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Converting venous acid-base and oxygen status to arterial in patients with lung disease

Stephen E. Rees[1], Anita Hansen[2], Marianne Toftegaard[3,1], Jan Pedersen[4], Søren Risom Kristiensen[4], Henrik Harving[2]

1 -Center for Model Based Medical Decision Support Systems, Department of Health Science and Technology, Aalborg University, Denmark.

2 - Department of Respiratory Diseases, Aalborg Hospital, Aarhus University Hospital, Denmark.

3 - Department of Anaesthesia and Intensive Care, Aalborg Hospital, Aarhus University Hospital, Denmark

4 – Department of Clinical Biochemistry, Centre of Cardiovascular research, Aalborg Hospital, Aarhus University Hospital, Denmark

Corresponding author:
Stephen Rees
Center for Model Based Medical Decision Support,
Aalborg University
DK-9220 Aalborg
Denmark
Email: sr@hst.aau.dk
Tel: +45 99408793
Fax: +45 98154008

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Abstract

Objective **–** To evaluate a method for calculating arterial values of pH, PCO_2 and PO_2 from peripheral venous values.

Methods – 40 patients were studied. Arterial and peripheral venous blood were sampled at a department of respiratory diseases. Arterial values were calculated from venous and measured and calculated values of arterial pH, PCO_2 and PO_2 compared.

Results – Measured and calculated values of pH and PCO_2 correlated well (pH $r^2 = 0.95$, PCO_2 $r^2 = 0.98$) with the difference between them having a very small bias and standard deviation (pH -0.001 ± 0.013, PCO_2 -0.09 ± 0.28 kPa) within those considered acceptable for laboratory equipment and clinical practice. All but 4 patients had $SpO_2 \leq 96\%$, and for these measured and calculated PO_2 correlated well ($r^2 = 0.86$) with a difference such that the bias and standard deviation suggested that calculated PO_2 may be clinically useful (PO_2 0.11 ± 0.53 kPa).

Conclusion – This paper evaluates a method for calculating arterial pH, PCO_2 and PO_2 from venous blood. It has been shown that arterial pH and PCO_2 can be calculated precisely, and that PO_2 can be calculated with reasonable precision in the vast majority of patients. This method might be useful in reducing the need for painful arterial punctures.

Introduction

Arterial blood gas analysis is an important tool in assessing patient status. For patients residing in intensive care units (ICU), with indwelling arterial catheters the sampling of arterial blood is routine. In other departments blood is sampled via an arterial puncture with an increased risk of pain and hematoma [1,2,3].

Recently, studies have shown that values of acid-base status measured in peripheral venous blood correlate well with those measured in arterial blood, at least for values of pH, HCO_3 and PCO_2 [4,5,6]. Large numbers of peripheral venous samples are taken easily and safely in medical departments, and these results therefore imply a role for peripheral venous blood in the monitoring of acid-base status. In addition, a method has been recently proposed [7] which enables calculation of values of arterial acid-base and oxygenation status (i.e. pH, PCO_2 and PO_2) from measurements performed in the peripheral venous blood. This method has been shown [8] to have good accuracy and precision when calculating arterial pH (0.002 ± 0.027, bias ± 2SD) or arterial PCO_2 (-0.04 ± 0.52 kPa, bias ± 2SD). For calculation of PO_2, precision was dependent on the oxygenation level such that for peripheral oxygen saturation (SpO_2) values greater than 96% the method was not considered useful for calculating PO_2, and for $SpO_2 \leq 96$ % the accuracy and precision of calculated PO_2 was 0.21 ± 1.85 kPa (bias ± 2SD) [8].

The previous evaluation of this method [8] was in patients admitted to the wards of either ICUs or a department of pulmonary medicine, and these patients studied under experimental conditions. These experimental conditions differ from routine clinical practice in medical departments in several important respects. The majority of ICU patients have arterial catheters and are relatively immobile, making blood sampling simpler and less prone to error. Medical patients present as both admitted and outpatients with admitted patients tending to have a poorer condition than outpatients potentially giving larger arterial –venous differences in blood gas values and hence a greater signal

to noise ratio for application of the conversion method. In experimental conditions peripheral venous blood sampling was performed using a needle attached directly to a syringe, rather than the butterfly sampling needle and tube often used to sample venous blood in medical departments. In addition, the vast majority of patients included in the previous study, i.e. ICU patients, required supplementary oxygen as part of their clinical management, meaning that for the majority of patients SpO_2 was greater than 96 %.

