PROGRESS IN THE DEVELOPMENT OF A FLUORESCENT INTRAVASCULAR BLOOD GAS SYSTEM IN MAN

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ABSTRACT. In vitro and in vivo animal studies have shown accurate measurements of arterial blood pH (pHa), carbon dioxide tension ($PaCO_2$), and oxygen tension (PaO_2) with small intravascular fluorescent probes. Initial human clinical studies showed unexplained intermittent large drops in sensor oxygen tension (PiO_2). Normal volunteers were studied to elucidate this problem. In the first part of this study, the probe and cannula were manipulated and the probe configuration and its position within the cannula were varied. The decreases in PiO_2 were judged to be primarily due to the sensor touching the arterial wall. Retraction of the sensor tip within the cannula eliminated the problem. In the second part of this study, the accuracy of the retracted probe was evaluated in 4 subjects who breathed varying fractions of inspired oxygen and carbon dioxide. The arterial ranges achieved were 7.20 to 7.59 for pH, 22 to 70 mm Hg for $PaCO_2$, and 46 to 633 mm Hg for PaO_2. Linear regression of 48 paired sensor (i) versus arterial values showed pHi = 0.896 pHa + 0.773 (r = 0.98, SEE = 0.017); $PiCO_2$ = 1.05 $PaCO_2$ − 1.33 (r = 0.98, SEE = 2.4 mm Hg); and PiO_2 = 1.09 PaO_2 − 20.6 (r = 0.99, SEE = 21.2 mm Hg). Bias (defined as the mean differences between sensor and arterial values) and precision (SD of differences) were, respectively, −0.003 and 0.02 for pHi, 0.77 and 2.44 mm Hg for $PiCO_2$, and −2.9 and 25.4 mm Hg for PiO_2. The mean in vivo 90% response times for step changes in inspired gas were 2.64, 3.88, and 2.60 minutes, respectively, for pHi, $PiCO_2$, and PiO_2.

KEY WORDS. Equipment: fiberoptic sensors. Blood gas analysis. Monitoring.

Fluorescent-based sensor technology has advanced to the point where these devices can now accurately measure blood pH, carbon dioxide tension (PCO_2), and oxygen tension (PO_2) [1–4]. The major advantages of these sensors are that they can be easily miniaturized and that, with fiberoptics, the patient can be electrically isolated. When the sensors are placed at the tip of a probe, sufficiently small to be passed through a 20-gauge radial artery cannula, continuous in vivo blood gas monitoring can be achieved. The characteristics and performance of such an intravascular blood gas system (CDI System 1000, Cardiovascular Devices, Inc, Irvine, CA) have been described [5]. In vitro studies in tonometered bovine blood showed high correlations and small standard deviations of the sensor values from the corresponding blood gas values [5,6]. In vivo studies in dogs confirmed these observations [6,7]. Initial developmental clinical studies were performed at Northwestern University (Dr B. Shapiro), Loma Linda University (Dr M. Allard), and the Long Beach Veterans Administration Medical Center (Dr K. Mahutte). The data in

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critically ill patients showed very poor and inconsistent results and have not been published for that reason. In particular, aberrant sensor values occurred frequently and erratically. These aberrancies tended to fall into two classes: (1) a downward drop in the sensor PO_2 ("down") and (2) a simultaneous "down-up-down" pattern in the pH, PCO_2, or PO_2 values, respectively (Fig 1). Pre- and poststudy calibration of the sensors suggested that these down and down-up-down patterns could not be attributed to system errors. Thus, the aberrancies were suspected of being due to the presence of the probe tip in the environment of the radial artery itself.

A number of possibilities were formulated to explain these effects: (1) clotting at the probe tip with associated gas value changes, perhaps due to local metabolic effects associated with the clotting process; (2) a longitudinal gradient in arterial blood gas values due to compromised flow at the radial sample site (i.e., the blood is different at the wrist than it is at the left ventricle in some patients); or (3) a "wall effect" caused by the sensor touching the vessel wall and hence reading some average of blood and tissue.

Subsequent animal studies where clotting was induced confirmed our suspicion in human trials that clotting, when it occurs, is associated with the down-up-down pattern (see Fig 1). This pattern could be consistent with a localized metabolic process that consumes oxygen (low PO_2), releases carbon dioxide (high PCO_2), and causes subsequent higher acidity (low pH).

To clarify the situation of frequent low sensor PO_2 values (down), we studied normal volunteers. Flow, sensor position, and sensor configuration were all varied in these experiments. When we retracted the probe tip within the cannula tip, so that the former could no longer touch the arterial wall, the down effect was eliminated. We then assessed the accuracy of the modified system in 4 normal subjects who breathed different mixtures of inspired gas.

MATERIALS AND METHODS

Fluorescent Blood Gas System

The system is illustrated in Figure 2. It consists of a disposable fiberoptic probe, an electrooptic patient interface module, the monitor, and a pole-mountable display module.

The operation of the probe is based on the phenomenon of fluorescence. When exposed to light of appropriate frequencies, molecules of certain dyes are excited into higher electronic states. Subsequent return to the lower ground state is accompanied by the emission of so-called fluorescent light. The emitted light has a lower frequency than the excitation light, and, by manipulating the dye and its matrix, the intensity of the emitted light can be affected by the concentration of blood constituents. It is to be noted that the sensors do not consume oxygen and carbon dioxide. The pH, PCO_2, and PO_2 sensor chemistries have been described in more detail elsewhere [5,6]. The probe tip is illustrated in Figure 3. The sensor chemistries are situated at the tip of three 140-μm-diameter optical fibers and are coated with a permeable film. A thermocouple to measure temperature is also incorporated near the probe tip. Heparin, covalently bonded, coats the assembled probe. The optical bundle is sealed in a Y connector to allow

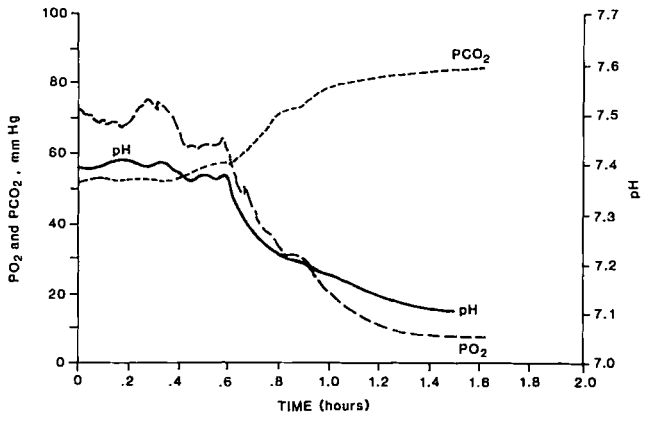

Fig 1. Pattern frequently observed in patients. The oxygen tension (PO_2) went down, the carbon dioxide (PCO_2) went up, and the pH went down. Similar down-up-down patterns were observed when clots were induced at the probe tip in animal studies.

