

# Improved breath alcohol analysis in patients with depressed consciousness

Annika Kaisdotter Andersson · Bertil Hök ·  
Daniel Rentsch · Gernot Ruecker · Mikael Ekström

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**Abstract** Many patients in pre-hospital and emergency care are under the influence of alcohol. In addition, some of the more common pathological conditions can introduce a behaviour that can be mistaken to be related to alcohol inebriation. Fast quantitative determination of the breath alcohol concentration (BrAC) in emergency patients facilitates triage and medical assessment, but shallow expirations performed by non-cooperative patients reduce the measurement reliability. The aim of this study was to evaluate if breath alcohol analysis in non-cooperative patients can be improved with use of simultaneous measurement of the expired carbon dioxide ( $\text{CO}_2$ ). With prototypes of a handheld breath alcohol analyser based on infrared transmission spectroscopy the alcohol and  $\text{CO}_2$  concentration in expired breath from 37 cooperative and non-cooperative patients were measured. The results show that enhanced breath sampling with use of a pump and estimation of the end expiratory BrAC with use of the ratio between the measured partial pressure of  $\text{CO}_2$  ( $P_{\text{CO}_2}$ ) and a reference value of the alveolar  $P_{\text{CO}_2}$ , provided adequate correlation with the blood alcohol concentration (BAC).

This pre-clinical study has shown that breath alcohol analysis in shallow expirations from non-cooperative patients can be improved with use of  $\text{CO}_2$  as a tracer gas.

**Keywords** Breath alcohol analysis · Infrared transmission spectroscopy · Passive expirations · Test subject study · Depressed consciousness

## 1 Introduction

Rapid medical assessment and correct diagnosis are of great importance in emergency care. The medical assessment is made more difficult if the patient has a depressed consciousness and is under the influence of alcohol, which many patients in need of emergency care are [11, 16, 18, 20]. Dependent on the level of alcohol intoxication the patient's mental status and behaviour might be affected, and additional symptoms might occur, whereas other pathological symptoms can become diminished or shadowed. However, it is more serious if alcohol intoxication is falsely believed to be the cause of the patient's medical condition. This is a considerable risk due to the high incidence of alcohol inebriated patients and since some of the more common pathological conditions in emergency medicine can introduce a behaviour that resembles the behaviour of a person under the influence of alcohol, e.g. brain and head injuries, psychomotor seizures, acute or diagnosed physiological illness, carbon dioxide narcosis, and acute hypo-glycemia [6, 7, 11, 20, 22, 27]. With determination of the blood or breath alcohol concentration the risk of relying on a suspicion of involvement of alcohol would be eliminated in the medical assessment. With a negative alcohol test or a result indicating a low or high alcohol concentration, the medical staff can continue the

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A. Kaisdotter Andersson (✉) · B. Hök  
Hök Instrument AB, Västerås, Sweden  
e-mail: annika@hokinstrument.se

D. Rentsch  
Institute of Forensic Medicine, University of Rostock,  
Rostock, Germany

G. Ruecker  
Department of Anaesthesiology and Intensive Therapy,  
University of Rostock, Rostock, Germany

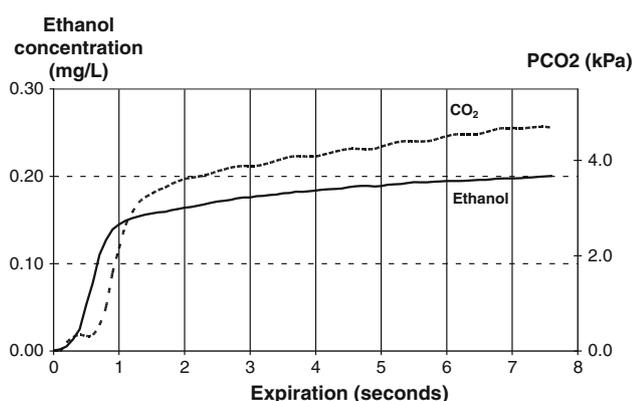
A. Kaisdotter Andersson · M. Ekström  
School of Innovation, Design and Engineering, Mälardalen  
University, Västerås, Sweden

assessment with the knowledge whether the patient's symptoms could be alcohol induced or not, and if the sensory and pain responses are likely to be diminished or shadowed due to intake of alcohol [3, 6, 7, 10, 22, 23, 26]. Thereby delay of the diagnosis and misdiagnosis are avoided.

