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Continuous Intravascular Monitoring of P_{O_2} and P_{CO_2}. A Comparative *in vitro-in vivo* Study*

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Abstract. Two electrodes placed at the tip of catheters for *in vivo* determinations of P_{CO_2} and P_{O_2} respectively, were tested in dogs. Results were satisfactory when compared to a highly accurate reference method, correlation coefficients were close to 1 ($P < 10^{-9}$). Means of the differences were respectively -1.74 ± 1.14 torr for the P_{O_2} probe ($P < 0.01$) and -1.62 ± 0.72 torr for the P_{CO_2} sensor ($P < 0.0001$). While no drift was detected in the P_{CO_2} electrode, that of the P_{O_2} was significant but negligible compared to the variability of measurements. Thus, for P_{CO_2} values between 20 and 85 torr, and P_{O_2} values between 20 and 140 torr, *in vivo* monitoring is sufficiently reliable for clinical use.

Key words: Catheter electrode, Oxygen and carbon dioxide measurements, *in vitro* and *in vivo* comparisons.

During the last 15 years, the *in vitro* techniques for blood gas measurements have become reliable enough to permit a better understanding of the laws that govern both *hematosis* and acid-base balance. But they provide only pinpoint information and there is a need for the development of new methods for continuous monitoring. Such devices should meet criteria of accuracy, reproducibility, shortness of the response time and tolerance *in vivo*.

The proteic film coating the surface of the platinum cathode in P_{O_2} polarographic measurements precludes its clinical use. Indeed, in 1953, Clark (2) built a stable system consisting of a cathode protected by a polyethylene film and an anode embedded in saline-soaked cotton. Once miniaturised, this electrode allowed the first continuous P_{O_2} measurements to be made (11, 12), but it is an expensive and fragile sensor with significant drift.

Since 1956, the response time of most of the latest electrodes have been shortened, but their stability remains dependent on the electrode coating. On the other hand although a probe with a cathode, a ring-shaped anode and a reference central electrode keeps all its properties over a long period of time (6), it does not resolve the technical problems related to blood-membrane contact. Some methods including withdrawal and subsequent reinfusion of blood (9, 10) necessitate a total heparinisation with risks of haemorrhage and blood disorders.

More recently the P_{CO_2} electrodes were miniaturised, and this paper describes the testing of two sensors for the continuous *in vivo* monitoring of P_{O_2} and P_{CO_2}.

Material and Method

1. Preparation and Monitoring of Dogs

Six mongrel dogs, weighing 17 to 24 kg, were premedicated with 10 mg. Droperidol i.m., and 30 min. later, 2 mg Phenoperidine i.v. Anaesthesia was achieved by an intravenous injection of Sodium penthiobarbital ($15 \text{ mg} \cdot \text{kg}^{-1}$) and was maintained throughout an eight-hour period by continuous infusion of Sodium-penthiobarbital ($0.1 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) and Succicurarium ($0.025 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$). Thereafter, the dogs were heparinized, intubated and artificially ventilated using a volume generated servo-ventilator (Elema) fed with various inspired oxygen concentrations in N_2. Temperature was continuously recorded with an oesophageal thermocouple.

Cournand catheters were placed in the femoral vein for anaesthesia, and the carotid artery for arterial pressure, cardiac output, heart rate recordings and blood

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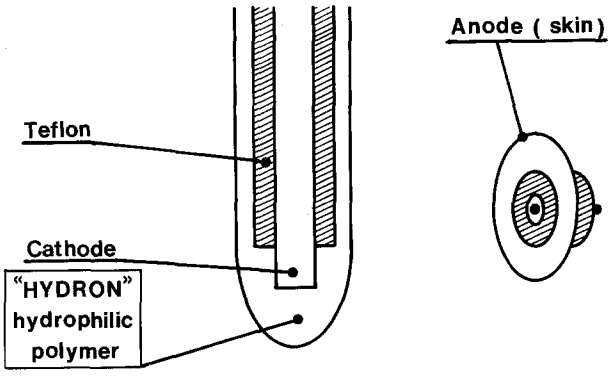

