REFLECTANCE PULSE OXIMETRY IN FETAL LAMBS: SUBCUTANEOUS VESSELS AND VASOCONSTRICTION AFFECT ITS RELIABILITY

Roel Nijland, Henk W. Jongsma, Ineke M. Verbruggen, and Jan G. Nijhuis

Nijland R, Jongsma HW, Verbruggen IM, Nijhuis JG. Reflectance pulse oximetry in fetal lambs: subcutaneous vessels and vasoconstriction affect its reliability

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ABSTRACT. Objective. Reflectance pulse oximetry (RPOX) has been introduced for intrapartum fetal surveillance. The purpose of this study was to describe two possible effects on the reliability of RPOX, namely the effect of the presence of a subcutaneous vein and the effect of vasoconstriction by adrenaline, both at fetal SaO_2 levels. **Methods.** In four anesthetized fetal lambs, a prototype 660/890 nm reflectance sensor (Nellcor Inc.) was placed on the fetal head, with the photodiode of the sensor precisely over a superficial subcutaneous vein. Measurements were made before and after coagulation of the vein. In five anesthetized fetal lambs, one or two reflectance sensors were placed on the fetal head and/or neck and adrenaline was administered in doses of 0.02 to 0.04 mg via a brachial artery. Pulse oximeter saturation readings (SpO_2) were compared with continuous arterial oxygen saturation (SaO_2) values obtained using a fiberoptic catheter (Opticath, Abbott) in the carotid artery. **Results.** When the sensor was placed over the vein, the pulse oximeter read 18% to 24% too low at a SaO_2 level of 20% to 50%. After coagulation of the vein, SpO_2 readings were in agreement with fiberoptic SaO_2 values. Administration of adrenaline resulted in a large overestimation of the SaO_2 in 6 of the 7 measurements. **Conclusions.** Subcutaneous veins and vasoconstriction can affect the reliability of reflectance pulse oximetry. As comparable situations may occur during labor, SpO_2 readings should be interpreted with caution when this kind or comparable types of RPOX sensors are used at low SaO_2 levels.

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

INTRODUCTION

Reflectance pulse oximetry (RPOX) is a technique for estimating arterial oxygen saturation (SaO_2) continuously and noninvasively. This technique uses light emitting diodes (LEDs) for red and infrared light to transilluminate the tissue. A photodiode receives the alternating back-scattered light intensities, caused by the pulsating blood volume in the tissue, from which an SaO_2 value can be estimated.

If the Lambert-Beer law could be applied to the propagation of light through tissue, the pulse oximeter oxygen saturation (SpO_2) would be a function of the ratio of the pulsatile red and infrared signals depending only on the extinction coefficients. In the literature [1–3] it was recognized that, due to the fact that for the propagation of light, both absorption and scattering have to be taken into account, the simple theory of transmission pulse oximetry based on the Lambert-Beer

From the Perinatal Research Group, Department of Obstetrics & Gynaecology, University Hospital Nijmegen, The Netherlands.

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

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law is not valid. Instead, an experimental calibration is performed, which has been shown to be accurate in the SaO_2 range of 70% to 100% for transmission pulse oximetry [1,3,4]. For RPOX similar experimental calibrations are performed [5,6]. In theoretical models in which the propagation of light is based on both absorption and scattering of light, the relation between SpO_2 and the measured ratio of pulsatile red and infrared signals becomes complex [7,8]. In these models the SpO_2 is, for instance, also dependent on the tissue blood volume. The influence of blood volume on the calibration is predicted to be of minor importance at high SaO_2 levels but becomes significant at low SaO_2 levels [7,8]. Tissue blood volume is determined by the presence of large subcutaneous arteries and veins and the vascular density in general. Under hypoxia, tissue blood volume may be reduced because of (sub)cutaneous vasoconstriction.

RPOX is used for monitoring the SaO_2 of the fetus during labor [9–11], where SaO_2 values are predominantly below 70%. During labor, the reflectance sensor has to be placed blindly on the presenting part of the fetus and may therefore be positioned over a subcutaneous artery or vein. During labor, hypoxia may occur, which can result in a (sub)cutaneous vasoconstriction. The effect of blood volume differences cannot be studied in the human fetus because SpO_2 readings cannot be compared to a correct standard. Nor could such a study be performed in the human neonate or adult because of the much higher SaO_2 levels. Therefore, we set out to investigate the effects of visible subcutaneous vessels under the reflectance sensor and of vasoconstriction by adrenaline, on the reliability of RPOX at low SaO_2 values in the fetal lamb.

