Accuracy of Oxygen Partial Pressure Measurements: An In-Vitro Study

Gary D. Reeder and Andrew G. Hood
RMI, Inc.
Westlake Village, California

Abstract

The accuracy of oxygen partial pressure (pO_2) analysis was examined in two commercially available systems, an IL 513 blood gas analyzer and a new in-line sensor from Orange Medical Instruments.

Data was obtained with each system after equilibration of an in vitro test circuit with specially formulated tonometry gases. The response of each system was examined over a pO_2 range from 19 Torr to 400 Torr. The effect of hypothermia on analytical accuracy of each system was evaluated over a range of 37°C to 21.5°C.

A high degree of temperature dependent error was found with analysis on an IL 513 system. This resulted in significant underestimation of true pO_2 under most conditions examined. In contrast, the in-line sensor was found to report significantly more accurate data with less temperature dependence.

Introduction

Among the many variables under perfusionist control during cardiopulmonary bypass, blood oxygenation is, perhaps, of the greatest importance. Arterialized blood, with oxygen partial pressures (pO_2) in excess of the normal range, has been implicated in microaeroemboli[1] and organ ischemia.[2] On the other hand, low pO_2 may create generalized tissue hypoxia with resultant anaerobic metabolism. In tissues with low metabolic reserves, such as the brain or ischemic myocardium, a sustained anaerobic insult may create irreversible cellular damage. Additionally, the monitoring of venous pO_2 has been shown to be an extremely sensitive measure of the adequacy of tissue oxygen supply.[3]

Because of the demonstrated importance of blood pO_2 monitoring during cardiopulmonary bypass, a vast body of literature has been promulgated dealing with the implications of pO_2 variations. Numerous regimens specifying ideal pO_2 tensions have been established and, for the most part, are rigorously followed. Virtually all of these studies and regimens are based on pO_2 measurements made on commercially available blood gas analyzers.

Such blood gas analyzers require that blood samples be removed from the patient, or extracorporeal circuit, prior to aspiration into a heated cuvette (usually 37°C).Once in the cuvette, the blood is in contact with a "Clark type" electrode, the current flow from which can be directly related to the pO_2 of the sequestered sample. When the patient, or sample site, temperature is significantly different from the measuring cuvette temperature, the measured pO_2 will be significantly different from the actual sample site pO_2. A variety of mathematical formulae and nomograms have been proposed[4,5,6] to allow for temperature correction of such thermally abberant samples.

Blood pO_2 measurements made on such ana-

Direct Communications to: Gary D. Reeder, 2500 Townsgate Rd., Suite E Westlake Village, CA 91361

lyzers have become an integral part of blood oxygenation management during cardiopulmonary bypass and the results are implicitly accepted as the foundation for both research studies and clinical judgments. Such analyzers require meticulous maintenance and frequent calibration against known standards.

In support of optimizing the accuracy of these measurements, much has been written about storage and blood handling techniques, and about various techniques for machine calibration. However, to the authors' knowledge, there is no documentation in the literature of the accuracy of commercial blood gas analyzers under the relatively abnormal conditions of hypothermic, cardiopulmonary bypass.

This paper, in part, examines the accuracy of an IL 513 blood gas analyzer[a] over the expected range of variables to be encountered by the contemporary perfusionist. This is accompanied by a comparative evaluation of accuracy for a new, continuous, in-line pO_2 monitor[b] designed for use in the extra-corporeal circuit.

Methods

An in-vitro test circuit was constructed, a schematic diagram of which is depicted in Figure 1. The circuit utilized a bubble oxygenator,[c] roller pump, two calibrated thermistor temperature probes[d] and six extracorporeal pO_2 sensors.[b] Provision for direct blood sampling was made by the inclusion of stopcock sample sites in the test line immediately preceding and following the test sensors.

The pre-sensor and post-sensor electronic temperature probes were connected to a multichannel, electronic thermometer[d] and calibrated against a mercury thermometer throughout the expected range of test temperatures.