Fig. 1. In vivo $P_{O_2(IBC)}$ electrode

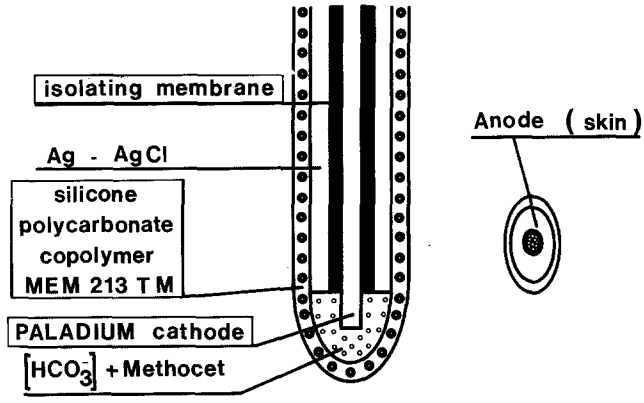

Fig. 2. In vivo $P_{CO_2(GE)}$ electrode

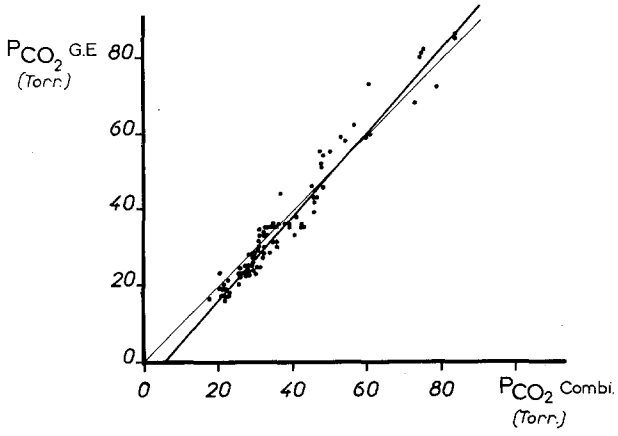

Fig. 3. Relationship of $P_{CO_2(Combi)}$ versus $P_{CO_2(GE)}$. Thin line = identity line, thick line = regression line; $P_{CO_2(GE)} = 1.1\ P_{CO_2(Combi)} - 5.2$

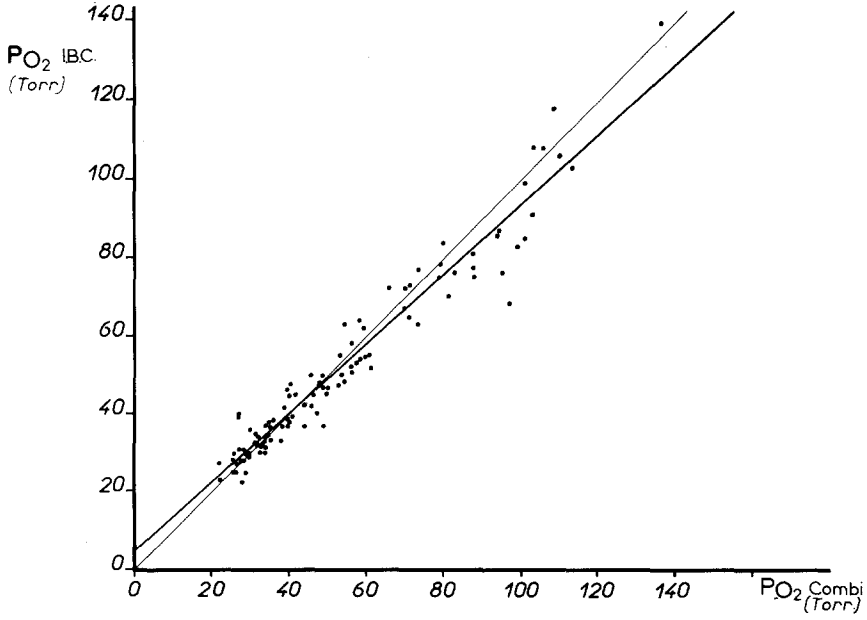

Fig. 4. Relationship of $P_{O_2(Combi)}$ versus $P_{O_2(IBC)}$. Thin line = identity line, thick line = regression line; $P_{O_2(IBC)} = 0.9\ P_{O_2(Combi)} + 4.3$

sampling. A fiberoptic catheter (Edwards) was placed in the aorta via the other carotid artery and permitted a continuous recording of haemoglobin saturation (SaO_2) to be made.