The purpose of this study was to evaluate the method for conversion of peripheral venous values of acid-base and oxygenation status to arterial values in patients presenting at the department of pulmonary medicine, using sampling technology and blood samples routinely collected as part of clinical care.

Materials and Methods

Patients

Arterial and peripheral venous blood was sampled from 40 patients (22 admitted and 18 outpatients) at the Department of Respiratory Diseases at Aalborg Hospital, Denmark, median age 68 years (range 35–93 years), 22 females. Patients were all previously diagnosed with chronic lung disease resulting in hypercapnia and/or hypoxia, and were either acutely admitted or visiting the Department for their bi-annual clinical assessment. The arterial acid-base and oxygenation status of the patients is summarized in table 1.

Age	pH	PCO_2 (kPa)	PO_2 (kPa)
68(35 – 93)	7.418 (7.237 – 7.508)	6.26 (3.92 – 11.2)	8.97 (6.11 – 15.70)

Tabel 1 : Values of pH, PCO_2 and PO_2 measured in arterial blood. Values are described as median (range).

Data acquisition.

All patients had arterial blood sampled as a routine part of clinical care. These samples were drawn via an arterial puncture into a syringe suitable for blood gas analysis (PICO70; Radiometer AS, Brønshoj, Denamark), and processed immediately to obtain values of arterial acid-base, oxygen, metabolism and electrolyte status (ABL 800, Radiometer AS, Brønshoj, Denamark).

All patients had venous blood sampled as a routine part of clinical care. A butterfly needle (Multifly; Sarsted AG & Co., Nübrecht, Germany), was inserted into a vein at the elbow. This butterfly includes an 20 cm long and 0.8 mm diameter tube connected to a sealed sample adapter. Blood was sampled into a standard venous blood collection tube (S-Monovette; Sarsted AG & Co., Nübrecht, Germany) using the vacuum principle, and into a syringe suitable for blood gas analysis (PICO50; Radiometer AS, Brønshøj, Denmark), fitted with an adapter (Membran adapter; Sarsted AG & Co., Nübrecht, Germany) to enable sampling from the butterfly's sample adapter. Blood was analysed immediately for values of acid-base, oxygenation, metabolism and electrolyte status. Venous and arterial blood samples were taken within a ten minute period as part of normal clinical practice. In addition, the measurement of peripheral oxygen saturation (SpO_2) was obtained from a pulse oximeter (Nonin Onyx 9500, Nonin Medical, Minneapolis, USA) placed on an index finger. The data from 2 patients was excluded, due to sample error, and the pulse oximeter running out of battery during blood sampling.

Blood sampling was performed in this study as for routine clinical practice, and following contact to the local ethics committee the investigators were informed that application for ethical approval was not required.

Venous to Arterial Conversion Method

A brief description of the venous to arterial conversion method, summarising [7], follows. Figure 1 illustrates the method for calculating arterial acid-base and oxygenation status from measurements in the venous blood and pulse oximetry, described in detail previously [7]. The method calculates arterial values using mathematical models [9] to simulate the transport of venous blood back through the tissues until simulated arterial oxygenation matches that measured by pulse oxymetry. In this simulation oxygen is added to and carbon dioxide removed from venous blood using a constant value of the respiratory quotient (RQ) selected here to be 0.82 [7] and no strong acid is removed from the blood on its simulated passage from the veins to the arteries, i.e. $\Delta BE_{av} = 0$ mmol/l.

Calculated arterial values of pH, PCO_2 and PO_2 are compared with the simultaneously measured arterial values using Bland Altman plots and scatter plots of measured versus calculated. Values of bias and standard deviation between measured and calculated arterial values are reported, along with values of correlation coefficients (r^2) and parameter values for regression lines.

Results

Figure 2 compares measured arterial values (a) and calculated arterial values (ca) using the venous to arterial conversion method.

