oxygen monitoring in neonates.^{4,5}

However, the traditional method of transmission pulse oximetry (TPO) has several limitations. In conditions of poor peripheral perfusion or cardiovascular collapse, the measurements of this method are not accurate, and in case of arm or leg movements, motion artifacts may emerge.^{3,6,7} The reflectance pulse oximetry (RPO) is a potential alternative to the traditional TPO. Few investigators have tried to use this method in neonates.^{8–10} A novel RPO (with innovated sensor and internal algorithm) capable of measuring from core body of neonates is presented. Its major advantage would be in overcoming the limitations of TPO.

The aim of our study was to compare the RPO SpO₂ from core body to arterial oxygen saturation in neonates and infants. TPO was measured simultaneously for comparison.

METHODS

We monitored 18 infants by the two methods (RPO and TPO) simultaneously, and data were collected on a computer placed at the bedside. The reflectance oximetry (PRO2, ConMed Corporation, Utica, NY) was measured on the upper back or chest, while the transmission oximetry (N395-Nellcor, Pleasanton, CA) was measured from the finger of the infant on the left hand or the foot. Data from the two methods were compared to functional arterial oxygen saturation (SaO₂) derived from blood samples drawn from an arterial line placed for patient care. SaO₂ (%HbO₂/

Department of Neonatology, Bnai Zion Medical Center, B Rappaport Faculty of Medicine, Technion-IT, Haifa, Israel

Data were presented in part as a poster at the Pediatric Academic Society meeting in Baltimore 2002 (“late breaker” session) and in the ATS meeting in Seattle 2003. This work was supported by ConMed Corporation, Utica, NY, USA.

Address correspondence and reprint requests to Amir Kugelman, MD, Department of Neonatology, Bnai Zion Medical Center, 47 Golomb Street, Haifa 31048, Israel

$[100\% - (\%HbCO + \%MetHb)] \times 100$) was measured by a co-oximeter (Ilex 482, Instrument Lab., Lexington, MA). Informed consent was obtained from all parents whose infants participated in the study, which was approved by the Investigational Review Board in our center.

The PRO2 reflectance pulse oximeter consists of a sensor that emits and detects red and infrared light, holder and a microprocessor-controlled monitoring signal processing unit. The sensor is based on unique geometry, in which light source derives light from the center of the chip in three different wavelengths (one red, 660 nm, and two infrared, 850 and 940 nm). The effective detecting areas are defined two optic rings, which are arranged concentrically around the central light sources. Since the rings constitute an angular shape, the detection area is capable of acquiring signals from a larger tissue zone (multipath) than with TPO. The internal algorithm enables analysis of signals obtained from newborns and adults. We used for TPO the Nellcor model N395 that represents the group of modern pulse oximeters that was found to be reliable in combination of the most challenging situations of motion and reduced perfusion.⁶ Figure 1 illustrates the differences between the RPO and the TPO oximeters.

Statistical Analysis

Linear regression analysis was used to compare the SpO₂ determined by the two methods (reflectance and transmission) to functional SaO₂ measured by a co-oximeter. We calculated bias

and precision of the reflectance and transmission oximetry when compared to functional SaO₂; $p < 0.05$ was considered significant. Data are presented as mean \pm SD.

RESULTS

Patients' Characteristics

Our patients' characteristics are shown in Table 1. They comprise of infants with a relatively low and wide range of oxygen saturation (mean \pm SD by RPO was 88.3 \pm 9.8%, by the TPO 84.2 \pm 10.1%, and the functional SaO₂ was 88.2 \pm 11.7%) (Figure 2a, b). The infant's weight ranged from 1.2 to 14.7 kg (3.7 \pm 3.0 kg) and the study age ranged from day 1 in a premature infant (gestational age 29 weeks) to 618 days (median: 4.5 days). The mean blood pressure was 52 \pm 12 mmHg. The RPO was placed on core-body sites (back or chest). All infants had an indwelling arterial catheter for clinical care: eight umbilical, one left radial, and two femoral. No side effects were seen during the study.

Reflectance and Transmission Pulse Oximetry vs Functional SaO₂

We used for analysis of the reflectance (PRO2) method 56 measurements (3.1 \pm 1.8 measurements per patient) and for the transmission (N395-Nellcor) method 32 measurements from the 18 patients (some transmission oximetry data collected by other instruments were omitted from analysis for consistency). Both, reflectance and transmission oximetry significantly correlated with functional SaO₂ ($p < 0.0001$); correlation coefficients were 0.93 (0.90 for $n = 32$) and 0.88, respectively (Figure 2a, b).

Mean difference (bias) and SD of the differences (precision) for the RPO and the TPO compared to functional SaO₂ were $-0.09 \pm 4.5\%$ ($0.86 \pm 5.4\%$ for $n = 32$) and $1.26 \pm 5.9\%$, respectively (Figure 3a, b). The absolute errors were $3.2 \pm 3.1\%$ ($3.7 \pm 3.9\%$ for $n = 32$) and $4.4 \pm 4.0\%$, respectively. Analysis of the data with SaO₂ below 85% includes 23 RPO measurements and 21 TPO measurements. The regression analysis for RPO and TPO as compared with functional SaO₂ had a correlation coefficient of 0.58 ($p < 0.005$) and 0.35 ($p = 0.11$, NS), respectively. The mean difference was $2.4 \pm 5.4\%$ and $2.9 \pm 6.6\%$, and the SD of the absolute errors was 4.4 and 4.1%, respectively. Thus, the accuracy of both methods in the low range of oxygen saturation ($< 85\%$) was diminished, but remained significantly correlated to functional SaO₂ only with the RPO method. The following case report illustrates the potential significance of the RPO measured from core body in a premature newborn.

Case Report

A preterm male infant, the third of a triplet, was born via cesarian section at 32 weeks of gestation with a birthweight of 1370 g. His course was uneventful until day 9 of life when the diagnosis of necrotizing enterocolitis was made, which required surgery. The infant returned from the operating room to the NICU in

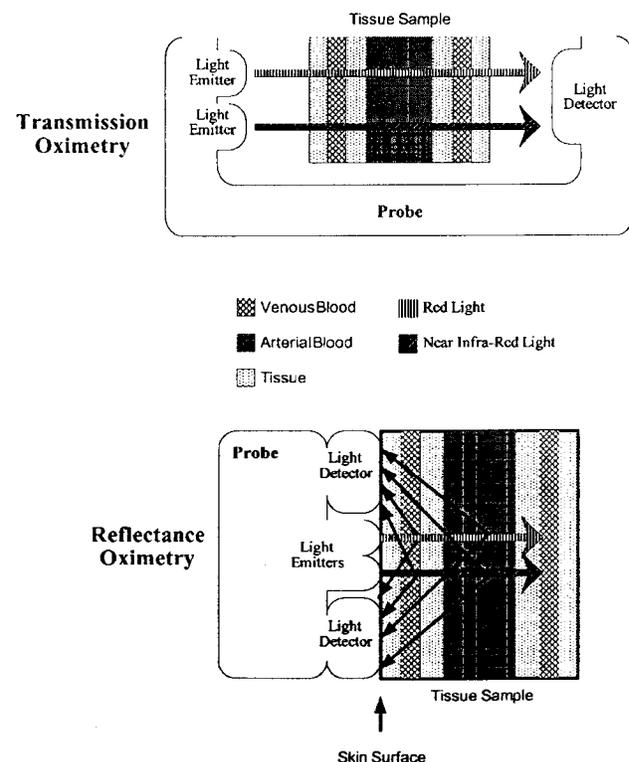


Figure 1. The principle difference between transmission and reflectance pulse oximetry.

Table 1 Patients' Characteristics

	BW*	SW*	GA*	SA*	Race [†]	Sex	Diagnosis [‡]
1	2.25	2.2	34	1	H	M	RDS, PDA, cardiomegaly
2	2.60	2.8	37	8	C	M	Asphyxia, PPHN, RDS
3	3.03	2.2	39	4	C	F	Poor LV function
4	2.99	2.9	37	3	C	F	RDS, PPHN
5	3.47	3.38	37	3	A	F	Ebsteins anomaly
6	3.87	3.84	40	1	C	F	RDS, sepsis
7	2.53	2.58	34	2	C	M	RDS
8	1.58	1.52	36	2	H	M	RDS
9	2.47	2.47	35	1	H	M	RDS
10	2.88	2.81	39	5	C	F	HLHS
11	4.5	4.25	38	21	C	F	Dextrocardia, ASD, VSD, BT shunt
12	2.74	3.00	40	19	C	M	HLHS, s/p Norwood
13	—	5.00	—	95	A	M	HLHS, s/p Norwood
14	4.19	4.55	40	9	C	M	HLHS, s/p Norwood
15	3.05	14.7	40	618	Af.	M	DORV, TAPVR Mitral stenosis
16	2.63	5.9	38	124	C	F	Ebstein anomaly, VSD
17	1.52	1.5	29.5	1	C	F	RDS
18	1.22	1.2	29	5	C	M	RDS, PDA

*BW = birth weight (kg), SW = study weight (kg), GA = gestational age (weeks), SA = study age (days).

[†]C = Caucasian, A = Asian, Af. = African, H = Hispanic.

[‡]RDS = respiratory distress syndrome, VSD = ventricular septal defect, ASD = atrial septal defect, HLHS = hypoplastic left heart syndrome, PDA = patent ductus arteriosus, PPHN = persistent pulmonary hypertension, DORV = double outlet right ventricle, BL shunt = Blalock Taussig shunt, LV = left ventricle.

cardiovascular collapse due to hypovolemic or septic shock. His heart rate was 170 b/min, noninvasive blood pressure 32/17 mmHg and mean of 19 mmHg, temperature 36.6°C, with poor peripheral perfusion and oxygen saturation of 94% by TPO. The hematocrit was 19.3% and platelet count 37,000. It was impossible to obtain a blood gas by inserting an arterial line or by a peripheral or capillary stick. A transfusion of red blood cells, fresh frozen plasma and platelets as well as dopamine and dobutamine were administered. Within an hour, the TPO signal was lost and could not be obtained on any limb. The RPO was placed on his back and gave readings as presented in Figure 4. The capillary blood gas obtained after few hours of intensive treatment showed severe metabolic acidosis (pH 6.8, BE -23.7 meq, HCO₃ 10.6 meq, PO₂ 43 mmHg, PCO₂ 65 mmHg). He received bicarbonate and the ventilator settings were adjusted; however, the next venous blood gas was: pH 7.0, BE -22.5 meq, HCO₃ 9.1 meq, PO₂ 64 mmHg, and PCO₂ 37 mmHg. Despite the maximal support, his mean noninvasive blood pressure increased only temporarily to 32 mmHg for few hours but he remained anuric. The infant died 13 hours after the operation despite aggressive resuscitation efforts.

DISCUSSION

Our study showed that the RPO measured from core body of neonates and infants is accurate and reliable and is comparable to

the transmission SpO₂ when compared to functional SaO₂. The reflectance method is safe to use in neonates and infants. The presented case, demonstrates the potential advantage of measuring reflectance pulse oximetry from core-body in extreme situation of cardiovascular collapse, when no arterial blood gas or transmission SpO₂ are available because of poor peripheral perfusion.

There is a difference between different brands of instruments of TPO.¹¹ In this study, it was found that the Nellcor SpO₂ correlated best with functional SaO₂, that SpO₂ determined by different pulse oximeters is not interchangeable, and that this may be of clinical importance in predicting PaO₂ on the basis of SpO₂. Fetal hemoglobin (HbF) shifts the oxyhemoglobin dissociation curve to the left. Experimental data show that HbF has no clinically significant effects on pulse oximetry.¹¹⁻¹⁵ The degree of HbF of course affects the correlation of SaO₂ to PaO₂. Clinicians concerned with PaO₂ value must understand the effect of HbF when interpreting the SpO₂ reading. Accordingly, we elected to compare the new reflectance oximeter to functional SaO₂. Functional SaO₂ is calculated from measurements derived from co-oximeter (HbO₂, HbCO, MetHb) that determines the SaO₂ by spectrophotometry, and this method is accepted as a valid standard.¹² We also compared our results to the TPO that is currently the common pulse oximetry method used in critical care units of newborns and infants.

TPO can be used reliably for continuous monitoring in normotensive neonates with SaO₂ of 80 to 100%.¹⁶ However, TPO has performance limitations because of motion artifacts,

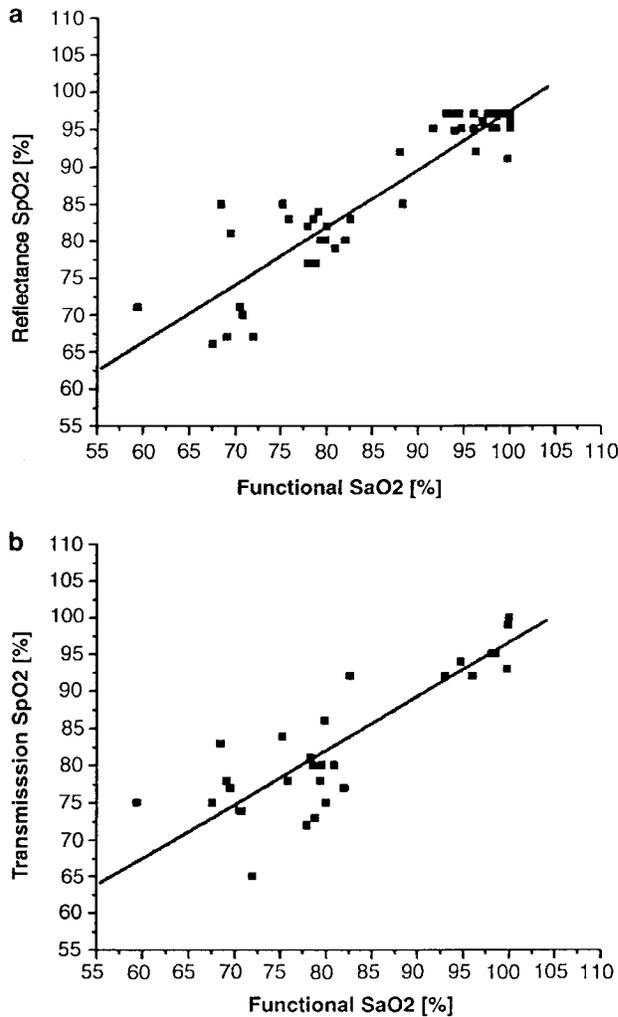


Figure 2. Correlation between reflectance (a) and transmission (b) pulse oximetry (SpO₂) and functional SaO₂ ($r = 0.93$ and 0.88 , respectively; $p < 0.0001$).

hypotension and vasoconstriction.^{3,6,7} While during control desaturation the SpO₂ of the new generation of TPO was within $\pm 3\%$ of the reference reading $>95\%$ of the time, during motion and reduced perfusion the error increased by 20 and 10%, respectively.⁶ In order to minimize these limitations, new transmission pulse oximeters were recently introduced.¹⁷ A different approach to solve these problems was to develop the RPO.

The RPO is designed to measure SpO₂ by reflectance of the signal from the tissue, and not by transmission of the signal through the tissue. Thus, it allows to obtain SpO₂ from core body (chest, back and forehead), and might be less dependent and less affected by peripheral perfusion and movements of the extremities. Faiss et al.⁸ showed close agreement between the reflectance and transmission oximetry in newborns. They had unreliable signals from the back because of breathing artifacts, and both systems were equally sensitive to motion artifacts. Fanconi and Tschupp⁹ reported on accuracy of a new transmittance–reflectance sensor

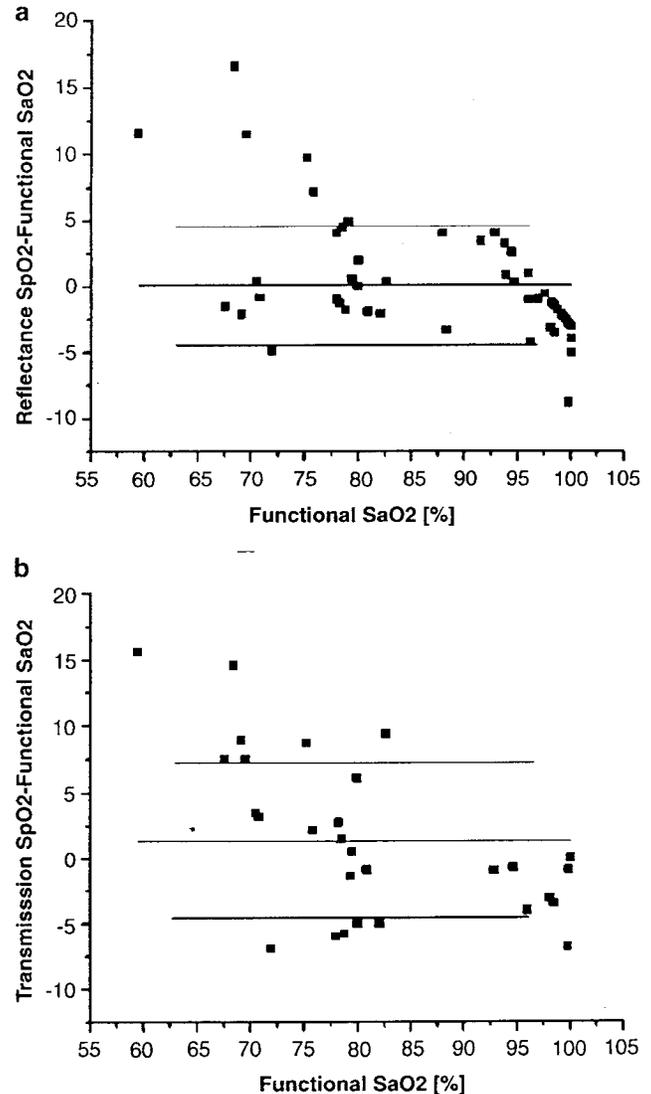


Figure 3. Differences of reflectance (a) and transmission (b) pulse oximetry (SpO₂) and functional SaO₂ (bias and precision: -0.09 ± 4.5 and $1.26 \pm 5.9\%$, respectively).

from hand, foot and calf of newborn infants. They compared SpO₂ from transmittance–reflectance sensor to SaO₂ derived from arterial blood SaO₂. Comparison of femoral or umbilical SaO₂ with lower limb transmittance–reflectance sensor had a mean difference of $1.44 \pm 3.51\%$ and correlation of $r^2 = 0.96$, and radial artery SaO₂ with upper limb transmittance–reflectance sensor had a mean difference of $0.66 \pm 3.34\%$ and $r^2 = 0.94$. The mean error was slightly larger for arterial saturation values $< 90\%$, a recognized limitation of several pulse oximetry devices.^{2,18} They did not report core-body measurements. Takatani et al¹⁰ reported in an animal study, the effect of temperature on TPO and RPO, and they also monitored 18 critical patients perioperatively with the reflectance sensor. To our knowledge, our study is the first to report

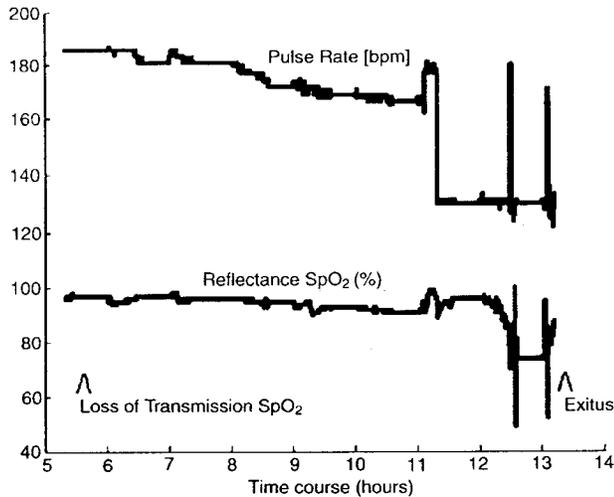


Figure 4. Time course of reflectance pulse oximetry in an infant with severe cardiovascular collapse.

accurate reflectance SpO₂ from core body (chest and back) in newborns and infants compared to functional SaO₂. Our patients were normotensive at the time of the study, but their characteristics (that included respiratory as well as cardiac diagnoses, Table 1) allowed us to evaluate the accuracy of the RPO along a wide range of oxygen saturations (including the low range <85%); SpO₂ obtained from RPO was 88.3±9.8% (range 66 to 97%), from TPO 84.2±10.1% (range 65 to 100%), and functional SaO₂ was 88.2±11.7 (range 59 to 100%); RPO and TPO had comparable accuracy, with correlation coefficient of 0.93 and 0.88, respectively (*p*<0.0001, Figure 2). The mean difference (bias) and the standard deviation of the differences (precision) between RPO and TPO compared to functional SaO₂ was 0.09±4.5% and 1.26±5.9% (Figure 3), and the standard deviation of the absolute errors was 3.1 and 4.0%, respectively. Thus, we found good accuracy (according to published literature⁹) between RPO from core-body of neonates and infants and functional SaO₂. The accuracy was comparable to TPO, which is now the prevailing method of pulse oximetry. Accuracy of pulse oximetry in the low range of oxygen saturation is problematic and several oximeters tend to overestimate the SaO₂ at this range.^{2,18} Analysis of the subgroup of measurements with SaO₂ below 85% includes 23 measurements with RPO and 21 measurements with TPO. The accuracy of both RPO and TPO in the low range of oxygen saturation (<85%) was diminished, but significant correlation with functional SaO₂ was maintained only with the RPO method (*p*<0.005). Our improved results with reflectance oximetry from core body in neonates and infants were probably achieved because of our innovative sensor and the internal algorithm of the PRO2 instrument.

While our patients were relatively well with adequate perfusion at the time of the study, the presented case demonstrated the possible advantage of the RPO compared to TPO in a hypoperfused

patient. The TPO probes need to be placed on tissue that can be easily transilluminated, usually at the periphery of the circulation (finger, toe and ear lobe), where in shock conditions, the changes in pulsatile capillary blood volume are much smaller and more susceptible to errors. In contrast, RPO may be placed on core body areas like the chest and back. In this premature infant with cardiovascular collapse and poor peripheral perfusion, we could not insert an arterial line or obtain an arterial blood gas by a stick, nor could we have continuous monitoring by TPO. The only way that was possible to monitor the oxygenation status of this infant for several hours until his death was SpO₂ measured by RPO (Figure 4).

This study is a preliminary report. Our case report is only an illustration of the potential advantage of the RPO in an extreme situation, and we should be cautious in coming to any conclusion from a single case. Our new RPO sensor needs further evaluation on large number of infants in different situations of hypotension, poor peripheral perfusion, hypothermia, phototherapy, high humidity and other possible physical limitations. It further needs an evaluation for prolonged continuous monitoring as compared to the commonly used TPO, and it needs to be compared to other modern transmission pulse oximeters like the Masimo SET that might be advantageous as compared to the Nellcor N395, according to few recent studies.¹⁷ One of the limitations of our study was the wide range of study weight and postnatal age, and in future studies, will evaluate the RPO in unique groups of infants like very low birth-weight infants (<1500 g).

We conclude that RPO measured from core-body sites of neonates and infants is accurate and reliable and is comparable to the transmission SpO₂ when compared to functional SaO₂. We speculate that the reflectance method might be advantageous in cases of poor peripheral perfusion in neonates and infants.

References

- Mower WR, Sachs C, Nicklin EL, Baraff LJ. Pulse oximetry as a fifth pediatric vital sign. *Pediatrics* 1997;99:681–6.
- Katzman GH. The newborn's SpO₂: a routine vital sign whose time has come? *Pediatrics* 1995;95:161–2.
- Sinex JE. Pulse oximetry: principles and limitations. *Am J Emerg Med* 1999;17:59–67.
- Hay WW, Brockway JM, Eyzaguirre M. Neonatal pulse oximetry: accuracy and reliability. *Pediatrics* 1989;83:717–22.
- Durand M, Ramanathan R. Pulse oximetry for continuous oxygen monitoring in sick newborn infants. *J Pediatr* 1986;109:1052–56.
- Gehring H, Hornberger C, Matz H, Konecny E, Schmuker P. The effect of motion artifact and low perfusion on the performance of new generation of pulse oximeters in volunteers undergoing hypoxemia. *Respir Care* 2002;47:48–60.
- Poets CF, Southall DP. Noninvasive monitoring of oxygenation in infants and children: practical considerations and areas of concern. *Pediatrics* 1995;95:161–2.