2. Modification of Arterial P_{O_2} and P_{CO_2}

By varying ventilation periods of hypo- (−30%), normo-, and hyperventilation (+80%) were induced. In each of them inspired Oxygen changes were monitored by the fiberoptic catheter so as to obtain different SaO_2. Hypercapnia was also induced in some cases by increasing the inspired carbon dioxide concentration.

3. Reference Measurements

Blood samples were anaerobically withdrawn using heparinized glass-syringes.

pH was determined by a glass microelectrode coupled with a calomel reference electrode (Radiometer type E 5021) thermostated at 37 °C and calibrated with two NBS buffer solutions whose values at 37 °C are respectively 7.383 and 6.841.

P_{O_2} and P_{CO_2} evaluations were performed simultaneously in each sample using a Combi analyzer V. D. (Eishweiler, Co Kiel).

The reference P_{CO_2} ($P_{CO_2\ Combi}$) was determined directly with the Gleichmann and Lubbers electrode, calibrated with three gas mixtures of different CO_2 concentrations titrated by the Scholander method, humidified and warmed to 37 °C. The reference P_{O_2} ($P_{O_2\ Combi}$) was polarographically determined using the Gleichmann and Lubbers platinum macro-electrode fitted with a magnetic stirring system and calibrated as above. Measurements of blood equilibrated with a given P_{O_2} allowed an estimate of gas-blood difference. The Hb concentration was estimated using the Drabkin method.

4. Electrodes

The $P_{O_2\,(IBC)}$ and $P_{CO_2\,(GE)}$ electrodes were placed respectively in either femoral artery and were rinsed with heparin every hour.

The P_{O_2} electrode (16) was built according to the polarographic principle illustrated in Fig. 1. At the tip of a teflon tube, the gold cathode, 100 μm. diameter, was coated with hydrophilic polymer gel and passed readily through an 18 gauge plastic cannula. The gel was inert and was not affected by tissue contact. The electrode required from 20 to 60 min. to reach its full equilibrium. The anode was fixed to the dog's skin. The oxygen diffused to the gold cathode where it was reduced and generated a current proportional to the oxygen partial pressure. Current was amplified, and was read on a torr-graded galvanometer.

The miniaturized P_{CO_2} cell (Fig. 2) enclosed in a membrane whose selective permeability was limited to blood gases and depended on Stow's principle, consisted of a metal-metal oxide sensor, a silver-silver chloride electrode in bicarbonate buffer solution. The membrane was made of silicone polycarbonate. A reference electrode was placed on the skin of the animal. When P_{CO_2} was to be read *in vivo* at a temperature different from 37 °C, this latter parameter had to be fed to a specific potentiometer, otherwise the P_{CO_2} value on the digital display would remain that of P_{CO_2} at 37 °C. Hence the characteristics of the sensor mean that changes in P_{CO_2} due to temperature variations are not taken into account. The device also included an alarm system and a graphic recorder.

5. Calibration

Calibration of both electrodes and computers was achieved in the same manner: 30 min. after the electrodes were positioned blood was withdrawn for *in vitro* P_{O_2} and P_{CO_2} determinations and the values on the computer were registered. Once the *in vitro* estimates were known, digits were corrected for the difference between direct readings at the time of withdrawal and at that of *in vitro* determinations.

6. Statistical Analysis

Results were analysed by the method of pairs; comparison of the difference to "O" used the "t" test; direct, partial and multiple correlations and regression coefficients were evaluated according to Galton's method. The 95% confidence limits of "y" for a given "x" about the regression line, were determined by estimating the variance $s_y^2 (1-r^2)$. Significances were read in the Student-Fisher table.