			SpO2 ≤ 96%	SpO2 ≤ 98%
	pH	PCO_2 (kPa)	PO_2 (kPa)	PO_2 (kPa)
Arterial – calculated arterial values (n=38)	-0.001 ± 0.026	-0.09 ± 0.55	0.11 ± 1.05 (n=34)	-0.13 ± 1.79 (n=38)
Laboratory acceptable performance criteria (acceptable range)	± 0.04	± 0.67[a]	± 0.6[b]	± 0.6[b]

Tabel 2: Bias ± 2SD for the difference between measured and calculated values of arterial blood, compared to laboratory performance guidelines. It is assumed that these guidelines are comparable to a 95% confidence interval given by 2 SD. [a]Original value given as ± 5 mmHg. [b]Original value given as ± 3 SD of measurement equipment error, where one SD is assumed to be 0.2 kPa according to Radiometer [10].

As illustrated in the Bland-Altman plots of figure 2 and in table 2, calculated values of arterial pH and PCO_2 have very small bias and standard deviation, with these errors being within those considered acceptable for the performance of laboratory equipment (table 2) and well within the limits of error acceptable in clinical practice [11,12]. Values of pH and PCO_2 measured (a) or calculated (ca) correlate extremely well (r^2 for pH = 0.95, r^2 for PCO_2 = 0.98) with regression lines comparing well to the lines of identity. As illustrated in figure 2, the error in calculated PO_2 values is greater at higher levels of PO_2. Table 2 reports values of standard deviation for PO_2 values corresponding to $SpO_2 \leq 96\%$ (34 patients) and $SpO_2 \leq 98\%$ (38 patients. These errors are outside those considered acceptable for the performance of laboratory equipment but may be useful in clinical practice. When excluding data points with $SpO_2 \geq 97\%$ (circles on figure 2), values of measured and calculated PO_2 correlate well ($r^2 = 0.86$).

Discussion

Arterial blood gas analysis is an important tool in assessing patient status, but outside the ICU blood sampling is typically performed from an arterial puncture and is associated with pain and increased risk of haematoma.

This study is a further evaluation of a method [7] for calculating arterial acid-base and oxygenation status from measurement taken in peripheral venous blood. Unlike the previous study [8] this study has evaluated use of the method using routinely available blood samples in a patient group where arterial catheters are uncommon, i.e patients presenting at a department of pulmonary medicine.

This study has illustrated the potential for application of the method as part of the routine management of patients presenting at the department of pulmonary medicine. Calculation of arterial values could be performed with a similar precision to that for patients studied previously, despite the potential for increased error due to the logistics of blood sampling in routine clinical practice, and the use of butterfly type needles and sample tubing. The accuracy and precision of calculated values of arterial pH and PCO_2 are almost identical to that reported previously [8], and the precision within laboratory acceptable performance criteria [12]. For SpO_2 values less than or equal to 96 % the method can calculate PO_2 with an average SD of 0.53kPa, which may be useful in clinical practice. This SD is lower than that seen previously [8] where SD was 0.93 kPa. This is due to the lower values of arterial oxygenation seen in the patients presenting here, with about 50% of patients having $SpO_2 \leq 92$ %. For SpO_2 values greater than 96% it has previously been argued that the calculation of PO_2 values becomes imprecise due to the flat shape of the oxygen dissociation curve at high levels of oxygenation. Only four of these patients presented with $SpO_2 \geq 97\%$, as illustrated in figure 2. The small number of patients with high levels of oxygen indicate that the method might be applicable for calculation of arterial pH, PCO_2 and PO_2 in the vast majority of patients visiting pulmonary medical departments.