At most emergency departments in Sweden it is general praxis to determine the alcohol concentration in patients with unclear unconsciousness or who are suspected to be under the influence of alcohol. Breath alcohol analysis provides convenient, fast and non-invasive quantification of the patient's alcohol concentration. The breath alcohol concentration (BrAC) increases with expired volume, see Fig. 1, and for best correlation with the blood alcohol concentration (BAC) a prolonged expiration shall be performed with sealing around a mouthpiece. This implies that for breath alcohol analysis in small expired volumes, e.g. oral or nasal expirations from uncooperative patients, the correlation with the BAC will be negatively affected [4, 5, 9, 24, 25].

With a new handheld breath analyser, the alcohol and  $\text{CO}_2$  concentrations in expired breath from cooperative and non-cooperative patients were measured. To evaluate if enhanced breath sampling improved the measurement quality of breath testing, two different prototypes were used: one which passively sampled the expired air, and one that facilitated the sampling with the use of a pump.

The aim of this study was to evaluate whether the difference between the alcohol concentration measured in blood and breath can be reduced with use of carbon dioxide ( $\text{CO}_2$ ) as a tracer gas.



**Fig. 1** The expiration profile (expirogram) for ethanol and carbon dioxide ( $\text{CO}_2$ ), which shows a steady positive slope; increase in breath alcohol concentration and carbon dioxide, during a prolonged expiration. The expirogram is recorded with an evidential breath analyser instrument equipped with a mouthpiece (Evidenzer, Nanopuls AB, Uppsala). The time of onset of the final phase of the  $\text{CO}_2$  expirogram occurs after approximately 1.2 s

## 2 Methods and materials

### 2.1 The breath alcohol analyser prototypes

Breath analysers based on infrared (IR) transmission spectroscopy enables high sensitivity, selectivity to ethanol and continuous measurement of the concentration during expiration, and in addition they are long-time stable [8]. IR spectroscopy is based on the substances' absorption of IR light at different wavelengths. The absorption originates from specific vibrations and rotations of the molecules which results in a unique absorption spectrum for each substance [1]. Ethanol shows strong absorption in the wavelength band 3.3 to 3.5  $\mu\text{m}$ , which is assigned to the C–H stretch vibrations of the molecule [1]. C–H bindings are found in most endogenous and exogenous substances in expired air. This implies that these substances have strong absorption in the same wavelength region as ethanol, but with use of at least two, ethanol specific wavelengths selectivity for ethanol is enabled. In order to achieve sufficient signal to noise ratio a long optical pathway is needed, which has been incompatible with the dimensions of a handheld breath analyser until now. The breath analyser tested in this study uses an optical measurement cavity (OBA3, SenseAir<sup>®</sup>), which enables the combination of a long optical path length at a large aperture with small dimensions (maximum width of 55 mm) [12]. The long optical path is achieved through use of multiple reflections in the high reflective gold coated surfaces inside the cavity [19]. The diverging beam from the IR source is reflected and focused several times on the elliptical surfaces of the cavity until it is detected by thermopiles.

The high  $P_{\text{CO}_2}$  in expired air enables high sensitivity already at a very short optical path length, whereas a long optical path length in the order of decimetres is necessary to achieve high sensitivity of the ethanol measurement. The placement of the thermopiles, with respect to how the light propagates within the optical cavity, gives an approximate path length of 4 and 210 mm for measurement of the  $P_{\text{CO}_2}$  and BrAC, respectively. A broad band IR source (HSL5/115/S, Heimann Sensors GmbH, Germany) with a modulation frequency of 2 Hz sets the sampling frequency for the two thermopiles (HMSJ21, Heimann Sensors GmbH, Germany). The two thermopiles were equipped with optical band pass filter: centre wavelengths of 3.45 and 4.26  $\mu\text{m}$  (optical windows of 90 nm) for measurement of the BrAC and  $P_{\text{CO}_2}$ , respectively. The use of a single detector for alcohol in this prototype does not assure selectivity for ethanol. Calibration was performed prior to and after the study with four different concentrations of  $\text{CO}_2$  (0.9, 3.6, 6.3, 9.1 kPa), and ethanol concentration of 1 and 2  $\text{mg l}^{-1}$ . The calibration after the tests, with 1  $\text{mg l}^{-1}$  ethanol and 0.9 kPa gave values of sensitivity and