8. Faisst K, Hannon W, Jorgensen JS, et al. Reflectance pulse oximetry in neonates. *Eur J Obstet Gynecol Reprod Biol* 1995;61:117–22.
9. Fanconi S, Tschupp A. Accuracy of a new transmittance–reflectance pulse oximetry sensor in critically ill neonates. *Crit Care Med* 1994;22:1142–46.
10. Takatani S, Davies C, Sakakibara N, et al. Experimental and clinical evaluation of a noninvasive reflectance pulse oximeter sensor. *J Clin Monit* 1992;8:257–66.
11. Thilo EH, Anderson D, Wasserstein ML, Schmidt J, Luckey D. Saturation by pulse oximetry: comparison of the results obtained by instruments of different brands. *J Pediatr* 1993;122:620–6.
12. Wukitsch MW, Petterson MT, Tobler DR, Pologe JA. Pulse oximetry: analysis of theory, technology, and practice. *J Clin Monit* 1988;4:290–301.
13. Ramanathan R, Durand M, Larrazabal C. Pulse oximetry in very low birth weight infants with acute and chronic lung disease. *Pediatrics* 1987;79:612–7.
14. Pologe JA, Raney DM. Effects of fetal hemoglobin on pulse oximetry. *J Perinatol* 1987;7:324–6.
15. Rajadurai VS, Walker AM, Yu Vy, Oates A. Effect of fetal haemoglobin on the accuracy of pulse oximetry in preterm infants. *J Paediatr Child Health* 1992;28:43–6.
16. Sardesai S, Durand M, MacEvoy C, Johnson C, Maarek JM. Pulse oximetry in newborn infants with birth weights of 620–4285 grams receiving dopamine and dobutamine. *J Perinatol* 1996;16:31–4.
17. Hay Jr WW, Rodden DJ, Collins SM, Melara DL, Hale KA, Fashaw LM. Reliability of conventional and new pulse oximetry in neonatal patients. *J Perinatol* 2002;22:360–6.
18. Fanconi S. Reliability of pulse oximetry in hypoxic infants. *Pediatrics* 1988;122:424–7.

FOREHEAD PULSE OXIMETRY COMPARED WITH FINGER PULSE OXIMETRY AND ARTERIAL BLOOD GAS MEASUREMENT

Eugene Y. Cheng, MD,
Margaret B. Hopwood, RN,
and Jonathan Kay, MD

Cheng EY, Hopwood MB, Kay J. Forehead pulse oximetry compared with finger pulse oximetry and arterial blood gas measurement.

J Clin Monit 1988;4:223-226

ABSTRACT. Usual monitoring sites for pulse oximetry involve the fingers, toes, ear lobe, and nasal septum. This study examined the performance of a forehead sensor compared with a finger sensor for the pulse oximeter and arterial blood gas (ABG) analysis. Ten healthy adult volunteers and 22 ventilator-dependent patients were studied. The arterial oxygen saturation detected by forehead pulse oximetry (SpO_2) correlated well with finger SpO_2 and arterial oxygen saturation (SaO_2) determined by arterial blood gas analysis in the healthy volunteers. Forehead SpO_2 in mechanically ventilated patients correlated well with finger SpO_2 and SaO_2 when heart rate detected by pulse oximeter differed less than 10% from apical heart rate. Factors that caused a difference in oximeter-detected heart rate and apical heart rate were extensive tissue edema, head movement, and difficulty securing good tape placement. This suggests that when signal strength is weak, causing poor pulse rate detection, there will also be problems associated with accurate SpO_2 .

The forehead pulse oximeter sensor works well on healthy, well-oxygenated volunteers. Difficulty was experienced when applying and using the sensor on critically ill patients. The reliability of the forehead pulse oximeter sensor has not been established at low saturations.

KEY WORDS. Measurement techniques: oximetry. Blood: gas analysis.

Early detection of untoward events in the operating room, postanesthesia care unit, or intensive care unit (ICU) can contribute to the prevention of hypoxic insults. Within the past several years use of the pulse oximeter to monitor a patient's arterial oxygenation has become widespread, both in the operating room and the ICU. Major advantages of pulse oximetry over measurement of arterial blood gases (ABGs) include ease of use, nearly continuous measurement of arterial oxygenation, and noninvasiveness. Standard probes for pulse oximeters are available for the finger, nasal septum, and ear lobe. This study evaluates the accuracy and utility of a new forehead sensor probe for the pulse oximeter when compared with a standard pulse oximeter finger sensor and ABG analysis.

METHODS AND MATERIALS

Ten healthy adult volunteers and 22 consecutive mechanical ventilator-dependent patients in the medical/surgical ICU were studied. Equipment used for pulse oximetry evaluation were the Criticare 501 + pulse oximeter, a standard finger probe, and a new forehead sensor (Criticare Systems, Waukesha, WI). The two Criticare 501 + pulse oximeters, each used exclusively

From the Department of Anesthesiology, Medical College of Wisconsin, 9200 W Wisconsin Ave, Milwaukee, WI 53226.

Received May 21, 1987. Accepted for publication Dec 28, 1987.

Address correspondence to Dr Cheng.

for either the finger or forehead probe, had similar electronic specifications from the factory. Healthy subjects were resting in a semirecumbent position and all ICU patients were supine. All healthy volunteers were breathing room air and all critically ill patients were receiving appropriate oxygen supplementation to keep arterial oxygen tension greater than 80 mm Hg. The finger sensor was placed on a forefinger on the hand opposite from which the ABG was sampled. The forehead sensor comprised two parts: the sensor portion and a part containing two light-emitting electrodes, each measuring $14 \times 20 \times 5$ mm. These probes were placed side by side with no more than 2 to 3 mm between them. The sensor unit was taped to the head with 25-mm-wide microfoam tape. The tape was secured so as to apply only enough pressure to keep the probes flat on the forehead surface.

When stable pulse oximeter readings of oxygen saturation (SpO_2) were reached for 10 seconds, arterial blood was drawn for analysis of ABGs. In volunteers, the radial artery was punctured. In the ICU patients, finger and forehead pulse oximeter sensors were placed shortly before scheduled arterial sampling for ABGs. Blood was obtained via arterial catheters already in place as part of clinical management. ABGs were analyzed and arterial oxygen saturation (SaO_2) was calculated by an ABL-1 blood gas analyzer (Radiometer Emdrupvej 72, Copenhagen).

Simultaneous pulse rate and SaO_2 readings were obtained from each oximeter probe, as was apical pulse rate when arterial blood was drawn. Current ventilator settings and temperature were noted for each ICU patient. Ten individual data points were collected from the

volunteers and 45 data points from the ICU patients, some patients contributing more than 1 data point.

Statistical analysis was by Student's paired *t* test. Values are expressed as mean \pm standard error; $P < 0.05$ was considered significant.

RESULTS

The mean age of the volunteers was 30.2 ± 5.6 years (range, 26 to 43 years). The mean age of the critically ill patients was 42.9 ± 4.9 years (range, 16 to 73 years). The fraction of inspired oxygen was 0.44 ± 6.6 on the ventilated patients (range, 0.3 to 1.0). Their mean temperature was $37.5 \pm 0.2^\circ\text{C}$ (range, 35.6 to 38.3°C). In the 10 volunteers there was a small but statistically significant difference between finger and apical pulse rates. The pulse rate detected by the forehead probe and SpO_2 detected by both probes did not differ significantly from the apical pulse rate and ABGs, respectively (Table).

In the ICU patients, 45 data sets were collected. The pulse rates detected by the forehead sensor were significantly lower than those from the finger probe and apex. SpO_2 from the forehead was significantly lower than from the ABGs (see Table). In 2 ICU patients who were severely edematous we were unable to obtain any readings from the forehead probe. Data from these patients were not included in the analysis. In 4 other ICU patients yielding 7 data points the forehead probe showed an SpO_2 less than 90% at the same time ABGs showed SaO_2 greater than 90%. The difficulty in forehead pulse detection seemed to occur with agitated or perspiring patients in whom the probe could not be properly secured.

Comparison of Measurements in Volunteers and Critically Ill Patients

Group	Pulse (beats/min)			Oxygen Saturation (%)		
	Forehead	Finger	Apical	Forehead	Finger	Laboratory
Volunteers ($n = 10$)						
Mean \pm SEM	73.9 ± 3.4	75.2 ± 2.9^a	73.4 ± 3.1	96.6 ± 0.5	97.3 ± 0.3	97 ± 0.4
Range	54-90	61-90	56-88	93-98	96-98	95-99
Critically ill patients ($n = 45$)						
Mean \pm SEM	96.3 ± 2.9^a	102.8 ± 2.8	104.2 ± 3.2	94.3 ± 1.3^b	96.1 ± 0.3	97.4 ± 0.3
Range	52-127	52-141	52-140	50-99	91-99	91-100
Critically ill patients ($n = 38$) ^c						
Mean \pm SEM	98.9 ± 3.1	101.6 ± 3.1	101.6 ± 3.3	96.3 ± 0.4	96.2 ± 0.3^b	97.4 ± 0.3
Range	52-129	52-120	52-133	89-99	92-99	92-100

^a $P < 0.05$ when compared with apical pulse.

^b $P < 0.05$ when compared with laboratory O_2 saturation.

^cSeven data points were deleted because of a greater than 10% difference in pulse rate.

It was noted that the false desaturation points tended to occur when the forehead pulse rate differed by more than 10% from the apical pulse rate. When all points in which forehead pulse differed from apical pulse rate by $\pm 10\%$ were removed, we obtained a good correlation between forehead SpO_2 and SaO_2 (see Table). Looking at the difference of the means of this group we found that the maximum difference between pulses was 2.7 beats/min, while the maximum difference between SaO_2 values was 0.7%.

DISCUSSION

Pulse oximetry functions by positioning a pulsating arterial vascular bed between a light source emitting at two different wavelengths and a detector. The variation in amplitude of light transmitted or scattered across the tissue during arterial pulsation is measured, and saturation is estimated from empiric evidence of the effect of oxygen on the relative pulse amplitudes in the red and infrared light transmission.

The site used for noninvasive detection of SaO_2 should have a profuse blood supply and a minimal amount of vasoactivity in response to vasoconstrictive stimuli. The usual pulse oximeter sensor clips onto the toe or finger. In some circumstances, especially in the operating room or when the patient's extremities are bandaged or covered, access to these sites becomes difficult. Alternative sites such as the nasal septum and ear lobe have been used.

Brinkman et al [1] were the first to develop a forehead pulse oximeter. However, their forehead reflexometer, "Cyclops," never was easy to use.

Theoretically the forehead should be a good site for pulse oximetry. In 1938, Hertzman [2] estimated blood supply of various skin areas by photoelectric plethysmography. He found that next to digits the ear lobe and forehead had the richest arterial supply when compared with the dorsum of finger, hand, foot, forearm, knee, and tibia. In addition Hertzman noted an absence of vascular reactivity of the forehead and ear lobe to the cold pressor test in contrast to lability of the arterial supply to the finger tip.

Even though the forehead should have a good arterial blood supply we experienced several episodes of poor forehead pulse detection that affected the monitor accuracy.

Small differences of 1 to 2% between pulse oximeter and apical pulse rate, even though different statistically, as seen with our healthy volunteers, did not affect the accuracy of SpO_2 when compared with SaO_2 . These small differences between the pulse rate detected by the pulse oximeter and the apical pulse rate should be ex-

pected because of variabilities in normal sinus rhythm and the different times at which the pulse rate is determined by pulse oximeter, electrocardiographic monitor, or auscultation.

Larger differences between forehead pulse oximeter and apical pulse rates did produce a significant difference between SpO_2 and SaO_2 in our critically ill subjects. When we removed the data points in which there was a greater than 10% difference between forehead pulse oximeter and apical heart rate there was good correlation between SpO_2 and SaO_2 .

One of the common causes of large differences between actual and pulse oximetry-determined pulse rates is poor tissue perfusion. Poor peripheral perfusion is commonly associated with hypotension or the effect of therapy with vasopressive drugs. In our study neither of these two specific causes was noted; however, severe forehead edema could decrease tissue perfusion.

Another factor that contributed to poor pulse correlation was the inability to securely place the forehead sensor because of forehead wetness or excessive head movement.

In 1972 several investigators demonstrated that the forehead could be used as a location to monitor arterial oxygen saturation [1,3], but they did not quantitate the oxygen saturation changes or test the accuracy in relation to ABGs. In 1981 Mendelson et al [4] demonstrated in a group of volunteers a good quantitative correlation between an ear pulse oximeter and their "skin reflectance oximeter system" that was placed on the forehead. They believed that the function of their instrument was based on optical reflectance rather than on detection and analysis of transmitted light. At that time, Mendelson et al surmised that the reflectance photoplethysmograph would be applicable to other centrally located body surface areas. In actuality the light used for analyzing SaO_2 was the scatter through the tissue rather than the light reflected by the skin [5].

We encountered two patients in whom forehead SpO_2 was undetectable and who also had extensive head edema. Edema increases the distance from surface to bone and may have decreased the scatter back to the pulse oximeter sensor. In addition, in several patients we placed the forehead sensor on the neck over the carotid artery, and on the abdomen, thigh, and upper arm; none of these areas proved useful for the detection of SaO_2 . Thus, we surmise that noninvasive assessment of SaO_2 by using the sensor probe depends on analysis of light scatter returning from the cranial bone through the tissue rather than reflected from the skin.

A potential source of error in this study was the use of the ABL-1 blood gas analyzer rather than a bench oximeter for determining SaO_2 . The ABL-1 calculates

rather than directly measures the SaO_2 . This may create a 1 to 2% overestimation of SaO_2 readings because hemoglobin species other than oxyhemoglobin and deoxyhemoglobin are not considered (i.e., methemoglobin and carboxyhemoglobin). In our study methemoglobin or carboxyhemoglobin should not be an important variable since all the volunteers were non-smokers and the mechanically ventilated patients were not exposed to any known sources of carbon monoxide or drugs that could potentiate the development of methemoglobin.

During the testing period the performance of the forehead probe at low saturation values could not be assessed because the clinical staff diligently tried to prevent significant desaturation and administered supplemental oxygen. However, information obtained from Severinghaus and Naifeh (personal communication, December 1987) shows that forehead pulse oximetry, like finger pulse oximetry, is not always accurate at very low SaO_2 values. Severinghaus and Naifeh also tested the Criticare 501 + pulse oximeter and forehead sensor on two different sets of healthy volunteers subjected to hypoxic gas mixtures via a technique previously described [6]. In the first study group of 3 subjects, 18 desaturation events were recorded. The mean measured SaO_2 was $52.97 \pm 2.18\%$. The mean difference between SaO_2 and SpO_2 from two forehead sensors tested simultaneously was $5.41 \pm 2.18\%$ and $13.56 \pm 6.7\%$.

In a group of 10 subjects tested at a later time the mean measured SaO_2 was $54.76 \pm 5.39\%$. Again, two forehead sensors were tested at the same time. For one sensor 60 desaturation events were recorded, with a mean difference from measured SaO_2 of $8.88 \pm 5.47\%$. For the other forehead sensor 54 desaturation events were recorded. The mean difference between SaO_2 and SpO_2 was $1.11 \pm 8.85\%$.

The relatively large errors between SpO_2 and SaO_2 have several causes. Severinghaus and Naifeh [6] noted that errors at low levels are due in part to lack of suitable calibration data. This is because, at an oxygen saturation of less than 70%, development of an accurate formula is hampered by the relationship between saturation and the optical signals at the two wavelengths usually used, which are not linear or logarithmic, but variable. Another factor may be the qualitative differences in the production of the forehead sensor. Lack of adequate plateau times for equilibrium to take place also may play a role.

The forehead pulse oximeter sensor for noninvasively determining SaO_2 deserves more study. Further modification and refinement are needed to calculate low saturation and to secure the sensor on the forehead before

this method can become an acceptable alternative to the common finger or ear-lobe sensors.

Supported in part by Criticare Systems, Inc. The authors thank Debbie Schmidling and Kathy Bernardo for manuscript preparation and Kim Stommel for data organization.

REFERENCES

1. Brinkman R, Zijlstra WG, Koopmans RK. A method for continuous observation of percentage oxygen saturation in patients. *Neth J Surg* 1950;1:333-334
2. Hertzman AB. The blood supply of various skin areas as estimated by the photoelectric plethysmograph. *Am J Physiol* 1938;124:318
3. Cohen A, Wadsworth W. A light emitting diode skin reflectance oximeter. *Med Biol Eng Comput* 1972;10:385-391
4. Mendelson Y, Cheung PW, Neuman MR, et al. Spectrophotometric investigation of pulsatile blood flow for transcutaneous reflectance oximetry. *Adv Exp Med Biol* 1981;159:93-102
5. Severinghaus JW, Astrup PB. History of blood gas analysis. VI. Oximetry. *J Clin Monit* 1986;2:270-288
6. Severinghaus JW, Naifeh KH. Accuracy of response of six pulse oximeters to profound hypoxia. *Anesthesiology* 1987;67:551-558

Pulse oximetry in pediatric intensive care: Comparison with measured saturations and transcutaneous oxygen tension

We evaluated a new pulse oximeter designed to monitor beat-to-beat arterial oxygen saturation (SaO_2) and compared the monitored SaO_2 with arterial samples measured by co-oximetry. In 40 critically ill children (112 data sets) with a mean age of 3.9 years (range 1 day to 19 years), SaO_2 ranged from 57% to 100%, and PaO_2 from 27 to 128 mm Hg, heart rates from 85 to 210 beats per minute, hematocrit from 20% to 67%, and fetal hemoglobin levels from 1.3% to 60%; peripheral temperatures varied between 26.5° and 36.5° C. Linear correlation analysis revealed a good agreement between simultaneous pulse oximeter values and both directly measured SaO_2 ($r = 0.95$) and that calculated from measured arterial PaO_2 ($r = 0.95$). The device detected several otherwise unrecognized drops in SaO_2 but failed to function in four patients with poor peripheral perfusion secondary to low cardiac output. Simultaneous measurements with a $tcPO_2$ electrode showed a similarly good correlation with PaO_2 ($r = 0.91$), but the differences between the two measurements were much wider (mean 7.1 ± 10.3 mm Hg, range -14 to +49 mm Hg) than the differences between pulse oximeter SaO_2 and measured SaO_2 ($1.5\% \pm 3.5\%$, range -7.5% to -9%) and were not predictable. We conclude that pulse oximetry is a reliable and accurate noninvasive device for measuring saturation, which because of its rapid response time may be an important advance in monitoring changes in oxygenation and guiding oxygen therapy. (*J PEDIATR* 1985;107:362-366)

Sergio Fanconi, M.D., Patrick Doherty, M.D., John F. Edmonds, M.D.,
Geoffrey A. Barker, M.D., and Desmond J. Bohn, M.D.
Toronto, Ontario, Canada

CONTINUOUS AND PRECISE MONITORING of arterial oxygenation is important in the management of critically ill patients.¹⁻³ Currently, the most frequently used noninvasive device for measuring arterial oxygenation is the $tcPO_2$ monitor. This allows for continuous measurements, but response time varies, frequent calibration is necessary, and change of site is required to prevent skin damage. There may also be a poor correlation with PaO_2 , depending on age of the patient, site of electrode, oxygen levels, cardiac output, peripheral perfusion, and condition of the skin.⁴⁻⁹ Arterial SaO_2 can be measured noninvasively with oxymet-

ric techniques, but such devices have thus far been inconvenient because of technical difficulties.^{3, 10-23} Recently a pulse oximeter has been developed (Nellcor, Hayward, Calif.) that measures saturation beat by beat.²⁴⁻²⁶ Our study was performed to evaluate this machine in infants and children with cardiorespiratory problems and to compare its performance with $tcPO_2$ monitoring and measured saturation from arterial blood samples.

METHODS

We studied 40 consecutive patients in our pediatric intensive care unit who had initial PaO_2 values <100 mm Hg. Indwelling arterial lines had been placed in all patients as part of routine clinical management. The informed consent of the parents or guardians of the children was obtained. The mean age of the patients was 3.85 years (range 1 day to 19 years); 11 were younger than 1 month, 10 between 1 month and 1 year, nine between 1 and 3

From the Intensive Care Unit, The Hospital for Sick Children.
Submitted for publication June 25, 1984; accepted Feb. 6, 1985.

Reprint requests: Desmond J. Bohn, M.D., Intensive Care Unit,
The Hospital for Sick Children, 555 University Ave., Toronto,
Ont. M5G 1X8, Canada.

years, and 1 acute life-th (cardiac su airway obst aspiration, l wall with s patients ne severe cardi two had nor inotropic su tion with ni mine.

Pulse oxi saturation a extremity. T and measur infrared lig absorption i vascular be pulse rate. audibly wit provides que an audible t tion. Audibl and for high saturation f: posed of a l the tissue to completely : pling.

Transcuta applied to th newborn inf: the hand. A: tion was not position of th avoid discre persistent pa play mode w pulse oximet beats from t tor.

The $tcPO_2$ (Kontron An sensor temp probe was re: ed for a max: fixed to the possible pers: of the chest place. Blood drawn from i

years, and 10 between 3 and 19 years. Each patient had an acute life-threatening respiratory or circulatory condition (cardiac surgery, 29 patients; neurosurgery, five; upper airway obstruction, cardiac arrest, diaphragmatic hernia, aspiration, heart failure, and severe deformity of the chest wall with scoliosis, one each. Twenty-eight of the 40 patients needed respiratory support. Ten patients had severe cardiac failure, six moderate, and 18 mild failure; two had normal cardiac function. Seven patients required inotropic support, and five were receiving afterload reduction with nitroprusside, nitroglycerine, or phenoxybenzamine.

Pulse oximetry is a noninvasive method for monitoring saturation and pulse rate via a single sensor located on an extremity. The instrument is controlled by a microprocessor and measures saturation by the absorption of red and infrared light as it passes through tissue. Changes in absorption related to the pulsation of blood through the vascular bed are used to determine both saturation and pulse rate. This information is displayed digitally and audibly with each heart beat. A linear array of lights provides qualitative indication of perfusion combined with an audible tone, which varies in pitch according to saturation. Audible alarm limits can be set for low saturations and for high and low heart rates. The machine "reads" the saturation from the peripheral oxisensor, which is composed of a light-emitting diode that passes light through the tissue to a photocell detector. Calibration of the unit is completely automatic and requires no blood or gas sampling.

Transcutaneous SaO_2 was measured with the sensor applied to the big toe or the finger in older children; in the newborn infants, the sensor was fixed to the foot or palm of the hand. Any limb with compromised peripheral circulation was not used. The sensor was placed according to the position of the arterial catheter and $tcPO_2$ probe in order to avoid discrepancies resulting from shunting through a persistent patent ductus arteriosus. The beat-to-beat display mode was used, and the value was accepted only if the pulse oximeter monitored heart rate did not differ by >5 beats from that on the independent bedside ECG monitor.

The $tcPO_2$ was measured with a transcutaneous monitor (Kontron Analytical, Redwood City, Calif.). The electrode sensor temperature was maintained at 44° C, and the probe was recalibrated for each patient. $tcPO_2$ was recorded for a maximum of 3.5 hours. The electrode was usually fixed to the right side of the chest or, in neonates with possible persistent pulmonary hypertension, to the left side of the chest when an umbilical arterial catheter was in place. Blood for arterial blood gas determinations was drawn from indwelling arterial lines, and PaO_2 and calcu-

Table. Summary of clinical data (three sets per patient) in 36 children

	Mean	SD	Range
Age (yr)	3.6	5.6	1 day to 19 yr
Blood pressure (mm Hg)	66.0	16.0	40 to 110
Heart rate (bpm)	127.0	20.0	85 to 210
Hematocrit (%)	41.0	10.0	20 to 67
Fetal hemoglobin (% total Hb)	13.5	16.4	1.3 to 59.8
PaO_2 (mm Hg)	67.0	23.0	27 to 128
$tcPO_2$ (mm Hg)	60.0	18.0	30 to 106
Measured SaO_2 (%)	88.9	8.4	57.3 to 99.8
Calculated SaO_2 (%)	89.6	8.3	53 to 99
Pulse oximeter SaO_2 (%)	87.5	8.9	55 to 100

lated SaO_2 were measured with a Corning 175 oximeter (Corning Medical and Scientific, Corning, N.Y.), the results being corrected for the patients' temperature and hemoglobin. SaO_2 was measured using an IL 182 co-oximeter (Instrumentation Laboratory, Inc., Lexington, Mass.), and each blood sample was analyzed twice. SaO_2 was calculated for the total hemoglobin content but was not corrected for carboxyhemoglobin. Blood pressure was monitored continuously using a pressure transducer and was displayed on a bedside monitor together with heart rate and ECG. Core and toe temperatures were measured using a probe and temperature monitor (Yellow Springs Instrument Co., Yellow Springs, Ohio). Hematocrit and hemoglobin were measured in all patients. In addition, fetal hemoglobin was measured in 13 patients younger than 1 year. The results were expressed as percent of total hemoglobin. Dye dilution cardiac output determination was performed in nine children without intracardiac shunts; in the remainder, output was estimated clinically.

The study period was 3 to 3.5 hours. Monitors were applied to the patient and the $tcPO_2$ monitor was allowed to equilibrate for a period of 10 to 20 minutes. When all monitors were functioning correctly, blood was drawn for blood gas analysis, calculated SaO_2 , direct SaO_2 measurement, and hematocrit, hemoglobin, and fetal hemoglobin estimation. Simultaneously, pulse oximeter SaO_2 , $tcPO_2$, core and peripheral temperature, mean blood pressure, and heart rate on both the pulse oximeter and bedside monitor were recorded. Two specimens were drawn at hourly intervals for arterial blood gas analysis and calculated and direct oxygen SaO_2 measurements. Pulse rate and $tcPO_2$ were recorded simultaneously.