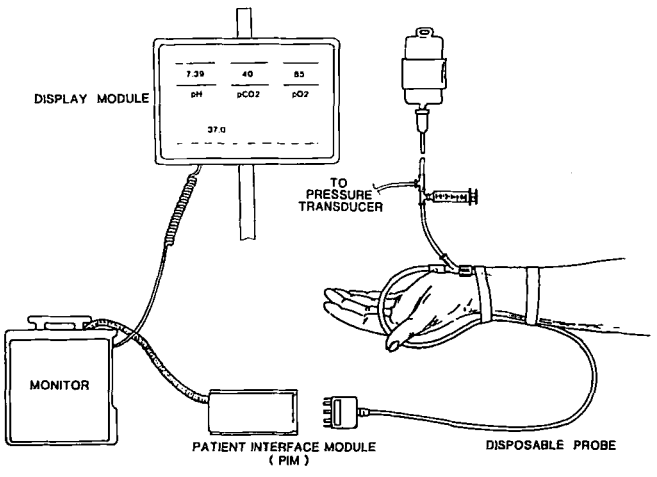

Fig 2. CDI system 1000. PCO2 = carbon dioxide tension; PO2 = oxygen tension.

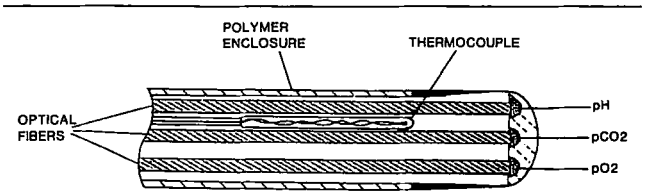

Fig 3. Fiberoptic probe tip. Three 140-μm-diameter optical fibers conduct light to and from the sensors. The sensors are 0.13 mm long. A thermocouple to measure temperature is reset 8 mm from the probe tip. Heparin coats the assembled probe. PCO2 = *carbon dioxide tension;* PO2 = *oxygen tension.*

standard drip infusion and pressure monitoring when the probe is inserted in a 1¾-in (4.5-cm) 20-gauge radial artery cannula. The probe tip is sterile and stored in a calibration cuvette. The proximal end of the probe connects to the patient interface module.

The patient interface module contains the electrooptical interface and separates the emitted fluorescent light from the excitation light. Silicon photodiodes in the patient interface module convert the intensities of the emitted light into the electronic signals [7]. The system monitor contains the excitation light source (a pulsed xenon lamp), power supply, and microprocessor. The microprocessor controls the flash lamp and filter wheel, automatically sequences the two-point tonometry calibration procedure, and converts the digitized signal intensities using proprietary algorithms [1,5] to pH, PCO_2, and PO_2 values. During calibration, the probe is placed in a buffered solution in a cuvette with two calibrated gas concentrations, each containing different precisely known concentrations of oxygen and carbon dioxide. Calibration takes approximately 20 minutes. The display panel, updated every 2 seconds, has the usual alarm functions and is also used for in vivo calibration of the probe.

Subjects

The protocols were approved by the hospital's Human Experimentation Committee and all subjects signed informed consents. Eighteen normal conscious subjects were studied: physicians (8), respiratory therapists (6), intensive care unit nurses (2), and research personnel (2). In some subjects two probes were inserted in the in situ cannula. The wrists of the subjects were prepared in the usual manner and 20-gauge cannulas (Jelco or Arrow) were placed in the radial artery.

Part 1. Probe/Cannula Configuration

In the early clinical trials in patients, the probe tip extended approximately 6 mm beyond the tip of the cannula. Since this configuration produced the intermittent low sensor PO_2 value (down), we attempted to produce a down result under controlled laboratory conditions. We also varied both the probe and cannula configurations. The most important experiments with the different configurations are described.

The effect of decreased flow on sensor values was studied with intermittent inflation of the blood pressure cuff. The effect of probe position was systematically altered by hyperextension and relaxation at the wrist, applying lateral pressure on the probe, and rotating the probe. These maneuvers were repeated when a down pattern occurred. In addition, once a down effect occurred, blood was drawn slowly from the Y port to determine whether the down pattern was due to decreased flow at the sensor tip (thereby drawing "fresher"upstream blood over the probe).

These experiments were then repeated using probes that had three PO_2 sensors rather than a pH, PCO_2, and PO_2 sensor. The probe tip was arranged in a staggered (i.e., PO_2 sensor at the probe tip, another recessed slightly back from the tip, and the third recessed twice that distance from the probe tip) or nonstaggered (i.e., all three PO_2 sensors flush at the probe tip) fashion. The probes were produced with varying lengths so that all sensors protruded beyond the cannula tip or so that the distal end of the probe extended just beyond the cannula tip, was flush with it, or was recessed just within the cannula tip.

In the final set of experiments, the pH, PCO_2, and PO_2 sensors were flush at the probe tip. The probes themselves were retracted to just within the cannula tip. To decrease the effects of flush solution on sensor accuracy, cannulas with several holes near the cannula tip were studied. Finally the effects of flush solution were minimized by enhancing the tidal action (due to blood pressure) at the tip of the cannula with the introduction of additional compliance in the pressure transducer circuit. The damping coefficient and frequency response of the circuit were studied on the bench. A fast flush was applied against a pressure head, as suggested by Gardner [8]. The experiments described below were carried out with this system.