To understand whether the results presented here would be reflected in a broader population it is necessary to consider the sensitivity of calculations to measurement error and to the assumptions contained in the method. The method does not include calculation for the effects of varying blood temperature. All blood samples are measured at 37^{o}C and all calculations performed at this temperature. Any necessary corrections for temperature can be performed using existing algorithms present in commercial blood gas analysers. It has previously been shown [7] that calculations performed using the method are insensitive to errors in measurement of venous blood gases, being linear over a range of input conditions and of an order of magnitude similar to the direct measurement of arterial blood. This analysis of variation to venous measurements implicitly includes any variation in parameters describing the shift of the oxygen dissociation curve, e.g. P_{50} or 2,3-DPG concentration. Similar analysis has also been performed for variation in the values of RQ and ΔBE_{av} [7]. Variation in ΔBE_{av} of 0.2 mmol/l gives rise to errors in calculated pH, PCO_2 and PO_2 of 0.006, 0.08 kPa and 0.07 kPa respectively. These errors are small, but it is clear that errors in ΔBE_{av} amouting to several milimoles would be significant. The results presented here, and previously [8] are inconsistent with large changes in BE across the peripheral sampling site even during sepsis. It is possible however, that some caution is warranted in situations of acute changes in peripheral perfusion or acid-base status such as hypovolaemic shock. Previous analysis of the sensitivity to variation in RQ, has shown that literature reported values of RQ variation equal to 0.08 [13] gives rise to small errors in calculated values of pH, PCO_2 and PO_2 equal to 0.005, 0.10 kPa and 0.06 kPa. The largest source of measurement error is due to the pulse oximetry measurement of SpO_2. Figure 3 illustrates the sensitivity of calculations of arterial pH, PCO_2 and PO_2 to error in SpO_2. Each of the subplots represent simulation of one of these variables when a standard venous blood sample (pH = 7.370, PCO_2 = 6.1 kPa, PO_2 = 5.5 kPa, SO_2 = 75 %, Hb = 9.3 mmol/l, FMetHb = 0 mmol/l, FCOHb = 0 mmol/l) is used to calculate arterial values using a SpO_2 value ranging from 80 to 96%. Solid lines represent conversion at the mean SpO_2 value, and dashed

at SpO_2 ± 4% repectively, consistent with 2 times the reported standard deviation for measurement of SpO_2 [14, 15]. Errors in SpO_2 of ± 4% give rise to small variation in calculated arterial pH with a SD = ±0.0025 (figure 3A), which is rather constant over the range of SpO_2 values and has a maximum of 0.005. A similar picture can be seen in the error in calculation of arterial PCO_2 (figure 3B). Errors in SpO_2 of ± 4% give rise to a small variation in calculated arterial PCO_2 with a SD = 0.06 kPa which is again rather constant over SpO_2 values and has a maximum of SD= 0.12 kPa. The errors in calculation of arterial PO_2 are illustrated in figure 3C and 3D. These are a little more complex to interpret that for pH and PCO_2, but some important conclusions can be drawn, as follows. From a clinical perspective, a pulse oximeter that reads too low, as represented by the bottom dashed line on figure 3C, results in an underestimate of arterial PO_2 and potentially more aggressive treatment of the patient with supplementary oxygen, fluids or other intervention. These interventions carry their own risk, but the risk of hypoxaemia associated with a pulse oximeter that reads too high is not present. For a pulse oximeter that overestimates oxygen saturation, the maximal error exists when the true value is 96% and the pulse oximeter reads 100%. As shown on figure 3C the error at this level is large, but clinically unimportant as both the true and overestimated PO_2 levels are normal or above. In neither case would the patient require oxygen therapy. The effects of error in SpO_2 on the important clinical assessment, i.e. does the patient have a low arterial PO_2 can be seen in figure 3,D which is a zoom in on figure 3,C. If we consider three situations where a pulse oximeter over-estimated SpO_2, labelled ‘a’, ‘b’, and ‘c’ on figure 3D, we can conclude the following. From the difference in calculated and ‘true’ arterial PO_2 indicated by label ‘a’ on figure 3D we can see that if the calculated PO_2 is at or above 12.5 kPa, then the true value is above 9 kPa. From the point labeled ‘b’ we can see that if the calculated PO_2 is at or above 10 kPa, then the true value is above 8 kPa. From the point labelled ‘c’ we can see that if the calculated PO_2 is at or above 8 kPa, then the true value is above 7 kPa. This analysis shows that errors in SpO_2 are unimportant to the calculation of pHa and PCO_2. It also shows the potential of calculated values of PO_2 to identify patients in need of supplementary oxygen, or where an arterial

sample might be most beneficial. The improving precision of calculated values of PO_2 at lower oxygenation shows that the error in SpO_2 is least important in the most critical clinical situations. This is seen in both this sensitivity analysis, and from the results of this study (figure 2), where the errors in calculated PO_2 illustrated in the Bland-Altman plot are reduced with lower oxygen levels.

