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## Agreement between arterial and non-arterialised fingertip capillary blood gas and acid-base values

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### ABSTRACT

**Background:** Arterial puncture is considered the gold standard for obtaining blood gas and acid-base values and facilitates the assessment of acutely and critically ill patients, as well as control of patients in long-term oxygen therapy (LTOT). Substitutional capillary sampling has been proposed, as researchers cite lower complication rates, physician independence, lower degree of invasiveness and higher degree of patient comfort. An arterialised earlobe is considered the method of choice to obtain capillary blood sampling, but in an acute setting, the need for vasodilating pastes may be time-consuming and impractical.

The aim of this study is to examine whether accurate blood gas and acid-base measurements can be obtained using non-arterialised fingertip blood.

**Materials and methods:** Consecutive arterial punctures and non-arterialised capillary blood samples were drawn from 62 patients with stable-phase chronic obstructive pulmonary disease (COPD), and subsequently analysed. Agreement between arterial and capillary blood gas values was compared using the method recommended by Bland and Altman.

**Results:** Results show that limits of agreement (LoA) regarding PO<sub>2</sub> (LoA: -1.27–4.45 kPa); Base Excess (LoA: -1.35–0.55); lactate (LoA: -0.77–0.20 mmol/l) and SO<sub>2</sub> (LoA: -0.02–0.06) are wider than what would be applicable for clinical use. However, clinically acceptable LoA were obtained regarding PCO<sub>2</sub> (LoA: -0.64–0.38 kPa); pH (LoA: -0.02–0.03), and HCO<sub>3</sub><sup>-</sup> (LoA: -1.06–0.55 mmol/l).

**Conclusion:** LoA for PCO<sub>2</sub>, pH and HCO<sub>3</sub><sup>-</sup> indicate that measurement of these parameters in non-arterialised capillary blood may be useful in clinical practice/an acute setting.

What this paper adds:

- Capillary blood sampling provides a fast, non-invasive means of obtaining blood gas-values;
- Traditionally, capillary blood sampling for blood gas analysis is obtained from the earlobe using arterialisation;
- The present study presents accurate measurements of PCO<sub>2</sub>, HCO<sub>3</sub><sup>-</sup> and pH using non-arterialised fingertip capillary blood;
- The present study is the first to show this in a population of stable-phase COPD patients.

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Arterial blood gas analysis; capillary blood gas analysis; carbon dioxide; oxygen; oximetry; arterial puncture; arterial blood sample; capillary blood sample; arterialised blood sample

## Background

Arterial blood gas and acid-base analysis is a quick and useful tool in the assessment of acutely and critically ill patients, as well as the management of patients with chronic pulmonary diseases. Its application spans nearly every field of medicine and surgery and guides the assessment and management of e.g. respiratory failure, circulatory failure and endocrine disturbances.

Arterial puncture remains the gold standard for obtaining arterial blood gas and acid-base values, but requires trained personnel and is associated with patient discomfort [1,2] and a risk of potential complications such as hematoma and pseudoaneurysm formation [3].

The use of capillary blood sampling as a substitute for direct arterial puncture has been investigated, with researchers citing lower complication rates, physician independence, lower degree of invasiveness and higher degree of patient comfort as arguments for the use of capillary blood sampling [1,2,4–10]. Generally, studies have found that partial pressure of oxygen (PO<sub>2</sub>) and oxygen saturation (SO<sub>2</sub>) agree poorly between arterial and capillary blood samples [2,6,7,11–14], while partial pressure of carbon dioxide (PCO<sub>2</sub>) and pH exhibit acceptable agreement [2,6–8,11–15]. Few studies [5–7,11,16] have investigated the agreement regarding bicarbonate concentration (HCO<sub>3</sub><sup>-</sup>), BE and lactate, generally finding

poor agreement between the two sampling methods regarding these parameters.

The most widely accepted optimal means of obtaining accurate capillary blood gas values involve using the ear-lobe, with prior arterialisation using a vasodilating paste [9,10], with some studies using the fingertip as sampling site [5,11,16].