Part 2. Accuracy of the Retracted Probe

Four subjects were studied using the probe slightly retracted within the cannula tip and compliance in the circuit. The 1¾-in (4.5-cm) 20-gauge cannulas (Arrow) were placed in the radial artery. A second cannula was then placed via a guidewire. This was done to minimize deformity at the cannula tip. We have observed that deformity of the cannula tip can enhance clotting when

a probe is in the cannula. After the second cannula was placed, in vitro calibration of the probe was performed according to the manufacturer's instructions. This calibration took approximately 20 minutes, after which the probe was placed. The pressure signal was then noted, and pressure transducer circuit compliance was increased just until the point where the fidelity of the blood pressure signal would appear to become impaired. After a 10-minute stabilization period, a blood gas sample was drawn and analyzed (IL 1312, Instrumentation Laboratories, Lexington, MA) and in vivo recalibration was performed. This was done to (1) examine the bias of the in vitro calibration and (2) improve the subsequent data. Probe blood gases were automatically (via the built-in thermocouple) corrected to 37°C. Blood pressure was monitored throughout these experiments on an oscilloscope or four-channel recorder (Hewlett-Packard 7754B). End-tidal carbon dioxide was also continuously recorded with an infrared carbon dioxide analyzer (LB3, Sensormedics, Anaheim, CA). Subjects then breathed different concentrations of inspired oxygen and carbon dioxide for 10-minute periods each. Hyperventilation to lower carbon dioxide was performed also. Arterial blood was drawn at each steady-state level (at the end of each 10-minute period) for blood gas analysis. Thirteen blood gases were drawn in each subject during the experiment.

For the hyperoxic studies the subject was breathing spontaneously (continuous positive airway pressure = 0 mode) on a ventilator (Puritan-Bennett 7200, Carlsbad, CA). Inspired oxygen concentrations of 30, 40, 50, and 100% were studied sequentially. We prepared hypoxic mixtures of 14, 16, and 18% concentrations of inspired oxygen by mixing air with 100% nitrogen. A Tissot spirometer was filled with the hypoxic mixture. The subject inspired each of the mixtures via a nonrebreathing valve for 10-minute periods.

Hypercapnia was similarly induced by having the subject inspire steady-state hypercapnic mixtures for 10-minute periods. These were prepared by mixing 100% carbon dioxide with air and filling the spirometer. The resulting inspired PCO_2 values ranged from 45 to 60 mm Hg. Hypocapnia was induced by having the subject breathe on the ventilator in the controlled mode. The tidal volume was set at 1 L and the frequency ranged from 15 to 25 breaths/min. Each subject breathed for 10-minute periods at several fixed frequencies.

Data Analysis

For the accuracy study, the sensor versus blood gas values were analyzed by least-squares linear regression, eliminating, of course, the in vivo calibration point. Sensor values were also plotted against the corresponding arterial values over the whole range and separately for the clinically relevant range of arterial PO_2 values less than 200 mm Hg. The data were also analyzed as suggested by Altman [9]. Accordingly, differences (and percent differences) between simultaneously obtained probe values and blood gas values were calculated. Bias is defined as the mean of these differences; the standard deviations of the differences are a measure of precision. Bias and precision between the in vivo and in vitro calibrations were also calculated from the in vivo calibration data, that is, the first drawn blood gas.

Ninety percent response times of the system to step changes in inspired gas mixtures were also calculated and averaged for each sensor. All the step changes—both up and down—were used in the calculation of these averages.

RESULTS

Part 1. Probe/Cannula Configuration

Inflation of the blood pressure cuff above arterial pressure produced decreases in sensor PO_2 (and smaller increases in PCO_2) (Fig 4A). Typically, PO_2 would drop to values of around 35 to 45 mm Hg over 5 minutes. This interval was longer than that associated with a typical down effect previously observed in the clinical environment. Typical down patterns could be induced easily by relaxing an otherwise hyperextended wrist (Fig 4B). Subsequent hyperextension would bring the PO_2 back up. The decreased PO_2 during a down phenomenon could not be easily attributed to decreased flow past the sensor, since slow blood withdrawal ($\approx$50 ml over 4 minutes) from the artery would not increase the PO_2 (Fig 4C). The flush following blood withdrawal and hyperextension did increase the PO_2.

To study the role of the probe geometry on these effects, the normal three-sensor probe (pH, PCO_2, and PO_2) was replaced by special triple PO_2 probes. The geometries studied were a design with each of the three PO_2 sensors attached flush at the probe tip and a "staggered" design where the three PO_2 sensors were distributed axially, with two sensors located at different positions back from the probe tip. As might be expected with staggered probes protruding beyond the catheter, the most distal sensor had the lowest PO_2 (since this was the most likely to touch the arterial wall) (Fig 5A). The most distal PO_2 sensor in the staggered probes was also the most sensitive (showed the largest drops in PO_2) to changes in position of the probe induced by hyperextension and relaxation at the wrist. Rotation 180 degrees of

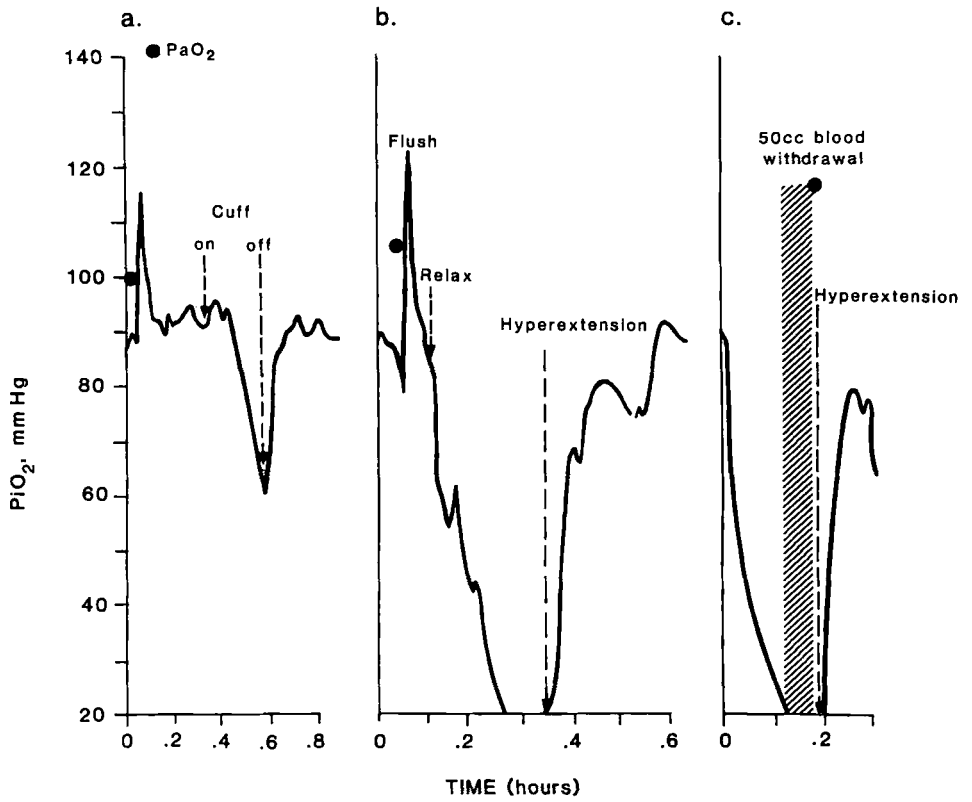

Fig 4. The effects of various manipulations on sensor oxygen tension (PiO_2) *of a probe extending beyond the cannula tip.* PaO_2 = *arterial oxygen tension. (A) Effect of blood pressure cuff inflated to 130 mm Hg over 7 minutes. The subject's blood pressure was 115/75 mm Hg. (B) Effect of wrist relaxation followed by hyperextension. The wrist was initially hyperextended. (C) Effect of slow withdrawal of 50 ml of blood.* PiO_2 *increased only with the flush and hyperextension.*