RESULTS

One hundred eight data sets from 36 patients (three samples per patient) were obtained (Table). In four (10%) patients the pulse oximeter did not provide useful data,

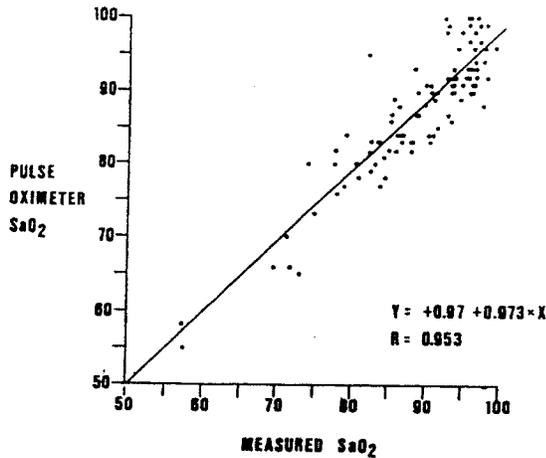


Fig. 1. Relationship between measured SaO_2 and pulse oximeter SaO_2 .

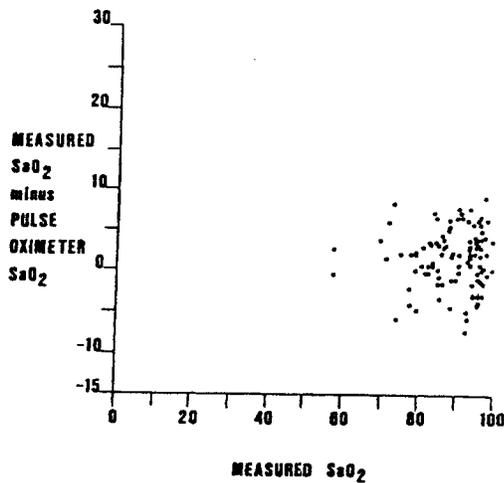


Fig. 2. Relationship between measured SaO_2 and error of pulse oximeter SaO_2 .

inasmuch as the machine could not detect a pulse because of low cardiac output. Peripheral pulses were not palpable but could be detected by Doppler technique.

Linear regression analysis of pulse oximeter SaO_2 compared with measured SaO_2 produced an r value of 0.95 ($P < 0.01$), with a regression equation of $y = +0.97 + 0.973 \times X$ (Fig. 1). Regression analysis of pulse oximeter SaO_2 vs calculated SaO_2 showed an r value of 0.95 with an equation of $y = -0.04 + 0.977 \times X$. The mean difference between measured SaO_2 and pulse oximeter SaO_2 was $+1.51\% \pm 3.49\%$ (range -7.5% to $+9\%$) (Fig. 2); the mean difference between calculated SaO_2 and pulse oximeter SaO_2 was

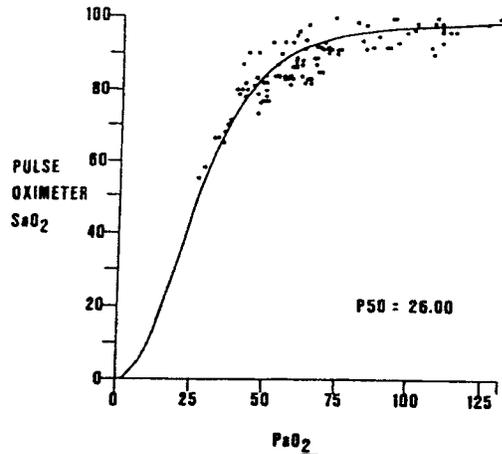


Fig. 3. In vivo oxygen dissociation curve plotting PaO_2 vs pulse oximeter SaO_2 . Regression line is normal oxygen dissociation curve for adult patient with pH 7.4, PCO_2 40 mm Hg, temperature $37^\circ C$.

$+2.15\% \pm 3.67\%$ (range -8% to $+9\%$). The mean difference between measured and calculated SaO_2 was $+0.62\% \pm 3.59\%$ (range $+8.2\%$ to -9.7%). The in vivo oxygen dissociation curves constructed with PaO_2 vs measured SaO_2 , pulse oximeter saturation (Fig. 3), and calculated SaO_2 all showed similar curves. The oxygen dissociation curve constructed with the calculated SaO_2 represented, in fact, a reliable mean dissociation curve of all our patients. There was no significant correlation between age, blood pressure, heart rate, peripheral core temperature, hematocrit, fetal hemoglobin level, or PaO_2 and the difference between pulse oximeter SaO_2 and measured SaO_2 . Good correlation was also obtained in two patients with elevated serum bilirubin levels (total bilirubin 9.7 and 7.4 mg/dl, 165 and 126 mmol/L, respectively). Linear regression analysis of PaO_2 vs $tcPO_2$ revealed a correlation coefficient of $r = 0.91$ ($P < 0.01$), with an equation of $y = 11.72 + 0.719 \times X$ (Fig. 4). The mean difference between PaO_2 and $tcPO_2$ was 7.08 ± 10.28 mm Hg (range -14 to $+49$ mm Hg). Linear regression analysis of PaO_2 vs $PaO_2 - tcPO_2$ showed a correlation coefficient of $r = 0.64$ ($P < 0.01$), with an equation of $y = -11.72 + 0.281 \times X$ (Fig. 5). This demonstrates an increasing difference between PaO_2 and $tcPO_2$ with increasing PaO_2 . There was no statistically significant correlation between $PaO_2 - tcPO_2$ and blood pressure, heart rate, age, peripheral or core temperature, hemoglobin, fetal hemoglobin, and cardiac output for the whole group of patients. However, poor peripheral perfusion with low toe temperature, high systemic vascular resistance, or low cardiac output were

probably re-
ous probe
between Pa_2
than 1 year

DISCUSS

The goo-
vivo pulse
demonstrat-
and childre
remained a
128 mm H
temperatur-
correlation
 SaO_2 showe
between pu-
slightly larg
 SaO_2 and n
constructed
calculated
measureme-
of the real
oxygen diss
detected sev
but the diff
independent
because an
indication o
fact, malpos
young and
attachment
oximeter fa-
with extrem
absent peri-
within 24 ho

The trans-
for monitori
trend monit
nately, the t
is unreliabl
indeed, hype
ancies betwe
Poor periph
systemic vas
also respons
probe in sev
almost as go
and measure
 PaO_2 and tc
between the
were not pre
Most inte

probably responsible for underreading by the transcutaneous probe in seven patients. The largest differences between P_{aO_2} and $tcPO_2$ were found in patients younger than 1 year.

DISCUSSION

The good linear relationship between simultaneous in vivo pulse oximeter SaO_2 and in vitro measurements demonstrates the reliability of the pulse oximeter in infants and children with cardiorespiratory problems. Readings remained accurate over a wide range of SaO_2 , P_{aO_2} (27 to 128 mm Hg), ages, heart rates, core temperatures, toe temperatures, hematocrit, and fetal hemoglobin levels. The correlation between pulse oximeter SaO_2 and calculated SaO_2 showed the same good correlation. The difference between pulse oximeter SaO_2 and calculated SaO_2 was slightly larger than the difference between pulse oximeter SaO_2 and measured SaO_2 . The oxygen dissociation curves constructed with pulse oximeter SaO_2 , measured SaO_2 , and calculated SaO_2 were all similar. Within the error of measurement, the pulse oximeter is a very good indication of the real SaO_2 , which depends on the position of the oxygen dissociation curve.^{3,23,27-30} The device immediately detected several otherwise unrecognized changes in SaO_2 , but the difference between pulse oximeter heart rate and independent ECG heart rate had to be monitored closely because an increasing discrepancy was often the only indication of malposition or malfunction of the probe. In fact, malposition was a frequent problem, especially in the young and restless patient, and improvement in sensor attachment would be helpful. Nevertheless, the pulse oximeter failed to function in only four (10%) patients, with extremely low cardiac output, poor perfusion, and absent peripheral pulses. Three of these children died within 24 hours.

The transcutaneous oxygen monitor is used extensively for monitoring oxygenation in neonates and is a reliable trend monitor in older children and adults.^{5,7,9} Unfortunately, the $tcPO_2$ monitor has a varying response time and is unreliable during low flow and hyperoxic states^{4,8}; indeed, hyperoxia was the most frequent cause of discrepancies between P_{aO_2} and $tcPO_2$ in our series of 10 patients. Poor peripheral perfusion with low temperature, high systemic vascular resistance, or low cardiac output was also responsible for underreading by the transcutaneous probe in seven other patients. P_{aO_2} and $tcPO_2$ showed almost as good a correlation ($r = 0.91$) as pulse oximetry and measured SaO_2 ($r = 0.95$), but the difference between P_{aO_2} and $tcPO_2$ was much wider than the differences between the pulse oximeter SaO_2 and measured SaO_2 and were not predictable.

Most intensive care specialists and neonatologists use

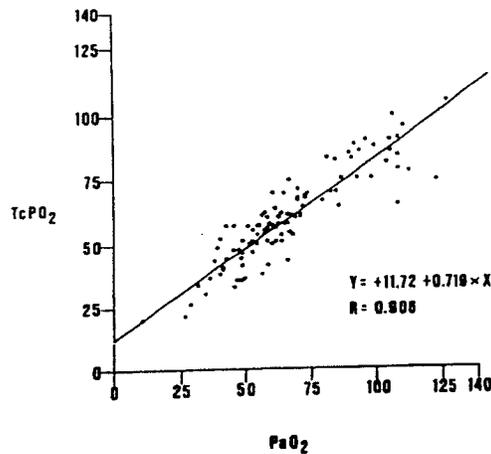


Fig. 4. Relationship between P_{aO_2} and $tcPO_2$.

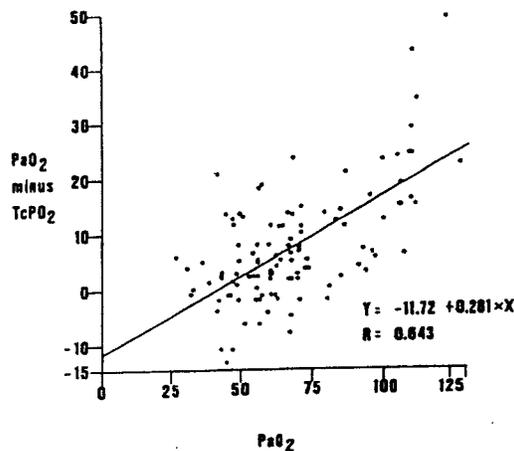


Fig. 5. Relationship between P_{aO_2} and error of $tcPO_2$.

P_{aO_2} , not SaO_2 , as a guide to oxygen therapy.^{3,6,9,15} Over the steep portion of the oxygen dissociation curve, changes in blood oxygen are reflected by SaO_2 more precisely than by P_{aO_2} . Continuous measurement of SaO_2 is a more reliable indicator of hypoxemia than P_{aO_2} , because it will detect inadequate oxygenation (which may occur despite P_{aO_2} of ≥ 50 mm Hg) related to a shift of the oxygen dissociation curve to the right. It will also detect those situations in which the curve is shifted to the left and SaO_2 is adequate despite $P_{aO_2} < 50$ mm Hg. On the other hand, in the upper part of the oxygen dissociation curve a small change in SaO_2 corresponds to a large change in P_{aO_2} .^{3,27} This confirms that both SaO_2 and P_{aO_2} are important in the management of oxygen therapy,^{3,9,27,29,30} especially in pre-

term infants, in whom hyperoxia is probably one of the most important causes of retrolental fibroplasia. To avoid P_{aO_2} levels >100 mm Hg, pulse oximeter S_{aO_2} should not exceed 90%; a pulse oximeter reading of 85% to 90% is a clinically safe target range.^{1-3, 27}

Our data demonstrate that the pulse oximeter is a reliable, noninvasive device for monitoring oxygen therapy in the pediatric age group. It offers the advantage of real-time readings and is independent of peripheral perfusion except in extremely low output states. In these cases, any inaccurate reading is readily apparent from the pulse display, whereas the t_{cPO_2} may continue to present inaccurate data. The device facilitates oxygen therapy by early detection of otherwise recognized hyperoxic and hypoxic episodes. Further studies will show if continuous and exact measurement of S_{aO_2} will help in reducing pulmonary oxygen toxicity.

We thank Miss L. Urmson for technical assistance, Dr. M. Yelderman and M. K. Allen for providing statistical analysis, and Dr A. O. Poon for measurement of fetal hemoglobin levels.

REFERENCES

- Barber RE, Lec J, Hamilton WK: Oxygen toxicity in man: A prospective study in patients with irreversible brain damage. *N Engl J Med* 283:1478, 1970.
- Singer MM, Wright F, Stanley LK, Roe BB, Hamilton WK: Oxygen toxicity in man: A prospective study in patients after open-heart surgery. *N Engl J Med* 283:1473, 1970.
- Wilkinson AR, Phibbs RH, Gregory GA: Continuous in vivo oxygen saturation in newborn infants with pulmonary disease: A new fiberoptic catheter oximeter. *Crit Care Med* 7:232, 1979.
- Beran AV, Tolle CD, Huxtable RF: Cutaneous blood flow and its relationship to transcutaneous O_2/CO_2 measurements. *Crit Care Med* 9:736, 1981.
- Gregory GA: Transcutaneous oxygen monitoring. In Spence AA, editor: *Respiratory monitoring in intensive care*. New York, 1982, Churchill-Livingstone.
- Huch R, Huch A, Albani M, Gabriel M, Schulte FJ, Wolf H, Rupprath G, Emmrich P, Stechele U, Duc G, Bucher H: Transcutaneous PO_2 monitoring in routine management of infants and children with cardiorespiratory problems. *Pediatrics* 57:681, 1976.
- Luebbers DW: Theoretical basis of the transcutaneous blood gas measurements. *Crit Care Med* 9:721, 1981.
- Tremper KK, Shoemaker WC: Transcutaneous oxygen monitoring of critically ill adults, with and without low flow shock. *Crit Care Med* 9:706, 1981.
- Venus B, Patel KC, Pratap KS, Konchigeri H, Vidyasagar D: Transcutaneous PO_2 monitoring during pediatric surgery. *Crit Care Med* 9:714, 1981.
- Anderson NM, Sekelj P: Reflection and transmission of light by thin films of nonhaemolyzed blood. *Phys Med Biol* 12:185, 1967.
- Burchell HB: An introduction to the clinical applications of oximetry. *Proc Staff Meet Mayo Clinic* 25:377, 1950.
- Crehan EL, Kennedy RLJ, Wood EH: A study of the oxygen saturation of arterial blood of normal newborn infants by means of a modified photo-electric oximeter. *Proc Staff Meet Mayo Clinic* 25:392, 1950.
- Kramer K: Bestimmung des Sauerstoffgehaltes und der Haemoglobin Konzentration in Haemoglobinloesungen und haemolysiertem Blut auf lichtelektrischem Wege. *Z Biol* 95:126, 1934.
- Kramer K, Elam JO, Saxton GA, Elan WN: Influence of oxygen saturation, erythrocyte concentration and optical depth upon the red and near-infrared light transmittance of whole blood. *Am J Physiol* 165:229, 1951.
- Krauss AN, Waldman S, Frayer W, Auld PA: Noninvasive estimation of arterial oxygenation in newborn infants. *J PEDIATR* 93:275, 1978.
- McClure RD, Behrmann VG, Hartman FW: The control of anoxemia during surgical anesthesia with the aid of the oxyhemograph. *Ann Surg* 128:685, 1948.
- Nilsson NJ: Oximetry. *Physiol Rev* 40:1, 1960.
- Perkins JF: The photoelectric oximeter: New tools for research. *Mod Med* 24:117, 1956.
- Rebuck AS, Chapman AD: The accuracy and response characteristics of a simplified ear oximeter. *Chest* 6:860, 1983.
- Scoggia C, Nett L, Petty TL: Clinical evaluation of a new ear oximeter. *Heart Lung* 6:121, 1977.
- Schotz S, Bloom SS, Helfmworth FW, Dodge HC, Birkmire EL: The ear oximeter as a circulatory monitor (preliminary report). *Anesthesiology* 19:3, 1958.
- Stephen CR, Slater HM, Johnson AB, Sekelj P: The oximeter: A technical aid for the anesthesiologist. *Anesthesiology* 12:541, 1951.
- Wood E: Oxymetry. *Med Phys* 3:416, 1950.
- Swedlow DB, Sterns: Continuous non-invasive oxygen saturation monitoring in children with a new pulse-oximeter [abstract]. *Crit Care Med* 11:228, 1983.
- Yoshiya I, Shimada Y, Tanaka K: Spectrophotometric monitoring of arterial oxygen saturation in the fingertip. *Med Biol Eng Comput* 18:27, 1980.
- Yelderman M, New W: Evaluation of pulse oximetry. *Anesthesiology* 59:349, 1983.
- Wilkinson AR, Phibbs RH, Heilbron DC, Gregory GA, Versmold HT: In vivo oxygen dissociation curves in transfused and untransfused newborns with cardiopulmonary disease. *Am Rev Respir Dis* 122:629, 1980.
- Martin WE, Cheney FW, Dillard DH, Johnson C, Wong KC: Oxygen saturation versus oxygen tension. *J Thorac Cardiovasc Surg* 65:409, 1973.
- Oeseburg B, Landsman MLJ, Mook JA, Zijlstra WG: Direct recording of oxyhaemoglobin dissociation curves in vivo. *Nature* 237:49, 1972.
- Papadopoulos MD, Roncevic NP, Oski FA: Postnatal changes in oxygen transport of term, premature, and sick infants: The role of red cell 2,3-diphosphoglycerate and adult hemoglobin. *Pediatr Res* 5:235, 1971.

SINCE it has been demonstrated that the use of pulse oximetry in the study of oxygen toxicity is a significant contribution to the major problem of monitoring the effectiveness of a therapeutic intervention.

From the Supportive Unit, Submitted 1985. Reprint requests to Kinderklinik, West Ger.

Noninvasive arterial hemoglobin oxygen saturation versus transcutaneous oxygen tension monitoring in the preterm infant

RAINER DECKARDT, MD; DAVID J. STEWARD, MD, FRCP(C)

We found that results from a transcutaneous arterial hemoglobin oxygen-saturation monitor correlated well with those from a co-oximeter. The monitor was not disturbed by differing hematocrit levels, the presence of fetal hemoglobin, or hypotension.

We also found that the results of simultaneous transcutaneous arterial hemoglobin oxygen saturation ($S_{tc}aO_2$) and transcutaneous oxygen tension ($P_{tc}O_2$) monitoring were predictably correlated over a wide range of hemoglobin saturations in preterm infants. When $S_{tc}aO_2$ was between 80% and 95%, $P_{tc}O_2$ was at a safe level of 40 to 80 torr in 94% of the patients studied. $S_{tc}aO_2$ monitoring as an index of arterial oxygenation has several advantages for the preterm infant.

Continuous noninvasive monitoring of transcutaneous oxygen tension ($P_{tc}O_2$) in infants and children is often unreliable as a means to measure PaO_2 when the patient is very sick and poorly perfused.¹⁻³ We evaluated a new noninvasive monitor which continuously measures transcutaneous arterial hemoglobin oxygen saturation ($S_{tc}aO_2$), by comparing $S_{tc}aO_2$ readings with hemoglobin saturation measured in arterial blood samples. We also compared the $S_{tc}aO_2$ monitor with the $P_{tc}O_2$ monitor in premature infants.

CLINICAL SERIES

Thirty-one moderately to severely sick children were studied on 52 different occasions. Patients were randomly selected from the ICU population or from those scheduled for surgery.

The patients were divided into two different groups according to age: the mean age of the 23 in group 1 was 28 months (range 3 months to 9 yr), thus assuming an adult hemoglobin level of more than 90%. In this group, six children had tetralogy of Fallot, five had transposition of the great arteries (TGA), three had ventricular septal defect, three patent ductus arteriosus (PDA), one aortic stenosis, one hypoplastic right pulmonary artery, one sarcoma, and three suffered from asthma. Group 2 consisted of eight newborn infants with a mean gestational age (GA) of 32.8 wk (range 26 to 39) and con-

sequently 90% to 95% of fetal hemoglobin.⁴ In this group, one child had a diaphragmatic hernia, one had TGA, and six had moderate to severe respiratory distress syndrome (RDS). Mean birth weight was 1562 g (range 700 to 3500). No group 2 infants received a blood transfusion before the study was performed.

PROCEDURE

A noninvasive, microprocessor-based pulse oximeter (Nellcor 100, Nellcor Incorporated, Hayward, CA) was used to measure the pulse rate and amplitude and $S_{tc}aO_2$. The instrument probe, which consists of two light-emitting diodes and a photosemiconductor, is attached to a digit, palm, or forefoot in infants, because low-intensity light at both the visible red and infrared wave lengths is transmitted through this highly vascular body tissue. Skin, flesh, bone, and capillary blood absorb a constant amount of light. Arterial blood flow, by contrast, absorbs varying amounts of light due to pulsatile blood flow. The light-absorption characteristics of oxygenated and nonoxygenated hemoglobin at each measured wave length are used to compute the oxygen saturation of arterial blood. No calibration of the monitor is necessary, and a reading for arterial hemoglobin oxygen saturation is presented automatically.

Arterial blood samples for comparison were obtained from a radial or an umbilical artery catheter, and were stored on ice until arterial hemoglobin saturation was measured with an oximeter.

In the second part of the study, ten moderately to severely sick infants from the neonatal ICU were randomly selected. Mean GA was 31.1 wk (range 28 to 40), and mean weight was 1145 g (range 810 to 2230). All infants were intubated and on artificial ventilation at the time of the study. Five had moderate to severe RDS, four had bronchopulmonary dysplasia, and one was confirmed as trisomy 18 with transient, tachypneic RDS. During the study all infants were kept in incubators. The lowest recorded rectal temperature was 35.5°C, the highest was 37.1°C. The lowest measured arterial pH was 7.3, the highest 7.5. The range of $PaCO_2$ was from 28 to 59 torr. All infants studied were normotensive. All but one infant had received a packed-cell transfusion at least once before the study. The $P_{tc}O_2$

From the Department of Anaesthesia, The Hospital for Sick Children, and The University of Toronto, Toronto, Canada.

probe (TC075-1, Narco Air-Shields Inc., Hatboro, PA) was applied to the abdominal or chest wall of each infant according to the manufacturer's instructions, with a temperature setting of 44°C. The probe was allowed to stabilize for at least 15 min before measurements started. The probe was repositioned every 4 to 5 h. The $S_{i,c}aO_2$ monitor was used simultaneously in each infant. Its probe was taped to the patient's palm or forefoot. In incubators where phototherapy lights were used, the $S_{i,c}aO_2$ probe was covered with a piece of foil to avoid interference from extraneous light. The pulse rates shown by the $S_{i,c}aO_2$ monitor and ECG monitor were confirmed to be identical before measurements were taken. Total monitoring time was 67.5 h.

RESULTS

The correlation of the in vivo and in vitro oxygen saturations derived from both groups is shown in Figure 1. The range of arterial oxygen saturation was 70% to 100% in group 1 and 42% to 99% in group 2. At the time the comparisons were made, the hematocrit values ranged from 33% to 61.5%. Systolic blood pressures ranged from 20 to 140 mm Hg, and pulse rates from 120 to 210 beat/min. The correlation of in vivo and in vitro oxygen saturations for group 2 patients alone (Fig. 2) was not significantly different from the entire patient population.

In the second part of the study, 337 data pairs were collected. Figure 3 compares in vivo $S_{i,c}aO_2$ and $P_{t,c}O_2$. $S_{i,c}aO_2$ ranged from 63% to 100%, and $P_{t,c}O_2$ ranged from 24 to 96 torr. Figure 4 shows these correlated data pairs plotted against oxygen dissociation curves for the

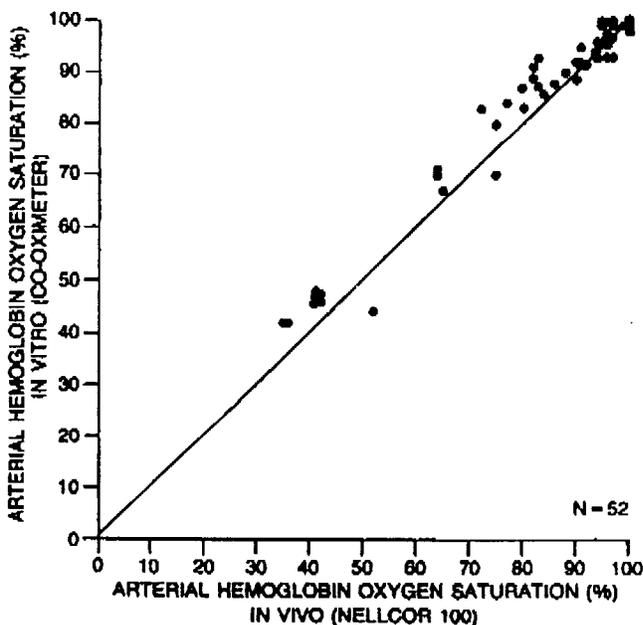


FIG. 1. Comparison of 52 simultaneous measurements of arterial hemoglobin oxygen saturation (S_{aO_2}) in groups 1 and 2.