Results

Comparisons were performed in a hundred measurements ranging from 18 to 84 torr for $P_{CO_2\,(GE)}$ versus $P_{CO_2\,(Combi)}$, and in 113 measurements ranging from 22 to 136 torr for $P_{O_2\,(IBC)}$ versus $P_{O_2\,(Combi)}$.

1. Mean of the Difference (Table 1a) and 95% Confidence Intervals ($= \pm ts/\sqrt{n}$)

The difference between the P_{CO_2} values as provided by either probes, namely Δ (GE-Combi), was as much as −1.62 torr (±0.72), significantly different from O ($P < 10^{-4}$).

Table 1. Direct, partial and multiple correlations between
a) $P_{CO_2(Combi)}$ level, Δ (Ge-Combi), and lag of time (t) from calibration to measurements
b) $P_{O_2(Combi)}$ level, Δ (IBC-Combi), and lag of time (t) from calibration to measurements
N. S. = non significant; ■ : $P < 0.05$; ■■ : $P < 0.01$; ■■■ : $P < 0.001$
r and r* = respectively, direct and partial correlation coefficient
R = multiple correlation coefficient

1 a	P_{CO_2}	ΔP_{CO_2}	t
P_{CO_2}	R: 0.4327 ■■■	r: 0.4324 ■■■	r: 0.0482 N. S.
ΔP_{CO_2}	r*: 0.4305 ■■■	R: 0.4355 ■■■	r: 0.0728 N. S.
t	r*: 0.0186 N. S.	r*: 0.0577 N. S.	R: 0.0751 N. S.
1 b	P_{O_2}	ΔP_{O_2}	t
P_{O_2}	R: 0.4235 ■■■	r: −0.4231 ■■■	r: 0.0855 N. S.
ΔP_{O_2}	r*: −0.4163 ■■■	R: 0.4711 ■■■	r: −0.2427 ■
t	r*: 0.0196 N. S.	r*: −0.2288 ■	R: 0.2434 ■

Table 2. Comparison of in vivo and in vitro paired measurements for P_{O_2} and P_{CO_2}.
a) Mean differences ΔP and standard error : Δ (IBC-Combi) P_{O_2} and Δ (GE-Combi) P_{CO_2} are compared to zero. "t" values are given with their significance level (P)
b) Correlation coefficients (r) and regression lines coefficients (p = slope; q = zero intercept) and their 95% confidence limits $\pm t s\sqrt{1-r^2}$, with t = (N − 2) degrees of freedom.

2a	N	Δp	$S/\sqrt{n}$	t	p
P_{O_2}	113	−1.74 −2.88 −0.60	0.581	2.99	$P < 0.01$
P_{CO_2}	100	−1.62 −2.71 −0.99	0.371	4.36	$P < 0.0001$
2b	N	r	p	q	$\pm t S\sqrt{1-r^2}$
P_{O_2}	113	0.973 $P < 10^{-9}$	0.89	+ 4.32	10.69
P_{CO_2}	100	0.972 $P < 10^{-9}$	1.10	− 5.24	6.67

The difference between the P_{O_2} values as provided by either probes, namely Δ (IBC-Combi), was as much as −1.74 torr (±1.14), significantly different from O ($P < 0.01$).

2. Correlation Coefficients

Correlation coefficients are given in Table 1b and the regression lines are delineated in Fig. 3 for P_{CO_2} and Fig. 4 for P_{O_2}.

3. Direct, Partial and Multiple Correlations

a) In Table 2a data refer to the level of $P_{CO_2(Combi)}$, Δ (GE-Combi) and the lag of time between calibrations and measurements. The correlation coefficients were significant ($P < 0.001$) between Δ (GE-Combi) and $P_{CO_2(Combi)}$ level and not significant between the former and the lag of time.

b) In Table 2b data refer to the level of $P_{O_2(Combi)}$, the difference Δ (IBC-Combi) and the lag of time between calibrations and measurements. The correlation coefficients were significant either between Δ (IBC-Combi) and $P_{O_2(Combi)}$ level ($P < 0.001$) or between the former and the lag of time ($P < 0.05$).