The in-line pO_2 monitors, previously described by Parker et al.,[7] were assembled and calibrated with strict adherence to the manufacturer's recommended instructions. A schematic of the sensor components is depicted in Figure 2. A membrane ring filled with electrolyte was screwed onto a bi-

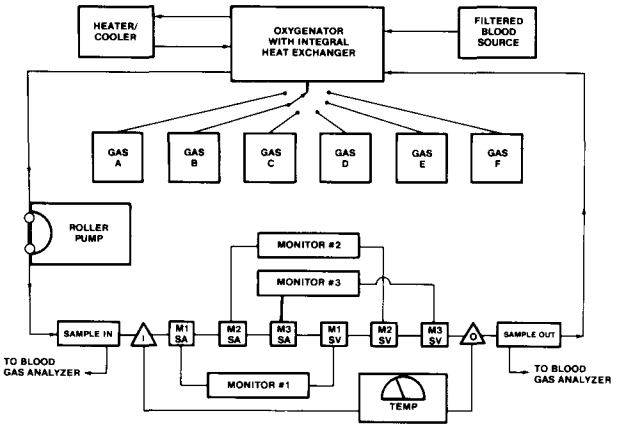

FIGURE 1. In vitro test circuit.

polar electrode (platinum cathode/silver anode) forming a "Clark type" polarographic sensor. This assembly was in turn connected by cable to a battery powered monitor.

After a brief equilibration period, nitrogen gas was delivered onto the surface of the sensor membrane until a stable "null" reading on the monitor could be effected with the zero calibration potentiometer. The intact sensor was then inserted into a specially designed connector, and following the application of additional electrolyte, it was calibrated to room air as a high gas standard.

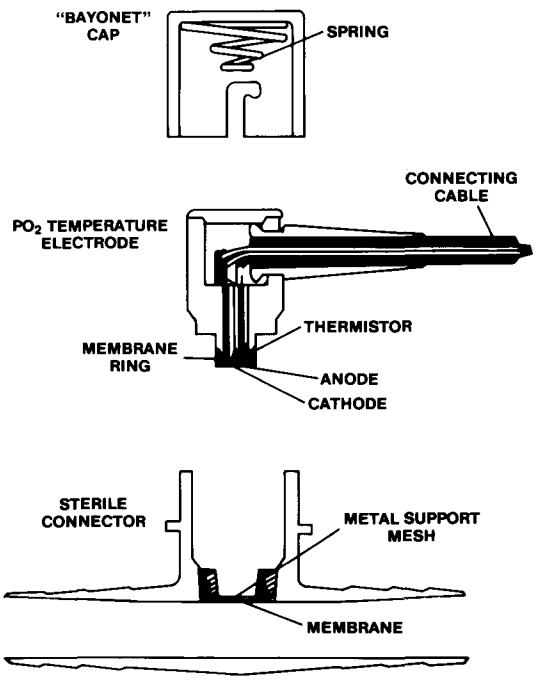

FIGURE 2. Extracorporeal pO_2 sensor.

[a] Instrumentation Laboratory, Lexington, MA 02173
[b] Orange Medical Instruments, Costa Mesa, CA 92626
[c] Model H-1500, C. R. Bard, Santa Ana, CA 92705
[d] Yellow Springs Instruments, Yellow Springs, OH 45387

The connector, otherwise similar to a conventional extracorporeal tubing connector, contains a silicone rubber membrane supported by a stainless steel mesh. The sensor is designed such that the electrode can rapidly equilibrate through the membrane and assess the pO_2 of liquids or gases within the lumen of the connector. Once calibrated, the sensor assembly was removed from the calibration connector and inserted into a similar connector in the test circuit configuration depicted in Figure 1. During the course of the study, no further adjustments were made to the calibration of the extracorporeal sensors.

The circuit was primed with 2000 cc. of heparinized, bovine blood, collected within three hours of the onset of testing. This blood was filtered through a cardiotomy reservoir[e] prior to introduction into the test circuit. The blood prime was then hemodiluted with 5% Dextrose in Lactated Ringers to a final volume of 3000 cc. Additional heparin[f] was added (40,000 IU) to ensure that anticoagulation would remain adequate for the duration of the procedure. The degree of hemodilution was assessed by cyanomethemoglobin determination in a Beckman DBG-T[g] spectrophometer against known quality control standards. The volume of hemodiluted blood introduced into the circuit was sufficient to allow for all sampling during the course of the procedure, thereby precluding the possibility of any further volume additions.