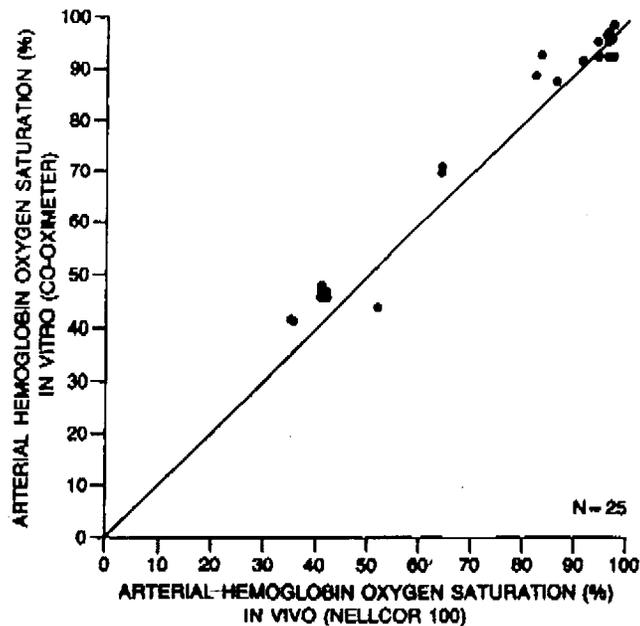


FIG. 2. Comparison of 25 simultaneous measurements of arterial hemoglobin oxygen saturation (S_{aO_2}) in group 2.

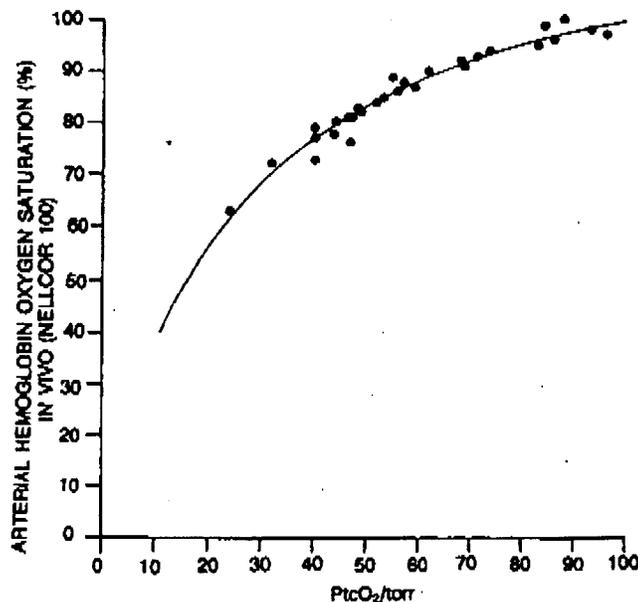


FIG. 3. Comparison of in vivo arterial hemoglobin oxygen saturation (S_{aO_2}) and transcutaneous oxygen tension ($P_{t,c}O_2$) in ten preterm infants. The regression coefficient (r) is .96 and the slope is described by the equation: $y = 0.4 E^{2.55x}$.

lowest and highest temperatures, P_{aCO_2} and arterial pH values.⁵ The mean P_{50} was assumed to be 26.6 torr.⁶ Ninety percent of all recorded data points fell within these curves.

The $S_{i,c}aO_2$ monitor produced readings which closely approximated those obtained by in vitro measurement of saturation in blood from arterial samples. Application of the probe to a patient's digit, hand or forefoot required no special skill. The readout of saturation

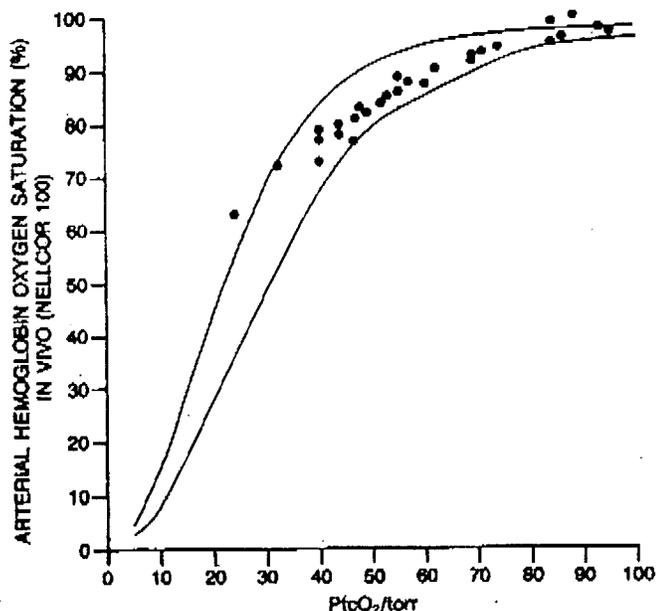


FIG. 4. Transcutaneous arterial hemoglobin oxygen saturation ($S_{tc}aO_2$) and transcutaneous oxygen tension ($P_{tc}O_2$) in ten preterm infants plotted against calculated oxyhemoglobin-dissociation curves. These curves were derived for temperature of 35.5°C, pH 7.5 and PCO_2 28 torr; and for temperature 37.1°C, pH 7.3 and PCO_2 7.31 torr. The mean P_{30} was assumed to be 26.6 torr.

occurred within a couple of heart beats, as soon as a pulsatile flow was picked up by the monitor. Comparison of the pulse shown by the $S_{tc}aO_2$ monitor and the pulse indicated by the ECG monitor was a good method of ensuring reliability of saturation readings. Correlation between simultaneous in vivo pulse-oximeter readings and in vitro oxyhemoglobin concentrations was good over a wide range of arterial oxygen saturations. Changes in blood pressure or different hematocrits did not affect the monitor's accuracy, even in one premature infant whose systolic blood pressure was 20 mm Hg. Reliable measurements of arterial hemoglobin oxygen saturation were obtained both in patients with adult hemoglobin and in patients with high amounts of fetal hemoglobin.

ILLUSTRATIVE CASES

Patient 1

A male infant with a corrected GA of 30 wk (GA at birth was 26 wk by dates and ultrasound, birth weight 710 g) was ventilated via a nasotracheal tube for RDS, and required surgery for PDA. Postoperatively the baby was monitored in the neonatal ICU with ECG leads, rectal temperature probe, blood pressure cuff, low-pressure and high-pressure alarm settings on the ventilator, a $P_{tc}O_2$ probe attached to the abdominal wall, and an $S_{tc}aO_2$ probe taped to his left forefoot. Both oxygenation variables were measured over a period of 12 h. The $P_{tc}O_2$ probe was changed every 4 h. Figure 5 compares $P_{tc}O_2$ and $S_{tc}aO_2$ readings.

The infant required intermittent suctioning to improve oxygenation. Both lungs had scattered rales and rhonchi. Bagging after a drop in oxygenation produced no improvement. Air entry was diminished, and suctioning at this time proved impossible. The infant was rein-

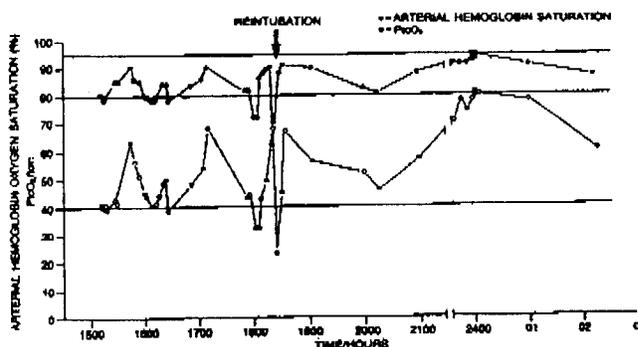


FIG. 5. Simultaneous transcutaneous arterial hemoglobin oxygen saturation ($S_{tc}aO_2$) and transcutaneous oxygen tension ($P_{tc}O_2$) measurements over a period of 12 h in patient 1.

tubated; the old tube was almost completely blocked. The $S_{tc}aO_2$ monitor provided an accurate continuous record of oxygenation.

Patient 2

A male infant with a GA of 26 wk (by dates and ultrasound) and a birth weight of 800 g was transferred from the neonatal ICU to the operating room for ligation of a PDA. At this time his weight was 710 g. The infant was ventilator-dependent (pressures 23/5 cm H_2O , ventilatory rate 20 breath/min, inspired oxygen fraction 0.24). His temperature was 31°C. The infant had a secure iv line. He was anesthetized using fentanyl-citrate (30 $\mu g/kg$ body weight) and pancuronium-bromide (50 $\mu g/kg$). A heated humidified anesthesia circuit and controlled positive-pressure ventilation were used to deliver a mixture of air and oxygen. The infant was placed in a right decubitus position. Monitoring devices consisted of a blood pressure cuff, Doppler flowmeter, esophageal stethoscope, rectal and esophageal temperature probe, and ECG and $S_{tc}aO_2$ monitors. Because access to the ductus arteriosus proved difficult, the left lung was retracted. The patient seemed to tolerate this well, but his arterial saturation immediately decreased. Heart rate and blood pressure remained unchanged. However, saturation continued to decrease (Fig. 6) and bradycardia occurred. Inflation of the lung was followed by immediate recovery. A second decrease in $S_{tc}aO_2$ was caused by repeated retraction of the left lung to check for bleeding. However, this time the period of decreased oxygenation was so brief that it was not followed by a drop in heart rate. In this patient, early warning of impending hypoxia was indicated by the $S_{tc}aO_2$ monitor before any other circulatory variables changed.

DISCUSSION

At least 30% of intraoperative complications in preterm infants are due to hypoxia.⁷ Unrecognized hyperoxia may also cause serious morbidity.⁸ Hypotension, hypovolemia, hypothermia, and acid/base derangements all affect the accuracy of the $P_{tc}O_2$ electrode as a monitor of arterial oxygenation.^{9,10} During anesthesia and surgery, the anesthetic gases and vapors, and high levels of circulating catecholamines may also disturb the accuracy of $P_{tc}O_2$ monitoring.^{1,11} Skin burns may occur if the probe is left on one site for prolonged periods, or if skin perfusion is decreased.¹² By contrast, the $S_{tc}aO_2$ probe transmits light of low intensity only, and therefore there is no risk of skin burns. Light transmission and reception through the tissues are such that the monitor will function independently of changes in superficial skin blood flow. Although the probe should be covered with foil during phototherapy, op-

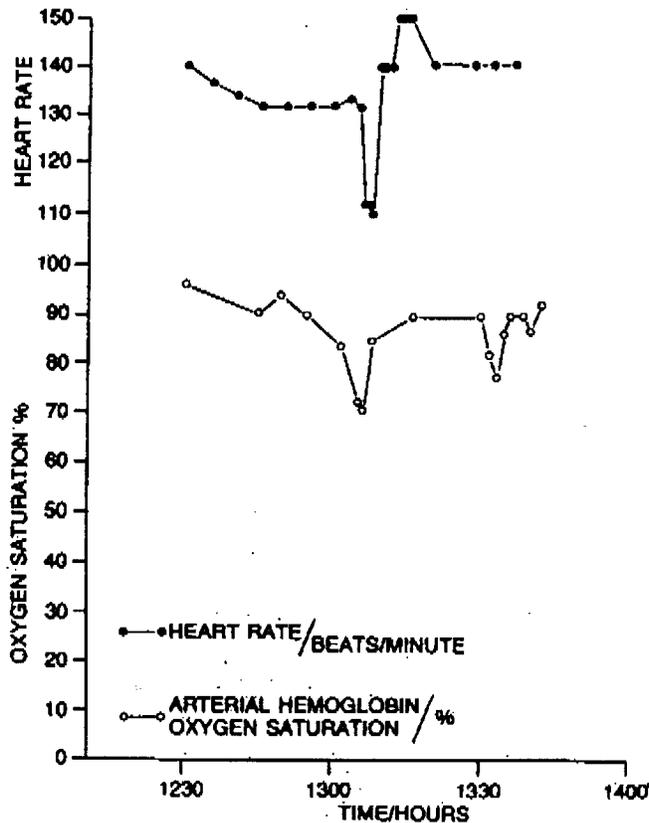


FIG. 6. Simultaneous arterial hemoglobin oxygen saturation ($S_{a}O_2$) and heart rate during an operation for ligature of a PDA in patient 2. Note the decrease in oxygen saturation followed by a drop in heart rate after compression of the left lung.

erating room lights did not interfere with monitored readings. Also, anesthetic gases and vapors did not affect the $S_{t}cO_2$ monitor's accuracy. In the second part of the study, we only included patients who were normothermic and normotensive, thereby assuring a close correlation between $P_{t}cO_2$ and PaO_2 .¹² There was a predictable correlation between $P_{t}cO_2$ and $S_{t}cO_2$ over a wide range of saturations (63% to 100%).

Physicians treating sick neonates have been accustomed to measure arterial oxygen tension as an index of oxygenation. Safe limits for the level of oxygen in the blood of the preterm infant, a level which ensures adequate available oxygen but minimizes the risk of retrolental fibroplasia, have been defined in terms of oxygen tension.¹³ Now that instruments are available to monitor $S_{t}cO_2$ continuously, this custom will have to be re-evaluated. As a consequence of the shape of the oxyhemoglobin dissociation curve, the oxygen content of the blood of hypoxemic infants is more sensitively expressed in terms of hemoglobin saturation than arterial oxygen tension. On the steep portion of the curve, a large change in saturation is accompanied by only a small change in oxygen tension. Furthermore, defining blood oxygenation in terms of hemoglobin saturation avoids factors which may displace the oxy-

hemoglobin-affinity curve (e.g., hypothermia, acidosis, blood transfusion) and thus influence the oxygen content of blood at a given oxygen tension. Thus, in the diagnosis of hypoxemia, the hemoglobin saturation level is a more useful index. On the other end of the scale, as oxygenation increases, the hemoglobin saturation becomes a less sensitive index than the arterial oxygen tension, and a larger change in PaO_2 will be reflected in only minor changes in hemoglobin saturation. Thus, it might be argued that monitoring of hemoglobin saturation is a less sensitive method of avoiding hyperoxia.

In fact, the $P_{t}cO_2$ monitor has a similar problem in detecting arterial hyperoxia in the sick neonate. This is partly because the accuracy of $P_{t}cO_2$ readings in reflecting PaO_2 declines at higher levels of PaO_2 . Also, in any condition that decreases skin perfusion (e.g., hypotension, hypovolemia, hypothermia), the gradient between PaO_2 and $P_{t}cO_2$ widens. Thus, an acceptable $P_{t}cO_2$ level could be accompanied by dangerously high PaO_2 . Therefore, even at the upper end of the oxyhemoglobin-affinity curve, when the performance characteristics of the presently available equipment are considered, monitoring of arterial saturation may offer equal safety. When $S_{t}cO_2$ was between 80% and 95%, the $P_{t}cO_2$ fell between 40 and 80 torr in 94% of our patients (in all these patients, the circulatory status was such that $P_{t}cO_2$ could be expected to correlate closely with PaO_2). Similar results have been obtained in other investigations of the relation between arterial saturation and arterial oxygen tension.¹⁴ Thus, it would seem advantageous to monitor saturation continuously in the sick neonate, especially when conditions exist which make it likely that $P_{t}cO_2$ readings differ from PaO_2 .

We found that the $S_{t}cO_2$ monitor performed well under many different clinical conditions. In the sick infant undergoing surgery or treatment in the ICU, this monitor offers a safe, reliable noninvasive method to monitor oxygenation continuously.

ACKNOWLEDGMENTS

The authors thank Lynn Urmson and George A. Volgyesi for their helpful cooperation during the study, and the nurses and staff of the neonatal ICU of the Women's College Hospital for their assistance. Special thanks go to Drs. Martin Skidmore and J. J. Edmonds for their help during the study.

REFERENCES

1. Dent JG, Netter KJ: Errors in oxygen tension measurements caused by halothane. *Br J Anaesth* 1976; 48:195
2. Vermold HT, Linderkamp O, Holzmann M, et al: Transcutaneous monitoring of PO_2 in newborn infants. Where are the limits? Influence of blood pressure, blood volume, blood flow, viscosity and acid base state. *Birth Defects* 1979; 15:285
3. Le Souef PN, Morgan AK, Soutter LP, et al: Continuous comparison of transcutaneous and arterial oxygen tension in newborn infants with respiratory illnesses. *Acta Anaesth Scand* 1978; 68(Suppl):91
4. Garby L, Sjolín S, Vuille JC: Studies on erythro-kinetics in

- infancy: II. The relative rate of synthesis of haemoglobin F and haemoglobin A during the first months of life. *Acta Paediatrica* 1962; 51:245
5. Kelman GR, Nunn JF: Computer Produced Physiological Tables. London, Butterworths, 1968, p 3
 6. Oski FA, Naiman JL: Hematologic Problems in the Newborn. Philadelphia, WB Saunders Company, 1982, pp 250-253
 7. Finucane BT, Symbas PN, Braswell R: Ligation of patent ductus arteriosus in premature neonates: Anesthetic management. *South Med J* 1981; 74:21
 8. Betts EK, Downes JJ, Schaffer DB, et al: Retrorenal fibroplasia and oxygen administration during general anesthesia. *Anesthesiology* 1977; 47:518
 9. Le Souef PN, Morgan AK, Soutter LP, et al: Comparison of transcutaneous oxygen tension with arterial oxygen tension in newborn infants with severe respiratory illnesses. *Pediatrics* 1978; 62:692
 10. Wijdan A-S, Hill DW: The importance of an elevated skin temperature in transcutaneous oxygen tension measurement. *Birth Defects* 1979; 15:149
 11. Eberhard P, Mindt W: Interference of anesthetic gases at oxygen sensors. *Birth Defects* 1979; 15:65
 12. Peabody JL, Gregory GA, Willis MM, et al: Transcutaneous oxygen tension in sick infants. *Am Rev Respir Dis* 1978; 118:83
 13. Klaus MH, Fanaroff AA: Care of the High Risk Neonate. Second Edition. Philadelphia, WB Saunders Company, 1979, p 176
 14. Wilkinson AR, Phibbs RH, Gregory GA: Continuous in vivo oxygen saturation in newborn infants with pulmonary disease. A new fiberoptic catheter oximeter. *Crit Care Med* 1979; 7:232

Effects of Fetal Hemoglobin on Pulse Oximetry

JONAS A. POLOGE*
DENA M. RALEY†

To date, all pulse oximeters are programmed with only one calibration curve. This is a curve empirically derived by inducing a hypoxic state in healthy adult volunteers and correlating their arterial blood saturation, as measured on a co-oximeter, with the ratio of light absorbance measured by the oximeter. This calibration curve corresponds to one set of extinction curves, in this case those of adult hemoglobin (Figure 1). Oximeters are not able to differentiate between fetal hemoglobin (HbF) and adult hemoglobin (HbA). As a result, the same data processing and calculations are done on the data received by the oximeter whether it is monitoring a premature infant or an adult. The intention of this research was to investigate the expected accuracy of a pulse oximeter calibrated on adults and used on neonates with high HbF levels.

If a different calibration curve is required for HbF, one would need a series of calibration curves. This is because the neonate or premature infant being monitored does not have 100 per cent HbF but has a combination of HbF and HbA, varying between 0 and 100 per cent HbF. A different calibration curve would be required for each percentage of HbF being monitored. The oximeter would have to be equipped with a "dial" so that one could dial in the infant's actual per cent HbF, and the oximeter would select the corresponding calibration curve. This would mean that the per cent HbF would need to be determined on a periodic basis for each infant monitored.

The question is, is there a difference between the extinction curves for HbF and HbA and if so, is there a clinically significant difference in the resulting error in oxygen saturation?

Dr. Zijlstra of the University of Groningen, recently completed a set of extinction curves that he obtained by scanning washed, lysed HbF and HbA. He obtained curves for the hemoglobin in the fully oxygenated and fully deoxygenated states. These curves were used as the basic data for our research.

The curves that Dr. Zijlstra sent us ranged from 450 nm to 750 nm. Oximetry uses wavelengths of light from approximately 600 nm to 1,000 nm, so Dr. Zijlstra's curves were extended by 300 nm into the near-infrared range by appending the published extinction curves to the end of his curves. The published curves were shifted up or down as required to make them continuous with Dr. Zijlstra's (Figure 2). Using only the HbA curves for oxy- and reduced hemoglobin, a computer model of an oximeter was generated, complete with a calibration curve. HbF at known saturations was *digitally input* to the model, which then calculated saturation. Any difference between the known saturation and the calculated saturation would be due to the differences between the extinction curves of HbF and HbA. Figure 3 shows the HbF and HbA curves plotted on the same graph. Notice the lines broaden in some regions. The errors caused

* Research Manager, Ohmeda, Boulder, Colorado.

† Research Engineer, Ohmeda, Boulder, Colorado.

Address correspondence and reprint requests to Mr. Pologe: Research Manager, Ohmeda, 4765 Walnut Street, Boulder, CO 80301.

0743-8346/87 \$0.00 + .25

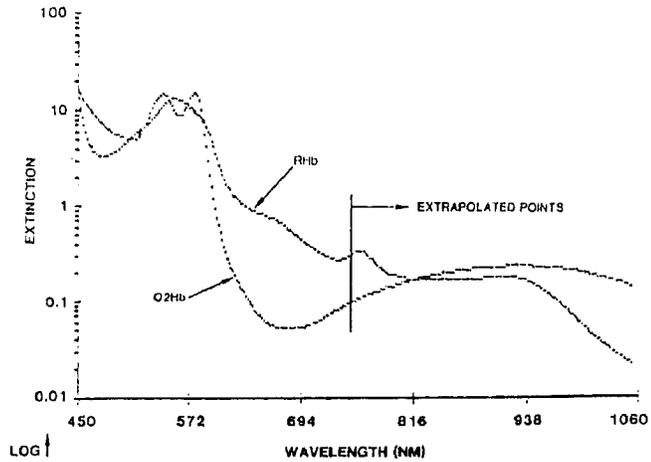
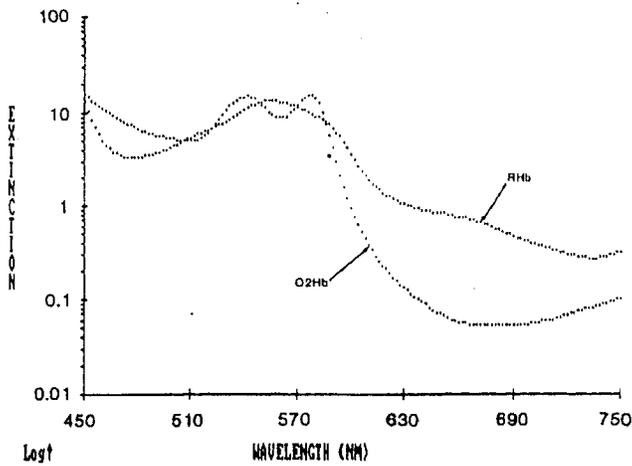


Figure 1 — (left) Extinction curves for adult reduced (RHb) and oxygenated hemoglobin (O2Hb).

Figure 2 — (right) Extinction curves for adult reduced (RHb) and oxygenated hemoglobin (O2Hb) showing the extrapolated points.

by these differences are shown in Table I. There is some shift in the saturation but the errors generated are clinically insignificant, ranging from approximately 0.41 per cent at 100 per cent saturation to a maximum of 1.12 per cent at 50 per cent saturation.

The assumption in this analysis is that Zijlstra's curves would continue out into the near-infrared region in the manner previously described. Although this treatment would not be expected to be exact, the comparison of the extinction curves of various species (of animals) suggests that this method provides at least a close approximation. The computer model used has been extensively tested, both experimentally with known factors and by hand computations.

More significant proof of the model lies in the fact that the results coincide with what one would expect on a theoretical basis. The hemoglobin consists of four globin chains with a heme bound to each. The light absorption properties of hemoglobin lie primarily within the heme. The difference between HbF and HbA is in the globin chains: HbA consists of two alpha and two beta chains whereas, HbF consists of two alpha and two

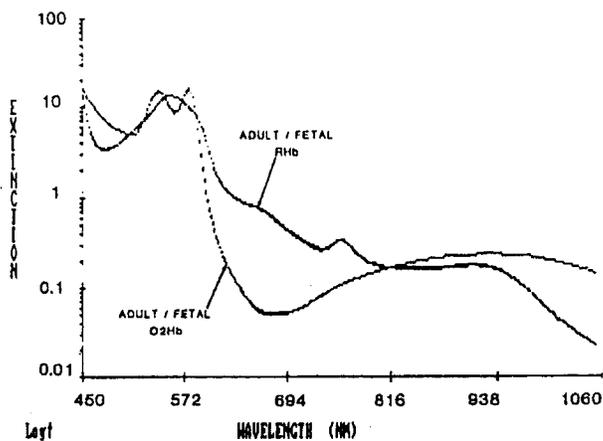


Figure 3 — Combined extinction curves for reduced and oxygenated Hb, showing by the darker areas where the fetal and adult curves differ.

Known SaO ₂	Calculated SaO ₂	SaO ₂ Difference
0.00	0.28	0.28
10.00	10.57	0.57
20.00	20.80	0.80
30.00	30.97	0.97
40.00	41.07	1.07
50.00	51.12	1.12
60.00	61.10	1.10
70.00	71.01	1.01
80.00	80.87	0.87
90.00	90.67	0.67
100.00	100.41	0.41

* The difference between the known SaO₂ and the SaO₂ that would be calculated in the presence of fetal hemoglobin.

gamma chains. The structure of the heme itself remains unchanged, so, one would expect the absorption of light by hemoglobin would remain virtually unchanged with the replacement of the two globin chains.