However, in an acute setting, the use of vasodilating pastes may be time-consuming and delay diagnosis and treatment.

Considering the findings of existing literature, and the fact that capillary blood is a mixture of arterial and venous blood, we hypothesise that adequate agreement between capillary and arterial samples can be obtained in all parameters, except partial pressure of oxygen (PO<sub>2</sub>) and oxygen saturation (SO<sub>2</sub>).

Thus, the purpose of the present study was to examine the agreement between arterial and non-arterialised fingertip blood, regarding blood gas and acid-base parameters.

## Materials and methods

### Sample population

From the outpatient clinic at Aalborg University Hospital, Aalborg, Denmark, 62 patients suffering from stable-phase chronic obstructive lung disease (COPD) treated with LTOT, were recruited for the study.

The inclusion criteria were:

- (1) Patient prescribed a routine arterial blood gas analysis in connection with the outpatient visit;
- (2) Age  $\geq 18$  years;
- (3) Ability to understand and accept written and oral information pertaining to the study.

To achieve a power value of 90% at a significance level of 5% and with a correlation coefficient of  $\pm 0.6$ , a sample size of 25 participants was intended; 62 were included to increase method reliability.

Prior to data collection, written consent was given by each patient and the study protocol was submitted to, and approved by, the local ethics committee (approval number RN20100103).

### Procedure

Data collection took place between May and November 2011. During the patients' visit to the clinic, an arterial blood sample was drawn via the radial artery, using a heparinised PICO 70 syringe (Radiometer, Copenhagen, Denmark). Within minutes, a capillary blood sample was drawn from a lateral aspect of the third, fourth or fifth finger using a 125  $\mu$ l capillary tube

(Radiometer, Copenhagen, Denmark). An Accu-Chek lancet (Roche, Basel, Switzerland) was used to pierce the skin.

Great care was taken to avoid exposing the blood droplet to air, and the arterial samples were continuously turned so as to avoid clotting.

The blood samples were analysed for the following parameters: pH, PCO<sub>2</sub>, PO<sub>2</sub>, SO<sub>2</sub>, BE, HCO<sub>3</sub><sup>-</sup>, Hgb, K<sup>+</sup> and Lactate. Reference intervals for these variables are presented in Table 1.

Blood sampling and analysis were performed by two certified technicians.

The blood gas analyser was calibrated automatically daily and controlled manually every 14 days.

The results of the paired samples were printed out and entered into the data entry application EpiData 3.1 (EpiData association, Odense, Denmark, <http://www.epidata.dk>). Data were entered by two separate individuals, and the results were compared.

### Statistical analysis

Limits of Agreement (LoA) between the two sampling methods were analysed using the method recommended by Bland and Altman [18] and Bland-Altman plots were constructed using SPSS 24 (IBM corp., Armonk, NY, USA). Prior to this, the mean difference (MD) between sampling methods had been calculated by means of a paired sampled t-test, which also yielded the standard deviation (SD). Upper and lower LoA were calculated using the formula  $LoA = MD \pm (SD \cdot 1.96)$ .

MD and LoA for Hgb were calculated as a control for sample dilution.

No indeterminate or missing values were found.

## Results

Patient age ranged from 34 to 89 years (median 73.5 years). Thirty-seven patients (59.7%) were female. Forty-two patients (67.7%) received long-term oxygen therapy (0.5–5 litres/min; mean 1.38; median 1.5).

The time from arterial sampling to capillary sampling was 2–13 min, with a median of 3 min.