The venous - arterial calculation method assumes that the peripheral venous sampling site is from a limb with a clearly recognisable pulse and a normal capillary response, such that the anaerobic metabolism at the tissue site is negligible The present study used routinely available blood samples and as such no attempt was made to ensure that this was the case, above that of normal clinical practice. It is therefore interesting then that the results are in line with previous, experimentally controlled conditions.

This paper has evaluated a method for calculating arterial values of pH, PCO_2 and PO_2 from measurements in peripheral venous blood and a pulse oximeter, for patients presenting at a department of pulmonary medicine. It has been shown that values of arterial pH and PCO_2 can be calculated precisely from peripheral venous blood and that values of arterial PO_2 can be calculated with precision which may be clinically useful, at least when $SpO_2 \leq 96\%$. This study has shown the potential for use of the method in departments of pulmonary medicine where it might replace routinely taken arterial samples eliminating the need for painful arterial punctures.

Conflict of interest

SER and MT authors are board members and shareholders of OBI APS. OBI APS is currently applying for a patent on the method presented in this manuscript.

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Figure legends

Fig.1 - Calculation of arterial blood acid-base status from venous blood and arterial oxygen saturation measured using a pulse oximeter. A-E represent the mathematical steps included in the method [7]. (Reproduced with permission of Elsevier).

Fig.2 – Bland-Altman and scatter plots comparing measured arterial (a) and calculated arterial (ca) values of pH, PCO_2 and PO_2 in peripheral venous blood. On Bland Altman plots, bias (mean difference) and 95 % limits of agreement (± 2SD) are shown for pH and PCO_2., with only the line representing bias drawn for PO_2. For scatter plots solid lines represent linear regression between measured and calculated values, and dashed lines the associated line of identity. Correlation coefficients (r^2) and regression equations are included for each of the comparisons. In the plot of PO_2, circles represent data with $SpO_2 \geq 97\%$, these data are not included in calculation of the bias or regression line for PO_2.

Figure 3 – Simulations performed using the method to illustrate the sensitivity of calculate values of arterial pH (A), PCO_2 (B) and PO_2 (C,D) to variation in SpO_2, over a range of values of SpO_2 (80-96 %). Plots are drawn for calculation of pHca, PCO_2ca and PO_2ca for mean SpO_2 (solid line) and mean SpO_2 ± 2SD, i.e. ± 4% (dashed lines).