METHODS AND MATERIALS

Surgery

Under general anesthesia (2% enflurane in 1:1 oxygen and nitrous oxide), six pregnant ewes of the Dutch Texel breed were operated on between 134 and 139 days of gestation (term 147 days). Fetal lambs were prepared with a catheter in the left fetal brachial artery for arterial sampling, and a fiberoptic catheter (Abbott Opticath®, U440, 4 French, Oximetrix Inc, Mt. View, CA) in the fetal carotid artery for continuous intravascular recording of the SaO_2. Both catheters remained with the tip in a pre-ductal position. Three electrocardiogram (ECG) electrodes were sutured subcutaneously, and RPOX sensors (660/890 nm sensor, Nellcor Inc, Pleasanton, CA) were placed on the shaved skin of the fetal head or neck. The sensors were fixed in place by an elastic band; sensors made proper contact with the skin and compression of the circulation was prevented. The fetal head and neck remained exposed during the experiment and cooling of the fetal lamb was prevented by a thermostatic heating pad under the ewe and a warming lamp above the fetus. The sensors were covered by a warm, saline-soaked towel and the operation lights were turned off.

The RPOX sensor contained a combination of 660 and 890 nm LEDs, and one photodiode that was placed 10 mm from the two LEDs. The sensors and the ECG-electrodes were connected to prototype oximeters (Nellcor Inc. Pleasanton, CA). The ECG was used to cardio-synchronize the optical pulses (C-lock, Nellcor Inc.). The prototype oximeter was provided with a calibration line based on measurements on human volunteers (SaO_2 range 50–100%) and fetal sheep (SaO_2 range 10–50%). The fiberoptic catheter was connected to an Oximetrix computer (Oximetrix Inc, Mt. View, CA); the operation mode was set to SaO_2. Fiberoptic SaO_2 values were linearly calibrated off-line with the blood sample SaO_2 values. Heparinized blood samples were analyzed within 5 minutes to assess SaO_2 (Instrumentation Laboratory 482®, Lexington, MA) and corrected for fetal sheep blood [12]. All continuous signals of RPOX and fiberoptic oximetry were collected on a personal computer and analyzed off-line.

Experiments

Experiments described in this study were part of a validation study for RPOX using six ewes, starting with one or two fetal desaturations in each lamb and taking blood samples at 10%-steps in oxygen saturation level. These data have been published elsewhere [13]. After each desaturation, fetal lambs were allowed to recover for at least 30 minutes.

At the start of the experiments, maternal inspired oxygen concentration was lowered to achieve a fetal SaO_2 level of between 20% and 50%. In four of the six fetal lambs, a subcutaneous vein was located visually and the RPOX sensor placed with the photodiode over the vein. The sensor was placed with the LED-photodiode axis perpendicular to the vein. The pulse oximeter SpO_2 readings and fiberoptic SaO_2 values were obtained at an SaO_2 level that was stable for at least one minute. Thereafter, the sensor was removed and the vein was coagulated with a needle until it could no longer be visually observed. The sensor was then replaced in the same position and the measurements were repeated.

The influence of adrenaline was studied in five of the six fetal lambs. The sensor was placed on the neck in four

lambs and on the head in three lambs, a total of 7 measurements. Adrenaline was administered as a bolus via the catheter in the brachial artery in doses of 0.02 mg to 0.04 mg.

The investigation was approved by the local ethical committee for animal experiments.