such a staggered probe, moving it presumably away from the wall, increased the distal PO_2, but the PO_2 of another sensor on the opposite side dropped (Fig 5B). Dramatic wall effects were also demonstrable with three PO_2 sensors flush at the tip of a probe that extended beyond the cannula tip. Lateral pressure, presumably forcing the probe tip against the arterial wall, caused a down effect in one PO_2 sensor. Rotation 180 degrees in the same position moved the down pattern to the opposite sensor (Fig 5C). Another staggered triple PO_2 probe with the distal probe extending beyond the cannula, and the other sensors flush with and inside the cannula, demonstrated that a down effect could be induced only in the distal sensor. Once we studied probes whose tips remained within the cannula tip, down patterns could no longer be induced with the simple manipulations described, that is, relaxation at the wrist, extension, or exertion of lateral pressure.

Sensor response time to step changes in PO_2 with a retracted staggered PO_2 probe was also studied, and it was evident that response times were slowest in the most proximal PO_2 sensor. In this experiment the most distal PO_2 sensor was just inside the cannula tip and had a 90% response time of 3.7 minutes, whereas the most proximal sensor, set back twice as far, had a 90% response time of 11 minutes. To avoid the down effect and to enhance the response time, the probe tip has to reside just within the cannula tip. To minimize the interference caused by flush solution, we introduced an adjustable compliance in the tubing system. The damping coefficient and frequency response of the circuit were 0.14 and 27.3 Hz without a probe in the cannula and 0.28 and 26.5 Hz with a probe in the cannula.

Part 2. Accuracy of the Retracted Probe

No down patterns were observed during these studies in 4 subjects, confirming our expectation from the design studies that the retracted probe within the cannula eliminates the large and erratic drops in sensor PO_2.

We studied only 4 subjects; thus, the data on the bias and precision of the in vitro calibration of the sensors are limited. Yet, in vitro calibration yielded values close to

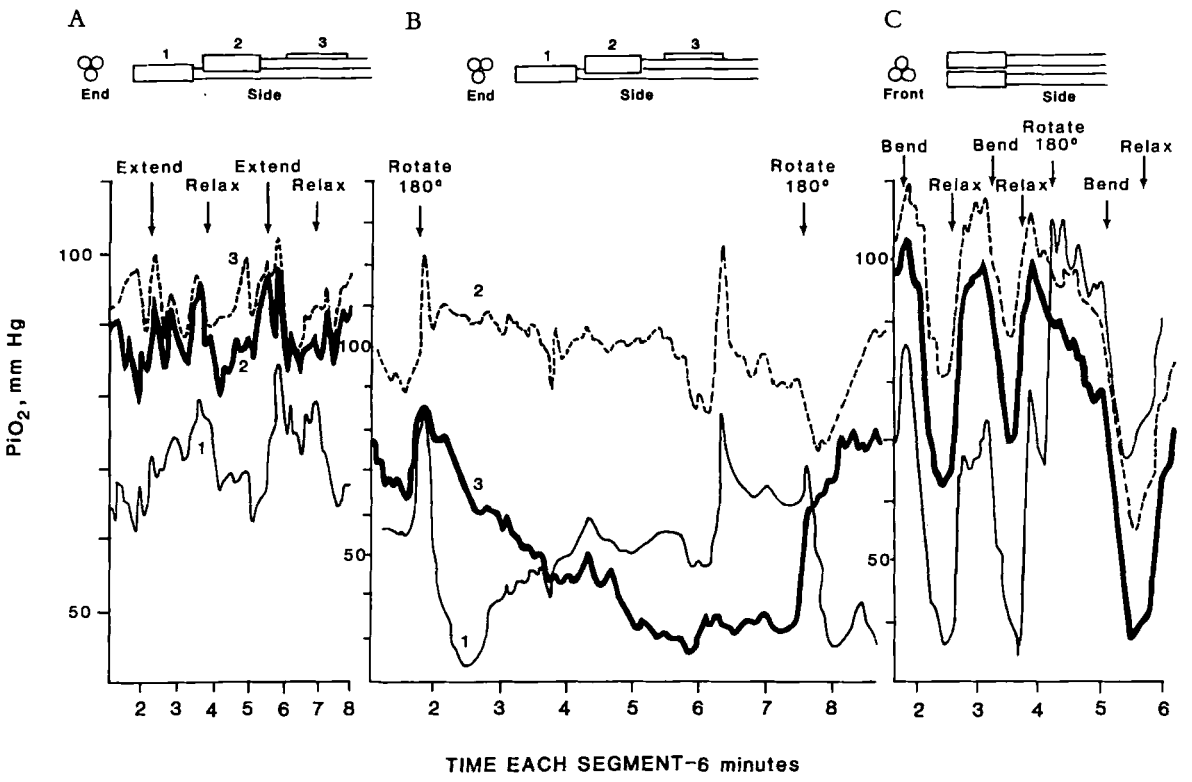

Fig 5. Manipulations with probes consisting of three sensors of oxygen tension (PiO_2) arranged in a staggered fashion (A and B) and side-by-side (sensors flush at the probe tip) fashion (C). Each probe tip extended beyond the cannula tip. (A) Most distal sensor has the lowest oxygen tension and is most influenced by relaxation and hyperextension. The most distal sensor extended just beyond the cannula tip. (B) This shows that 180-degree rotation raised the most distal oxygen tension above that of the most proximal sensor. A subsequent 180-degree rotation reversed the situation. The most proximal sensor extended just beyond the cannula tip. (C) The same effect as in (B) can be obtained with 180-degree rotation in three sensors flush at the probe tip. The probe tip extended slightly beyond the cannula tip.

the first obtained set of arterial blood gases. The bias, as measured by the mean differences between sensor value minus the first simultaneously obtained blood gas value, and precision (±SD) were 0.05 ± 0.02 for pH, −1.0 ± 1.6 mm Hg for PCO_2, and −12.8 ± 3.1 mm Hg for PO_2.