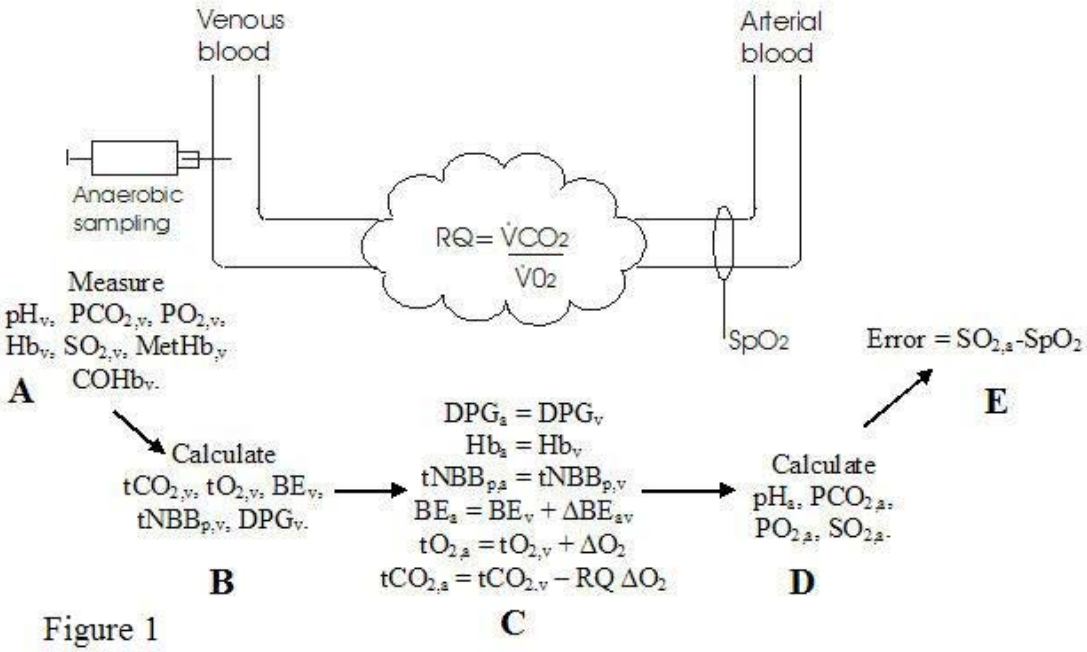
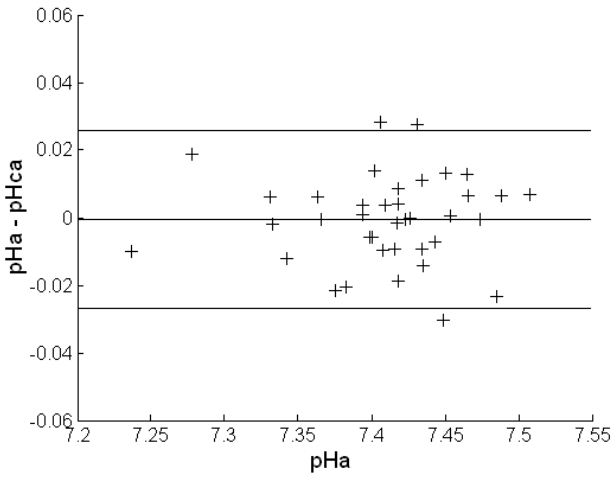
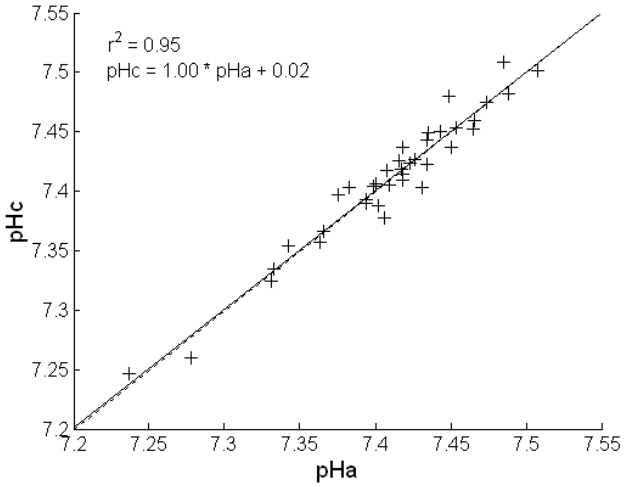
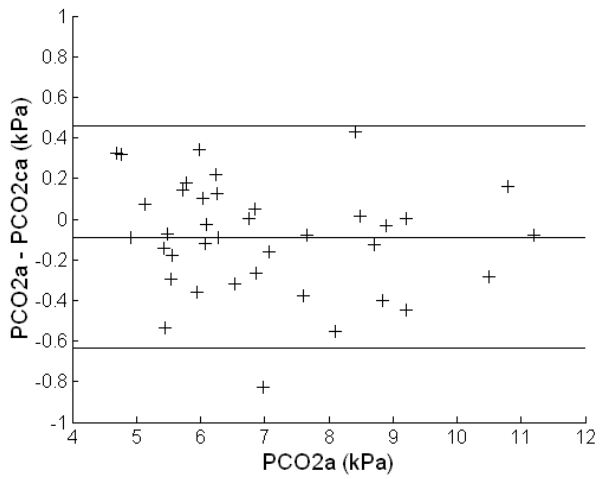