Data analysis

The amplitudes of the pulsatile (ac) components of the red and infrared plethysmographic waveforms were divided by the corresponding nonpulsatile (dc) components of the red and infrared signals. The percentages of ac/dc for red and infrared light, respectively, were used to calculate the red to infrared ratio $[=(ac_R/dc_R)/(ac_{IR}/dc_{IR})]$. The prototype pulse oximeter uses a calibration table to convert this ratio to an SpO_2 value. The pulse oximeter displays the fetal heart rate (FHR) up to a maximum of 255 beats/min. During the adrenaline administration, FHR often exceeded this maximum value. FHR was then calculated by counting the numbers of ECG complexes in a 10-second period. The pulse oximeter uses a scoring system for signal quality, based on multiple factors such as pulse synchrony and pulse amplitude. All signals with a quality $\geq 50\%$ resulted in an SpO_2 display and were accepted for analysis. The plethysmographic waveforms were also visually verified to ascertain that the red and infrared peak and trough were adequate and in phase. To obtain signals of sufficient intensity, the pulse oximeter automatically regulates the intensity of the red and infrared LEDs and the amplification of the output of the photodetector. Therefore, ac and dc components of red and infrared signals were corrected for amplifying differences for each heart beat.

For the experiments with the subcutaneous vein, values before and after coagulation of this vein were compared. For the experiments with adrenaline, values before and after administration of adrenaline at the lowest ac components of the signals were compared.

RESULTS

Off-line calibration of the fiberoptic SaO_2 values resulted in an accurate continuous SaO_2 standard for comparison to the RPOX SpO_2 readings; the standard deviation of residuals for the fiberoptic oximeter was $<3\%$ absolute. During two experiments with adrenaline, additional blood samples were drawn; fiberoptic SaO_2 values agreed with the sample SaO_2 values.

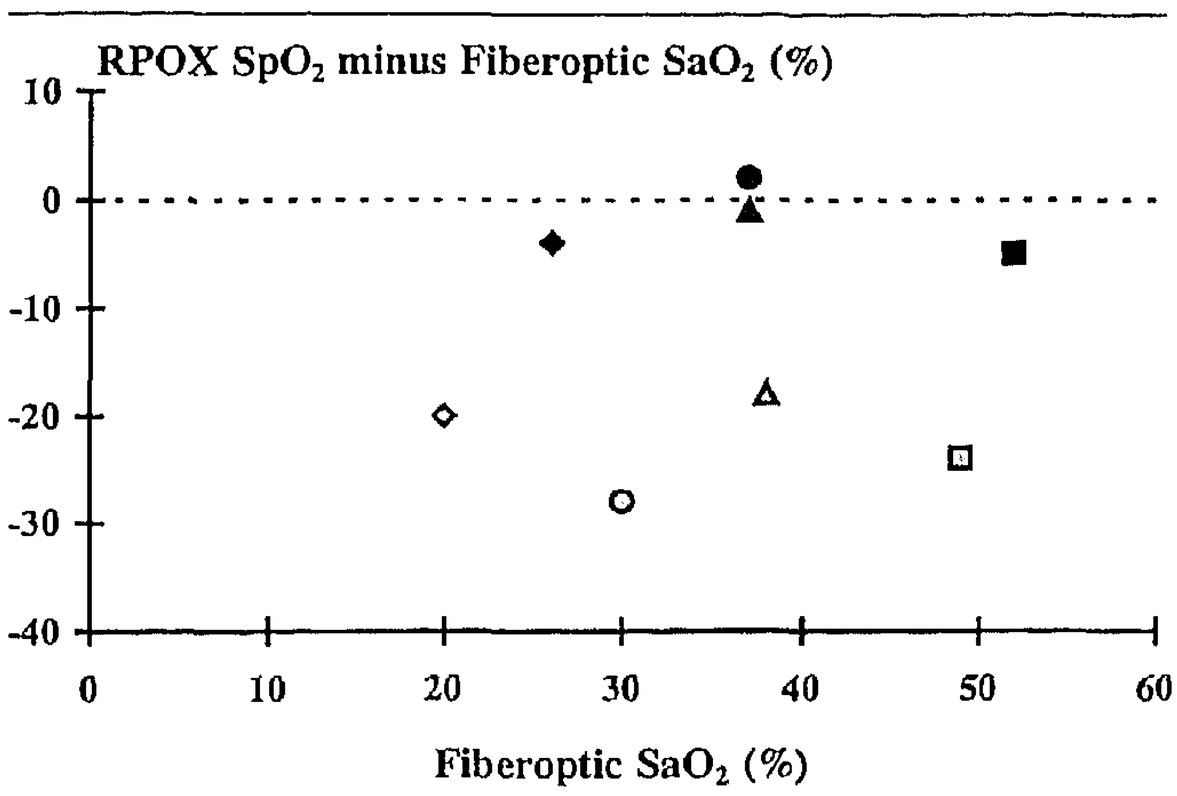

Fig 1. The differences of RPOX SpO_2 reading minus fiberoptic SaO_2 value against fiberoptic SaO_2 values in four fetal lambs, before (grey symbol) and after (black symbol) coagulation of the vein. Each animal is represented by a different symbol.