**Table 1.** Reference intervals for the examined variables.

	Reference value
PO <sub>2</sub>	9.6–13.7 kPa
PCO <sub>2</sub>	4.5–6 kPa
pH	7.37–7.45
BE	–2–2
SO <sub>2</sub>	0.92–0.99 (92–99%)
HCO <sub>3</sub> <sup>-</sup>	Q: 21.8–26.2 mmol/l; σ: 22.5–26.9 mmol/l
Lactate	0.36–0.75 (mmol/l) [17] 0.5–2.5 (mmol/l) [21]

**Table 2.** Means, standard deviations (SD) and ranges for the arterial and capillary blood gasses.

	Arterial blood			Capillary blood		
	Mean	SD	Range	Mean	SD	Range
PO <sub>2</sub> (kPa)	9.75	2.20	5.03–16.90	8.16	1.22	4.95–10.60
PCO <sub>2</sub> (kPa)	6.62	1.51	4.19–11.40	6.76	1.53	4.18–11.80
pH	7.41	0.04	7.32–7.48	7.41	0.04	7.30–7.48
BE	6.07	4.37	–4.00–16.20	6.47	4.60	–4.00–17.40
SO <sub>2</sub>	0.94	0.05	0.70–1.00	0.93	0.04	0.72–0.99
HCO <sub>3</sub> <sup>–</sup> (mmol/l)	29.32	3.60	21.20–38.30	29.58	3.80	21.20–39.50
Lactate (mmol/l)	1.24	0.73	0.50–4.50	1.53	0.74	0.70–5.20

Blood analysis was performed within a median of 12 min after blood sampling, using an ABL 800 Flex blood gas analyser (Radiometer, Copenhagen, Denmark). For the capillary samples, time from sampling to analysis was 3–9 min. For the arterial samples, time from sampling to analysis ranged from 8 to 18 min; in only 2 instances did this time exceed 15 min. These specific samples had PO<sub>2</sub> values of 12.4 kPa and 8.62 kPa, respectively, which is well within the range of the dataset in general, as seen in Table 2.

Arterial and capillary means and ranges are displayed in Table 2, and the comparative data used for the Bland-Altman plots are shown in Table 3. The Bland-Altman plots are visualised in Figure 1(a–g).

The capillary blood sample had a tendency to underestimate PO<sub>2</sub>, especially at higher PO<sub>2</sub> values. Furthermore, there was a poor agreement between arterial and capillary PO<sub>2</sub>, with a high MD and quite wide LoA (Figure 1(a)). Conversely, the capillary PCO<sub>2</sub> had a tendency to slightly overestimate PCO<sub>2</sub> but displayed better agreement with a low MD and narrow LoA (Figure 1(b)).

The results for pH displayed excellent agreement with an MD close to zero and narrow LoA (Figure 1(c)).

**Table 3.** Mean differences (MD) including p-values (*p*), standard deviations (SD) and Limits of Agreement (Upper Limit = MD+1.96SD; Lower Limit = MD-1.96SD) for arterial and capillary blood gasses.

	MD	SD	Upper limit	Lower limit
PO <sub>2</sub> (kPa)	1.59 ( <i>p</i> = 0.00)	1.46	4.45	–1.27
PCO <sub>2</sub> (kPa)	–0.13 ( <i>p</i> = 0.00)	0.26	0.38	–0.64
pH	0.00 ( <i>p</i> = 0.21)	0.01	0.03	–0.02
BE	–0.40 ( <i>p</i> = 0.00)	0.48	0.55	–1.35
SO <sub>2</sub>	0.02 ( <i>p</i> = 0.00)	0.02	0.06	–0.02
HCO <sub>3</sub> <sup>–</sup> (mmol/l)	–0.25 ( <i>p</i> = 0.00)	0.41	0.55	–1.06
Lactate (mmol/l)	–0.28 ( <i>p</i> = 0.00)	0.25	0.20	–0.77

Statistical analysis of Hgb concentrations showed an MD of –0.23 mmol/l and LoA of –0.77–0.31 mmol/l (*p* = 0.00, *SD* = 0.28). Bland-Altman plots of this result will not be presented.

As for BE and HCO<sub>3</sub><sup>–</sup>, capillary blood samples tended to overestimate the values (Figure 1(d,f)), while the capillary samples underestimated SO<sub>2</sub> measurements (Figure 1(e)).

Lactate concentration, on the other hand, was overestimated by the capillary blood samples (Figure 1(g)).

No adverse events using either sampling method were recorded.