Finally, it is also worth noting that although we have seen no published study to date of the accuracy of oximetry in cases of high HbF levels, we also have not seen anything that indicates a reduced accuracy. The data that have come in from neonatal intensive care units, where oximetry has been compared with invasive arterial saturation measurements, have shown correlations similar to those found in the case of HbA.

In conclusion, with pulse oximetry having a specified accuracy of approximately ± 2 per cent in the 90 to 100 per cent saturation range, any error generated by HbF in pulse oximetry is clinically insignificant.

Acknowledgment

The curves in Figures 1-3 were plotted from data generated by Dr. W. G. Zijlstra, Department of Physiology, University of Groningen, Groningen, The Netherlands.

ABSORPTION CHARACTERISTICS OF HUMAN FETAL HEMOGLOBIN AT WAVELENGTHS USED IN PULSE OXIMETRY

Andrew P. Harris, MD, Michael J. Sendak, MD, Robert T. Donham, MD, PhD, Michael Thomas, PhD, and Donald Duncan, PhD

Harris AP, Sendak MJ, Donham RT, Thomas M, Duncan D. Absorption characteristics of human fetal hemoglobin at wavelengths used in pulse oximetry.

J Clin Monit 1988;4:175-177

ABSTRACT. The absorption characteristics of fetal and adult human hemoglobin samples were determined for the range of 600 to 1,050 nm. Over this range, fetal hemoglobin absorption is nearly identical to that of adult hemoglobin. Since currently available two-wavelength pulse oximeters base their calculations of arterial oxyhemoglobin saturation on absorption at the wavelengths of 660 and 920 nm, we conclude that the accuracy of two-wavelength pulse oximetry previously demonstrated in adults can be extrapolated to infants with high concentrations of fetal hemoglobin.

KEY WORDS. Monitoring, pulse oximetry: neonatal. Blood: hemoglobin, fetal.

The measurement of arterial oxyhemoglobin saturation using pulse oximetry in the care of critically ill patients is becoming widespread. Although its use was first described in adults, its use in infants is increasing also. Although clinical studies indicate that pulse oximetry may be accurate in infants [1-3], the algorithms used by these instruments have been determined from studies in adult humans, presumably with normal adult hemoglobin. These algorithms derived from studies in adults may not be applicable to infants with a high percentage of fetal hemoglobin (i.e., in the early postnatal period), unless the absorption characteristics of fetal and adult hemoglobin are similar at the wavelengths of light used in pulse oximetry. We sought to determine whether differences exist in absorption by fetal and adult hemoglobin in the spectrum that includes the wavelengths of light used by the two-wavelength pulse oximeters.

METHODS AND MATERIALS

Heparinized fetal blood was obtained from the clamped umbilical cord of a 34-week-gestation human placenta immediately after delivery. The red blood cells were washed three times in normal saline. A volume of 2.5 ml of packed red blood cells was suspended in 4 ml of normal saline. The hemoglobin concentration of this red cell suspension was determined by a CO-Oximeter (Instrumentation Laboratory, Model IL 282). A 2% solution of octylphenoxy polyethoxyethanol in saline (diluent used to lyse the red blood cells) was combined with the red cell suspension in a 1:4 ratio. The resulting mixture was gently agitated and then centrifuged at 10,000 rpm at 4°C for 30 minutes. The supernatants, which contained free hemoglobin, were collected and oxygenated for 10 minutes before spectral analysis.

From the Department of Anesthesiology and Critical Care Medicine of the Johns Hopkins University School of Medicine, and the Applied Physics Laboratory of the Johns Hopkins University, Baltimore, MD.

Received Aug 11, 1987, and in revised form Dec 8. Accepted for publication Dec 21, 1987.

Address correspondence to Dr Harris, Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Hospital, 600 N Wolfe St, Meyer 294, Baltimore, MD 21205.

The percentage of fetal hemoglobin was determined in an aliquot of the cord blood by the alkali denaturation method. In our laboratory, the upper limit of resolution of this method is 64% fetal hemoglobin.

A scanning Fourier transform spectrophotometer (Bomen, DA3.02) was used for spectral analysis of the hemoglobins. Samples were analyzed in a 1-cm path-length cuvette. The optical density was measured in the wavelength spectrum of 600 to 1,050 nm, and the millimolar extinction coefficients were calculated. Oxygenated diluent was used as a reference for the oxygenated hemoglobin solution. After analysis of the oxygen-saturated solution, analysis of the deoxygenated solution was performed. To deoxygenate the solution, 15 mg of sodium dithionite was added to both the diluent and the hemoglobin solution immediately before spectral analysis. The cuvettes were covered with paraffin film and analyzed in a nitrogen-purged chamber. The deoxygenated diluent was used as a reference for the deoxygenated hemoglobin solution. The absorption spectra obtained for fetal oxygenated and reduced hemoglobin were compared with those previously determined in our laboratory for the adult [4].

RESULTS

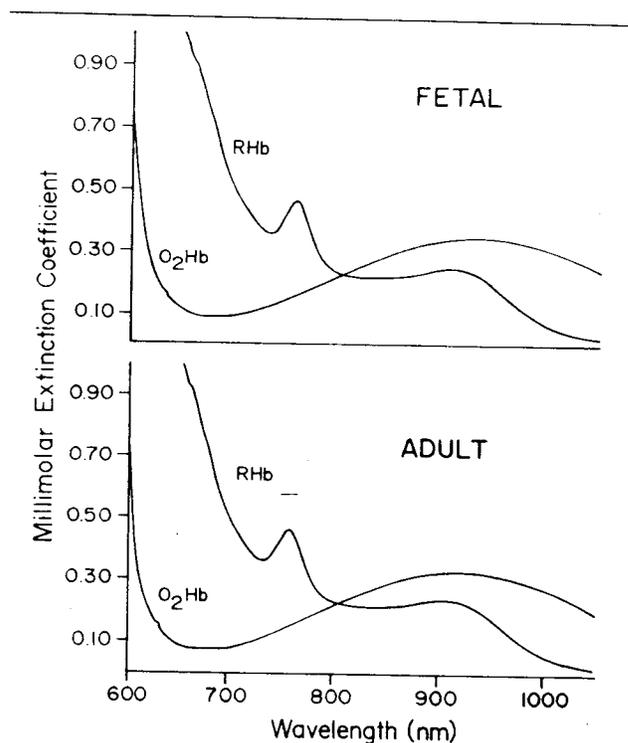
The fetal blood sample contained >64% fetal hemoglobin. The absorption spectra for fetal and adult oxygenated and reduced hemoglobin are depicted in the Figure. The irregularity of the oxygenated hemoglobin curves around 630 nm reflects the internal calibration point of the spectrophotometer and is an artifact of the method. The other irregularity, occurring around 660 nm, is a true characteristic of hemoglobins.

The Table lists the millimolar extinction coefficients at wavelengths near those used by pulse oximeters (i.e., 620 to 700 nm and 880 to 960 nm).

DISCUSSION

The absorption spectra of fetal and adult reduced and oxygenated hemoglobin are almost identical. Specifically, at 660 and 920 nm, the millimolar extinction coefficients of fetal oxygenated and reduced hemoglobin are nearly identical to those we have previously measured for the adult [4]. In addition, our measures of millimolar extinction coefficients for adult oxygenated and reduced hemoglobin are similar to those published by van Assendelft [5].

The ability to accurately measure arterial oxyhemoglobin saturation with pulse oximetry in infants with high percentages of fetal hemoglobin is useful in various clinical settings. The basis of two-wavelength pulse ox-



Absorption spectra for fetal and adult [4] oxyhemoglobin (O₂Hb) and reduced hemoglobin (RHb). Y-axis is millimolar extinction coefficient, expressed as (cm · mmol/L)⁻¹; x-axis is wavelength (nm).

imetry is that light at both a visible and near-infrared wavelength (660 and 920 nm, nominal) is passed through a tissue bed, and the absorbance is measured. Because oxygenated and reduced hemoglobin have differing millimolar extinction coefficients at these wavelengths, arterial oxygen saturation can be determined by algorithms that analyze plethysmographic waveforms and incorporate solutions of Beer's law.* Therefore, the algorithms employed by pulse oximeters are based on differential absorption of oxygenated and reduced hemoglobin at these wavelengths. Although the use of two-wavelength pulse oximeters has been reported in infants, these instruments were developed specifically for use in adults. There have been few attempts to validate, either theoretically or experimentally, the accuracy of such instruments when used in patients with a relatively high concentration of fetal hemoglobin. Such verification would seem essential, since in vitro IL 282 CO-Oximeter measurements are inaccurate in the pres-

* Beer's law: $P = P_0 10^{-\alpha LC}$. P = radiant power transmitted from the substance being analyzed, P_0 = radiant power applied to the substance being analyzed, α = absorptivity of the sample, L = length of the path through the sample, and C = concentration of the absorbing substance.

Millimolar Extinction Coefficients^a for Fetal and Adult Hemoglobins

Wavelength (nm)	Reduced Hemoglobin		Oxyhemoglobin	
	Fetal	Adult	Fetal	Adult
620	1.41	1.48	0.24	0.23
630	1.18	1.19	0.17	0.16
640	1.08	1.08	0.13	0.12
650	1.00	1.01	0.10	0.090
660	0.91	0.92	0.090	0.077
670	0.79	0.80	0.086	0.075
680	0.69	0.69	0.085	0.075
690	0.57	0.57	0.084	0.074
700	0.49	0.49	0.086	0.076
880	0.22	0.22	0.32	0.31
890	0.23	0.23	0.33	0.32
900	0.24	0.23	0.33	0.32
910	0.24	0.23	0.34	0.33
920	0.23	0.23	0.34	0.33
930	0.22	0.22	0.34	0.33
940	0.20	0.20	0.34	0.32
950	0.17	0.17	0.34	0.32
960	0.14	0.15	0.33	0.31

^aOptical density of an absorbing substance in a concentration of 1 mmol/L measured with a path length of 1 cm.

ence of high-concentration fetal hemoglobin and require correction [6]. This probably is due to differences in reduced and oxygenated fetal hemoglobin absorption at the wavelengths used by the IL 282 CO-Oximeter, namely 548, 568, and 578 nm.

Two factors affect the ability to extrapolate the accuracy of pulse oximeters in adults to infants: (1) whether the tissue beds in which pulse oximeter arterial oxygen saturation is being measured are similar in infants and adults and (2) whether the absorptions of fetal and adult hemoglobin are similar [7]. Relative to the first point, there is no evidence to suggest that the characteristics of light transmission by neonatal tissues are different from those of adult tissues (e.g., across the flesh of the hand, finger, or foot). Therefore, the main obstacle to extrapolation would be a difference in absorption characteristics between fetal and adult hemoglobin at the wavelengths used by the pulse oximeter.

We could find only one previous study that examined the absorption characteristics of fetal hemoglobin, especially in reference to contrasting these absorption characteristics to adult human hemoglobin. In that study, absorptions of oxygenated and reduced hemoglobins were measured over the range of 535 to 627 nm (the

range used by the IL 282 CO-Oximeter) and were similar for fetal and adult hemoglobin [8]. We found striking similarities in hemoglobin absorption in the entire 600 to 1,050 nm range.

There is good reason for the virtually identical absorption characteristics of fetal and adult oxygenated and reduced hemoglobins over this spectrum. It is predominantly the heme moiety that absorbs light at these wavelengths, and although the globin chains are different in fetal and adult hemoglobin, the prosthetic group of heme, ferroprotoporphyrin IX, is common to both adult and fetal hemoglobins and, indeed, to all vertebrates [9]. One might postulate that under similar tissue bed conditions, the pulse oximeter may be accurate in any vertebrate.

Our results form a theoretical basis for the conclusion that two-wavelength pulse oximeters that base their algorithms on differential absorption of oxygenated and reduced hemoglobins at wavelengths of light in the 600 to 1,050 nm spectrum should be as accurate in patients with a high concentration of fetal hemoglobin as they are in patients with normal adult hemoglobin.

REFERENCES

1. Deckhardt R, Steward DJ. Noninvasive arterial hemoglobin oxygen saturation versus transcutaneous oxygen tension monitoring in the preterm infant. *Crit Care Med* 1984;12:935-939
2. Jennis MS, Peabody JL. No burns, no gradient—pulse oximetry, an alternative to transcutaneous PO_2 . *Pediatr Res* 1985;19:142A
3. Durando M, Ramanathan R. Pulse oximetry for continuous oxygen monitoring in sick newborn infants. *J Pediatr* 1986;109:1052-1056
4. Sendak MJ, Harris AP, Donham RT. Accuracy of pulse oximetry during severe arterial oxyhemoglobin desaturation in dogs. *Anesthesiology* 1988;68:111-114
5. van Assendelft OW. Spectrophotometry of haemoglobin derivatives. Springfield, IL: Thomas, 1970:8-73
6. Comelissen PJH, van Woensel CLM, van Oel WC, deJong PA. Correction factors for hemoglobin derivatives in fetal blood, as measured with the IL 282 CO-Oximeter. *Clin Chem* 1983;29:1555 (Letter)
7. Ryan CA, Barrington KH, Vaughan D, Finer NN. Directly measured arterial oxygen saturation in the newborn infant. *J Pediatr* 1986;109:526-529
8. Zijlstra WG, Buursma A, Koek J, Zwart A. Correction factors for hemoglobin derivatives in fetal blood, as measured with the IL 282 CO-Oximeter. *Clin Chem* 1983;29:1556 (Reply)
9. Bunn HF, Forget BG, Ranney HM. Human hemoglobins. Philadelphia: Saunders, 1977:1-4

Variations in Optical Absorption Spectra of Adult and Fetal Hemoglobins and Its Effect on Pulse Oximetry

YITZHAK MENDELSON, MEMBER, IEEE, AND JOEL C. KENT, MEMBER, IEEE

Abstract—One of the concerns clinicians have relates to the interpretation of noninvasive pulse oximeters in newborns since at birth high levels of fetal hemoglobin (HbF) is present in the blood. Accurate *in vivo* studies of pulse oximeters in infants with predominantly HbF cannot be easily performed. Therefore, the objective of this *in vitro* study was to determine whether the presence of high levels of HbF in the blood can significantly affect the accuracy of noninvasive pulse oximeters.

It is evident from our results that there is no perceptible difference in the 650–1000 nm wavelength region, which is commonly used in pulse oximetry, between the optical absorption spectra of hemolyzed whole adult and fetal blood. Our observations are in good agreement with *in vivo* studies published by other investigators showing considerable correlations between SpO_2 measured by a pulse oximeter and So_2 values analyzed *in vitro* by an IL 282 CO-Oximeter.

I. INTRODUCTION

PULSE oximeters measure arterial hemoglobin oxygen saturation (SpO_2) by detecting changes in the absorption of red and infrared light resulting from arterial blood pulsation in a vascular bed [1]–[3]. Recently, the use of pulse oximeters has been reported in the clinical management of pediatric patients and critically ill newborn infants with cardiac and pulmonary diseases [4]–[10].

At birth, fetal hemoglobin (HbF) constitutes 60–95 percent of the total hemoglobin in the erythrocytes of both preterm and full term newborns, with the remainder being adult hemoglobin (HbA) [11]–[13]. At approximately nine months postnatal age, HbF levels higher than 2 percent often indicate an anemia, such as sickle-cell anemia or beta-thalassemia major. Since pulse oximeters are calibrated empirically by inducing hypoxia in healthy adults, one of the concerns relates to the interpretation of pulse oximeter measurements in newborns with high levels of HbF.

Zwart *et al.* [14] and Zijlstra *et al.* [15], [16] first drew attention to the finding that the standard laboratory IL 282 CO-Oximeter (Instrumentation Laboratory Inc., Lexington, MA), which is commonly used as a standard for calibrating pulse oximeters, gives fictitiously high carboxyhemoglobin (HbCO) readings in the presence of high HbF levels in blood. This finding was based on the observation that there is a slight, but significant, difference between

the optical absorption spectra of HbA and HbF in the visible wavelength range between 535 and 627 nm. Cornelissen *et al.* [17] described a systematic method for correcting the apparent elevated HbCO fraction in fetal blood as measured with the IL 282 CO-Oximeter.

The spectrophotometric studies of HbA and HbF by Zwart *et al.* [14], Zijlstra *et al.* [15], [16], and Cornelissen *et al.* [17] have been confined to the low visible portion of the spectrum. In a few cases the observations were extended into the ultraviolet region [18]. The IL 282 CO-Oximeter determines the total hemoglobin (THb), oxyhemoglobin (HbO₂), HbCO and methemoglobin (Hi) by measuring the optical absorption of a blood sample at four visible wavelengths: 535.0, 585.2, 594.5, and 626.6 nm. The wavelengths used by pulse oximeters, however, are typical¹, in the red (e.g., 660 nm) and infrared (e.g., 940 nm) regions of the spectrum.

Accurate *in vivo* studies of pulse oximeters in infants with predominantly HbF can not be easily performed. Therefore, the objective of this *in vitro* study was to determine whether the presence of high levels of HbF in the blood can affect the accuracy of pulse oximeters.

II. METHODS

A. Sample Preparation

Outdated packed red blood cells and plasma obtained from a local Red Cross blood bank and freshly collected fetal blood obtained from the umbilical cords of several placentas immediately after delivery were pooled separately. The fetal blood samples were collected in Vacutainer tubes containing EDTA as an anticoagulant. Each blood sample (approximately 100 ml) was thoroughly mixed and filtered through separate transfusion filter sets to remove microaggregates.

The filtered whole adult and fetal blood samples were diluted to a THb content of 5 ± 0.1 g/dl by the addition of distilled water. The blood was agitated and then hemolyzed using a Sonifer cell disrupter. The mean THb content of the adult and fetal hemolysates were determined by averaging the values from five different blood samples analyzed by the IL 282 CO-Oximeter. HbO₂ was obtained by exposing the blood to pure oxygen gas for 10 minutes. The pH of each hemolysate was adjusted to 7.40 ± 0.05 by the addition of sodium bicarbonate.

The fully oxygenated hemolyzed blood sample was then pipetted into the optical cuvette for spectrophotometric

Manuscript received July 10, 1988; revised December 2, 1988. This work was supported in part by grants from the Datascope Corporation and the Whitaker, W. M. Keck and Surdna Foundations.

The authors are with the Department of Biomedical Engineering, Worcester Polytechnic Institute, Worcester, MA 01609.

IEEE Log Number 8928351

analysis. Following the spectral analysis of each HbO₂ sample by the spectrophotometer, several crystals of powdered sodium dithionite (Na₂S₂O₄) were added to the cuvette to obtain fully deoxygenated Hb. Immediately thereafter the spectra of deoxygenated Hb were recorded.

B. HbF Determination

The HbF fraction in each blood sample was determined using radial immunodiffusion (RID). The Helena HbF QUIPlate kit (Helena Laboratories, Beaumont, TX), which is designed for the rapid quantitation of HbF levels between 1 and 10 percent, was used. To accurately quantify levels of HbF above 10 percent, such as those present in cord blood, the fetal blood samples were diluted with adult whole blood which had previously been analyzed and found to have less than 0.5 percent HbF. Supplied HbF standards and the unknown blood sample were applied to wells in the agarose plate of the RID kit. The antigens in the blood sample are allowed to diffuse into the agarose matrix where HbF in the sample reacts with the HbF specific antiserum, producing an opaque precipitin ring around the wells. The diameter squared of the precipitin ring is directly proportional to the HbF concentration after a 24 h of incubation. Utilizing this technique it was determined that the amount of HbF in the fetal and adult blood samples was greater than 95 percent and less than 0.5 percent, respectively.

C. Spectral Determination

The optical absorption spectra of the adult and fetal blood samples were independently recorded using a Shimadzu UV 160 double-beam scanning spectrophotometer (Shimadzu Scientific Instruments, Columbia, MD). The spectral band width and wavelength accuracy of this spectrophotometer are approximately 3 and ± 0.5 nm, respectively. The scanning range was set to cover a wavelength band between 600 and 1000 nm. Each blood sample was scanned repeatedly three times. The absorption spectra readings were taken at 2 nm intervals.

The spectra of the adult and fetal hemolysates were recorded from 1 mm pathlength (volume: 0.4 ml) quartz optical cuvettes (NSG Precision Cells, Inc., Farmingdale, NY). Distilled water was used for the reference blank cuvette. All blood samples were kept at ambient temperature before they were pipetted into the cuvette and placed in the cell holder of the spectrophotometers.

D. Calculations

Because Beer-Lambert's Law holds for hemoglobin solutions over a wide range of concentrations [19], [20], the specific extinction coefficients of blood can be calculated using the relationship

$$A(\lambda) = C\epsilon(\lambda)d \quad (1)$$

where $A(\lambda)$ is the absorbance at wavelength λ , C is the concentration of the absorbing sample expressed in mmol/l, $\epsilon(\lambda)$ is the specific millimolar absorptivity at wavelength λ expressed in $\text{mmol}^{-1} \times 1 \times \text{cm}^{-1}$, and d

the light pathlength in centimeters. This relationship is valid only when monochromatic light is used and the material investigated does not scatter light.

To convert the absorbances measured to that of a standard 1.0 cm pathlength, the average absorbances measured at each wavelength were divided by the light pathlength of the optical cuvette used (1 mm). Since hemoglobin has four iron-containing groups, the extinction coefficients obtained refer to one heme group plus globin moiety, i.e., one-quarter of the molecular weight of the Hb tetramer (64, 458).

For the purpose of assessing the error in S_pO_2 due to variations in the extinction coefficients of HbA and HbF, a simple mathematical relationship was derived as follows.

Assuming that Beer-Lambert's Law can be used to describe the change in optical density of a pulsating vascular tissue bed [1], and that the incident light propagates through a homogeneous mixture of blood and bloodless tissue, the total absorbance of the tissue bed is equal to the sum of the optical absorbances of each component. If $C(\text{Hb})$, $\epsilon(\text{Hb})$, and $d(\text{Hb})$ denotes the concentration, extinction coefficient, and optical path length of the Hb component, $C(\text{HbO}_2)$, $\epsilon(\text{HbO}_2)$ and $d(\text{HbO}_2)$ denotes the concentration, extinction coefficient and optical path length of the HbO₂ component and $C(t)$, $\epsilon(t)$ and $d(t)$ denotes the concentration, extinction coefficient and optical path length of the bloodless tissue component, then the total absorbance of the tissue bed (A_T) is equal to

$$\begin{aligned} A_T = & C(\text{Hb}) \epsilon(\text{Hb}) d(\text{Hb}) \\ & + C(\text{HbO}_2) \epsilon(\text{HbO}_2) d(\text{HbO}_2) \\ & + C(t) \epsilon(t) d(t). \end{aligned} \quad (2)$$

Since pulse oximetry relies on the difference in optical absorbance of a vascular tissue bed produced by the time-variant pulsatile flow of arterial blood, by differentiating (2) with respect to time we obtain

$$\begin{aligned} \frac{d[A(T)]}{dt} = & \frac{d}{dt} [C(\text{Hb}) \epsilon(\text{Hb}) d(\text{Hb}) + C(\text{HbO}_2) \\ & \cdot \epsilon(\text{HbO}_2) d(\text{HbO}_2)] \\ & + \frac{d}{dt} [C(t) \epsilon(t) d(t)]. \end{aligned} \quad (3)$$

Note that the tissue parameters are constant with respect to time and, therefore, the last term in (3) has a zero derivative. Furthermore, since the absorbance is defined as $-\ln(I_t/I_o)$ where I_t and I_o denote the transmitted (time variant) and incident (time invariant) light intensities, respectively, (3) can be written as

$$\begin{aligned} -\frac{d(\ln I_t)}{dt} = & \frac{d}{dt} [C(\text{Hb}) \epsilon(\text{Hb}) d(\text{Hb}) + C(\text{HbO}_2) \\ & \cdot \epsilon(\text{HbO}_2) d(\text{HbO}_2)]. \end{aligned} \quad (4)$$

Utilizing two different wavelengths, e.g., $\lambda(R) = 660$ nm and $\lambda(IR) = 940$ nm, and calculating the ratio of the

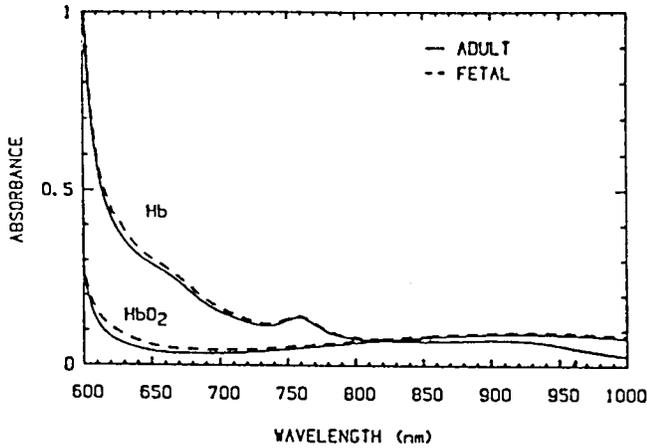


Fig. 1. Optical absorption spectra recorded by the Shimadzu UV160 spectrophotometer from fully oxygenated and deoxygenated hemolyzed whole adult and fetal blood. THb content = 5 g/dl.