Subcutaneous vein

In all four fetal lambs, RPOX underestimated the oxygen saturation over a wide SaO_2 range if the sensor was placed with the photodiode over the subcutaneous vein. Signal quality of all SpO_2 readings was $\geq 75\%$. FHR ranged from 128 to 160 beats/min and did not change during coagulation. In Figure 1 results are shown before and after coagulation of the subcutaneous vein at an SaO_2 level of 20% to 50%. Before coagulation the difference between the RPOX SpO_2 reading and fiberoptic SaO_2 value ranged from -16% to -28%. After coagulation, the differences ranged from -1% to $+6\%$ oxygen saturation. For both the red and infrared signals, the ac components increased or decreased, and the dc components remained the same or decreased after coagulation.

Vasoconstriction by adrenaline

An example of the effect of a bolus injection of adrenaline is given in Figure 2. In all but one of the seven measurements, SpO_2 readings increased while fiberoptic SaO_2 values decreased or remained the same. Within one minute after injection, SpO_2 readings started to increase, reaching the maximum between one and two minutes. In three of the seven measurements the quality of the pulse oximeter signal dropped below 50% two minutes after the injection of adrenaline and the oximeter stopped displaying SpO_2 values. In all seven measurements, percentages ac/dc of the red signal and infrared signal decreased between two-fold and seven-fold, reaching the lowest level between one and two minutes. The dc components of red and infrared signals did not