[e] Extracorporeal, Inc, King of Prussia, PA 19406

[f] Upjohn, Inc., Kalamazoo, MI 49001

[g] Beckman Instruments, Inc., Fullerton, CA 92634

Thermal stability was maintained at each test condition by recirculation of water from a temperature control module through the integral heat exchanger of the oxygenator. Stable gas tensions were achieved at each desired test level by maintaining direct exposure of the blood to specially formulated, laboratory analyzed, gas mixtures (Table 1). Recirculation of the blood through the oxygenator was maintained with each source gas until a stable gas tension was achieved prior to the commencement of data acquisition. When necessary during the procedure, aliquants of sodium bicarbonate (1 mEq/ml) were added to the perfusate to maintain base excess within normal limits.

Blood gas data was obtained by syringe collection of blood samples from each of the pre-sensor and post-sensor sample collection sites. A minimum of four samples was collected at each test condition and immediately analyzed on an IL 513 blood gas analyzer. Analysis was conducted per manufacturer's recommended procedures, with full system calibration against known source gases and buffers following every fourth sample analysis. Blood gas data obtained at circuit temperatures less than 36° C were temperature corrected according to the Kelman-Nunn equations.[4] Percent oxyhemoglobin saturations were calculated using the Hill equation.[9]

Results

Table 1 defines the formulations of the specially prepared gas mixtures utilized to establish known gas tensions at each test condition. The table pre-

TABLE 1
Analyzed Oxygen and Carbon Dioxide Contents of Tonometry Gases and the Resulting Calculated pO_2 and pCO_2 Values

	Analyzed Gas Content		Calculated pO_2 at Test Temperatures			Calculated pCO_2 at Test Temperatures		
Gas Mixture	% O_2	% CO_2	37°C	28°C	21.5°C	37°C	28°C	21.5°C
A	2.82	5.48	19.2	19.8	20.0	37.4	38.4	38.9
B	5.52	5.72	37.6	38.7	39.2	39.0	40.1	40.6
C	10.9	5.60	74.3	76.4	77.4	38.2	39.2	39.7
D	20.3	5.43	138	142	144	37.0	38.0	38.5
E	33.6	5.46	229	235	238	37.2	38.3	38.8
F	57.2	5.33	390	401	406	36.3	37.3	37.8

Barometric pressure = 729 Torr; pH_2O at 21.5°C = 19.2 Torr, at 28°C = 28.3 Torr, at 37°C = 47.1 Torr. 8

TABLE 2
Blood Gas Data Collected at 37°C Test Condition

Gas Mixture	A	B	C	D	E	F
True pO_2 (Torr)	19.2	37.6	74.3	138.0	229.0	390.0
True pCO_2 (Torr)	37.4	39.0	38.2	37.0	37.2	36.3
pO_2 Measured (IL513)	23.3 ± 0.4	44.9 ± 3.1	81.0 ± 3.9	137.6 ± 10.9	218.1 ± 12.4	337.8 ± 3.3
pO_2 Measured (OMI)	17.2 ± 0.4	33.8 ± 0.9	66.8 ± 2.8	130.7 ± 3.2	221.3 ± 7.9	385.2 ± 16.7
Percent Saturation	31.3 ± 0.8	73.5 ± 3.8	93.3 ± 0.6	98.3 ± 0.3	99.5 ± 0.1	99.9 ± 0.0

sents the percentage oxygen and carbon dioxide present in each formulation with the balance being nitrogen. Additionally, this table presents the partial pressures which resulted following equilibration of the blood with each gas at every thermal test level. It will be noted that the pCO_2 is held relatively constant within normal ranges throughout the experiment. The pO_2, however, spans a range from 19.2 to 406 Torr.

Table 2 presents the mean and standard deviation of the blood gas data obtained at a 37°C test condition. Reported in this table are the oxygen tensions reported by both the OMI sensor and the IL 513 blood gas analyzer as well as the oxyhemoglobin saturation levels.