The results of sensor values and arterial blood gases with different inspired gases in a representative subject are shown in Figure 6 for pH and PCO_2 and in Figure 7 for PO_2.

After dropping the initial in vivo calibration values from the regression analysis, a total of 48 paired sensor and blood gas variables were obtained. The arterial pH ranged from 7.20 to 7.59, the arterial PCO_2 from 22 to 70 mm Hg, and the arterial PO_2 from 46 to 633 mm Hg.

The sensor pH is plotted against the arterial pH in Figure 8, sensor PCO_2 verus arterial PCO_2 in Figure 9, and sensor PO_2 versus arterial PO_2 in Figure 10 for all data points; in Figure 11 PO_2 values less than 200 mm Hg are plotted. The overall regression equations are summarized in Table 1. The bias and precision of sensor values are summarized in Table 2.

The in vivo 90% response time to a step change in inspired gas was calculated. The mean (±SD) 90% response times were 2.64 ± 1.15 minutes for pH, 3.88 ± 1.02 minutes for PCO_2 and 2.60 ± 1.22 minutes for PO_2.

DISCUSSION

In vitro and in vivo animal studies with the fluorescent fiberoptic blood gas system have shown excellent results [5–7]. The poor results (unpublished) obtained in the initial developmental studies in patients indicated that the optimal probe/cannula design had not yet been achieved. One might have expected that to achieve optimal blood gas measurement, the probe would have to reside within the artery. Contrary to expectation, we found that in order to circumvent the large drops in PO_2, the probe tip had to be retracted within the can-

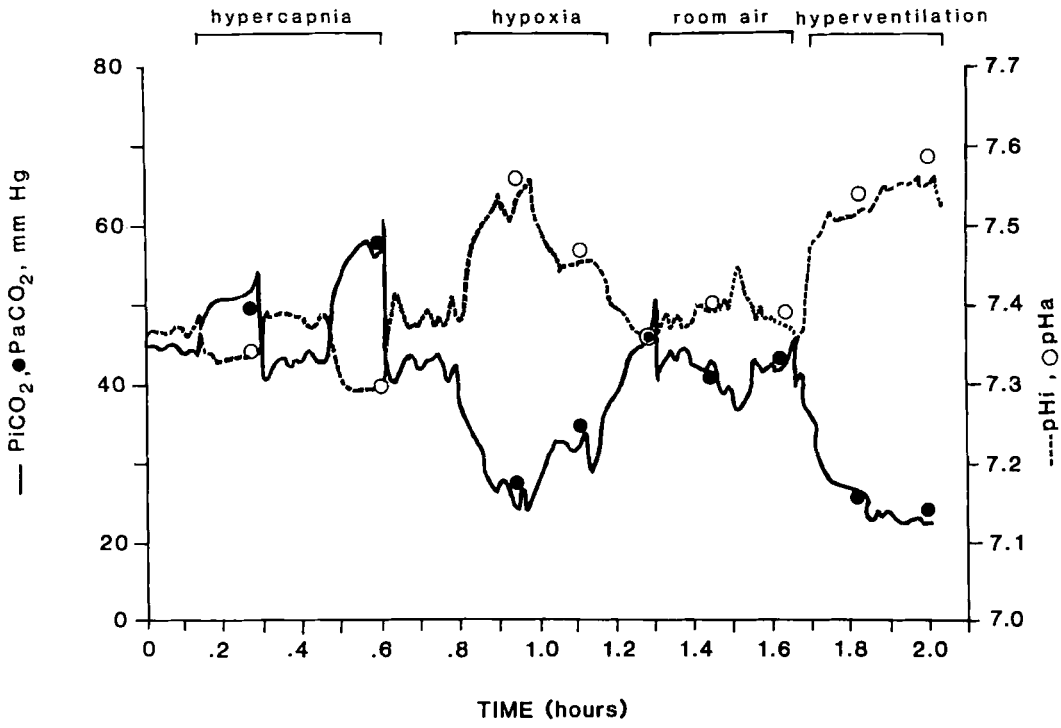

Fig 6. A tracing of sensor pH (pHi, *broken line) and carbon dioxide tension* ($PiCO_2$, *solid line) and corresponding arterial* (pHa *and* $PaCO_2$) *values, indicated by open and solid circles, respectively, in 1 subject.*

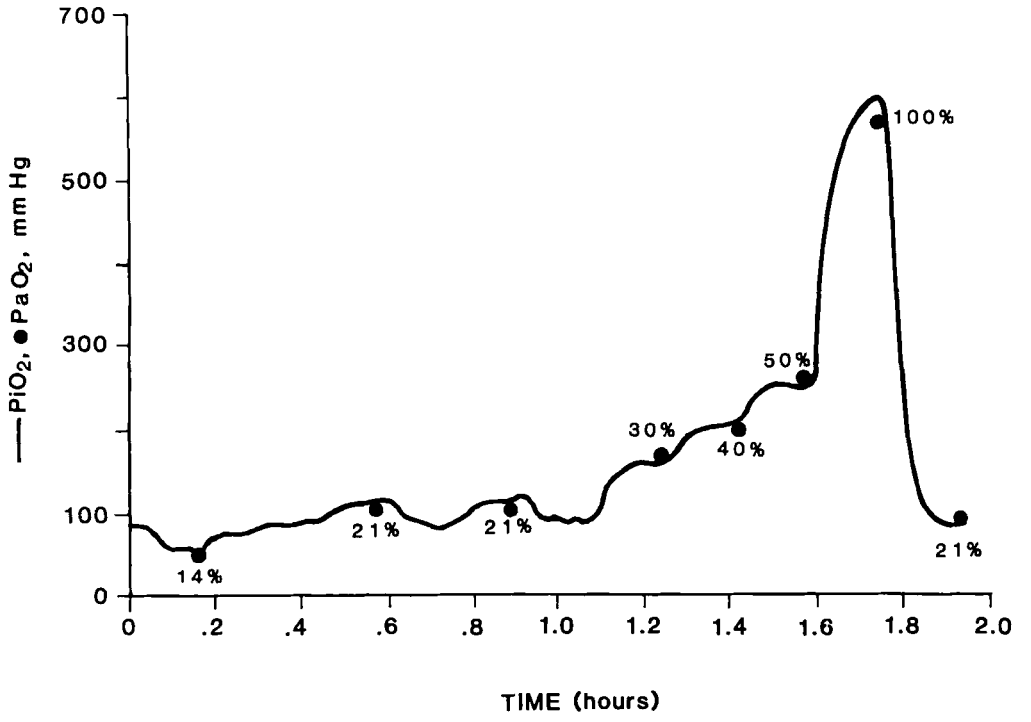

Fig 7. Tracing of sensor (PiO_2) *and arterial* (PaO_2) *oxygen tensions in the same subject as in Figure 6.*