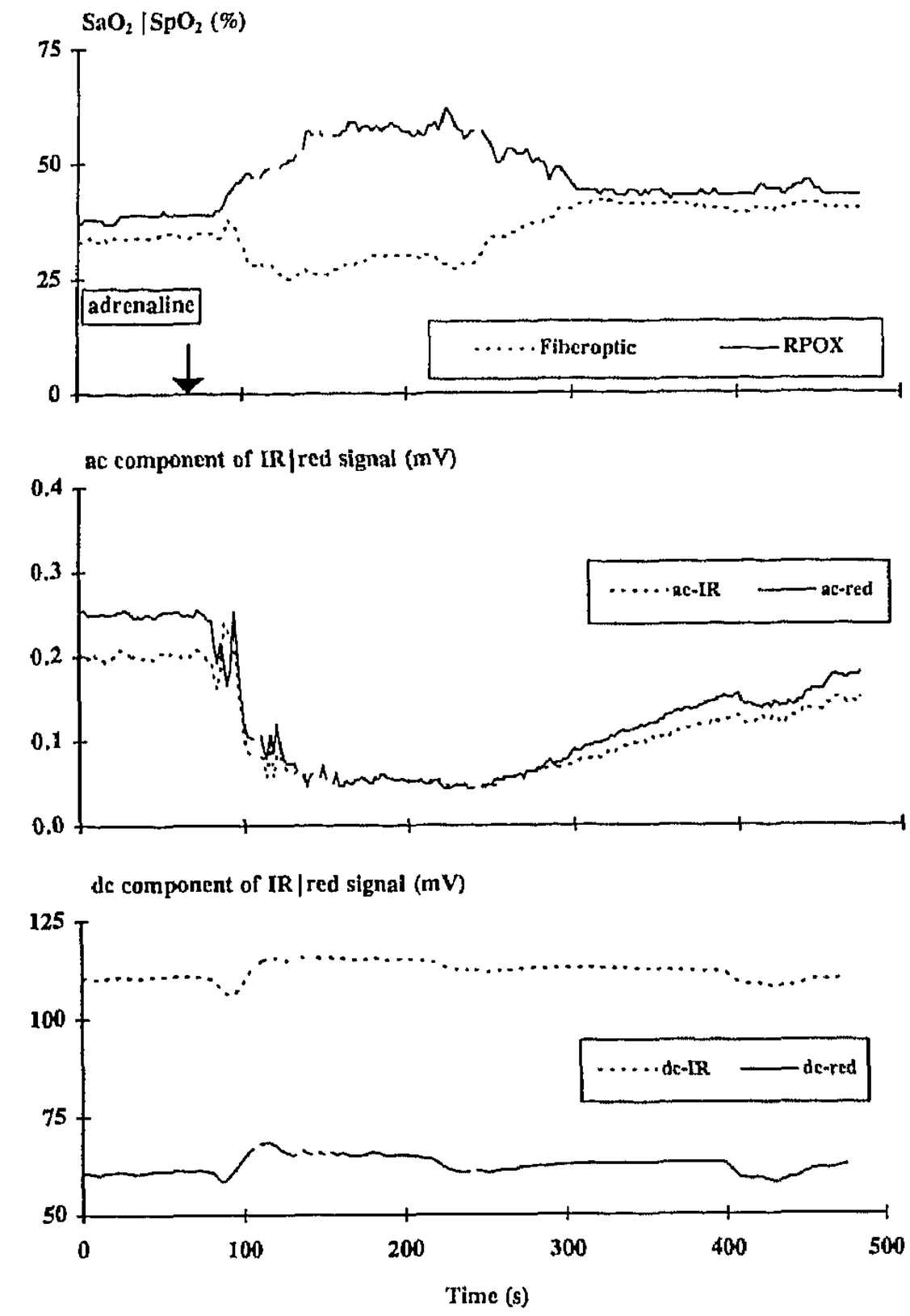

Fig 2. The effect of administration of a bolus injection of adrenaline of 0.04 mg on the fiberoptic SaO_2 values and pulse oximetry SpO_2 readings (upper panel), ac components (middle panel) and dc components (lower panel) of the red and infrared signal. The RPOX sensor was placed on the fetal neck.