Tables 3 and 4 similarly report results obtained at thermal test conditions of 28°C and 21.5°C respectively. The information reported here is similar to the format of Table 2 with the inclusion of temperature corrected pO_2 for IL 513 data.

Figure 3 depicts the correlation between true pO_2 and the mean pO_2 reported by the OMI sensor at each test condition. The "line of identity" represents absolute correlation between reported data and the true value. Figure 4 depicts a format identical to that of Figure 3, except that the experimental comparative is the temperature corrected pO_2 established by traditional blood gas analysis on the IL 513.

Figure 5 depicts the absolute deviation (Torr) of each data acquisition method from the true oxygen partial pressure at each thermal state. These data are listed in Table 5. A statistical analysis was made employing Student's "t" test, comparing the absolute value of the deviation shown by the two test measurement systems at each set of conditions studied.

Discussion

Blood gas analysis with traditional analyzer systems has been an accepted standard of medical practice for many years. Its application to the management of patients subjected to cardiopulmonary bypass seems a natural extension of the technique's usefulness. However, it may be seen from the data presented in Figures 4 and 5 that pO_2 evaluation by traditional methods, during hypothermic cardiopulmonary bypass, may result in gross underestimation of the true partial pressure. Such erroneous data could affect bypass management decisions, resulting in true operational oxygen tensions in excess of 300 Torr during the course of the procedure. The pathophysiologic impact of such errors may be found in the work of Kuntz & Maurer[1] which demonstrated the generation of significant quantities of microaeroemboli as a result of cavitation occurring at the arterial

TABLE 3
Blood Gas Data Collected at 28°C Test Condition

Gas Mixture	A	B	C	D	E	F
True pO_2 (Torr)	19.8	38.7	76.4	142.0	235.0	401.0
True pCO_2 (Torr)	38.4	40.1	39.2	38.0	38.3	37.3
pO_2 Measured (IL513)	30.5 ± 0.3	58.0 ± 0.04	94.7 ± 3.4	116.0 ± 13.2	157.3 ± 17.6	226.5 ± 36.5
pO_2 Corrected (IL513)	15.7 ± 0.2	29.8 ± 0.0	48.9 ± 1.8	62.9 ± 9.6	94.8 ± 15.7	161.4 ± 35.2
pO_2 Measured (OMI)	17.0 ± 1.2	34.7 ± 1.4	67.7 ± 1.8	127.0 ± 5.0	216.3 ± 12.5	390.0 ± 29.7
Percent Saturation	49.5 ± 0.4	85.2 ± 0.3	95.7 ± 0.7	97.5 ± 0.8	98.8 ± 0.3	99.6 ± 0.2

TABLE 4
Blood Gas Data Collected at 21.5°C Test Condition

Gas Mixture	A	B	C	D	E	F
True pO_2 (Torr)	20.1	39.3	77.6	144.0	239.0	407.0
True pCO_2 (Torr)	39.0	40.7	39.8	38.6	38.8	37.9
pO_2 Measured (IL513)	42.8 ± 0.8	71.8 ± 1.8	88.8 ± 3.9	106.0 ± 7.6	87.3 ± 3.9	201.0 ± 39.4
pO_2 Corrected (IL513)	13.5 ± 0.2	22.8 ± 0.6	28.1 ± 1.3	33.6 ± 2.4	27.7 ± 1.2	74.5 ± 22.7
pO_2 Measured (OMI)	18.3 ± 2.0	33.3 ± 2.7	61.7 ± 3.7	115.7 ± 6.3	209.8 ± 14.9	375.5 ± 27.9
Percent Saturation	72.0 ± 0.6	91.3 ± 0.8	95.0 ± 0.9	96.8 ± 1.2	94.7 ± 0.9	99.4 ± 0.3

cannulation site. Their work clearly demonstrated the dependent relationship between elevated pO_2 and cannula pressure drop in the generation of gaseous microemboli. Additionally, the work of Pearson[2] has confirmed the presence of significant numbers of microemboli, in excess of 10μ, within the carotid artery during cardiopulmonary bypass. This work further demonstrated a direct relationship between the number of such embolic doppler counts and the oxygen partial pressure.