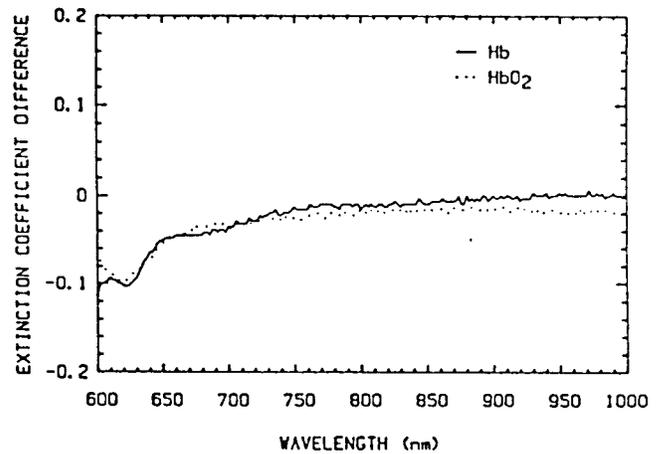


Fig. 3. Spectral difference in extinction coefficients between HbA and HbF (HbA-HbF) for fully oxygenated and deoxygenated hemolyzed whole blood.

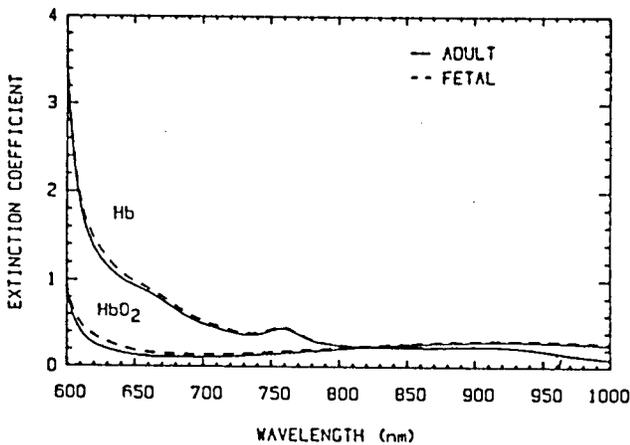


Fig. 2. Optical extinction coefficient spectra calculated from the optical absorption spectra recorded by the Shimadzu UV160 spectrophotometer from fully oxygenated and deoxygenated hemolyzed whole adult and fetal blood. THb content = 5 g/dl.

changes in transmitted light intensities, we obtain the following relationship

$$\frac{\frac{d}{dt} [\ln I_t(R)]}{\frac{d}{dt} [\ln I_t(IR)]} = \frac{\frac{d}{dt} [C(Hb) \epsilon_R(Hb) d(Hb) + C(HbO_2) \epsilon_R(HbO_2) d(HbO_2)]}{\frac{d}{dt} [C(Hb) \epsilon_{IR}(Hb) d(Hb) + C(HbO_2) \epsilon_{IR}(HbO_2) d(HbO_2)]} \quad (5)$$

where ϵ_R and ϵ_{IR} denote the extinction coefficients of blood for the red and infrared wavelengths, respectively.

If we denote the ratio of the time-variant changes in transmitted light intensities $d/dt [\ln I_t(R)] / (d/dt) [\ln I_t(IR)]$ in (5) by R/IR and assume that

$$SpO_2 = \frac{C(HbO_2)}{C(Hb) + C(HbO_2)} \quad (6)$$

and

$$d(Hb) = d(HbO_2) \quad (7)$$

the relationship in (5) can be expressed as

$$SpO_2 = \left[\frac{-\epsilon_R(Hb) + \epsilon_{IR}(Hb) \times (R/IR)}{[\epsilon_R(HbO_2) - \epsilon_R(Hb)] + [\epsilon_{IR}(Hb) - \epsilon_{IR}(HbO_2)] \times (R/IR)} \right] \quad (8)$$

RESULTS

The optical absorption spectra recorded from hemolyzed adult and fetal blood samples in the wavelength range between 600 and 1000 nm are shown in Fig. 1. The corresponding extinction coefficients for the spectra in Fig. 1, which were calculated from (1), and the difference in the extinction coefficients for HbA and HbF are plotted in Figs. 2 and 3, respectively. These spectra represent the average values based on three repeated scans for a THb content of 5 g/dl. It is clearly evident from these figures that the spectral analysis of HbF yielded extinction coefficients that are virtually identical to those of HbA. The extinction coefficients for 660 and 940 nm, the two wavelengths typically used in pulse oximeters, are reported in Table I.

The extinction coefficients in Table I were substituted into (8) in order to determine the error in SpO_2 for the adult and fetal hemoglobin derivatives. The result of these theoretical simulations are plotted in Fig. 4 for the complete range of oxygen saturation. These curves reveal that

a maximum error of approximately 3 percent in SpO_2 could be expected when measurements from adult and fetal blood are compared.

DISCUSSION

The main purpose of this *in vitro* study was to determine the difference in the extinction coefficients of HbA and HbF for wavelengths typically used in pulse oximetry. The results in Table I are in good agreement with values reported by Van Assendelft [20]. The small discrepancy with respect to the absolute value of the HbO_2

TABLE I
MILLIMOLAR EXTINCTION COEFFICIENTS OF ADULT AND FETAL BLOOD
EXPRESSED IN ($l \times \text{mmol}^{-1} \times \text{cm}^{-1}$)

λ	Hb		HbO ₂		Hb*	HbO ₂ *
	A	F	A	F	A	A
660 nm	0.86	0.90	0.12	0.16	0.80	0.08
940 nm	0.20	0.20	0.29	0.30	0.20	0.30

*From Van Assendelft [20].

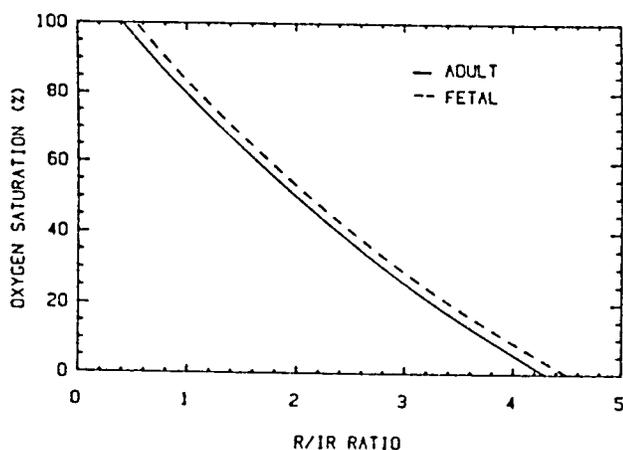


Fig. 4. Theoretical simulations showing the error in SpO_2 for adult and fetal hemoglobin derivatives.

extinction coefficient for the adult blood samples at 660 nm reported by Van Assendelft may be attributed to the presence of small amounts of HbCO (<2 percent) and Hi (<3 percent) in our blood samples.

Several investigators [4]–[8] found a high correlation between pulse oximeter readings and simultaneous *in vitro* SaO_2 measurements in newborn infants. They concluded that the presence of elevated levels of HbF does not affect the accuracy of pulse oximeters. Other investigators [9], [10], however, noticed that the presence of HbF may cause differences between *in vitro* determinations of SaO_2 and pulse oximeter measurements. Both groups used a Nellcor pulse oximeter (Nellcor, Inc., Hayward, CA) in their studies and corrected for the fictitiously high HbCO values measured in fetal blood by the IL 282 CO-Oximeter [17].

The present *in vitro* spectrophotometric study was undertaken since it is difficult to determine accurately whether the differences reported are due to the predominantly high levels of HbF in newborn blood or other factors which are not related to the spectral difference between HbA and HbF. It is evident from our results that there is no significant difference in the 650–1000 nm region between the absorption spectra of hemolyzed whole adult and fetal blood.

Our observations are in good agreement with related studies reported by Mendelson *et al.* [21], Pologe *et al.* [22], and Harris *et al.* [23]. Therefore, it may be concluded that it is improbable that spectrophotometric differences between HbA and HbF have caused the notice-

able discrepancies in oxygen saturation measurements reported by Fait *et al.* [9] and Jennis *et al.* [10].

The theoretical equations which were used to derive the relationship between SpO_2 and the optical properties of a pulsating vascular bed assume the validity of Beer–Lambert's law. In reality, however, the attenuation of the incident light caused by multiple scattering due to the different tissue structures and red blood cells cannot be entirely ignored. In theory, the general form of (8) is similar to the typical relationship used for calibrating pulse oximeters [24]

$$SpO_2 = \frac{K_1 - K_2(R/IR)}{K_3 - K_4(R/IR)} \quad (9)$$

where K_1 , K_2 , K_3 , and K_4 are empirically derived coefficients that are related to the extinction coefficients of oxyhemoglobin and deoxyhemoglobin. In practice, however, the values of the empirical coefficients in (9) are not identical to the extinction coefficients in (8). Although the principal relationship between SpO_2 and the R/IR ratio remains the same, it is important to realize this discrepancy when quantitative predictions of errors in pulse oximetry based on these theoretical simulations are attempted.

ACKNOWLEDGMENT

The authors would like to thank J. Widness, M.D. and L. Brown, R.N., B. S. for supplying the fetal blood.

REFERENCES

- [1] I. Yoshiya, Y. Shimada, and K. Tanaka, "Spectrophotometric monitoring of arterial oxygen saturation in the fingertip," *Med. Biol. Eng. Comput.*, vol. 18, pp. 27–32, 1980.
- [2] I. Yoshiya, and Y. Shimada, "Noninvasive spectrophotometric estimation of arterial oxygen saturation," in *Noninvasive Physiological Measurements*, P. Rolfe, Ed. New York: Academic, 1983, pp. 251–286.
- [3] M. Yelderman and J. Corenman, "Real time oximetry," in *Computing in Anesthesia and Intensive Care*, O. Prakash, S. H. Mey, and R. W. Patterson, Eds. Martinus Nijhoff, 1983, pp. 328–341.
- [4] T. D. Brooks and N. Gravenstein, "Pulse oximetry for early detection of hypoxemia in anesthetized infants," *J. Clin. Monitor.*, vol. 1, no. 2, pp. 135–137, 1985.
- [5] R. Deckardt and D. J. Steward, "Noninvasive arterial hemoglobin oxygen saturation versus transcutaneous oxygen tension monitoring in the preterm infant," *Crit. Care Med.*, vol. 12, no. 11, pp. 935–939, 1984.
- [6] M. Durand and R. Ramanathan, "Pulse oximetry for continuous oxygen monitoring in sick newborn infants," *J. Pediatrics*, vol. 109, no. 6, pp. 1052–1056, 1986.
- [7] L. G. Maxwell, A. P. Harris, M. J. Sendak, and R. T. Donham, "Monitoring the resuscitation of preterm infants in the delivery room using pulse oximetry," *Clin. Pediatrics*, vol. 26, no. 1, pp. 18–20, 1987.
- [8] S. Fanconi, P. Doherty, J. F. Edmonds, G. A. Barker, and D. J. Bohn, "Pulse oximetry in pediatric intensive care: Comparison with measured saturations and transcutaneous oxygen tension," *J. Pediatrics*, vol. 107, no. 3, pp. 362–366, 1985.
- [9] C. D. Fait, R. C. Wetzel, J. M. Dean, C. L. Schleien, and F. R. Gioia, "Pulse oximetry in critically ill children," *J. Clin. Monitor.*, vol. 1, no. 4, pp. 232–235, 1985.
- [10] M. S. Jennis and J. L. Peabody, "Pulse oximetry: An alternative method for the assessment of oxygenation in newborn infants," *Pediatrics*, vol. 79, no. 4, pp. 524–528, 1987.
- [11] R. M. Schmidh and E. M. Brosious, *Basic Laboratory Methods of Hemoglobinopathy Detection*, 8th ed., U.S. Dep. Health, Educ.,

Welfare, DHEW Pub. No. (CDC) 76-8266, Atlanta, ch. 15, pp. 6-7, 1976.

- [12] E. R. Huehns and G. H. Beaven, "Developmental changes in human haemoglobins—chapter VIII," *Clin. Development. Med.*, vol. 37, 1971.
- [13] H. F. Bunn and B. G. Forget, *Hemoglobin: Molecular, Genetic, and Clinical Aspects*. Philadelphia: Saunders, 1986.
- [14] A. Zwart, A. Buursma, B. Oeseburg, and W. G. Zijlstra, "Determination of hemoglobin derivatives with the IL 282 CO-oximeter as compared with a manual spectrophotometric five-wavelength method," *Clin. Chem.* vol. 27, no. 11, pp. 1903-1907, 1981.
- [15] W. G. Zijlstra, A. Buursma, J. Koek, and A. Zwart, Letter to the Editors, *Clin. Chem.*, vol. 29, no. 8, pp. 1556, 1983.
- [16] —, "Problems in the spectrophotometric determination of HbO₂ and HbCO in fetal blood," in *Proc. Intern. Fed. Clin. Chem. Workshop*, Oslo, Norway, 1983, pp. 45-55.
- [17] P. J. H. Cornelissen, C. L. M. Van Woensel, W. C. Van Oel, and P. A. De Jong, "Correction factors for hemoglobin derivatives in fetal blood as measured with the IL 282 CO-oximeter," *Clin. Chem.*, vol. 29, no. 8, pp. 1555-1556, 1983.
- [18] G. H. Beaven, H. Hoch, and E. R. Holiday, "The haemoglobins of the human foetus and infant—Electrophoretic and spectroscopic differentiation of adult and foetal types," *Biochem. J.*, vol. 49, no. 1, pp. 374-381, 1951.
- [19] B. L. Horecker, "The absorption spectra of hemoglobin and its derivatives in the visible and near infrared regions," *J. Biol. Chem.*, vol. 148, pp. 173-184, 1943.
- [20] O. W. Van Assendelft, *Spectrophotometry of Haemoglobin Derivatives*. The Netherlands: Royal Vangorcum Ltd., Assen, 1970.
- [21] Y. Mendelson, J. C. Kent, J. A. Widness, and L. J. Brown, "The effect of HbA and HbF on pulse oximetry," in *Proc. Ninth Ann. Conf. IEEE Eng. Med. Biol.*, Nov. 13-16, 1987.
- [22] J. A. Pologe and D. M. Raley, "Effects of fetal hemoglobin on pulse oximetry," *J. Perinat.*, vol. 7, no. 4, pp. 324-326, 1987.
- [23] P. A. Harris, M. J. Sendak, R. T. Donham, M. Thomas, and D. Duncan, "Absorption characteristics of human fetal hemoglobin at wavelengths used in pulse oximetry," *J. Clin. Monit.*, vol. 4, no. 3, pp. 175-177, 1988.
- [24] J. P. Payne and J. W. Severinghaus, Eds., *Pulse Oximetry*. New York: Springer-Verlag, 1986.



Yitzhak Mendelson (S'79-M'82) was born in Tel-Aviv, Israel, in 1949. He received the B.S. and M.S. degrees in electrical engineering from the State University of New York, Buffalo, in 1975 and 1976, respectively, and the Ph.D. degree in biomedical engineering from Case Western Reserve University, Cleveland, OH, in 1983.

He is currently an Associate Professor of Biomedical Engineering at Worcester Polytechnic Institute, Worcester, MA. His research interests are in developing invasive and noninvasive techniques for blood gas measurements, biomedical sensors, microprocessor-based medical instrumentation, and the study of light interaction with biological media.

Dr. Mendelson is a member of the Biomedical Engineering Society, AAMI, and the Optical Society of America.



Joel C. Kent (S'82-M'86-S'86-M'87) was born in Boston, MA, in 1962. He received the B.S.E. degree in electrical engineering in 1984 from Duke University, Durham, NC, and the M.Sc. degree in Biomedical Engineering in 1987 from Worcester Polytechnic Institute, Worcester, MA.

From 1987 to 1988 he was employed as Staff Engineer in the Biomedical Engineering Department at Worcester Polytechnic Institute where his research in the area of biomedical sensors included pulse oximetry, spectrophotometry, and mathematical modeling. He is currently employed as Senior Project Engineer and Research and Development Laboratory Manager at Tonometrics, Inc., Worcester, MA.

Mr. Kent is a member of the International Society for Optical Engineering, Tau Beta Pi, and Eta Kappa Nu.

Effect of fetal haemoglobin on the accuracy of pulse oximetry in preterm infants

V. S. RAJADURAI,¹ A. M. WALKER,² V. Y. H. YU¹ and A. OATES²

¹Department of Paediatrics and ²Centre for Early Human Development, Monash Medical Centre, Melbourne, Victoria, Australia

Abstract Pulse oximeters are programmed with a calibration curve derived from studies done in adults. Whether fetal haemoglobin levels affect their reliability is unclear. This study reports the accuracy of pulse oximetry in 22 preterm infants (mean 31 weeks, range 25–36 weeks gestation) between 1 h and 73 days of age. Oxygen saturation obtained from a Nellcor N-200 pulse oximeter (SpO_2) was compared with simultaneous arterial values (functional SaO_2) measured by a Radiometer OSM3 Hemoximeter over a SpO_2 range of 83–99%. Fetal haemoglobin (HbF), carboxyhaemoglobin (HbCO) and methaemoglobin (HbMet) measured by the hemoximeter ranged between 0–100%, 0–3.5% and 0–0.8% respectively. Linear regression analysis revealed a close correlation between SpO_2 and functional SaO_2 ($SpO_2 = 0.75 SaO_2 + 24.43$, $r = 0.88$, $P < 0.001$) over a wide range of values for PCV, heart rate, blood pressure, PaO_2 , $PaCO_2$ and pH. The mean SpO_2 - SaO_2 difference of 1.3, (s.d. 2.5%, $P < 0.001$) was unaffected by HgF, HbCO or HbMet but was increased in infants receiving inotropic support. We conclude that the Nellcor N-200 pulse oximeter gives reliable oxygen saturation measurements unaffected by the HbF level in preterm infants.

Key words: fetal haemoglobin; oxygen saturation; prematurity; pulse oximetry.

Pulse oximetry is a major advance in the non-invasive continuous monitoring of oxygen saturation. Its demonstrated reliability in adults and children has prompted its use in newborn infants.^{1–12} All pulse oximeters in use are programmed with a calibration curve derived from studies done in healthy adult volunteers who have adult haemoglobin (HbA) as their predominant haemoglobin. However oximeters do not differentiate between fetal haemoglobin (HbF) and HbA, and several characteristics of newborn infants such as high levels of HbF, a left-shifted oxyhaemoglobin dissociation curve and rapid heart rate compared with adults and children raise concerns regarding the applicability of this technique in neonatal medicine. The reliability of pulse oximetry also has been questioned in hyperoxic and hypoxaemic infants^{1,10} and in the presence of poor peripheral circulation.^{2,3,10} Data on the effect of HbF are contradictory.^{2,5,6,8,9} This study was designed to evaluate the performance of the pulse oximeter for assessment of oxygen saturation in sick preterm infants with emphasis on the possible effect of HbF on its accuracy.

PATIENTS AND METHODS

Twenty-two preterm infants with cardiorespiratory distress were studied between 1 h and 73 days of age (Table 1). Their clinical

problems included hyaline membrane disease (11), transient tachypnoea (3), pneumonia (2), apnoea (2), hypoplastic lung (1), congenital heart disease (1), persistent fetal circulation (1) and bronchopulmonary dysplasia (1). All required oxygen and ventilator therapy and had an indwelling arterial line inserted as part of their clinical management. The study was approved by the Research and Ethics Committee of the hospital.

Pulse oximetry was performed with a Nellcor N-200 pulse oximeter (Hayward, CA, USA). Disposable neonatal oximeters (N-25) were applied to the hand or foot according to the position of the arterial catheter thereby avoiding discrepancies resulting from shunting through a patent ductus arteriosus. For infants undergoing phototherapy or nursed under radiant warmers, precautions were taken to cover the sensor site. The oxygen saturation value obtained from the pulse oximeter (SpO_2) was accepted only in the presence of a clear and consistent pulsatile waveform display and when the pulse rate indicated by the oximeter matched that obtained from an independent cardiorespiratory monitor within 5 beats. SpO_2 and the pulsatile waveform were continuously recorded at 3 cm/min using a two channel recorder (Radiometer, Copenhagen).

Arterial oxygen saturation (SaO_2) was measured by an OSM3 Hemoximeter (Radiometer, Copenhagen) which determined fractions of oxyhaemoglobin (HbO₂), carboxyhaemoglobin (HbCO), methaemoglobin (HbMet) and HbF levels. The SaO_2 measured was corrected for the level of HbF in the blood. Zero calibration was done automatically every 2 h and quality control of the instrument was performed daily using the Qualichex reagents provided by the manufacturers. All measurements were performed in duplicate. The precision of the estimate calculated from the difference between duplicates was 0.18% and the 95% confidence intervals for the duplicate estimate were ± 0.26 . The fractional SaO_2 determined by the hemoximeter

Correspondence: Prof. V. Yu, Department of Paediatrics, Monash Medical Centre, 246 Clayton Road, Clayton, Vic. 3168, Australia.

V. S. Rajadurai, MB, BS, MD (Paed.), Neonatal Fellow. A. M. Walker, PhD, Deputy Director. V. Y. H. Yu, MD, MSc, FRACP, FRCP, DCH, Director of Neonatal Intensive Care. A. Oates, Research Assistant.

Accepted for publication 2 June 1991.

Table 1 Clinical and laboratory data

	Mean	s.d.	Range	n
Gestational ages (weeks)	31	3	25-36	22
Birthweight (g)	1680	690	805-3238	22
Heart rate (beats/min)	149	18	112-195	132
PCV (%)	45	7	33-65	85
Mean arterial pressure (mmHg)	42	9	24-68	131
Axillary skin temperature (°C)	36.8	0.3	35.8-37.8	131
Total serum bilirubin (µmol/L)	149	50	27-250	69
HbF (%)	55	33	0-100	64
HbCO (%)	1.4	0.7	0-3.5	138
HbMet (%)	0.4	0.2	0-0.8	138
SpO ₂ (%)	94	3	83-99	138
SaO ₂ (%) fractional	91	4	73-97	138
SaO ₂ (%) functional	93	4	78-98	138
PaO ₂ (mmHg)	56	10	29-86	138
pH	7.32	0.07	7.12-7.52	138
PaCO ₂ (mmHg)	43.7	8.8	22-66	138
Base excess (mmol/L)	-3.6	3.4	-10-+8	138

was converted to functional SaO₂ based on the following equation:

$$\text{Functional SaO}_2 = \frac{\text{HbO}_2}{100 - \text{HbCO} - \text{HbMet}} \times 100$$

Since the Nellcor pulse oximeter measures functional oxygen saturation, the SpO₂ readings obtained were compared with the calculated functional SaO₂ values. Blood gas analysis was performed on the same arterial blood sample using an ABL 30 Acid-Base Analyser (Radiometer, Copenhagen).

Heart rate and arterial blood pressure were monitored continuously on a Hewlett Packard cardiorespiratory monitor. Abdominal skin temperature was servocontrolled. Axillary temperature was recorded at the time of study and, if abnormal, the core temperature was measured. The central PCV was measured in all infants and the levels of serum bilirubin were determined in infants with jaundice. The peripheral perfusion status and use of vasopressor agents were also recorded for all infants.

Student's *t*-test, correlation and regression analyses and analysis of variance were performed using a commercial software package (Statview™, Brainpower Inc. CA, USA). A value of *P* < 0.05 was considered significant, with a Bonferroni correction for multiple comparisons.

RESULTS

Clinical and laboratory data from the study are shown in Table 1. The fractional SaO₂ ranged between 73 and 97% (mean 91%, s.d. 4%) and the corresponding functional values between 78 and 98% (mean 93%, s.d. 4%). The differences between functional and fractional SaO₂ were small and averaged 1.6% (s.d. 0.68%, range 0-3.6%) as they reflected the low levels of HbCO and HbMet in the study population. The 138 paired measurements of SpO₂ and functional SaO₂ were closely correlated (Fig. 1). Differences between SpO₂ and functional SaO₂ (ΔSaO₂) averaged 1.3% (s.d. 2.3%, range -4.2-7.2%, *P* < 0.001). This difference remained unchanged over a wide range of heart rate, mean arterial pressure, PCV, bilirubin, PaO₂, PaCO₂ and pH.

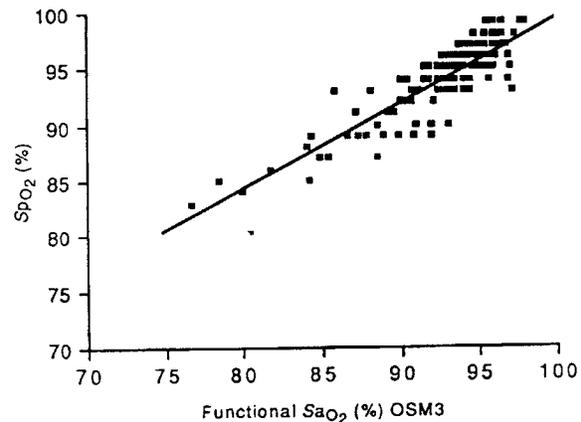


Fig. 1 Comparison of SpO₂ with functional SaO₂ (SpO₂ = 0.75 SaO₂ + 24.43, *r* = 0.88, *P* < 0.001).