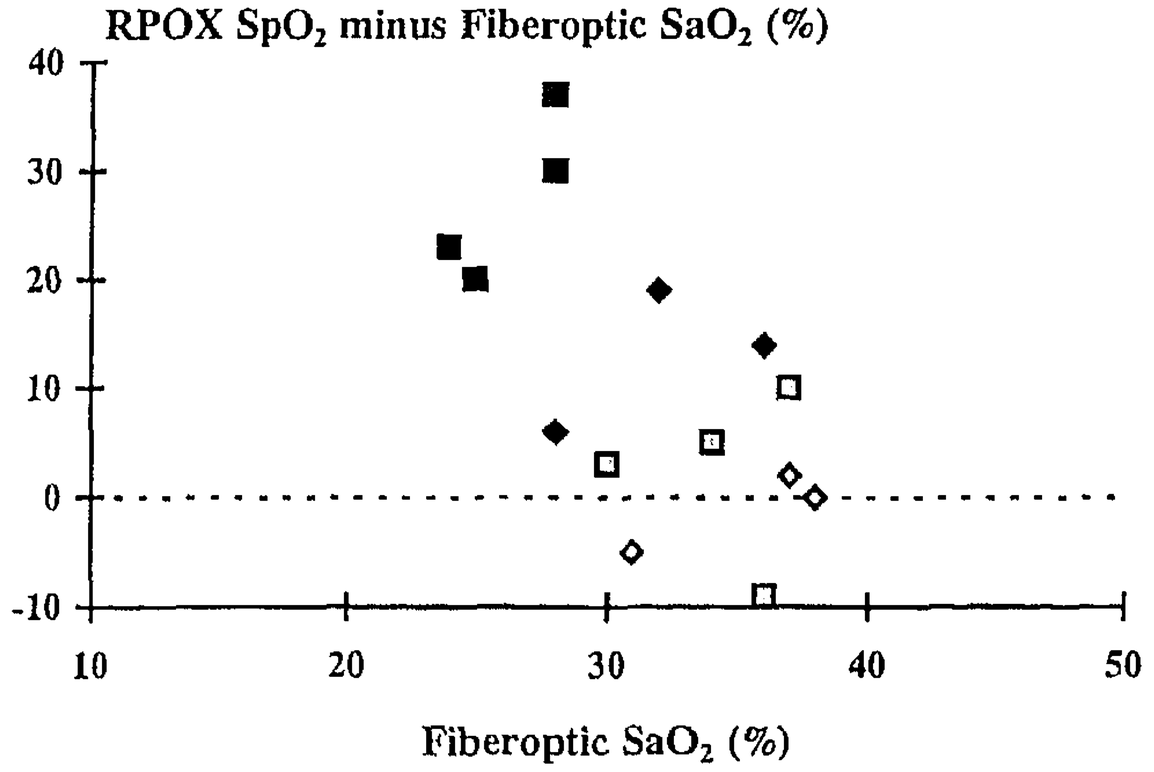

Fig 3. The differences of RPOX SpO_2 reading minus fiberoptic SaO_2 value against fiberoptic SaO_2 values of seven measurements in five fetal lambs, before (grey symbols) and one to two minutes after (black symbols) injection of adrenaline. Square = RPOX sensor on the neck, diamond = RPOX sensor on the head.

show a consistent change; in some experiments the dc component of the signal increased, in other experiments it decreased. The change in the dc component of the signal was maximally 10%. No difference in the dc components of the signal could be observed in the one experiment that did not show a clear increase in SpO_2 (the difference between RPOX SpO_2 and fiberoptic SaO_2 was 2% before and 6% after injection). FHR ranged between 130 and 185 beats/min before administration of adrenaline and rose to 240 to 285 beats/min after administration. SpO_2 readings increased before FHR values exceeded 255 beats/min.

In Figure 3, the results of the seven measurements in five fetal lambs are summarized. Before injection of adrenaline the difference between RPOX SpO_2 and fiberoptic SaO_2 ranged from −9% to +10%. One to two minutes after injection the difference ranged from 6% to 37%.

DISCUSSION

The usefulness of monitoring the fetus during labor with reflectance pulse oximetry will depend largely on whether a reliable estimation of the oxygen saturation can be obtained noninvasively and continuously. In the human fetus, arterial blood samples cannot be obtained to validate the correlation with the RPOX SpO_2 readings. We therefore used the fetal lamb to investigate the reliability of RPOX at low SaO_2 levels.

At these low SaO_2 levels, a continuous reliable SaO_2 recording is desirable for comparison with the RPOX SpO_2 recording. We therefore used a fiberoptic catheter to obtain a continuous SaO_2 recording between the intermittent blood samples. The fiberoptic system was calibrated off-line with blood sample values to improve its accuracy for SaO_2 values below 70% [14]. The standard deviation of residuals of the fiberoptic oximeter (<3%) is comparable with the standard deviation of residuals found in piglets over a SaO_2 range of 15% to 100%. The overall accuracy of the fiberoptic system is less than the 1% absolute accuracy stated for blood sample analysis by multi-wavelength photometers. However, inclusion of pre-analytical sampling errors will result in an overall accuracy of multi-wavelength photometers worse than 1% absolute. Considering the magnitude of the observed under- and overestimation of the SaO_2 by RPOX, the fiberoptic system has a satisfactory accuracy for this study.

When the RPOX sensor was placed over a subcutaneous vein, the pulse oximeter underestimated the SaO_2 by 16% to 28% at an SaO_2 level of 20% to 50%. This underestimation almost completely disappeared after co-

agulation of the vein. This finding is in agreement with our earlier study showing that placing the sensor with the photodiode over the temporal artery in neonates and adults resulted in an underestimation of 6% to 8% of the SaO_2 [15]. The underestimation is, however, in contradiction with the simulation models that predict an overestimation as a result of increased blood volume [7,8] instead of an underestimation. This discrepancy is hard to explain. In theoretical models homogeneous media, which may not be applicable for the heterogeneous *in vivo* situation, are used. The heterogeneity of the *in vivo* tissue may have a profound impact on the performance of RPOX as it can redistribute the light propagation. The theoretical models predict an overestimation of circa 25% at a 25% SaO_2 level, using 5% blood volume in the model instead of 1% blood volume [7,8]. The magnitude of the effect is, both in the theoretical models as well as in our *in vivo* model, significant. Venous pulsations are reported to give an underestimation of the SaO_2, for normal adult SaO_2 values around 96% SaO_2 [16]. We did not observe any pulsations of the subcutaneous vein, but we cannot exclude this completely as it may have been present but unnoticed. RPOX readings were, however, much lower, as the fetal venous oxygen saturation values would have been.