## Discussion

This study is the first to show acceptable agreement regarding PCO<sub>2</sub>, pH and HCO<sub>3</sub><sup>–</sup> between arterial and capillary samples, drawn from the non-arterialised fingertip, in stable-phase COPD patients. Conversely, PO<sub>2</sub>, SO<sub>2</sub> and BE showed poor agreement.

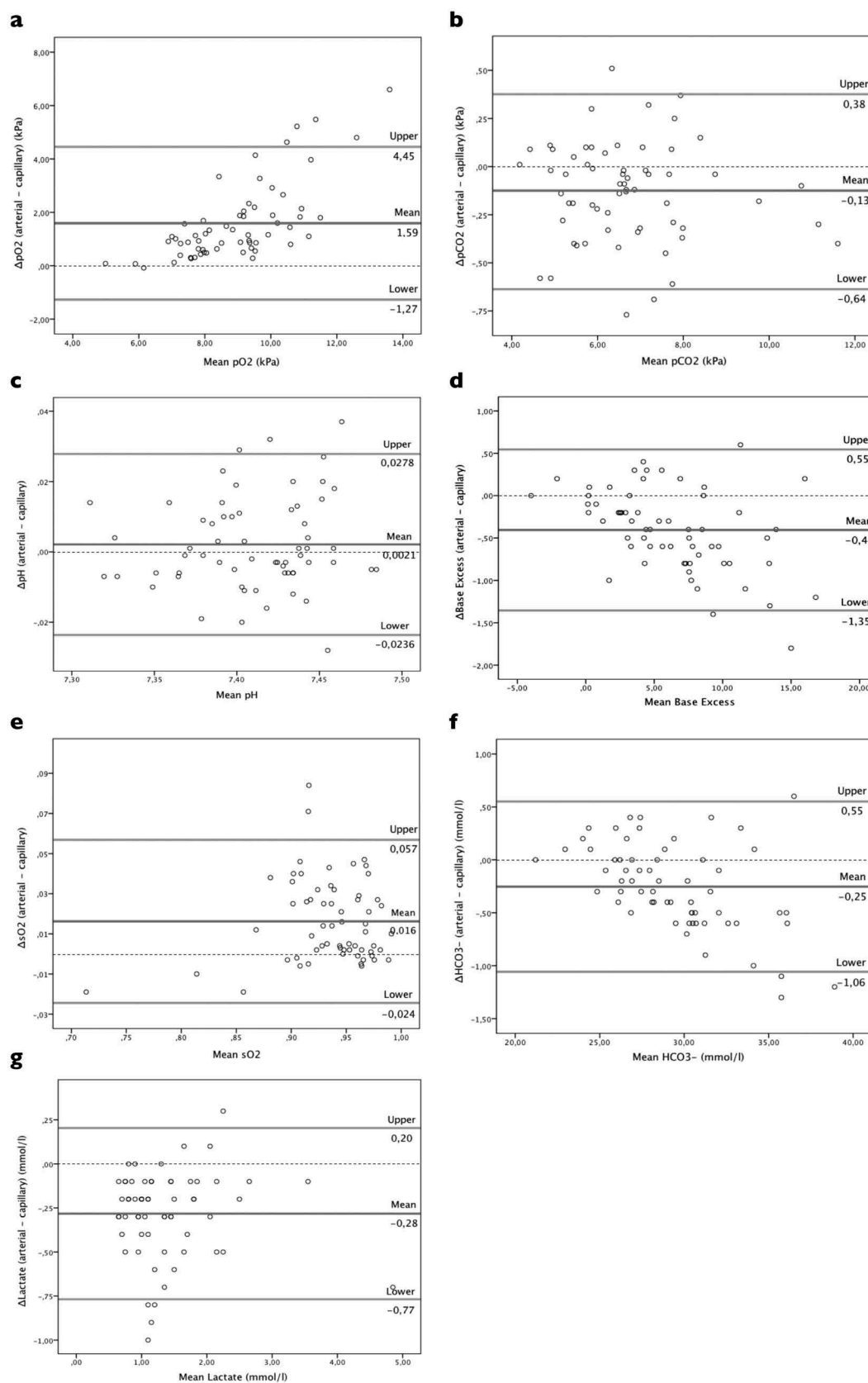
## PO<sub>2</sub> and SO<sub>2</sub>

Previous studies have published variable LoA regarding PO<sub>2</sub>; some found LoA consistent with those published presently [6,11,19], while others have published narrower LoA [2,8,12–14,16]. The latter publications are similar in the sense that they all used the arterialised earlobe capillary blood, likely accounting for the closer agreement between sampling methods. This is due to the reduction of the arterio-venous PO<sub>2</sub> difference caused by the increase in arterial blood flow in the capillary bed [20].

Some of the aforementioned studies were performed using healthy subjects [12,16] whereas others were performed on patients with pulmonary disease [2,8,14]. From this, it appears that more acceptable agreement can be achieved, regardless of pulmonary health status.

As hypothesised, our LoA for the measurement of PO<sub>2</sub> were wide, revealing poor agreement between capillary and arterial samples for the measurement of PO<sub>2</sub>. Given the reference interval [21], these LoA are too wide for capillary sampling to be considered clinically useful.

To the authors' knowledge, only two other studies [5,15] have investigated differences in SO<sub>2</sub> but did not use the Bland-Altman method to analyse their data, negating a direct comparison to our results.



**Figure 1.** Bland-Altman plots for the differences in arterial – capillary values ( $\Delta$ ) plotted against the mean. (a) Bland-Altman plot for  $pO_2$ . (b) Bland-Altman plot for  $pCO_2$ . (c) Bland-Altman plot for pH. (d) Bland-Altman plot for BE. (e) Bland-Altman plot for  $SO_2$ . (f) Bland-Altman plot for  $HCO_3^-$ . (g) Bland-Altman plot for lactate.



Our results revealed a lack of agreement between capillary and arterial readings of blood oxygen saturation levels. Given the reference interval for  $\text{SO}_2$ , our LoA are therefore not clinically acceptable.