absorbance for the ethanol channels, of the passive and active sampling prototypes, of 20 mV per mg l<sup>-1</sup> and 2.2% per mg l<sup>-1</sup>, and 41 mV per mg l<sup>-1</sup> and 2.3% per mg l<sup>-1</sup>, respectively. The corresponding values for the CO<sub>2</sub> channel were 285 mV per kPa and 15% per kPa, and 340 mV per kPa and 15% per kPa, respectively.

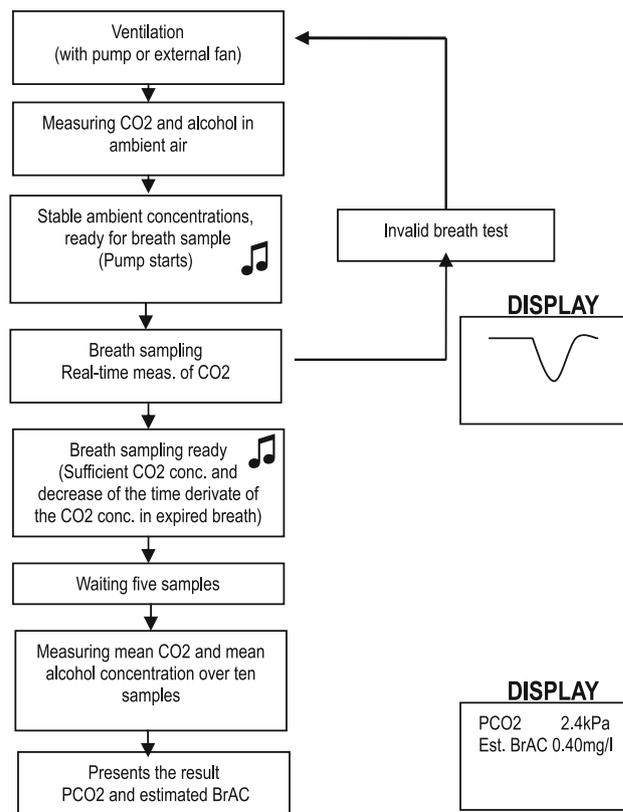
Patients influenced by alcohol or with depressed consciousness will not be able to cooperate for breath alcohol testing, thus they will passively exhale small volumes of breath, in the order of hundreds of millilitres. For this reason the sampling and quality assurance of the breath sample becomes critical in medical breath alcohol analysis. Collection of the expired breath from both the mouth and nose was ensured with a single use mask (7092, size 2, Intersurgical Ltd., U.K.) that was attached to the prototypes. The volume of the optical cavity was small (5 cm<sup>3</sup>), but the single-use mask and bacterial filter (Iso-Gard<sup>®</sup> Filter Small Gibeck, Teleflex Medical, Malaysia) added dead space (100 and 25 ml, respectively), Fig. 2. One of the two prototypes was equipped with a pump (Diaphragm pump 2002G, Rietschle Thomas Puchheim GmbH, Germany, maximum flow 380 ml min<sup>-1</sup>) for enhanced transport of the exhaled air into the optical cavity, henceforth called the active sampling prototype.

### 2.2 Measurement method and algorithm

The measurement algorithm was implemented in a microprocessor (Cypress 29566), Fig. 3. The analysis of ambient concentrations of alcohol and P<sub>CO<sub>2</sub></sub> prior to the



**Fig. 2** The passive sampling breath analyser with attached single use mask (Size2, Intersurgical Ltd., Country; ISO-Gard Filter Small, Gibeck) and bacterial filter (Iso-Gard filter small, Gibeck, Vårdkedjan AB, Sweden)



**Fig. 3** Flowgraph describing the measurement algorithm implemented in the microprocessor (Cypress 24894)

breath test is an advantage since relative measurement minimise the interference of ambient alcohol, i.e. from clothes and hand disinfection. Stable background concentration had to be achieved before the prototype was ready for breath testing. Continuous measurement of the P<sub>CO<sub>2</sub></sub> during the breath test enabled real-time presentation of the P<sub>CO<sub>2</sub></sub> in the sampled air on the display, similar to the respiration presentation with a capnograph.