Vasoconstriction with adrenaline led to an overestimation of the SaO_2. A complete recording could not be obtained in all experiments, but the direction of the change was the same in all experiments during the first two minutes after the injection of adrenaline. An overestimation was also occasionally observed in the course of our fetal lamb hypoxia experiments [13]. We never observed an underestimation of the SaO_2 in those hypoxia experiments. Vasoconstriction leads to a decrease in blood volume and the overestimation of the SaO_2 seems therefore to be in line with the other experiment in which an underestimation was observed by placing the sensor over the subcutaneous vein.

We tried to elucidate our findings by analyzing the signals in detail. The prototype pulse oximeter has an autogain, which automatically increases its output to obtain sufficient signals. We therefore corrected all measurements for amplifying differences. One might expect that an increased blood volume mimicked by the subcutaneous vein would lead to an increase of scattering of light, and therefore to a decrease in the dc components of the signals. However, our dc components for both red and infrared signals decreased or did not change significantly after the subcutaneous vein was coagulated. After injection of adrenaline, an increase in the dc component of the signal was expected but no consistent changes were observed. The dc components of the signal remained unaltered or showed a small increase or decrease. All ac components for red and infrared signals decreased after injection of adrenaline as result of vasoconstriction. Vasoconstriction will lead to a "centralization" of the blood. One might therefore hypothesize that the effect of vasoconstriction will be more pronounced in the skin and upper layers of the subcutaneous tissue than in the lower layers of the subcutaneous tissue. Infrared light penetrates deeper in the tissue than red light; with decreasing oxygen saturation, the amount of oxyhemoglobin decreases and deoxyhemoglobin increases, which causes even more attenuation of the red light. The effect of vasoconstriction on the ac component of the signal was larger for red than infrared light. A larger decrease in ac component of the red light than in the ac component of the infrared light (dc components of the signal hardly changed) results in a lower red to infrared ratio and, hence, a higher SpO_2 value.

A potential source of error may have been the high fetal heart rate after the injection of adrenaline. In some fetal lambs the fetal heart rate increased to 285 beats/min, while the prototype pulse oximeter is only validated up to 255 beats/min. The pulse oximeter clips the fetal heart rate at 255 beats/min and does not display rates above this value. Despite this, we could not explain the overestimation as a result of the high fetal heart rate because all red and infrared pulses were still cardiosynchronized and the pulse oximeter had already started to overestimate the SaO_2 before the FHR exceeded 255 beats/min.

The RPOX system used in this study is empirically calibrated using blood sample SaO_2 values over the total SaO_2 range. The SpO_2 values after coagulation of the vein, and before the administration of adrenaline are in the expected accuracy range of this RPOX system [5,13]. The same small difference in SpO_2 values between head and neck measurements was also observed earlier [13].

Explanations for incorrect SpO_2 readings are often thought to be found in disturbance factors such as malpositioning of the sensor [17], improper data analysis [18], caput succedaneum [18,19], or excessive pressure on the sensor. These factors, however, were carefully avoided in this study. Sensors made an appropriate contact with the skin, avoiding optical shunting of red and infrared light directly to the photodiode [17]. The pressure on the sensor was sufficient to keep the sensor in place and constant during the experiment. Compression of the circulation was carefully avoided. All the analyzed signals were based on cardiosynchronized and acceptable red and infrared pulses.

Other reflectance pulse oximetry sensors have been developed and could possibly be used for intrapartum fetal monitoring, but their reliability has not yet been widely tested [6,20]. It would be of interest to know whether these systems also show comparable results.

In conclusion, placement of a 660/890 nm reflectance sensor with the photodiode over a subcutaneous vein results in a substantial underestimation of the SaO_2, while vasoconstriction may lead to a substantial overestimation of the SaO_2. Results obtained with 660/890 nm reflectance pulse oximetry sensors in the human fetus during labor should therefore be interpreted with caution. Further development in theoretical models is desirable as homogeneous media as used currently in these models may not hold for the heterogeneous media of *in vivo* tissue.

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