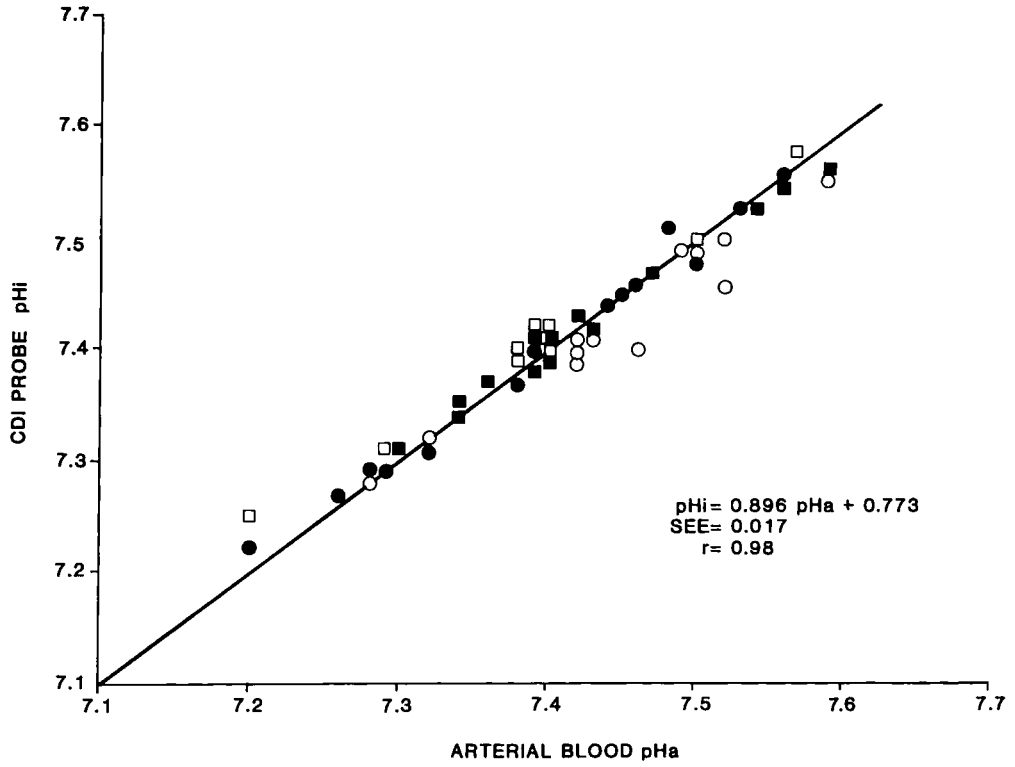

Fig 8. Relationship between sensor (pHi) *and arterial blood* (pHa) *pH values. Each symbol represents 1 of the 4 subjects. The line of identity and 48 data points are shown.*

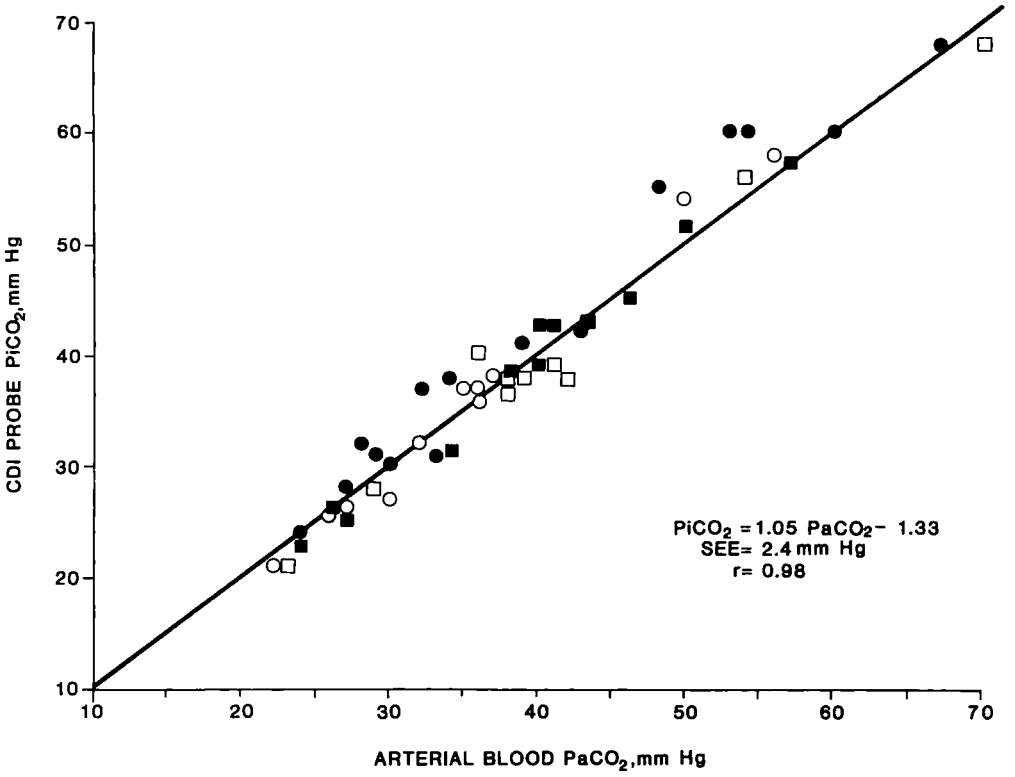

Fig 9. Relationship between sensor ($PiCO_2$) *and arterial blood* ($PaCO_2$) *oxygen tensions. Each symbol represents 1 of the 4 subjects. The line of identity and 48 data points are shown.*