As may be seen in Figures 3 and 5, the OMI sensor also demonstrated a tendency to slightly underestimate the true pO_2. There was a temperature dependent exaggeration of this error as found in the examination of the IL 513 data. However, as Table 5 shows, the errors from the IL 513 are significantly larger than those for the OMI sensor at conventional levels of hypothermia. In light of the reported findings, and the fact that the OMI sensor provides "real time" reporting as compared to "historic" reporting in traditional blood gas systems, it seems evident to the authors that the in-line sensor evaluated in this study provides more accurate data on which to base perfusion management decisions during hypothermic cardiopulmonary bypass. During normothermic procedures, the comparable accuracy and the continuous data availability make it the technique of choice.

Conclusions

In the course of this study we have examined two available systems for the evaluation of oxygen partial pressure during cardiopulmonary bypass. The extracorporeal sensor produced by Orange

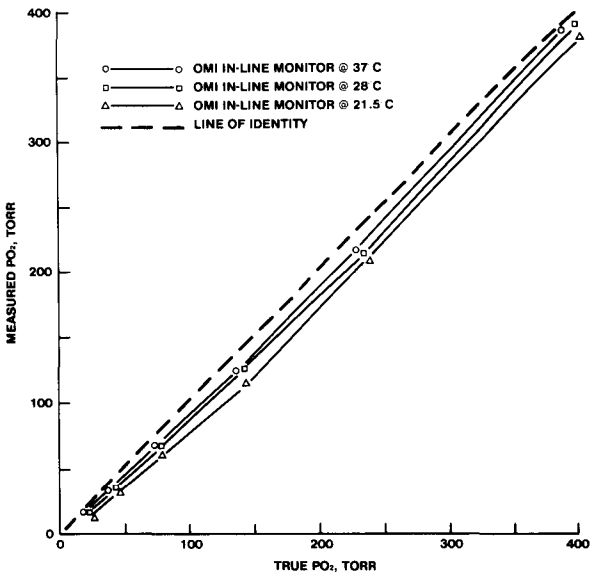

FIGURE 3. Effect of hypothermia on the mean pO_2 reported by OMI in-line sensors.

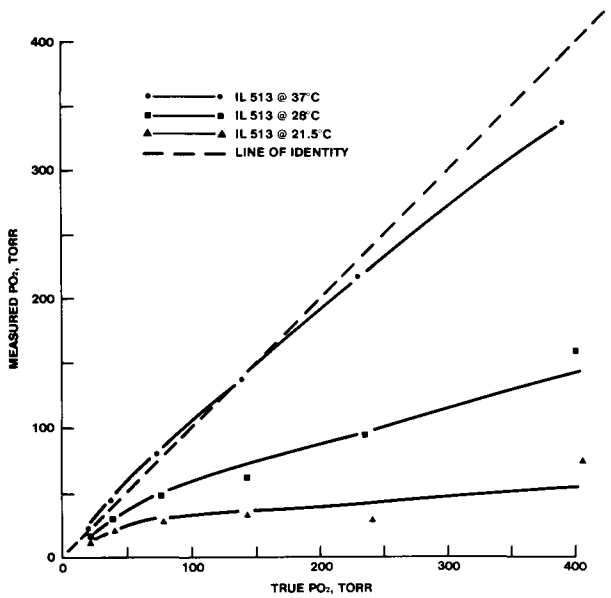

FIGURE 4. Effect of hypothermia on the mean pO_2 reported by IL 513 blood gas analyzer (Temperature corrected).