Comments

The results were generally satisfactory for both the IBC and the GE electrodes, since in each case, correlations were good, "r" was close to 1, significance levels were above 10^{-9}; most probably they would even have improved if the analysis had been effected probe by probe, each time readjusting gain and zero. They were valid for P_{O_2} and P_{CO_2} values ranging as defined above. In the present study the accuracy of the reference method is noteworthy.

A–$P_{CO_2(GE)}$

Mean difference between $P_{CO_2(GE)}$ and $P_{CO_2(Combi)}$ was −1.62 ± 0.72, demonstrating an underestimation of P_{CO_2} by the GE electrode. For a given P_{CO_2}, the value read on the digital display might vary from 1.1 P_{CO_2} + 1.43 to 1.1 P_{CO_2} − 11.91. In other respects no drift of the sensor existed throughout the 8-hour utilization since the correlation between the Δ (GE-Combi) and $P_{CO_2(Combi)}$ level was significant and since it was not between the former and the lag of time. Hence the variability of $P_{CO_2(GE)}$ can be characterized by the regression line of $P_{CO_2(GE)}$ versus $P_{CO_2(Combi)}$. Kampire *et al.* (8) have tested the $P_{CO_2(GE)}$ electrode in dogs and in surgical patients: mean differences were respectively 4.5 ± 3.8 and 4.3 ± 3.8. The *in vivo* drift in animals was as much as 6 torr, over a 12-hour period. These results do not compare with ours since the scatter found is wider and there is evidence of a drift. It might be explained by a larger variability of the reference method during calibration and by the difficulty of achieving valid P_{CO_2} comparisons in clinical practice.

B–$P_{O_2(IBC)}$

The IBC electrode gave an underestimation of P_{O_2} since the mean difference between $P_{O_2(IBC)}$ and $P_{O_2(Combi)}$ was −1.74 ± 1.14 torr. For a given P_{O_2}, the 95% confidence

limits of the electrodes ranged from 0.9 P_{O_2} – 6.34 to 0.9 P_{O_2} + 15.00 torr. The respective significance levels of the correlation coefficients between Δ(IBC-Combi) and $P_{O_2(Combi)}$ level ($P < 0.001$) on one hand, and the lag of time on the other hand ($P < 0.05$) indicate a slight influence of the sensor drift on $P_{O_2(IBC)}$ variability. Taking into account the time factor only slightly improves the correlation coefficient as $r_{(IBC, Combi)} = 0.42$ becomes 0.47 as far as the relationships between $P_{O_2(IBC)}$ and either $P_{O_2(Combi)}$ or time are concerned.

These results are in good agreement with those of other experiments performed in animals and in human beings. Strauss *et al.* (14) have tested the P_{O_2} IBC electrode placed in the umbilicalarlery of 25 new-born infants and studied 296 values. The results were the following : 0.77 for correlation coefficient; 15.9 for mean difference (in absolute value); and ± 34 torr for confidence interval out of the regression line. Reference measurements were achieved with a Corning 160 analyser. Harris *et al.* (7) performed 999 comparisons using 50 probes in 48 new-born infants, with a P_{O_2} varying from 10 to 252 torr. Depending on the situation of the probe, the mean difference (in absolute values) varied from ± 7.2 for the abdominal aorta to ± 28.8 torr for the left atrium; this deviation increased with the level of P_{O_2} . The reference measurements were carried out using an I. L. 213 or an I. L. 313 apparatus. The underestimation of P_{O_2} was confirmed by Diaz *et al.* (3) for levels above 240 torr. The lack of linearity of the results was in evidence away from the calibration point. Strauss *et al.* (14) documented a drift of ll torr during the first 24 hours, of 15 torr between 24 and 48 hours, followed by a 9 torr shift every subsequent 24 hours. According to Carlsen *et al.* (1), drift was 1.1 torr per hour during the first 12 hours, decreasing seemingly to an average 0.32 torr per hour during the following 36 hours. The scatter and the drift found by these authors proved larger than in the present study. Either a greater variability of the reference method or of the calibration, or even the variability inherent in clinical studies might explain this difference.