Table 2 HbF, HbCO and HbMet levels expressed as percentage of total haemoglobin

	Postnatal age (days)			
	1	4-7	10-14	> 14
HbF				
Mean	86	61	22	6
s.d.	10	29	17	8
Range	65-100	16-97	0-52	0-16
n	14	16	10	5
HbCO				
Mean	0.9	1.5	1.4	0.5
s.d.	0.4	0.7	0.7	0.4
Range	0-1.6	0.8-3.5	0.7-2.8	0.2-1
n	14	16	10	5
HbMet				
Mean	0.4	0.4	0.2	0.3
s.d.	0.2	0.1	0.1	0.1
Range	0.1-0.8	0.3-0.5	0.1-0.4	0.1-0.4
n	14	16	10	5

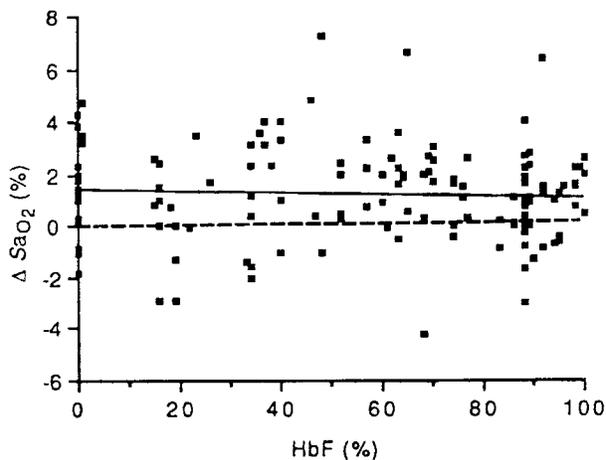


Fig. 2 ΔSaO_2 at different HbF levels ($\Delta\text{SaO}_2 = -0.003 \text{ HbF} + 1.43$, $r = 0.05$, $P = \text{NS}$).

Measurements were obtained in 21 instances in infants assessed clinically to have poor peripheral perfusion. Their mean ΔSaO_2 was not significantly different from that obtained in 117 instances in infants with normal peripheral perfusion: 1.4% (s.d. 1.8%) versus 1.3% (s.d. 1.98%). Measurements were obtained in 25 instances in infants receiving inotropic support in the form of dopamine 3–8 $\mu\text{g}/\text{kg}/\text{min}$; 17 of them also had dobutamine 5–10 $\mu\text{g}/\text{kg}/\text{min}$. Their mean ΔSaO_2 was significantly different from that obtained in 113 instances in infants not on inotropic support: 2.48% (s.d. 2.4%) versus 1.11% (s.d. 2.02%), $P < 0.005$.

HbF, HbCO and HbMet levels at different postnatal ages are shown in Table 2. HbF levels dropped progressively until 14 days postnatally ($P < 0.01$) while HbCO and HbMet levels remained unchanged. Regression analysis showed that ΔSaO_2 was not related to HbF levels (Fig. 2). The mean ΔSaO_2 values for HbF levels of 0–24%, 25–49%, 50–74% and 75–100% were 1.2% (s.d. 1.9%), 1.7% (s.d. 2.5%), 1.6% (s.d. 1.7%) and 0.9% (s.d. 1.5%) respectively. ΔSaO_2 was also unrelated to HbCO ($\Delta\text{SaO}_2 = 0.73 \text{ HbCO} + 0.26$, $r = 0.26$, $P = \text{NS}$) and to HbMet ($\Delta\text{SaO}_2 = 0.02 \text{ HbMet} + 1.25$, $r = 0.002$, $P = \text{NS}$).

DISCUSSION

Functional SaO_2 is the ratio of HbO_2 to the amount of haemoglobin capable of binding oxygen (HbO_2 and reduced haemoglobin) and, thus, this measurement includes only haemoglobin that is actually available for oxygen transport. Fractional SaO_2 is the ratio of HbO_2 to all forms of Hb measured, including measured dyshaemoglobin such as HbCO and HbMet.¹³ Some oximeters (e.g. Nellcor, Norin 8604D, Novamatrix, Spectramed Pulsat) are calibrated to measure functional SpO_2 whereas others (e.g. Radiometer Oxi pulse oximeter, Ohmeda 3700 and 3740, Sensormedics oxyshuttle, Physio-Control Lifestat 1600) are calibrated to measure fractional SpO_2 . In the same manner, devices designed for *in vitro* measurement of SaO_2 also differ. The Radiometer OSM2 Hemoximeter measures functional SaO_2 whereas IL282 and IL482 Co-Oximeter, Corning 2500 and Radiometer OSM3 Hemoximeter measure fractional SaO_2 . Since the Nellcor pulse oximeter used in the present study is calibrated

to measure functional SpO_2 , the fractional SaO_2 measured by the Radiometer OSM3 Hemoximeter was converted to functional SaO_2 before comparisons were made with SpO_2 .

We noted a rapid postnatal decline in HbF levels in our study population, down to <10% after 2 weeks. A study of infants <1500 g who required intensive care also reported a rapid decline of HbF levels to less than 10% by day 12.¹⁴ This is a result of frequent blood sampling and repeated replacement transfusions with adult blood in these high risk infants. By contrast, the transition from predominantly HbF to HbA takes place between 3 and 6 months in healthy infants.¹⁵

HbF and HbA have slightly different light absorption coefficients.^{16,17} As the calibration of currently available pulse oximeters is based upon the extinction curves of HbA, there has been concern whether the calibration is appropriate for patients with high levels of HbF. One study has shown that HbF levels greater than 50% interfered with the accuracy of pulse oximetry readings;⁸ the mean $\text{SpO}_2 - \text{SaO}_2$ difference was insignificant when HbF levels were less than 25% but increased to 3.6% when HbF levels were greater than 75%. In contrast, other studies have found that pulse oximeter readings were not influenced by HbF values.^{5,9,18} In the present study, we have shown that HbF levels do not have any significant effect on ΔSaO_2 . This is in keeping with theoretical estimates of errors arising from differences between the extinction curves for HbF and HbA; the errors generated are insignificant clinically, ranging from 0.41% at 100% saturation to a maximum of 1.12% at 50% saturation.¹⁶ Moreover the absorption characteristics of fetal and adult oxygenated and reduced haemoglobins are nearly identical over the spectrum of wavelength 600–1050 nm¹⁹ and most pulse oximeters (including the Nellcor N-200) base their estimation of SaO_2 on absorption at wavelengths of 660 and 920 nm. Thus even though the algorithms used by the pulse oximeters have been determined from studies in adults with high levels of HbA, theoretical and practical considerations suggest that they can be validly extrapolated to infants with high concentrations of HbF.

The levels of HbCO and HbMet found in the infants in the present study were not high enough to influence the accuracy of the pulse oximeter. However infants born to mothers who are heavy smokers are known to have HbCO levels as high as 5%.²⁰ Hereditary enzyme deficiency, exposure to toxins such as prilocaine, sulphur drugs and HbM disease can cause methaemoglobinaemia in the newborn period. In infants with significant methaemoglobinaemia or carboxyhaemoglobinaemia (levels >10% of total Hb), pulse oximetry is known to overestimate true SaO_2 .²¹

Decreased peripheral perfusion is not uncommon in sick preterm neonates. There are conflicting reports in the literature regarding its effect on the accuracy of the pulse oximeter.^{2,3,10,22} Measurement of oxygen saturation by pulse oximetry depends on a pulsating vascular bed. We have found the SpO_2 measured by the pulse oximeter to be reliable even in the presence of poor peripheral perfusion as long as a clear and consistent pulsatile waveform was obtained. Infusion of vasoactive drugs may affect pulsatility and impair the accuracy of the oximeter. Dopamine infusion was reported to result in poor correlation between SpO_2 and SaO_2 in infants as well as in adults.^{22,23} Although the mean ΔSaO_2 in infants receiving inotropic support in our study was statistically greater, the magnitude of the effect is insignificant clinically. However as the doses of inotropes we employed were low, we suggest that further research be done in order to investigate the possibility that there may be a dose-

dependent effect of dopaminergic inotropics on the accuracy of pulse oximetry.

In conclusion, the Nellcor N-200 pulse oximeter was found to give reliable oxygen saturation measurements over a range of 83–99% in sick preterm infants. Pulse oximeter saturations were unaffected by HbF values which ranged from 0 to 100% and were reliable in the presence of poor peripheral perfusion provided a clear and consistent pulsatile waveform was present. The low levels of HbCO and HbMet found in infants did not interfere with its accuracy but inotropic agents even at low doses were found to have a small but significant effect on pulse oximeter readings.

REFERENCES

- 1 Krauss A. N., Waldman S., Frayer W. W., Auld P. A. M. Noninvasive estimation of arterial oxygenation in newborn infants. *J. Pediatr.* 1978; **93**: 275–8.
- 2 Deckardt R., Steward D. J. Noninvasive arterial hemoglobin saturation versus transcutaneous oxygen tension monitoring in the preterm infant. *Critical Care Med.* 1984; **12**: 935–9.
- 3 Fanconi S., Doherty P., Edmonds J. F., Barker G. A., Bohn D. J. Pulse oximetry in pediatric intensive care: Comparison with measured saturations and transcutaneous oxygen tension. *J. Pediatr.* 1985; **107**: 362–6.
- 4 Solimano A. J., Smyth S. A., Mann T. K., Albersheim S. G., Lockitch G. Pulse oximetry advantages in infants with bronchopulmonary dysplasia. *Pediatrics* 1986; **78**: 844–9.
- 5 Durand M., Ramanathan R. Pulse oximetry for continuous oxygen monitoring in sick newborn infants. *J. Pediatr.* 1986; **109**: 1052–6.
- 6 Southall D. P., Bignall S., Stebbens V. A., Alexander J. R., Rivers R. P. A., Lissauer T. Pulse oximeter and transcutaneous arterial oxygen measurements in neonatal and paediatric intensive care. *Arch. Dis. Child.* 1987; **62**: 882–8.
- 7 Wasunna A., Whitelaw A. G. L. Pulse oximetry in preterm infants. *Arch. Dis. Child.* 1987; **62**: 957–71.
- 8 Jennis M. S., Peabody J. L. Pulse oximetry: An alternative method for the assessment of oxygenation in newborn infants. *Pediatrics* 1987; **79**: 524–8.
- 9 Ramanathan R., Durand M., Larrazabal C. Pulse oximetry in very low birthweight infants with acute and chronic lung disease. *Pediatrics* 1987; **79**: 612–17.
- 10 Fanconi S. Reliability of pulse oximetry in hypoxic infants. *J. Pediatr.* 1988; **112**: 424–7.
- 11 Reynolds G. J., Yu V. Y. H. Guidelines for the use of pulse oximetry in the non-invasive estimation of oxygen saturation in oxygen-dependent newborn infants. *Aust. Paediatr. J.* 1988; **24**: 346–50.
- 12 Hay W. W., Brookway B. A., Eyzaguirre M. Neonatal pulse oximetry: Accuracy and reliability. *Pediatrics* 1989; **83**: 717–22.
- 13 Tremper K. K. Pulse oximetry. *Chest* 1989; **95**: 713–15.
- 14 Ryan C. A., Barrington K. J., Vaughan D., Finer N. N. Directly measured arterial oxygen saturation in the newborn infant. *J. Pediatr.* 1986; **109**: 526–9.
- 15 Oski F. A., Delivoria-Papadopoulos M. The red cells, 2,3-diphosphoglycerate and tissue oxygen release. *J. Pediatr.* 1970; **77**: 941–56.
- 16 Pologe J. A., Raley D. M. Effects of fetal hemoglobin on pulse oximetry. *J. Perinatol.* 1988; **7**: 324–6.
- 17 Fogh-Anderson N., Siggaard-Anderson O., Lundsgaard F. C., Wimberley P. D. Spectrophotometric determination of hemoglobin pigments in neonatal blood. *Clin. Chim. Acta* 1987; **166**: 291–6.
- 18 Anderson J. V. The accuracy of pulse oximetry in neonates: Effects of fetal hemoglobin and bilirubin. *J. Perinatol.* 1988; **7**: 323.
- 19 Harris A. P., Sendak M. J., Donham R. T., Thomas M., Duncan D. Absorption characteristics of human fetal hemoglobin at wavelengths used in pulse oximetry. *J. Clin. Monit.* 1988; **4**: 175–7.
- 20 Farquharson R. G. The fetus and cigarette smoke (letter). *Pediatrics* 1983; **71**: 462–3.
- 21 Watcha M. F., Connor M. T., Hing A. V. Pulse oximetry in methemoglobinemia. *Am. J. Dis. Child.* 1989; **143**: 845–7.
- 22 Dziedzic K., Vidyasagar D. Pulse oximetry in neonatal intensive care. *Clin. Perinatol.* 1989; **16**: 177–97.
- 23 Mihm F. G., Halperin B. D. Noninvasive detection of profound arterial desaturations using a pulse oximetry device. *Anesthesiology* 1985; **62**: 85–7.

Absorption Spectra of Human Fetal and Adult Oxyhemoglobin, De-Oxyhemoglobin, Carboxyhemoglobin, and Methemoglobin

W. G. Zijlstra, A. Buursma, and W. P. Meeuwssen-van der Roest

We determined the millimolar absorptivities of the four clinically relevant derivatives of fetal and adult human hemoglobin in the visible and near-infrared spectral range (450–1000 nm). As expected, spectral absorption curves of similar shape were found, but the small differences between fetal and adult hemoglobin absorptivity were important enough that they should be taken into account in multicomponent analysis of hemoglobin derivatives. Common pulse oximeters, however, involving light of 660 and 940 nm, are so insensitive to the presence of fetal hemoglobin that they can be used safely in neonates. The error in pulse oximetry caused by the presence of carboxyhemoglobin is insubstantial, but methemoglobin gives either an underestimation or an overestimation at high or low oxygen saturation, respectively, the turning point being near 70% saturation.

Additional Keyphrases: oxygen saturation · multicomponent analysis · pulse oximeter

When spectrophotometric multicomponent analysis of hemoglobin derivatives came into more general use, incorrect results were occasionally obtained for fetal blood (1, 2). This proved to be caused by small differences between the light absorption spectra of human fetal (HbF) and adult hemoglobin (HbA) (3).¹ Some newer, common multiwavelength photometers for measuring hemoglobin derivatives have therefore been equipped with a "fetal mode," in which the differences in absorptivity between HbA and HbF have been taken into account as much as possible (4). Because few data are available concerning the absorptivities of the clinically relevant derivatives of HbF, and the proportion of HbF to HbA in the blood of newborn infants varies and rapidly declines in the first weeks of life, use of this fetal mode yields but an approximation, though a sufficiently close one for all practical purposes (5). However, possible differences between HbA and HbF in absorption of the various hemoglobin derivatives in the red and infrared spectral region have caused concern about the accuracy of pulse oximeter data from newborn infants (6, 7).

We have re-investigated the absorption spectra of the common derivatives of HbF, including carboxyhemoglobin (HbCO) and methemoglobin (hemoglobin, Hi), and

extended the spectral range to 1000 nm. The absorptivity data thus obtained are also applicable to multicomponent analysis for hemoglobin derivatives in fetal and neonatal blood with a general purpose diode-array spectrophotometer (8). New spectra of the common derivatives of HbA were determined for comparison with the corresponding HbF spectra.

Materials and Methods

Adult human blood was obtained from apparently healthy donors, and fetal blood by puncture of the umbilical cord immediately after delivery. The blood was anticoagulated with sodium heparin (100 USP units/mL of blood). The plasma was removed and the erythrocytes were resuspended in a 9 g/L NaCl solution. The total hemoglobin concentration (c_{Hb}) was kept between 100 and 150 g/L. Oxyhemoglobin (HbO₂), deoxyhemoglobin (Hb), and HbCO solutions were prepared by tonometry of the erythrocyte suspensions with O₂/CO₂, N₂/CO₂, and N₂/CO/CO₂ mixtures, respectively, as described previously (8). Hi was prepared from Hb by the addition of solid hexacyanoferrate III [K₃Fe(CN)₆]. Erythrolysis was performed differently from our earlier procedure. After tonometry for 2 h, 2 mL of a 100 mL/L solution of the nonionic detergent Sterox SE (Hartman, Leddon Co., Philadelphia, PA 19104) was introduced into the revolving tonometer; the solution was in equilibrium with the gas mixture flowing through the tonometer. After erythrolysis, tonometry was continued for ~20 min. For HbO₂ and HbCO, the spectrophotometer cuvetts were filled directly from the tonometers through cotton-wool filters; contact between the sample to be measured and the room air was avoided. For Hb, the cuvetts were filled by a slightly different procedure, allowing the addition of 3 mg of sodium dithionite (Na₂S₂O₄) per 2 mL of erythrolysate.

Absorbance measurements were made at room temperature (20–24 °C) with a Model HP8450 A diode-array spectrophotometer (Hewlett-Packard Co., Palo Alto, CA 94304) in the spectral range of 450–700 nm with a lightpath length (*l*) of 0.013 cm, and in the range of 600–800 nm with *l* = 1.000 cm for HbCO, *l* = 0.203 cm for HbO₂ and Hb, and *l* = 0.100 cm for Hi. The samples we used for the absorbance measurements in the latter range were subsequently measured in the range of 660–1000 nm at various intervals with an Optica CF4 grating spectrophotometer (Optica, S.p.A., Milan, Italy) and the same values for lightpath length. In each sample, c_{Hb} was measured by the standardized methemoglobin cyanide method (9). The absorptivities (ϵ expressed in L · mmol⁻¹ · cm⁻¹) were calculated by dividing the absorbances at each wavelength by c_{Hb} .

Department of Physiology, University of Groningen, 9712 KZ Groningen, The Netherlands.

¹ Nonstandard abbreviations: HbA, adult hemoglobin; HbF, fetal hemoglobin; Hb, de-oxyhemoglobin; HbO₂, oxyhemoglobin; HbCO, carboxyhemoglobin; Hi, methemoglobin; and c_{Hb} , total hemoglobin concentration in blood.

Received February 26, 1991; accepted June 28, 1991.

(mmol/L) and l (cm). The pH of Hi-containing samples was determined with a Model PHM28 pH meter (Radiometer A/S, Copenhagen, Denmark).

For Hi, this procedure yields correct values for ϵ^λ . For Hb, HbO₂, and HbCO, the measured values of ϵ^λ must be corrected for any contaminating Hi. To this end, the Hi fraction (F_{Hi}) of each sample was determined with a Hemoximeter OSM3 (Radiometer) (10), and the absorptivity of derivative x was calculated with the following equation:

$$\epsilon_x^\lambda = (\epsilon^\lambda - F_{\text{Hi}} \cdot \epsilon_{\text{Hi}}^\lambda) / (1 - F_{\text{Hi}}) \quad (1)$$

where ϵ_x^λ is the corrected absorptivity of Hb, HbO₂, or HbCO at wavelength λ , $\epsilon_{\text{Hi}}^\lambda$ is the absorptivity of Hi, and ϵ^λ is the absorptivity measured for the Hb, HbO₂, and HbCO solutions.

The absorptivities thus determined for hemoglobin solutions from adult blood specimens were assumed to be those of pure HbA. For the hemoglobin solutions from umbilical-cord blood, these absorptivities were assumed to be those of a mixture of HbA and HbF. In calculating the absorptivities of pure HbF, we used a procedure similar to that for eliminating the effect of any Hi in the Hb, HbO₂, and HbCO solutions. The HbF fraction of each sample (F_{HbF}) was determined by an alkaline denaturation method according to Jonxis and Visser (11), and was measured with the HP8450 A spectrophotometer ($\lambda = 576$ nm). The absorptivities of the various derivatives of HbF were calculated with the following equation:

$$\epsilon_{\text{HbF}}^\lambda = [\epsilon_{\text{HbA/HbF}}^\lambda - (1 - F_{\text{HbF}}) \cdot \epsilon_{\text{HbA}}^\lambda] / F_{\text{HbF}} \quad (2)$$

where $\epsilon_{\text{HbF}}^\lambda$ is the absorptivity of a derivative of HbF at wavelength λ , $\epsilon_{\text{HbA/HbF}}^\lambda$ is the absorptivity of the corresponding derivative as measured for the HbA/HbF mixture, and $\epsilon_{\text{HbA}}^\lambda$ is the absorptivity of the corresponding derivative of HbA.

The significance of the differences between the absorptivities of HbA and HbF was assessed by Student's t -test for unpaired samples, two-tailed. A difference was considered significant when P was <0.05 .

Results

Figure 1 shows the absorption spectra of Hb, HbO₂, HbCO, and Hi for HbA and HbF in the spectral range of 450–700 nm. The absorptivities of the various derivatives at wavelengths near the principal light-absorption maxima and minima are presented in Table 1. The data show that most of the differences between HbA and HbF, apparent from Figure 1, are statistically significant. Figure 2 shows the HbA and HbF absorption spectra of the various derivatives in the spectral range of 600–800 nm; an expanded ordinate is used because the absorptivities are lower in this region. In this range, the absorption spectra of Hb, HbO₂, and HbCO are not appreciably different between HbA and HbF. In the left panel of Figure 2, all four absorptivity curves converge to the isosbestic point of Hb and HbO₂, which is only slightly above 800 nm (12). Figure 2 shows that, for Hi, the absorptivities of HbA and HbF differ over almost the entire spectral region, the difference being statistically significant at most wavelengths. At (e.g.) 680 nm, $\epsilon_{\text{Hi}}(\text{HbF}) = 0.286 \pm 0.009$ and $\epsilon_{\text{Hi}}(\text{HbA}) = 0.257 \pm 0.004$ L · mmol⁻¹ · cm⁻¹ (mean \pm SEM; $P < 0.001$). This difference is not exclusively the result of a difference in pH between the Hi solutions of HbA and HbF; the pH of the Hi solutions of HbA was 7.275 (SD 0.027), and that of the Hi solutions of HbF was 7.068 (SD 0.023). Because the pH dependency of the light absorption spectrum of Hi depends on its OH⁻-binding affinity, which may be different for various kinds of hemoglobin (13), there was no point in eliminating the difference in pH. Moreover, this would have involved the unwanted use of either a lower p_{CO_2} or addition of buffer salts to the Hi solutions of HbF.

Table 2 shows a selection of absorptivities of the four

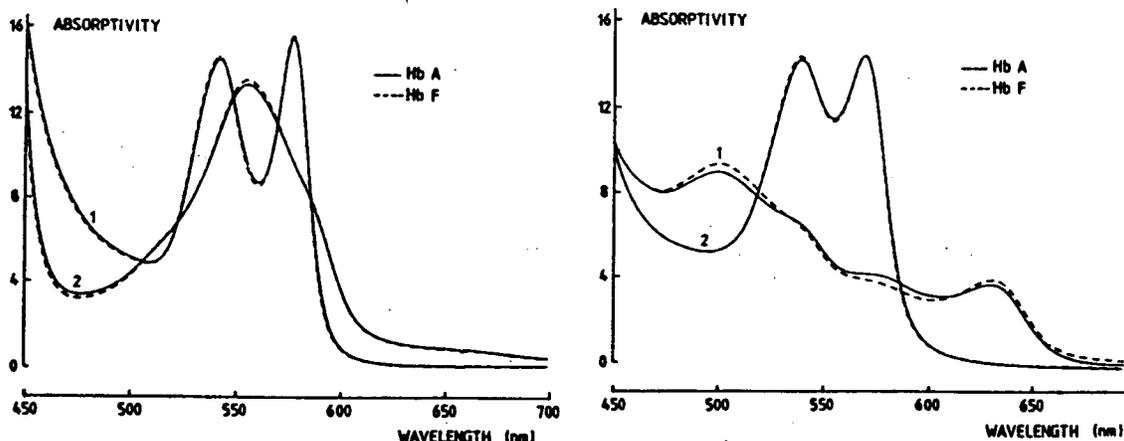


Fig. 1. Light absorption spectra of the common derivatives of HbA and HbF in the visible range

Left panel: oxyhemoglobin (1) and de-oxyhemoglobin (2); right panel: methemoglobin (1) and carboxyhemoglobin (2). The absorptivity is expressed in L · mmol⁻¹ · cm⁻¹

Table 1. Millimolar Absorptivities near Principal Peaks and Troughs in Spectra of HbF and HbA Derivatives

		ϵ^a , L · mmol ⁻¹ · cm ⁻¹ , mean ± SEM		
Min/Max	λ , nm	HbF (n=5)	HbA	P
Hb derivative				
Min	476	3.14 ± 0.028	3.33 ± 0.019 (6)	<0.001
Max	554	13.55 ± 0.054	13.35 ± 0.052 (6)	<0.05
HbO₂ derivative				
Min	508	4.83 ± 0.039	4.88 ± 0.008 (6)	—
Max	540	14.48 ± 0.037	14.32 ± 0.030 (6)	<0.01
Max	542	14.62 ± 0.040	14.52 ± 0.025 (6)	<0.10
Min	580	8.60 ± 0.049	8.77 ± 0.017 (6)	<0.01
Max	576	15.38 ± 0.041	15.27 ± 0.037 (6)	<0.10
Max	578	15.45 ± 0.038	15.36 ± 0.030 (6)	<0.10
HbCO derivative				
Min	496	5.22 ± 0.021	5.22 ± 0.018 (8)	—
Max	538	14.46 ± 0.033	14.30 ± 0.041 (8)	<0.05
Max	540	14.40 ± 0.035	14.27 ± 0.038 (8)	<0.05
Min	554	11.52 ± 0.022	11.63 ± 0.031 (8)	<0.05
Max	568	14.41 ± 0.030	14.43 ± 0.040 (8)	—
Max	570	14.42 ± 0.035	14.46 ± 0.042 (8)	—
Hi derivative				
Max	500	9.43 ± 0.043	9.07 ± 0.017 (6)	<0.001
Max	632	4.03 ± 0.033	3.80 ± 0.032 (6)	<0.001

^a n is listed in parentheses.

hemoglobin derivatives of HbF and HbA through the entire range of 450–1000 nm, including some wavelengths of interest for special purposes, e.g., 660 and 940 nm, which are used in pulse oximetry (14), and 700, 775, 805, 845, 880, and 904 nm, which are used in near-infrared spectrophotometry of organs and tissues in vivo (15, 16). The values for 450–600 nm are based on measurements with the HP8450 A diode-array spectrophotometer, and those for 600–1000 nm on measurements with the Optica CF4 grating spectrophotometer. Statistical analysis shows that for $\lambda > 800$ nm, there is no difference between HbA and HbF for HbCO, which absorbs hardly any light in this region, whereas for Hb,

HbO₂, and Hi, the differences are significant at most wavelengths. Table 3 shows this for the wavelengths commonly used in pulse oximetry.