Venous blood
Arterial blood
Anaerobic sampling
RQ= V̇CO2 / V̇O2
SpO2
Measure
pHv, PCO2,v, PO2,v,
Hbv, SO2,v, MetHb,v
COHbv.
A
Calculate
tCO2,v, tO2,v, BEv,
tNBBp,v, DPGv.
B
DPGa = DPGv
Hba = Hbv
tNBBp,a = tNBBp,v
BEa = BEv + ΔBEav
tO2,a = tO2,v + ΔO2
tCO2,a = tCO2,v – RQ ΔO2
C
Calculate
pHa, PCO2,a,
PO2,a, SO2,a.
D
Error = SO2,a-SpO2
E

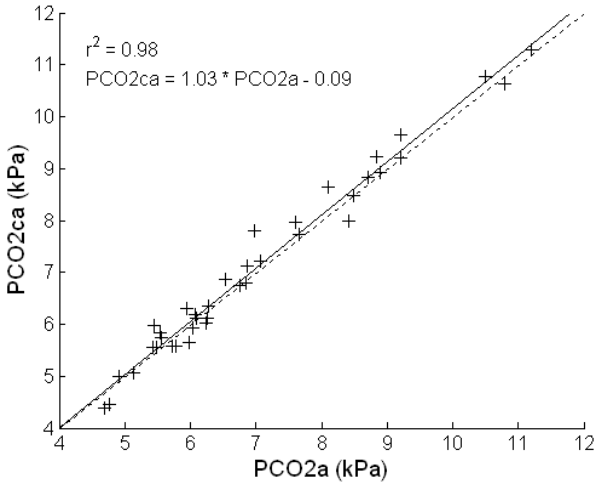
Figure 1

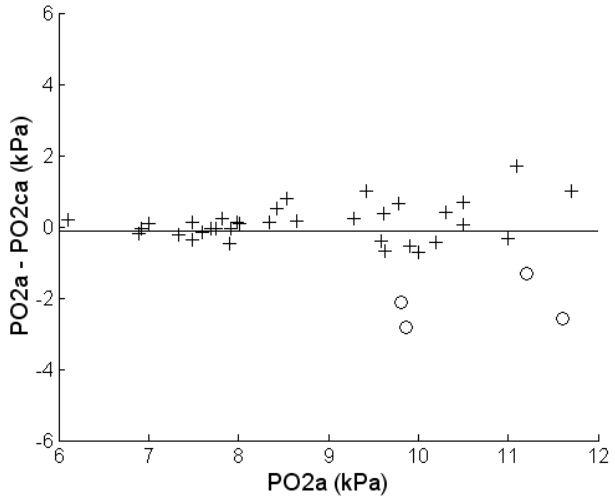
Figure 2


pHa - pHca
pHa


r2 = 0.95
pHc = 1.00 * pHa + 0.02
pHc
pHa


PCO2a - PCO2ca (kPa)
PCO2a (kPa)


r2 = 0.98
PCO2ca = 1.03 * PCO2a - 0.09
PCO2ca (kPa)
PCO2a (kPa)


PO2a - PO2ca (kPa)
PO2a (kPa)