$\text{PO}_2$  and  $\text{SO}_2$  have been found to decrease significantly if not analysed within 15 min or stored on ice [22]. However, in only two instances did time from sampling to analysis exceed 15 min, and we do not suspect this to have had a major influence on our results. If anything, the decrease in  $\text{PO}_2$  and  $\text{SO}_2$  should improve the agreement between arterial and capillary samples, as described above.

### **$\text{PCO}_2$**

Our results agree well with a number of previously published LoA [2,7,8,12,14,19] even though these have compared arterialised earlobe capillary blood with arterial blood. Compared to studies using the arterialised fingertip, results vary from narrower [16] to wider [6] than those found in the present study. This suggests that the value of  $\text{PCO}_2$  from non-arterialised fingertip blood is equal to that of arterialised earlobe blood. Given the reference interval, we deem capillary sampling sufficiently accurate for clinical use.

### **pH**

Similar to the present study, previous publications [8,16,19] have, with one exception [11], found narrow LoA in regards to arterial and capillary pH. Other studies did not use the recommended Bland-Altman method [1,5,6,15], and one opted to publish the  $\text{H}^+$  concentration rather than the pH value [7].

pH has a narrow reference interval, necessitating narrow LoA as well. As shown above, the LoA for pH in this study were narrow, demonstrating a clinically acceptable margin of error, and enabling the use of capillary pH as a substitute for the arterial analogue.

### **$\text{HCO}_3^-$**

The LoA of  $\text{HCO}_3^-$  in this study were narrower than what has so far been published [7,11].

Considering the reference intervals for  $\text{HCO}_3^-$ , these LoA are deemed clinically acceptable.

The fact that  $\text{PCO}_2$ , pH and  $\text{HCO}_3^-$  can all be reliably measured in capillary blood provides the clinician with a fast, non-invasive and virtually painless means of obtaining a quick overview of a patient's acid-base balance. These three parameters can be interpreted in conjunction to quickly differentiate between metabolic and respiratory causes of acid-base balance disturbances. The

less invasive method of capillary blood sampling, as well as the omission of the time-consuming arterialisation process, makes it a useful tool for managing conditions requiring serial sampling and has applications spanning the fields of pulmonary medicine, nephrology, endocrinology, emergency medicine and more.

