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Methodology investigation of expirograms for enabling contact free breath alcohol analysis

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Abstract

The present techniques for breath alcohol determination have usability limitations concerning practical use and the time and effort required for the test person. The rationale of the physiological assumptions in a recently demonstrated technique for breath analysis without a mouthpiece is investigated in this paper. Expirograms quantifying ethanol, carbon dioxide (CO_2) and water (H_2O) from 30 test subjects were analysed, with respect to the influence of individual variations in end-expiratory CO_2 and H_2O concentrations, and possible benefits from simultaneous measurement of CO_2 or H_2O. Both healthy subjects and patients suffering from pulmonary diseases performed breath tests with small and maximum volume expiration. The breath tests were recorded basically with a standard evidential instrument using infrared absorption spectroscopy, and equipped with a mouthpiece. Average concentrations were significantly higher for the maximum than for the small expirations. For the maximum expirations, the healthy subjects had a significantly higher end-expired PCO_2 of 4.4 ± 0.5 kPa (mean $\pm$ standard deviation) than the patients (3.9 ± 0.7 kPa). The corresponding values for H_2O were 39 ± 1 and 38 ± 1 mg l^{-1}. The results indicate that the CO_2 variability is consistent with the requirements of accuracy for alcohol ignition interlocks. In addition, CO_2 as tracer gas is preferable to H_2O due to its low concentration in ambient air. In instruments for evidential purposes H_2O may be required as tracer gas for increased accuracy. Furthermore, the study provides support for early determination of breath alcohol concentration, indicating that determination after 2 s will introduce an additional random error of 0.02 mg l^{-1} or less.

1. Introduction

In many countries, breath alcohol concentration (BrAC) limits are replacing, or are being used alongside blood alcohol concentration (BAC), as the evidential basis for prosecuting drunk drivers. In addition, breath analysers for general purpose applications, such as alcohol ignition interlocks (alcolocks), have become more common and are being used daily by a growing community of professional drivers.

On the other hand, the use of breath analysers has called attention to some of the major fallacies that are still prevailing. These are mainly related to the user interface of the equipment, combined with the physiological characteristics of the (possibly impaired or manipulative) test subject. Most of the basic problems of breath analysers become evident when examining the expirogram of a test subject, i.e., graphic representation of alcohol (or any other gas or vapour) concentration as a function of time during exhalation [1, 9]. The expirogram involves an initial phase related to the anatomic and physiological dead space, an intermediate

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mixing or washout phase, and a final phase often characterized by steadily increasing concentration. As a consequence of the increase, many breath analysers require a minimum of 5 s and a volume of 1 l of sustained exhalation, which is problematic to patients suffering from, e.g., chronic obstructive pulmonary disease (COPD). Conversely, a person with large vital capacity may manipulate the reading by delivering a shallow breath.

The mandatory use of a mouthpiece is a further limitation of the present breath analysers, both with respect to cost and practical use. Recently, contactless measurement by forced expiration towards a sampling point located 5–10 cm in front of the subject's mouth has been demonstrated, using simultaneous measurements of ethanol (EtOH) and CO_2 [10, 11]. The dilution of the breath sample is estimated by comparing the measured CO_2 concentration in the freely exhaled air and the estimated alveolar concentration. Lindberg *et al* [14] have demonstrated a corresponding procedure, using H_2O instead of CO_2 as tracer gas.

Assuming similar mixing of the gases involved, the end-expiratory ethanol concentration may be calculated from the diluted concentrations of ethanol and CO_2 (or H_2O), and the estimated end-expiratory (alveolar) CO_2 concentration (or H_2O) according to

$$\frac{C_{\text{end exp EtOH}}}{C_{\text{meas EtOH}}} = \frac{C_{\text{end exp CO}_2}}{C_{\text{meas CO}_2}}. \quad (1)$$

As can be understood from equation (1) the compensation for the dilution of ethanol requires a correct estimation of the end-expiratory CO_2 (or H_2O). Thus, before recommending the use of contactless measurements (without a mouthpiece), the variability of the end-expiratory CO_2 (or H_2O) and its influence on the calculated end-expiratory ethanol have to be analysed.

In the present study, we address the variability of alveolar CO_2 and H_2O concentrations between individuals. If large variations are prevailing, the estimation may require individual normalization, rather than accepting a common reference value. Differences between healthy persons and patients suffering from obstructive lung disease can be expected. The tolerance of variability will be different in different breath analyser applications. According to the industrial standards EN50436-2 and OIML R126 for alcolocks and evidential instruments, the accepted tolerances for the technical measurement error is ±15% and ±5%, respectively.