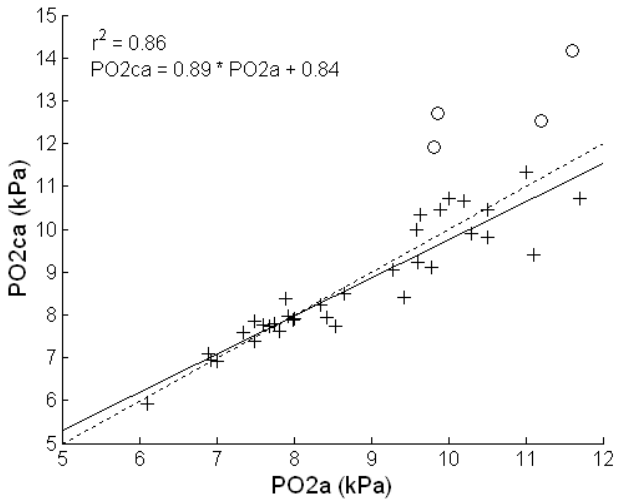
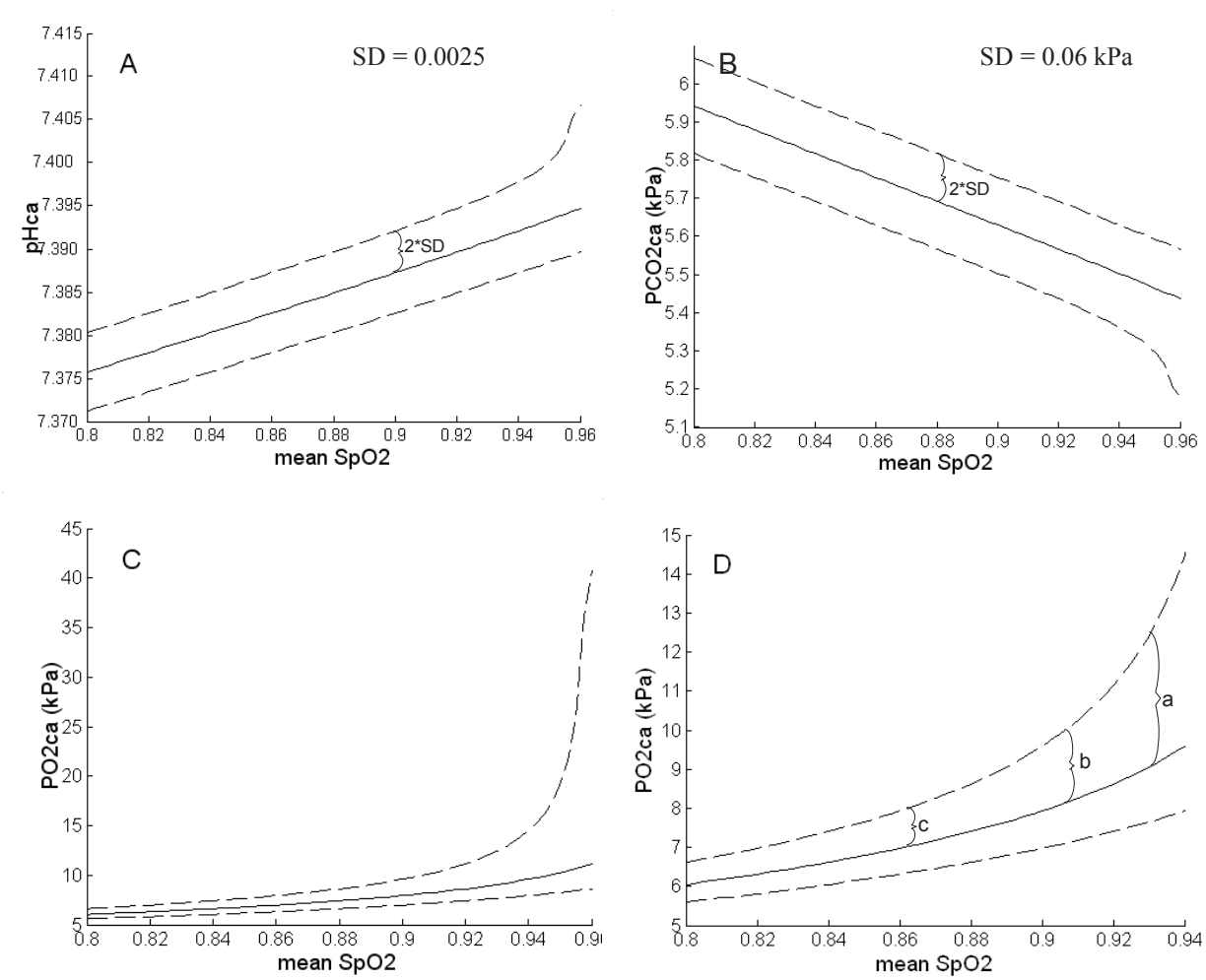

r2 = 0.86
PO2ca = 0.89 * PO2a + 0.84
PO2ca (kPa)
PO2a (kPa)

Figure 3


A
SD = 0.0025
pHca
2*SD
mean SpO2
B
SD = 0.06 kPa
PCO2ca (kPa)
2*SD
mean SpO2
C
PO2ca (kPa)
mean SpO2
D
PO2ca (kPa)
a
b
c
mean SpO2