In order to allow very shallow expirations to be performed a threshold level for CO<sub>2</sub> as low as 0.5 kPa was set. In addition, a criterion that the expiration had reached the final phase of the expirogram; the phase where the concentration steadily increases, prevailed. From earlier studies of expirograms the time to onset of the final phase of the CO<sub>2</sub> expirogram has been defined as when the time derivate of the P<sub>CO<sub>2</sub></sub> signal had decreased to half of its maximum value [15], which is related to knee of the expirogram, cf. Fig. 1. Results from these studies have shown that the onset of the final phase of both the ethanol and the CO<sub>2</sub> expirogram occur within 2 s, regardless of type of breath manoeuvre. When these two criteria were fulfilled an acoustic feedback was given to announce that the breath test was approved, and for the active sampling prototype the pump stopped. After a delay of 2.5 s (5 samples) the

mean alcohol concentration and  $P_{\text{CO}_2}$  over the following 5 s (10 samples) were calculated. The delay of 2.5 s was set to ensure that the expiration had stopped and that no adherent turbulent flow existed in the optical cavity during the measurement.

From the measured alcohol and  $\text{CO}_2$  concentrations, an estimation of the end expiratory BrAC valid for a prolonged (vital capacity) breath test was performed with use of Eq. 1, and as reference value of the alveolar  $P_{\text{CO}_2}$ , 4.8 kPa was used:

$$\text{BrAC}_{\text{Est}} = \frac{\text{CO}_{2\text{endexp}}}{\text{CO}_{2\text{measured}}} \cdot \text{BrAC}_{\text{measured}} \quad (1)$$

where,  $\text{BrAC}_{\text{Est}}$  = the BrAC estimated to be valid for the end expiratory concentration after a vital capacity breath test,  $\text{CO}_{2\text{measured}}$ ,  $\text{BrAC}_{\text{measured}}$  = the  $\text{CO}_2$  and alcohol concentration at the time of approved breath test,  $\text{CO}_{2\text{endexp}}$  = reference value of alveolar  $\text{CO}_2$  concentration (4.8 kPa).

The validity of the measurement method relies on the assumptions of similarities in the expirograms for ethanol and  $\text{CO}_2$ , and small intra- and inter-individual variations in  $P_{\text{CO}_2}$ . The estimation method of end expiratory BrAC has been found valid after performance of small and provocative breath tests [15, 17].

The estimated BrAC and the measured  $P_{\text{CO}_2}$  were presented to the user on the display of the breath analyser. Ventilation of the optical cavity after each breath tests was ensured with the pump in the active sampling prototype and an external fan in the passive sampling prototype. Complete data from the breath test; date and time of measurement, measured concentrations and presented result, were saved as a separate file in the internal memory of the prototype, which enabled traceability.

### 2.3 Subjects and measurement procedure

Thirty-seven patients who sought medical care at an emergency medical clinic set up at a music and cultural festival were enrolled in the study. When the patient arrived at the medical clinic, breath tests were taken with one or both of the prototypes and venous blood, from the dorsal side of the hand or the lower arm, was withdrawn for blood alcohol analysis. The blood alcohol analyses were performed by alcohol dehydrogenase method, an enzymatic procedure with photometric detection. This is a commonly used method for forensic and clinical purposes in Germany [13, 21]. The BAC presented is the mean value calculated from double analysis.

To the largest possible extent both the passive and active sampling prototype were used, but with the patients whose medical condition was more critical and who were unable to cooperate, only breath tests with the active sampling

prototype were taken. The conscious subjects were informed that there was no need for cooperation during the breath test, despite that some of the subjects did perform more forced expirations.

The  $P_{\text{CO}_2}$  and the estimated BrAC were documented for further analysis, together with the test subjects' level of consciousness at first contact which was graded by the nurses with use of the Glasgow coma scale (GCS). With the GCS scale the patient's eye, verbal and motor responses are graded, and the level graded from 3 to 15, where 15 means that no depression of the consciousness prevails. The data was collected by five different persons (four nurses and one of the authors, AKA). The study was approved by the ethical committee at the University hospital in Rostock and informed consent was obtained from the subjects. Full anonymity was given to all subjects enrolled.