Both temperature and pH were found to be of little importance whilst viscosity and hematocrit had no influence (7). Although the response of the IBC electrode *in vitro* is disturbed by small size molecules, the *in vivo* infusion of molecules of similar size do not have any effect. This might be due to the difference of the concentrations in the *in vitro* and *in vivo* studies.

The tolerance of *in vivo* P_{O_2} electrodes has been demonstrated. Strauss *et al.* (14) documented no difference in the incidence of complications (thrombosis, infections) in two groups of new-born infants, the first of which had umbilical catheters, the second the electrodes under test placed at the same site; in both instances only heparinized serum was injected. Carlsen *et al.* (1) have left in situ for two weeks two electrodes without any complications. The P_{O_2} and P_{CO_2} sensors are made of disposable material so as to eliminate any risk of infection.

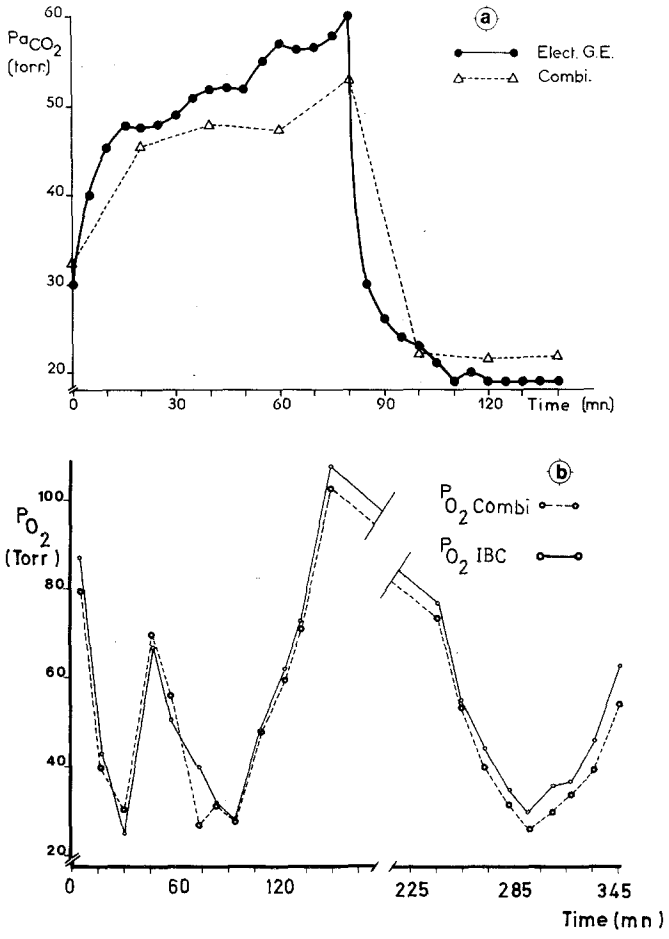

Fig. 5. Example of a continous recording: a) P_{CO_2} by the GE electrode; b) P_{O_2} by the IBC electrode

For physiological research or when an objective appreciation of a clinical picture is needed, the sensors we studied failed to provide accurate data for P_{O_2} and P_{CO_2}. Moreover, the response time of both sensors, namely 2 mn. between 10 and 60 torr for P_{CO_2} (8) and 45 to 74 seconds for P_{O_2} for a 95% response to step changes (1) preclude their use in servo-systems, and impairs the rapid detection of variations connected with the cardiac and respiratory cycles.

On the other hand, as long as systematic recalibration is made, such probes are accurate enough to define a trend of P_{O_2} and P_{CO_2} as illustrated in Fig. 5.