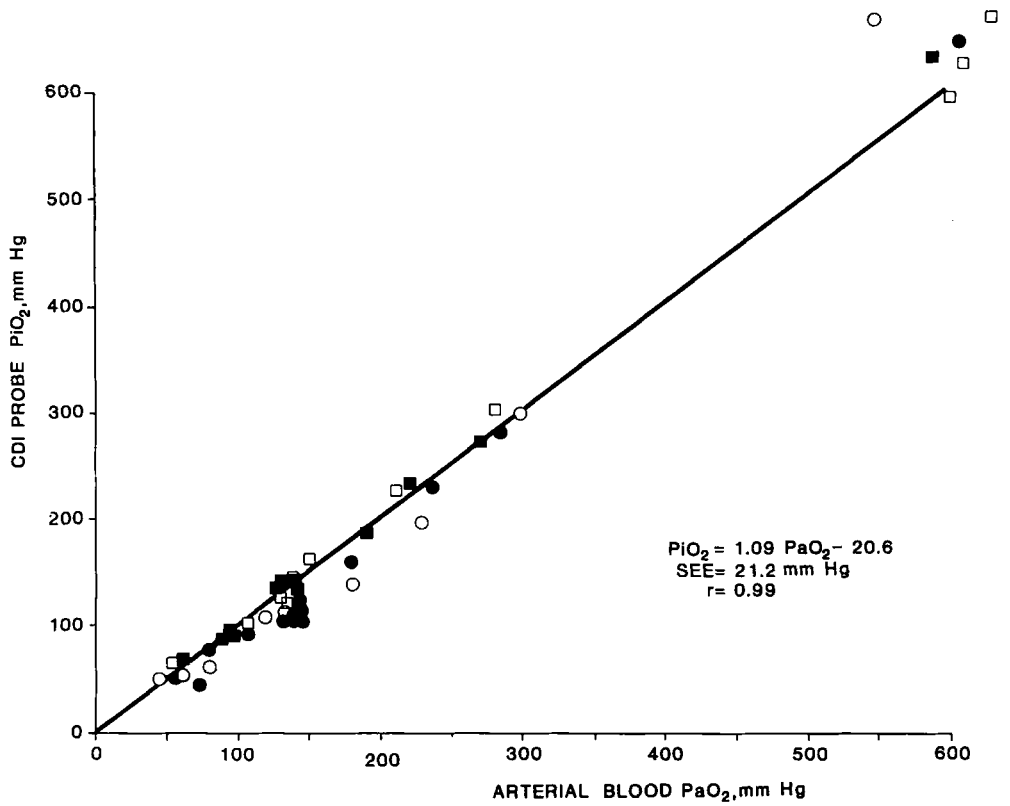

Fig 10. Relationship between sensor (PiO_2) *and arterial blood* (PaO_2) *oxygen tensions. Each symbol indicates 1 of the 4 subjects. The line of identity and 48 data points are shown.*

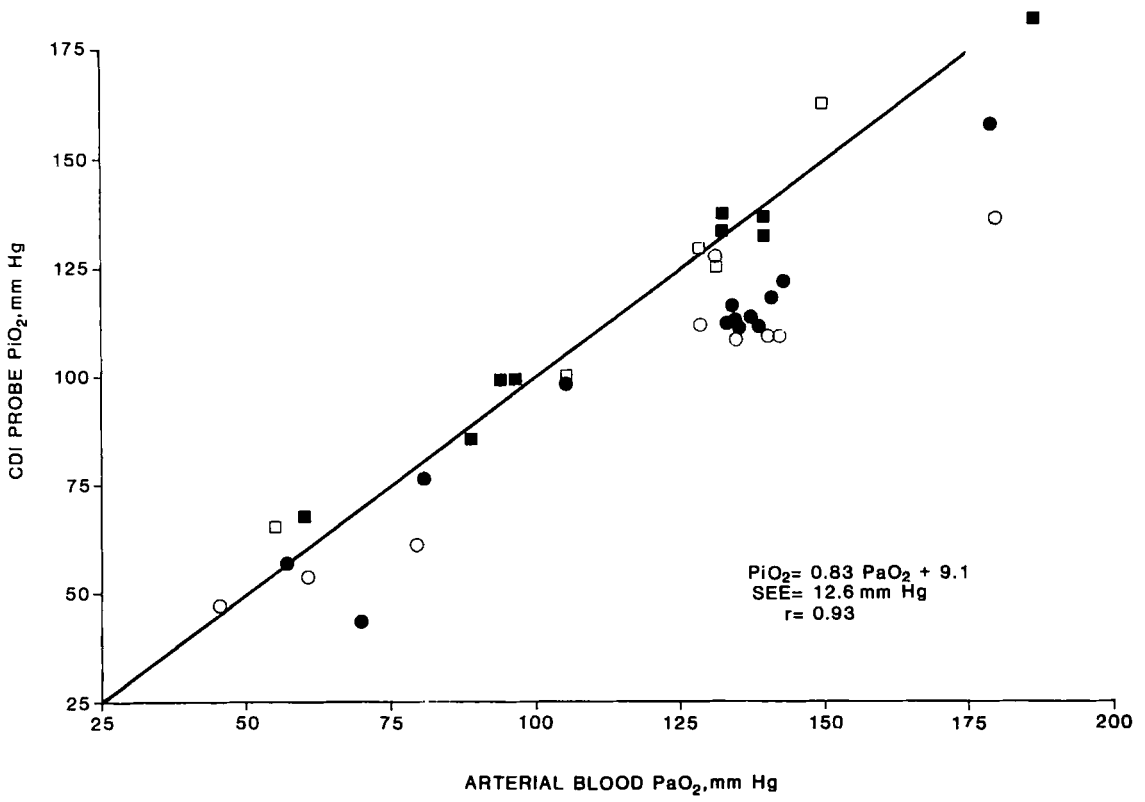

Fig 11. Relationship between sensor (PiO_2) *and arterial blood* (PaO_2) *oxygen tensions for arterial blood values less than 200 mm Hg. Each symbol indicates 1 of the 4 subjects. The line of identity and 36 data points are shown.*

Table 1. Least-Squares Linear Regression Equations of Fluorescent Sensors[a]

Equation	*r*	SEE
pHi = 0.896 pHa + 0.773	0.98	0.017
$PiCO_2$ = 1.05 $PaCO_2$ − 1.33	0.98	2.4 mm Hg
PiO_2 = 1.09 PaO_2 − 20.6	0.99	21.2 mm Hg
PiO_2[b] = 0.83 PaO_2 + 9.1	0.93	12.6 mm Hg

[a]pHi and pHa represent sensor (i) and arterial (a) pH values, respectively; $PiCO_2$ and $PaCO_2$ represent sensor (i) and arterial (a) carbon dioxide tensions, respectively; PiO_2 and PaO_2 represent sensor (i) and arterial (a) oxygen tensions, respectively.
[b]Denotes the regression equation for PaO_2 < 200 mm Hg. Data were obtained from 48 paired values in 4 subjects as described in Part 2 of the Results.