### 2.4 Data analysis

The prototypes presented the estimated BrAC and the measured  $P_{\text{CO}_2}$  and from the file of each breath test the measured alcohol concentration was extracted. The performed breath tests, with the passive and the active sampling prototypes, were regarded as single measurements, even in the case several breath tests were performed on the same subject. Each measured BrAC and estimated BrAC was paired with the corresponding BAC.

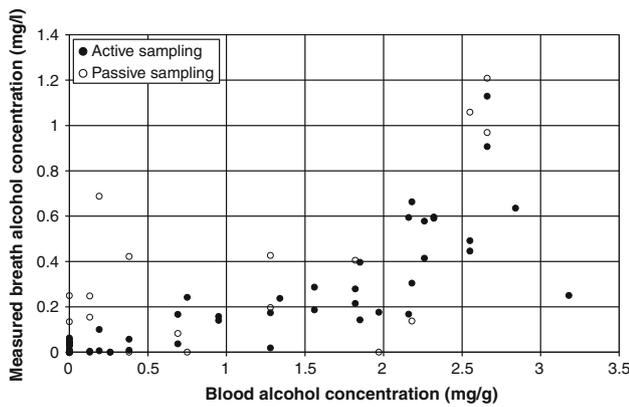
For evaluation of the performance of the two prototypes and evaluation of how use of  $\text{CO}_2$  as the tracer gas affect breath alcohol analysis, regression analyses were performed between the venous BAC and the measured BrAC, and the BAC and the estimated BrAC. Pearson's correlation coefficient was used for correlation analysis between the paired blood and breath tests. The average and random discrepancy between the blood and breath alcohol concentrations were analysed through the equation of the linear regression line and the residual standard deviation.

## 3 Results

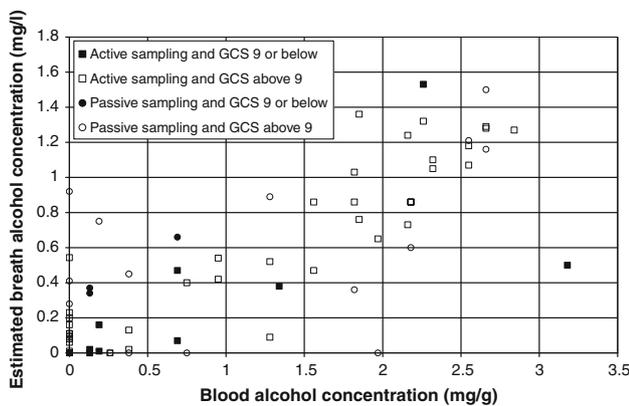
During 4 days, 37 patients (eight females) who sought emergency medical care were enrolled in the study. Seven of the 37 subjects had a GCS value of nine or lower. Twenty-three of the subjects had positive BAC, with a mean of  $0.94 \text{ mg g}^{-1}$ . Eighty-four breath tests were taken; 25 with the passive sampling, and 59 with the active sampling prototype.

As seen in Fig. 4, the alcohol concentration measured in expired air showed a relatively weak correlation to the BAC.

Figure 5 shows the relationship between the estimated BrAC and the BAC, for the passive and the active sampling prototype, with respect to the subject's level of



**Fig. 4** The relationship between the breath alcohol concentration measured with the passive (*open circle*,  $n = 25$ ) and active (*filled circle*,  $n = 59$ ) sampling prototypes and the blood alcohol concentration. The active sampling prototype showed a slightly higher correlation ( $r = 0.83$ ) than the passive sampling prototype ( $r = 0.69$ )