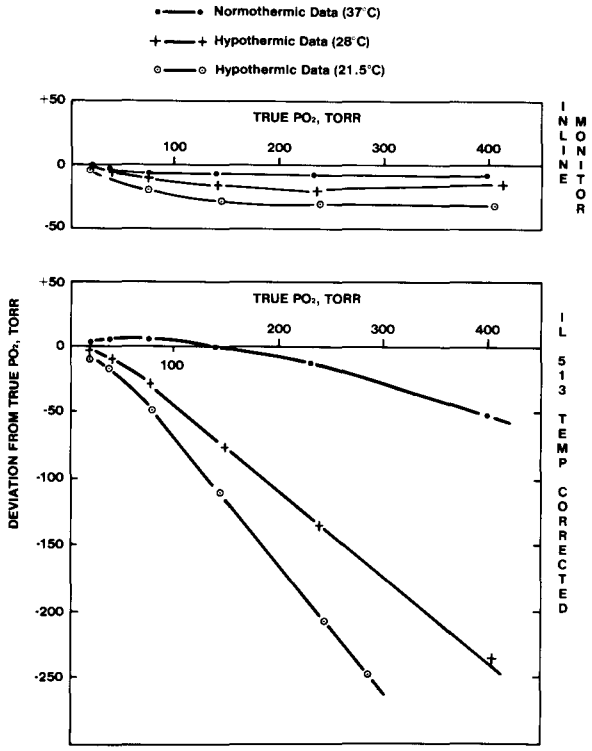

FIGURE 5. Deviation of reported pO_2 from true pO_2 for two types of pO_2 analyzers.

Medical Instruments was found to be superior to an Instrumentation Laboratory 513 blood gas analyzer in such evaluations. Furthermore, due to the degree of error encountered with traditional analyzer techniques, it seems obvious that such analytical techniques cannot be considered accurate during hypothermic cardiopulmonary bypass. Such analyzers should be utilized under these stated conditions only after thorough assessment to evaluate the magnitude of error in the reported data.

Additionally, it was observed that the commonly accepted temperature correction factors were not sufficient to correct the errors observed in traditional blood gas analysis under the conditions of hypothermia reported in this study.

Addendum

Although bovine blood has long been employed for the testing and evaluation of gas transfer and gas sensing devices, a criticism of this study may be its use with analyzer systems and temperature correction nomograms intended for application

TABLE 5
Deviation of Measured Values From True pO_2

Circuit Temp, °C	Gas Mixture	True pO_2, Torr	Deviation From True pO_2, Torr		p*
			IL 513, Temp Corr	OMI Sensor	
37	A	19.2	−4 ± 0.4	−2 ± 0.4	<0.005
37	B	37.6	−7 ± 4	−4 ± 1	N.S.
37	C	74.3	−7 ± 5	−8 ± 3	N.S.
37	D	138	0 ± 12	−7 ± 3	N.S.
37	E	229	−11 ± 14	−4 ± 7	N.S.
37	F	390	−53 ± 4	−5 ± 18	<0.005
28	A	19.8	−4 ± 0.2	−3 ± 1	<0.05
28	B	38.7	−9 ± 0	−4 ± 2	<0.005
28	C	76.4	−28 ± 2	−8 ± 2	<0.0005
28	D	142	−80 ± 11	−15 ± 6	<0.005
28	E	235	−140 ± 18	−17 ± 13	<0.005
28	F	401	−240 ± 41	−11 ± 33	<0.005
21.5	A	20.0	−7 ± 0.3	−2 ± 2	<0.005
21.5	B	39.2	−17 ± 1	−6 ± 3	<0.005
21.5	C	77.4	−43 ± 15	−15 ± 4	<0.025
21.5	D	144	−110 ± 3	−28 ± 7	<0.0005
21.5	E	238	−211 ± 1	−28 ± 16	<0.0005
21.5	F	406	−333 ± 26	−31 ± 31	<0.0005

* Student's "t" test; N.S. = Not Significant, $p > 0.05$

with human blood. However, the authors believe that any error introduced by the use of bovine blood would be minimal and would not account for the magnitude of error reported here for the IL 513.

Additionally, subsequent studies at Shadyside Hospital in Pittsburgh, Pennsylvania[10] using human blood have confirmed the trends reported in this paper. A further study on a Corning analyzer at the Brompton Hospital in England also showed results similar to those documented here.[11]

An explanation for the large errors reported with traditional blood gas analysis of hypothermic blood appears to be extremely complex. As Tables 3 and 4 clearly show, however, under the combined conditions of hypothermia and arterial range pO_2, the IL 513 analyzer reported values at 37°C which were *lower* than the known true pO_2 levels at hypothermia. Therefore, a major portion of the IL 513 data error reported here is the result of the blood gas machine measurement system itself. These machine-related errors may also be compounded by the use of temperature correction nomograms which are based on blood gas measurements that in turn may have been erroneous. Work in this area is continuing and will be reported at a later time.