Discussion

Table 1 does not show the exact wavelengths of maximum and minimum light absorption of the various hemoglobin derivatives because the spectral resolution of the diode-array spectrophotometer is limited, actually measuring light absorption at 2-nm intervals. This caused a little distortion in the spectra as depicted in Figure 1. The highest peak in the HbO₂ spectrum of HbA is measured at 578 nm, whereas the true α -peak is at 576.9 nm (13). Because locating the peaks and troughs in the absorption spectra exactly requires a spectral resolution of about 0.1 nm, which in our laboratory can be accomplished only when a laborious manual procedure is used, we preferred the method described. For comparing the absorption spectra of HbA and HbF, the limited spectral resolution of the diode-array spectrophotometer is hardly a disadvantage and it is amply outweighed by the accuracy with which the absorption is measured at each wavelength and the rapidity with which absorption spectra can be determined over a wide range of wavelengths.

The absorptivity data for HbA as given in Tables 1 and 2 are in fair agreement with those formerly released from our laboratory (13, 17, 18), although several technical modifications have been carried out over time. The slightly higher ϵ_{Hb} values in the red and near-infrared region reported previously (17), which cause a displacement of the isosbestic point of Hb and HbO₂ to 815 nm, are caused by adding sodium dithionite to oxygenated hemolysates. This produces Hb solutions with absorption spectra showing a minor upward displacement at $\lambda > 660$ nm; consequently, the crossover point for the HbO₂ spectra is shifted to longer wavelengths. In the present procedure we have added only a tiny amount of Na₂S₂O₄ to the solutions after the deoxygenation by tonometry with N₂/CO₂, to avoid any re-oxygenation in

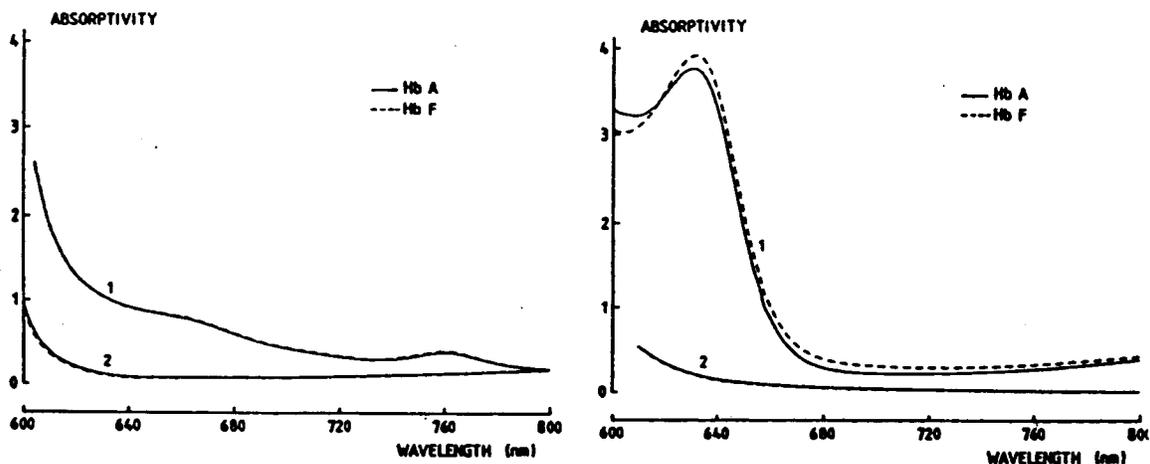


Fig. 2. Light absorption spectra of the common derivatives of HbA and HbF in the red- and near-infrared range. Left panel: de-oxyhemoglobin (1) and oxyhemoglobin (2); right panel: methemoglobin (1) and carboxyhemoglobin (2). The absorptivity is expressed in L · mmol⁻¹ · cm⁻¹.

Table 2. Millimolar Absorptivities ($L \cdot \text{mmol}^{-1} \cdot \text{cm}^{-1}$) of Four Hemoglobin Derivatives of HbF and HbA at Selected Wavelengths in the Visible and Near-Infrared Spectral Range

λ , nm	ϵ_{Hb}		ϵ_{HbO_2}		ϵ_{HbCO}		ϵ_{Hi}	
	HbF	HbA	HbF	HbA	HbF	HbA	HbF	HbA
	n = 5	n = 6	n = 5	n = 6	n = 5	n = 8	n = 5	n = 6
450	12.94	13.51	15.82	16.20	9.98	10.07	10.34	10.32
480	3.18	3.35	6.61	6.72	5.63	5.62	8.29	8.16
500	4.25	4.34	5.08	5.15	5.28	5.28	9.43	9.07
520	6.50	6.48	6.03	5.98	8.37	8.30	8.14	7.81
540	10.57	10.50	14.48	14.32	14.40	14.27	6.47	6.59
542	11.19	11.09	14.62	14.52	14.12	14.04	6.26	6.42
550	13.15	12.97	11.84	12.01	12.02	12.11	5.22	5.42
554	13.55	13.35	9.95	10.17	11.52	11.63	4.72	4.91
580	13.30	13.09	8.60	8.77	12.18	12.25	4.25	4.43
588	11.97	11.85	10.49	10.50	14.41	14.43	4.02	4.26
576	10.06	10.07	15.38	15.27	11.68	11.76	3.86	4.22
578	9.60	9.62	15.45	15.36	10.09	10.24	3.81	4.19
590	6.94	6.87	4.00	4.26	2.76	2.89	3.35	3.68
600	3.74	3.74	0.90	0.96	1.06	1.10	3.06	3.29
	n = 5	n = 7	n = 5	n = 6	n = 4	n = 6	n = 3	n = 6
630	1.05	1.06	0.10	0.11	0.18	0.19	3.95	3.80
660	0.83	0.81	0.07	0.08	0.07	0.06	0.87	0.81
680	0.62	0.61	0.08	0.09	0.04	0.03	0.29	0.28
700	0.45	0.44	0.08	0.09	0.03	0.02	0.23	0.20
750	0.40	0.39	0.13	0.14	0.02	0.01	0.26	0.25
775	0.29	0.29	0.16	0.17	0.02	0.01	0.32	0.31
800	0.21	0.20	0.19	0.20	0.01	0.01	0.40	0.39
805	0.20	0.20	0.19	0.21	0.01	0.01	0.41	0.40
840	0.18	0.19	0.23	0.25	0.01	0.01	0.53	0.51
845	0.18	0.19	0.24	0.25	0.01	0.01	0.54	0.51
880	0.19	0.20	0.27	0.28	0.01	0.01	0.62	0.58
904	0.20	0.21	0.28	0.30	0.01	0.00	0.68	0.63
920	0.20	0.21	0.29	0.30	0.01	0.00	0.72	0.66
940	0.17	0.18	0.28	0.29	0.00	0.00	0.75	0.69
960	0.12	0.14	0.27	0.28	0.00	0.00	0.77	0.71
1000	0.04	0.06	0.25	0.25	0.00	0.00	0.80	0.72

Table 3. Millimolar Absorptivities of HbA and HbF at Wavelengths Used in Pulse Oximetry

Derivative	λ , nm	ϵ_{HbF}^a	n	ϵ_{HbA}^a	n	P
Hb	660	0.826 ± 0.005	5	0.812 ± 0.006	7	ns.
	940	0.187 ± 0.002	5	0.181 ± 0.003	7	<0.01
HbO ₂	660	0.074 ± 0.002	5	0.080 ± 0.005	6	ns.
	940	0.284 ± 0.002	5	0.294 ± 0.002	6	<0.01
HbCO	660	0.065 ± 0.005	4	0.061 ± 0.003	6	ns.
	940	0.004 ± 0.003	4	0.001 ± 0.002	6	ns.
Hi	660	0.866 ± 0.004	3	0.811 ± 0.005	6	<0.001
	940	0.751 ± 0.009	3	0.691 ± 0.012	6	<0.02

^a $L \cdot \text{mmol}^{-1} \cdot \text{cm}^{-1}$, mean \pm SEM. ns., not significant ($P > 0.05$).

filling the cuvetts. This appeared to have no effect on the absorption spectra of the Hb solutions.

We measured the absorptivities of the Hi solutions at the pH prevailing after tonometry with N_2/CO_2 and addition of $\text{K}_3\text{Fe}(\text{CN})_6$. The significant difference between the pH values of the Hi solutions of HbA and HbF resulting from this procedure raises the question as to whether (and, if so, to what extent) the differences

between the absorption spectra are caused by differences in the degree of HiOH formation between HbA and HbF. This problem could not be solved by simply comparing the Hi spectra of HbA and HbF at the same pH, for it has been shown that different kinds of Hi may vary in OH^- -binding affinity. Comparing Hi solutions of human and dog hemoglobin, we found significant differences at pH 7.15, but increasing the pH of the Hi solution from dog blood modified the spectra to coincide almost completely. Thus, the affinity for OH^- of dog Hi was lower than that of human Hi (13).

In comparing the Hi spectrum of HbF with a family of Hi spectra of HbA made at different pH values, we did not find a single pH value at which the absorption spectra could be made to coincide. In Figure 1, the Hi spectrum of HbF exceeds that of HbA in both maxima (500 and 632 nm). If, by decreasing the pH of the Hi solutions of HbA, the peaks at 500 nm are made to coincide, the HbA peak at 632 nm exceeds that of HbF. The most prominent difference between the Hi spectra of HbA and HbF, however, is in the region between 560 and 610 nm, where the spectrum of HbF is definitely

flatter and lower than that of HbA. In deciding which Hi spectra of HbF and HbA to present in these figures and tables, we selected the spectra at the pH of the samples after lysis of erythrocyte suspensions at normal arterial p_{CO_2} . This most resembles what happens in the spectrophotometric multicomponent analysis of hemoglobin derivatives. This also enabled us to keep the procedure for preparing the Hi solutions as similar as possible to that used for the other derivatives, and identical for HbA and HbF. Although changes in pH have also been shown to influence the absorption spectra of HbO₂ and HbCO (5, 19), these effects are small enough to be neglected in all clinical applications of hemoglobin spectrophotometry.

The significant differences for Hb between HbF and HbA as shown in Figure 1 and Table 1 were not apparent in our original material. There are some technical differences between the two series of measurements, which may explain the observed differences. Our earlier measurements were made with hemolysates instead of the erythrolysates used in the present investigation, and no corrections were made for the possible presence of Hi in the solutions of the other derivatives.

Our absorption spectra of HbF show qualitatively the same differences in comparison with those of HbA as described by Fogh-Andersen et al. (4): the α and β peaks of HbO₂ and the β peak of HbCO are somewhat higher, and there is an increase in the maximum of the Hb spectrum near 554 nm. A more quantitative comparison between their data and ours is ruled out by the way in which their data were presented. We do not agree with Mendelson and Kent (14) and with Harris et al. (20) that there are no differences between HbF and HbA as to the absorption spectra of Hb and HbO₂ in the red and infrared spectral region, but we do agree with their conclusion that the performance of the usual pulse oximeters is not impaired through differences between the absorption spectra of HbF and HbA. In fact, ascertaining the reliability of pulse oximeters used on newborn infants was the principal objective of their investigations. Therefore, they did not need to measure as accurately as possible the absorptivities of the four derivatives of HbF and HbA. We did make this effort because previous experience showed that in multicomponent analysis of hemoglobin derivatives, these tiny differences are vital.

This has clearly been shown by the spurious HbCO fractions found when we measured oxygenated fetal blood with an IL 282 CO-Oximeter (1). The results of the present investigation enabled us to perform a realistic simulation of the IL 282 procedure, including all four relevant hemoglobin derivatives. When a matrix based on the absorptivities of Hb, HbO₂, HbCO, and Hi derivatives of HbA at the wavelengths of the IL 282 (535.0, 585.2, 594.5, and 626.6 nm) was used, introduction of the absorbance values calculated for a completely deoxygenated sample of 100% HbF yielded an HbCO fraction of 0%, whereas the absorbance values of a fully

oxygenated sample of 100% HbF yielded an HbCO fraction of 6.1%, which is in excellent agreement with the experimental data formerly obtained (1).

Predicting the influence of HbF on the oxygen saturation (s_{O_2}), as measured by a pulse oximeter calibrated in vivo on adult human volunteers, from the observed differences between the absorption spectra of HbA and HbF, is possible only with certain assumptions. A pulse oximeter does not measure absorbance as does a spectrophotometer, but extracts from the light transmitted by the tissue a signal that is regarded as representative for the light absorbed by the arterial blood. The ratio $d/dt (\ln I^{\lambda_1}) : d/dt (\ln I^{\lambda_2})$, where $\ln I^{\lambda_1}$ and $\ln I^{\lambda_2}$ are the natural logarithms of the (time variant) transmitted light at wavelengths λ_1 and λ_2 , respectively, is considered to relate to s_{O_2} as does the spectrophotometric ratio $A^{\lambda_1}/A^{\lambda_2}$ (14). This is not quite correct, because light scattering is not properly taken into account (21), but given the good clinical performance of the current pulse oximeters (6, 22), it seems to be a fair approximation. Consequently, we consider it justifiable to estimate the errors in pulse oximetry, which may result from differences in the absorptivities of HbF and HbA and from the presence of other hemoglobin derivatives in the blood, by calculating their effect on s_{O_2} in the case of a two-wavelength spectrophotometric method. If neither of the two wavelengths used is at an isosbestic point of the Hb and HbO₂ spectra, s_{O_2} may be calculated from the following equation (12):

$$s_{O_2} = \frac{\epsilon_{Hb}^{\lambda_1} - \epsilon_{Hb}^{\lambda_2} \cdot (A^{\lambda_1}/A^{\lambda_2})}{\epsilon_{Hb}^{\lambda_1} - \epsilon_{HbO_2}^{\lambda_1} - (\epsilon_{Hb}^{\lambda_1} - \epsilon_{HbO_2}^{\lambda_1}) \cdot (A^{\lambda_1}/A^{\lambda_2})} \quad (3)$$

Taking for λ_1 and λ_2 the wavelengths usually chosen in pulse oximetry (660 and 940 nm), we can use the absorptivity data of Table 3 to calculate the apparent s_{O_2} values resulting from the presence of HbF and other hemoglobin derivatives such as HbCO and Hi, when the absorptivities of Hb and HbO₂ of HbA have been substituted for the constants in equation 3. Some results of such calculations are shown in Table 4. The effect of the presence of HbF proves to be a slight underestimation of s_{O_2} , which is of no clinical importance. This is in agreement with the results of the only clinical investigation of the accuracy of pulse oximeter readings in infants in which the HbF fractions of the blood were quantitatively taken into account (6). There was a small, but statistically significant decrease of s_{O_2} at high fractions of HbF.

The limited effect of the presence of HbCO on s_{O_2} (Table 4) is also in agreement with clinical experience of pulse oximetry (23). Note that the opinion that pulse oximetry gives erroneous information in the case of CO intoxication because it does not signal the presence of HbCO (24) is based on a misunderstanding of the underlying spectrophotometric principles, as explained earlier by Eisenkraft (23). Mendelson and Kent (25) investigated the influence of HbCO on pulse oximetry readings by using a tissue model simulating the optical properties of biological tissue and arterial pulsations

Table 4. Influence of HbF, HbCO, and Hi on s_{O_2} by Spectrophotometric 2- λ Method with Wavelengths As Used in Pulse Oximetry (660/940 nm)

Hemoglobin derivatives in blood	s_{O_2} % ^a			
	100	80	60	40
HbA	100	80	60	40
HbA/10% HbCO ^b	99.1	79.2	59.3	39.4
HbA/10% Hi	93.0	77.8	62.1	46.7
40% HbF	99.9	79.6	59.2	38.8
80% HbF	99.7	79.1	58.4	37.6
40% HbF/10% HbCO ^c	98.9	78.7	58.5	38.2
40% HbF/10% Hi	92.7	77.2	61.7	46.1
80% HbF/10% HbCO	98.8	78.3	57.7	37.0
80% HbF/10% Hi	92.4	76.8	61.2	45.6

^a Calculated with equation 3 (see Discussion).

^b HbA/10% HbCO, 100% adult hemoglobin, of which 10% is liganded with CO.

^c 40% HbF/10% HbCO, 40% fetal and 60% adult hemoglobin, of which 10% is liganded with CO.

similar in size and shape to real photoplethysmograms. However, in such an approach, outdated blood bank blood is circulated through artificial tubes and repeatedly passes through a pump and an oxygenator, which causes some degree of hemolysis and deterioration of small amounts of hemoglobin into products with other spectral properties. We surmise that such a process has caused the reported overestimation of s_{O_2} by some 5% when 10% HbCO was present, which agrees with neither our results nor clinical experience.

As to the influence of Hi on s_{O_2} as measured at the wavelengths of pulse oximetry, Table 4 shows an underestimation and overestimation of s_{O_2} at high and low oxygenation, respectively. Given the limited usable data on the influence of Hi on pulse oximetry readings, these are in agreement with the results of our calculation (26). Most of the clinical papers on this subject, however, are difficult to interpret, because various definitions of oxygen saturation (27, 28) are used, and because methemoglobinemia is treated with methylene blue, which, through its color, has an effect on the pulse oximeter readings (29, 30).

References

- Zwart A, Buursma A, Oeseburg B, Zijlstra WG. Determination of hemoglobin derivatives with the IL 282 CO-Oximeter as compared with a manual spectrophotometric five-wavelength method. *Clin Chem* 1981;27:1903-7.
- Huch R, Huch A, Tuschmid P, Zijlstra WG, Zwart A. Carboxyhemoglobin concentration in fetal cord blood [Letter]. *Pediatrics* 1983;71:461-2.
- Zijlstra WG, Buursma A, Koek JN, Zwart A. Problems in the spectrophotometric determination of HbO₂ and HbCO in fetal blood. In: Maas AHL, Kofstad J, Siggaard-Andersen O, Kokholm G, eds. *Physiology and methodology of blood gases and pH*. Copenhagen, Denmark: Private Press, 1984:45-55.
- Fogh-Andersen N, Siggaard-Andersen O, Lundsgaard FC, Wimberley PD. Spectrophotometric determination of hemoglobin pigments in neonatal blood. *Clin Chim Acta* 1987;166:291-6.
- Wimberley PD, Siggaard-Andersen O, Fogh-Andersen N. Accurate measurements of hemoglobin oxygen saturation, and fractions of carboxyhemoglobin and methemoglobin in fetal blood using Radiometer OSM3: corrections for fetal hemoglobin fraction and pH. *Scand J Clin Lab Invest* 1990;50(Suppl)203:235-9.

- Jennis MS, Peabody JL. Pulse oximetry: an alternative method for the assessment of oxygenation in newborn infants. *Pediatrics* 1987;79:524-8.
- Ryan CA, Barrington KJ, Vaughan D, Finer NN. Directly measured arterial oxygen saturation in the newborn infant. *J Pediatr* 1986;109:526-9.
- Zwart A, Buursma A, van Kampen EJ, Zijlstra WG. Multicomponent analysis of hemoglobin derivatives with a reversed-optics spectrophotometer. *Clin Chem* 1984;30:373-9.
- International Committee for Standardization in Haematology. Recommendations for reference method for haemoglobinometry in human blood (ICSH standard 1986) and specifications for international haemoglobin cyanide reference preparation, 3rd ed. *Clin Lab Haematol* 1987;9:73-9.
- Zijlstra WG, Buursma A, Zwart A. Performance of an automated six-wavelength photometer (Radiometer OSM3) for routine measurement of hemoglobin derivatives. *Clin Chem* 1988;34:149-52.
- Jonxis JHP, Visser HKA. Determination of low percentages of fetal hemoglobin in blood of normal children. *Am J Dis Child* 1956;92:588-91.
- Mook GA, Buursma A, Gerding A, Kwant G, Zijlstra WG. Spectrophotometric determination of oxygen saturation of blood independent of the presence of indocyanine green. *Cardiovasc Res* 1979;13:233-7.
- Zijlstra WG, Buursma A. Spectrophotometry of hemoglobin: a comparison of dog and man. *Comp Biochem Physiol* 1987;88B:251-5.
- Mendelson Y, Kent JC. Variations in optical absorption spectra of adult and fetal hemoglobins and its effect on pulse oximetry. *IEEE Trans Bio Med Eng* 1989;36:844-8.
- Jensen JC, Amory D, Li JKJ. Near-infrared spectrophotometric assessment of brain blood oxygenation. *Ann Int Conf IEEE Eng Med Biol Soc* 1990;12:1150-1.
- Faris F, Thorniley M, Wickramasinghe Y, Rolfe P, Livera N, Spencer A. Near-infrared spectroscopy: in-vivo measurements of effective penetration depths and absorption coefficients. *Ann Int Conf IEEE Eng Med Biol Soc* 1990;12:1542-3.
- Van Assendelft OW. Spectrophotometry of haemoglobin derivatives. Groningen, The Netherlands: Thesis, 1970.
- Zwart A, van Kampen EJ, Zijlstra WG. Results of routine determination of clinically significant hemoglobin derivatives by multicomponent analysis. *Clin Chem* 1986;32:972-8.
- Wimberley PD, Fogh-Andersen N, Siggaard-Andersen O, Lundsgaard FC, Zijlstra WG. Effect of pH on the absorption spectrum of human oxyhemoglobin: a potential source of error in measuring the oxygen saturation of hemoglobin. *Clin Chem* 1988;34:750-4.
- Harris AP, Sendak MJ, Donham RT, Thomas M, Duncan D. Absorption characteristics of human fetal hemoglobin at wavelengths used in pulse oximetry. *J Clin Monit* 1988;4:175-7.
- Graaff R, Aarnoudse JG, De Mul FFM, Jentink HW. Light propagation parameters for anisotropically scattering media based on a rigorous solution of the transport equation. *Appl Optics* 1989;28:2273-9.
- Hay WW Jr, Brockway JM, Eyzaguirre M. Neonatal pulse oximetry: accuracy and reliability. *Pediatrics* 1989;83:717-22.
- Eisenkraft JB. Carboxyhemoglobin and pulse oximetry [Letter]. *Anesthesiology* 1988;68:300.
- González A, Gómez-Arnau J, Pensado A. Carboxyhemoglobin and pulse oximetry [Letter]. *Anesthesiology* 1990;73:573.
- Mendelson Y, Kent JC. An in vitro tissue model for evaluating the effect of carboxyhemoglobin concentration on pulse oximetry. *IEEE Trans Bio Med Eng* 1989;36:625-7.
- Eisenkraft JB. Pulse oximeter desaturation due to methemoglobinemia. *Anesthesiology* 1988;68:279-82.
- Zijlstra WG, Oeseburg B. Definition and notation of hemoglobin oxygen saturation. *IEEE Trans Bio Med Eng* 1989;36:872.
- Wimberley PD, Siggaard-Andersen O, Fogh-Andersen N, Zijlstra WG, Severinghaus JW. Haemoglobin oxygen saturation and related quantities: definitions, symbols and clinical use. *Scand J Clin Lab Invest* 1990;50:455-9.
- Watcha MF, Connor MT, Hing AV. Pulse oximetry in methemoglobinemia. *Am J Dis Child* 1989;143:845-7.
- Rieder HU, Frei FJ, Zbinden AM, Thomson DA. Pulse oximetry in methaemoglobinaemia. *Anaesthesia* 1989;44:326-7.