**Fig. 5** The relationship between the estimated breath alcohol concentration measured with the passive (*open circle and filled circle*,  $n = 25$ ) and active (*open square and filled square*,  $n = 59$ ) sampling prototypes and the blood alcohol concentration, with respect to the subject's value on the Glasgow Coma Scale (GCS). No difference in correlation was found for the active sampling prototype, with respect to GCS value of nine or below (*filled square*,  $n = 11$ ,  $r = 0.72$ ) or above nine (*open square*,  $n = 48$ ,  $r = 0.93$ ). Compared to the active sampling prototype, the correlation for the passive sampling prototype used in patients with GCS values above nine was lower (*open circle*,  $n = 22$ ,  $r = 0.64$ ). The correlation for the patients with GCS of nine or below, a very strong correlation was found, with can be explained by the small number of breath tests performed in only two subjects (*filled circle*,  $n = 3$ ,  $r = 1.0$ )

consciousness, defined from the individuals Glasgow Coma Scale (GCS) value determined at first contact. A GCS value equal to or below nine was regarded to might have affected the patient's cooperation during the breath tests. However, a GCS value higher than nine do not directly imply that the subject was cooperating during breath testing, since some of them were sleeping or as in one case, anaesthetised. The deviation in BrAC from the regression line does not seem to increase with increased BAC, for any of the prototypes.

In Table 1 all breath tests performed with respectively prototype has been analysed together regardless of the value of the GCS. For the active sampling prototype, estimation of end expiratory BrAC slightly increased the correlation with the BAC ( $r = 0.89$ ), as compared to the measured BrAC ( $r = 0.83$ ), see Table 1 and Fig. 4. The same applies for the passive sampling prototype ( $r = 0.69$  and  $r = 0.63$ , respectively). No significant offset existed for measurement performed with the active sampling prototype, whereas for the passive sampling prototype the small offset ( $0.06 \text{ mg l}^{-1}$ ) that existed in the measurement of BrAC significantly increased with estimation of the end expiratory BrAC ( $0.2 \text{ mg l}^{-1}$ ). Analysis of the regression line and the residual standard deviations for all breath tests performed with the active and passive prototypes are summarised in Table 1.

### 4 Discussion

In the conversion between BrAC and BAC a blood:breath ratio (BBR) is used. A commonly used BBR is 2100:1, which implies that 0.525 mg ethanol per ml blood (0.50 mg ethanol per gram blood) converts to 0.25 mg ethanol per litre exhaled air [14]. With knowledge about the physiological factors that determines the BrAC it is clear that there is nothing like a constant BBR valid for all individuals, nor for shallow and prolonged expirations [14]. The use of this BBR on our results, confirms the general opinion that measuring the BrAC in a shallow expiration from a patient who cannot cooperate is likely to give a false low BrAC.

For medical usage breath sampling and quality check of the breath sample are critical issues. In breath analysis the apparatus dead space is of importance. Large dead spaces in breath alcohol analysis imply that the last part of the expired breath will not enter the measurement cell. The dead space of the mask and filter used in this study was large in relation to the small volumes of breath expired. With use of a designated mask with a bacterial filter included, the total dead space of the apparatus can be greatly decreased. This is expected to improve the correlation between the BAC and the measured BrAC, and the estimated BrAC, respectively.

Quality check of the breath sample can be achieved with simultaneous measurement of the  $P_{CO_2}$  in expired breath. A low level of  $P_{CO_2}$  measured in the breath sample indicates that the quality of the breath test is low (possibly presenting a false low BrAC), which means that the expired air was either diluted with ambient air or that the expiration was very shallow, cf. Fig. 1. If no  $CO_2$  is detected the user becomes informed that the sample originates from ambient air.

The results from this study show that with compensation with use of the measured  $P_{CO_2}$  in the expired breath, the

**Table 1** Linear regression analysis and residual standard deviation for the relationship between the blood alcohol concentration (BAC) and the measured alcohol concentration in breath, and BAC and the

estimated breath alcohol concentration (BrAC) for the two prototypes, regardless of the patient's value of the Glasgow Coma Scale

	Passive sampling prototype ( $n = 25$ )		Active sampling prototype ( $n = 59$ )	
	Measured alcohol concentration	Estimated BrAC	Measured alcohol concentration	Estimated BrAC
Equation of the regression line	$y = 0.26x + 0.06$	$y = 0.32x + 0.21$	$y = 0.20x - 0.0052$	$y = 0.42x + 0.05$
Correlation coefficient ( $R$ value)	0.69	0.63	0.83	0.89
Residual standard deviation ( $\text{mg l}^{-1}$ )	0.05	0.07	0.02	0.03

active sampling prototype presented an estimated end expiratory BrAC which was only 16% lower than the BAC ( $y = 0.42x + 0.05$ , from Table 1), despite the shallow expirations performed by patients. Normalisation with use of  $\text{CO}_2$  seems to provide an opportunity to better determine the BrAC in non-cooperative patients. This is exemplified in the study where two of the breath tests recorded with the active sampling prototype were performed on an anaesthetised patient with a pharyngeal tube, and strong agreement between the BAC and the BrAC were found with use of a BBR of 2100:1 (BAC:  $2.3 \text{ mg g}^{-1}$ , estimated BrAC:  $1.1 \text{ mg l}^{-1}$ , for both breath tests).