The P_{O_2} electrode is used most of the time in new-born infants thus avoiding multiple withdrawals of blood (3, 7, 14). It provides reliable P_{O_2} values on some occasions when O_2 variations can no longer be expressed by changes in the saturation level as P_{O_2} is above 100 torr; it is a way to prevent the toxic effects of oxygen therapy. The P_{CO_2} electrode covers a similar experimental field. But it is of little interest to obtain this single information. Indeed, coupled with a P_{O_2} electrode it permits the continuous evaluation of the patient's ventilatory status, but is has to be complemented by an estimation of the pH level to

give a comprehensive picture. If, as seems probable, such a pH electrode is to be manufactured soon, it would provide a definite improvement in the acid-base and respiratory monitoring.

References

1. Carlsen, E. N., Bowyer, A. F.: Continuous blood P_{O_2} monitoring using a miniature indwelling catheter. Unpublished data from Loma Linda University Medical Center. Loma Linda, Calif. (1972)
2. Clark, L. C., Wolf, R., Granger, D., Taylor, S.: Continuous recording of blood oxygen tensions by polarography. J. Appl. Physiol. 6, 189–193 (1953)
3. Diaz, P. M., Gold, M. I., Duarte, I., Sohn, Y. J.: A disposable electrode for the continuous in vivo measurements of arterial oxygen tension during heart surgery. Department of anesthesiology. University of Miami 1974
4. Gaudebout, C., Blayo, M. C., Pocidalo, J. J.: A comparative study of technique for direct and indirect determinations of blood P_{CO_2}. Ann. N. Y. Acad. sci. 133, 66–72 (1966)
5. Gaudebout, C., Clavier, F., Blayo, M. C.: Mesures polarographiques "in vitro" de la pression partielle d'oxygène (P_{O_2}) dans les liquides biologiques sans hémoglobine. Importance de l'agitation de l'échantillon. Bull. Phys. Path. Resp. (Nancy) 5, 91–105 (1965)
6. Gaudebout, C., Quercy, J. F., Lacroix, Y., Muffa-Joly, M.: Contribution au développement d'électrodes intravasculaires pour la mesure continue de la pression partielle d'oxygène du sang. B 503, Imeko V, Versailles (1970)
7. Harris, T., Nugent, M.: Continuous arterial oxygen tension monitoring in the newborn infant. J. Pediat. 82, 929–939 (1973)
8. Kampine, J. P., Neumark, J.: Des capteurs CO_2 miniaturises pour la surveillance intravasculaire permanente de la P_{CO_2} du sang. Reunion ann. 1974. Society of critical Care Medicine
9. Koeff, S. T., Tsao, M. U., Vadnay, A., Wilson, T. O., Wilson, J. L.: Continuous measurements for intravascular oxygen tension in normal adults. J. clin. Invest. 41, 1,125-1,133 (1962)
10. Meyer, J. S., Gotoh, F., Tazaki, Y.: Continuous recording of arterial P_{O_2}, P_{CO_2}, pH and saturation in vivo. J. appl. Physiol. 16, 896–902 (1961)
11. Schuler, R.: Evaluation and design of rapid polarographic in vivo oxygen catheter electrodes. Ph. D. Thesis, Nijmegen 1966
12. Schuler, R., Kreuzer, F.: Rapid in vivo oxygen catheter electrodes. Resp. Physiol. 3, 90–110 (1967)
13. Schwartz, D.: Methodes statistiques à l'usage des médecins et des biologistes. Flammarion éditeur 1963.
14. Strauss, F. M., Escobedo, M., Goldeing, D.: Continuous monitoring of arterial oxygen tension in the newborn infant. J. Pediat. 85, 254–261 (1974)
15. Sussman, B. J., Barber, J. B., Goald, H.: Experimental intracerebral hematome. J. Neurosurg. 41, 177–186 (1974)
16. Watanabe, H., Siegelman, H., Welsh, H., Spracklen, S.: Continuous in vivo monitoring system. Proceeding of the San Diego biomedical symposium 12, 37 (1973)

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