### **Base excess**

As BE is not a measured but a calculated parameter, one could argue its eligibility in this study. However, it is often used in clinical settings in association with  $\text{PCO}_2$  and pH, and capillary BE would therefore be valuable in an acute setting when evaluating acid-base disturbances in critically ill patients.

The LoA for BE obtained from our data were wide, revealing poor agreement between capillary and arterial values. They are however narrower than those previously published [5,6,11], but given the reference interval, they are still too wide to allow capillary sampling to replace arterial sampling to estimate BE.

### **Lactate**

To our knowledge, only one previous study has investigated capillary lactate concentrations [16], finding close agreement between capillary versus arterial blood. Our results, however, displayed wider LoA for the measurement of lactate between the two sampling methods.

Current literature and guidelines state a number of different reference intervals for the lactate concentration, ranging from 0.36–0.75 mmol/l<sup>20</sup> to 0.5–2.5 mmol/l<sup>21</sup>, and therefore the clinical usefulness of capillary lactate measurements varies. Regardless of reference intervals, capillary lactate measurements may prove useful in the monitoring of patients with hyperlactatemia, where the relative values, rather than the absolute values, are monitored in conjunction with blood gas measurements.

### **Methodological considerations**

There are a number of methodological considerations in connection to this study. For one, drawing consecutive blood samples from the same person there is always a risk of sample degeneration before analysis. As arterial and capillary samples in this study were drawn with an inter-median time of 3 min and subsequently analysed, we do not suspect considerable degeneration before analysis.

Secondly, in two cases of fingertip sampling, increased massage of the finger was necessary to provide sufficient blood flow to obtain the sample. Theoretically, this could cause interstitial fluid to be



squeezed into the bloodstream, thereby diluting the blood sample. However, the MD of the haemoglobin concentration was in both cases investigated and indicated no dilution of the capillary blood sample.

Last, but not least, a possible source of error to consider lies within the study population, which consisted of outpatients from the COPD clinic. These patients suffer from chronic hypoxic failure, causing a right shift at the oxyhaemoglobin dissociation curve (ODC), and the arterial-venous differences of  $PO_2$  are lower compared to healthy individuals. Theoretically, this would cause more accurate  $PO_2$  values in the capillary blood when compared with arterial values. However, two-thirds of the patients received oxygen therapy during blood sampling resulting in a higher fractional-inspired oxygen concentration ( $FiO_2$ ), and this would naturally cause decreased accuracy, as the arterial-venous difference would increase.

### Perspectives

Today, Point of Care Testing (POCT) equipment is used to measure blood glucose levels, CRP, Hgb and other parameters. Future perspectives for capillary blood sampling could involve the development of POCT equipment that measures  $PCO_2$ , pH and  $HCO_3^-$  from capillary samples. This has potential application in the fields of prehospital care, general practice, home monitoring and hospital wards as a quick, minimally invasive way of assessing a patient's acid-base balance. Thus, capillary sampling may be applied in the early detection of COPD and asthma exacerbations, diabetic ketoacidosis and more.

Even though direct arterial sampling remains the gold standard for measuring blood gases and acid-base balance, increased awareness of the possibilities and limitations of capillary blood sampling may reduce the number of arterial punctures needed, in turn decreasing the risk of complications and increasing patient comfort.

### Conclusion

As expected, we have found that capillary samples generally agree poorly with arterial readings of  $PO_2$ . Furthermore, based on our data, the measurements of BE and  $SO_2$  agree insufficiently between arterial and capillary blood. Depending on the chosen reference interval, capillary and arterial measurements of lactate may or may not be interchangeable. However, readings of  $PCO_2$ , pH and  $HCO_3^-$  generally agree very well across the two sampling methods. Capillary blood sampling could therefore be useful in an acute setting for evaluation of acid-base disturbances.

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No potential conflict of interest was reported by the authors.

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