Analysis of some of the breath tests which deviated with respect to significantly low estimated BrAC in Fig. 5, has shown that in some of the breath tests the measured  $P_{\text{CO}_2}$  was below 2.5 kPa, which means that for diagnostic use of the BrAC a retest should have been recommended. On the contrary, a  $P_{\text{CO}_2}$  over 4.8 kPa which is regarded as the alveolar  $P_{\text{CO}_2}$ , were measured in two of the deviating breath tests performed with the passive sampling prototype. This means that the estimated BrAC becomes lower than the measured alcohol concentration, which in these cases already was falsely low.

A total of 12 breath tests, performed by eight different subjects, seem to be false positive. One possible explanation to the false positive breath tests is flow introduced noise, but since three of the subjects performed false positive breath tests in both of the prototypes, interference from other substances in breath might have occurred as well. The maximal estimated BrAC with a BAC of zero was  $0.92 \text{ mg l}^{-1}$ , presented by the passive sampling prototype but also the active sampling prototype gave a false positive breath test for this subject. The importance of selectivity in breath alcohol testing for medical use has been highlighted [5] and in the next generation of prototypes a wavelength around  $9.5 \mu\text{m}$  will be used for increased specificity for ethanol [8]. In addition to specificity for ethanol, a breath analyser based on IR transmission spectroscopy provides a possibility to detect intoxication from other substances that requires fast diagnosis and treatment, i.e. methanol or carbon monoxide.

In patients the alveolar  $P_{\text{CO}_2}$  might deviate from the assumed normal alveolar level of 4.8 kPa and the inter-

individual variation in  $P_{\text{CO}_2}$  is likely to be larger, which adds to the error in the estimation of the end expiratory BrAC. On the other hand, the degree of intoxication is not solely related to the measured BAC or BrAC but also to the patient's tolerance towards alcohol, which is partly dependent on the custom to consume alcoholic beverage [8]. Due to the large individual differences in alcohol tolerance, each measured alcohol concentration has to be assessed in the context of the patient's medical anamnesis and medical condition. This implies that the requirement of measurement accuracy of a breath analyser for medical use might be subordinated [9, 11, 26], unlike breath analysers used for traffic-law enforcement. An improved design of the mask, enhanced sampling of the breath test, and quality assurance of the breath test through simultaneous measurement of the  $P_{\text{CO}_2}$ , even without normalisation with  $\text{CO}_2$ , is likely to improve breath alcohol analysis, as compared to devices available today. In addition to the information regarding the sample quality, presentation of the  $P_{\text{CO}_2}$  measured at the end of the expiration also provides the physician with information about the patient's respiratory function.

With fast and simple on-site breath alcohol analysis, early exclusion of alcohol as the reason behind the medical condition can be done, in many of the severely ill emergency patients. This is likely to improve the outcome in terms of mortality and remaining injuries. Fast and non-laboratory measurement of the BrAC are also in line with the increased demand of triage in medical [18] and psychiatric emergency care [2], as well as in pre-hospital care [18, 20]. Additional advantages with breath analysis is the significantly lower cost compared to blood analysis, and the early determination is believed to save resources in the form of time, beds, but also use of diagnostic procedures [9, 16].

## 5 Conclusion

In this study two prototypes of a handheld breath alcohol analyser were evaluated; one passive and one active breath sampling prototype. With use of active breath sampling and

CO<sub>2</sub> as a tracer gas good correlation and fairly good agreement with the BAC were achieved with the prototypes in cooperative, sleeping, and unconscious patients. These results indicate that with simultaneous measurement of P<sub>CO<sub>2</sub></sub> in expired breath a more reliable breath alcohol testing can be achieved in patients.

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