Acknowledgements

The authors wish to acknowledge the technical assistance of Frederick Piazza and Sandra Pfefferkorn in the execution of this study.

Appendix

Formulae used in this study included the following:

(A) Hill equation;

$$SO_2 = \frac{(P/P_{50})^n}{1 + (P/P_{50})^n}$$

where P = measured pO_2 at 37°C and P_{50} is the pO_2 at an SO_2 of 50%. $P_{50} = 31$;[12] $n = 2.75$.[13]

(B) The P_{50} was adjusted for the Bohr effect by the relationship;[12]

$$\Delta \log P_{50} = (-0.49)\ \Delta\ pH$$

(C) The Kelman-Nunn equations are;[4]

$$pH_{corr} = pH_{37°C} - 0.015\ (T - 37)$$
$$pCO_{2\ corr} = pCO_{2\ 37°C} \times 10^{0.019(T\ -\ 37)}$$
$$pO_{2\ corr} = pO_{2\ 37°C} \times 10^{A(T\ -\ 37)}$$

where:

$$A = 0.0052 + 0.027\ (1 - 10^{-0.13(100\ -\ SO_2)})$$

(D) Student's "t" test is calculated for this study using the following formula modified to compare absolute values of deviation from a known true value;

$$t = \frac{|\bar{x}_1| - |\bar{x}_2|}{\sqrt{\frac{(s_1)^2}{n_1} + \frac{(s_2)^2}{n_2}}}$$

where $\bar{x}$ is the mean, s is the standard deviation, and n is the number of samples.

(E) The formula used to calculate true pO_2 from known gas oxygen concentrations is;

True pO_2 = Percent $O_2 \div 100 \times$ (Barometric Pressure $- pH_2O$)

References

1. Kuntz, R. A. and Maurer, W. G.: An Examination of Cavitation as It Relates to the Extracorporeal Arterial Infusion Model. J.E.C.T. 14(2), pp. 345–354, 1982.
2. Pearson, D.: Gaseous Emboli During Open Heart Surgery: Detection and Prevention, Presented 4th Annual Seminar on Cardiovascular Perfusion. AACP, San Diego, California, January 1983.
3. Stanley, T. H. and Isern-Amaral, J.: Periodic Analysis of Mixed Venous Oxygen Tension to Monitor the Adequacy of Perfusion During and After Cardiopulmonary Bypass. Canad. Anaesth. Soc. J. 21(5), pp. 454–460, 1974.
4. Kelman, G. R. and Nunn, J. F.: Nomograms for Correction of Blood pO_2, pCO_2, pH and Base Excess for Time and Temperature. J. Appl. Physiol. 21, pp. 1484–1490, 1966.
5. Kelman, G. R.: A Theoretical Study of Factors Affecting the In-vitro pO_2 Temperature Coefficient. Resp. Physiol. 4, pp. 301–308, 1968.
6. Severinghaus, J. W.: Blood Gas Calculator. J. Appl. Physiol. 21, pp. 1108–1116, 1966.
7. Parker, D., Delpy, D. T. and Halsall, D. N.: A New Approach to Inline Gas Monitoring: Development of an Oxygen Sensor. Med. & Biol. Eng. & Comp. 21, pp. 134–137, 1983.
8. Handbook of Chemistry and Physics, R. C. Weast, Ed., Chemical Rubber Co., p. D159, 1974.
9. Respiration and Circulation, P. L. Altman and D. S. Dittmer, Eds., Fed. Am. Soc. Exp. Biol. Bethesda, MD, p. 179, 1971.
10. Personal Communication, S. Stewart and D. Fallen.
11. Personal Communication, N. Walton.
12. Bartels, H. and H. Harms, Pfleugers Arch. Gesamte Physiol. 268, p. 334, 1959.
13. Riggs, A., J. Gen. Physiol., 43, p. 737, 1960.