Table 2. Bias and Precision of Fluorescent Sensors[a]

Variable	Bias	(SD)	% Bias	(% SD)
pHi	−0.003	(+0.02)	−0.027	(+0.27)
$PiCO_2$	0.77	(+2.44) mm Hg	1.6	(+6.2)
PiO_2	−2.9	(+25.4) mm Hg	−5.0	(+11.8)

[a]pHi, $PiCO_2$, and PiO_2 represent the sensor pH, carbon dioxide tension, and oxygen tension values, respectively. Bias is the mean sensor value minus arterial value; % bias is the mean sensor value minus arterial value expressed as a percentage.

nula tip. Once this was done we were able to demonstrate reasonable performance.

The aberrant decreases in PO_2 values (downs) that occurred in the initial attempts of using this system in human volunteers could most easily be explained by the tip of the sensor touching the arterial wall. Although cessation of blood flow showed values approximating tissue values within about 5 minutes, the drop in PO_2 was not as rapid as occurred with a down effect. Down patterns could be induced easily with positional manipulation of the probe. Positional manipulation with staggered triple PO_2 sensor probes showed that the down effect could be induced most easily in the most distal sensor. Slow blood withdrawal from the catheter pulling fresh blood past the probe did not improve the distal PO_2, which suggested that the effect could not be explained by decreases in flow alone. Rotation and reversal of the down effect to the opposite sensor with the three PO_2 sensors staggered or flush at the tip (see Figs 5B and 5C) also suggested a positional effect. Thus, the results could most easily be explained by the sensor tips touching the arterial wall. This was substantiated when the down phenomenon disappeared once the probe tip was retracted within the cannula tip.

Our wall effect appears to be different from the well-known vessel wall artifacts that can occur with intravascular fiberoptic oximeters. This latter wall effect is due to high peaks in reflected light that occur as the intravascular fiberoptic oximeter moves relative to the vessel wall [10]. It can be eliminated, at least with right heart venous oximetry catheters, by digital signal filtering techniques [11]. Since no light exits the distal end of our probe, we hypothesize that our wall effect, that is, drops in PO_2 (down), is due to the close proximity of the sensor to the wall and measuring tissue PO_2. We elected to avoid the wall effect by retracting the probe within the cannula.

Retraction of the probe within the cannula tip can cause other problems such as interference of flush solution and decreased response times. These were dealt with by selecting an appropriate fixed retraction distance and inserting a variable compliance in the pressure tubing. The arterial pressure was noted (without added compliance); then, compliance was increased until the fidelity of the pressure signal deteriorated as determined visually.

The probe occludes approximately one-third of the cross-sectional area of the cannula; this will clearly alter the fidelity of the pressure signal. Bench data on the frequency response and damping coefficient, without the compliance device, are given in the Results section. It has been shown (without a probe and compliance in the circuit) that a wide range of frequency responses and damping coefficients can be found in radial artery systems produced by the same manufacturer [12]. We would expect this variability to increase further in patients with a probe in a cannula, particularly with a variable compliance in the circuit. Positional changes (e.g., flexion at the wrist) will enhance the damping. For this reason, wrist immobilization via an arm board will be imperative to maintain adequate pressure signals in patients. The fidelity of the pressure signals will need to be studied in more detail in patients.

The results of the accuracy studies in normal subjects with varying arterial blood gas values were excellent overall. The American College of Pathologists [13] considers good blood gas analyzer performance to be ±0.03 for pH, ±3 mm Hg (or 7.5%) for PCO_2, and ±5 mm Hg (or 7.5%) for PO_2. In particular, both the pH and PCO_2 sensors performed well within these recommendations for adequate blood gas instrumentation performance. Although the correlation coefficients for the PO_2 sensor were high, the standard errors were substantial. Of all the PO_2 data points, only 60% fell within the acceptable arterial PO_2 range. In 2 of the subjects the PO_2 probe usually performed within specifications, with 20 of 22 values falling within 7.5% of the arterial PO_2. Thus, the large standard errors of the estimate

reflected the performance of the PO_2 probes in the other 2 subjects. In these subjects the probe PO_2 was less than the arterial PO_2 (see Fig 11). The presence of the cannula in the artery, intermittent arterial spasm, positional changes, or a clot near the cannula tip could lead to reduced blood flow past the cannula tip. Reduced blood flow in the artery in turn could result in a reduction of PO_2 along the artery and might account for the errors.

The response times of the system to step changes in inspired gas was somewhat slow for clinical purposes, although they do compare favorably with times measured in vitro. Miller et al [6] studied the 63% response time of the sensors in the in vitro closed-loop situation and reported values of 0.6, 1.6, and 1.0 minutes for pH, PCO_2, and PO_2, respectively. For an exponential, the 90% response time is 2.3 times the 63% response time. Thus, the calculated 90% in vitro response times of Miller et al of 1.4, 3.7, and 2.3 minutes compare favorably with our in vivo values of 2.64, 3.88, and 2.60 minutes for pH, PCO_2, and PO_2, respectively. In some of our experiments (e.g., hyperventilation), true step changes in pH could not be induced. We hypothesize that this is the reason the discrepancies between the in vitro and in vivo pH are the largest.

Other probes to measure pH, PCO_2, and PO_2 have been described [2,14–20]. None of these probes measures all variables simultaneously. It is not our purpose to review these sensors in detail, and we will compare only the commercially available intravascular PO_2 electrode (Continucath 1000, Biomedical Sensors, Kansas City, MO) and a prototype PO_2 optode. The former is based on the Clark electrode and has been studied by us [16] in critically ill patients. Bias and precision were found to be 9.1 and 19.6 mm Hg. The latter is based on the phenomenon of fluorescence and was studied in dogs [14]. Bias and precision were 2.7 and 37.3 mm Hg. The accuracy of our PO_2 sensor (see Table 2) is comparable.

We conclude that there is such a phenomenon as a wall effect and it will have to be dealt with in any small intravascular blood gas sensing device. The proposed solution to the wall effect—withdrawal of the sensor probe into the cannula—introduces other problems, such as interference of flush solution, necessitating compliance changes to enhance tidal action at the probe tip. Finally, a potential intermittent longitudinal PO_2 gradient along the radial artery may fundamentally interfere with the practicality of measuring intravascular PO_2 with a small sensor.

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