In the present study, we also investigate the possibility of reducing the time and effort of the breath test. We hypothesized that the ratio between ethanol and CO_2 (or H_2O) already at 2 s of expiration could be used to predict the end-expiratory BrAC. We tested this by using equation (1), inserting the 2 s values as $C_{\text{meas EtOH}}$ and $C_{\text{meas CO}_2}$ or $C_{\text{meas H}_2\text{O}}$.

In this study, expirograms of ethanol, CO_2 and H_2O were recorded and analysed, in 30 individuals, both healthy and with pulmonary disease. The equipment used was basically standard, using a mouthpiece for breath delivery.

2. Materials and methods

2.1. Subjects

Twenty-one healthy subjects and nine patients with obstructive pulmonary disease were enrolled in the study. The population size was a result of *a priori* power analysis based on the expected variability of end-expiratory CO_2 from the literature [2, 4, 5, 15, 16, 18, 19] and the measurement error. The adequate population size can be calculated by squaring the ratio between the expected variability (approximately 10%) and the measurement error (approximately 3%). The healthy subjects were recruited with the intention of setting a wide range in age and lung volume, including athletes and former athletes with large vital capacity. The variation in vital capacity and respiratory function was verified using a spirometry test.

All subjects were accustomed to consuming alcohol and were informed in advance about the test procedure. The study was approved by the Regional Ethical Review Board in Uppsala, and written consent was obtained from each subject.

2.2. Measurement of alcohol, CO_2 and H_2O concentration in exhaled air

An evidential breath analyser instrument (Evidenzer, Nanopuls AB, Uppsala, Sweden) based on infrared (IR) transmission spectroscopy [3] was used for recording expirograms of ethanol, CO_2 and H_2O. A combination of an optical filter at 3.41 μm and a reference filter at 3.80 μm allowed determination of the concentration of ethanol. The instrument had been modified by the supplier with additional optical filters for the measurement of H_2O and CO_2 concentrations, at wavelengths of 2.57 μm and 2.77 μm, respectively. At these wavelengths the interference from other endogenous and exogenous gases except methane is insignificant [13]. To avoid problem with condensation the inlet tube was heated with the mouthpiece attached to the tube during the procedure.

During the breath test, the breath analyser continuously measured the concentration of ethanol, H_2O and CO_2, with a sampling rate of 10 Hz. Afterwards, data from the breath test were presented in a data logger, containing date, time, duration of expiration, exhaled volume and mean ethanol concentration during the last second of the exhalation. In addition to this information, the raw data from the instrument were used to plot the ethanol, H_2O and CO_2 expirograms for each breath test.

The estimated total error for the reported H_2O concentrations was ±0.6 mg l^{-1}, and for the reported PCO_2 the estimated total error of the calibration curve was less than ±3%. The estimated total error for the reported ethanol concentrations was the largest of ±0.01 mg l^{-1} or ±3%.

2.3. Experimental procedure

The measurements were carried out during six separate days at the department of Clinical Physiology, Uppsala University Hospital. For the subjects, the measurement procedure took up to 2 h. With a spirometer (MasterScope, Jaeger, Spirofarma Cardiopulmonary, Sweden), the subjects' vital capacity (VC), forced expiratory volume (FEV) and forced expiratory volume during the first second of expiration (FEV_1) were measured among other respiratory parameters. After measurement of the respiratory function, a sequence of sober breath tests in

the breath analyser followed. Each sequence included two breath tests, where the subject was first asked to perform a low-volume breath test with a more or less normal inspiration and expiration, similar to a prolonged tidal breath. The expiration of the low-volume breath test should last at least for 2 s, and the exhaled volume should be about 0.5–1.0 l. In rapid succession after the low-volume breath test, the subject performed a breath test with maximum inspiration and maximal exhaled volume (vital capacity expiration). This manoeuvre is the recommended one for the breath analyser instrument used. The reason for the two different manoeuvres was to reveal any intra-individual variations in ethanol, H_2O and CO_2 concentrations during a small and large expiration, and to relate them to the inter-individual differences of the ethanol, H_2O and CO_2 concentrations.

After the breath test sequence under sober condition, the subject consumed 0.3 g alcohol per kilo body mass. The subject could choose to ingest the alcohol in the form of white or red wine, or spirit (straight or mixed with juice or soft drink). The amount of alcohol had to be consumed within 10 min, and 30 min later the two measurement sequences, each consisting of the two breath tests, were carried out. Each subject performed two sober and four alcoholic breath tests; three low-volume and three maximum volume breath tests. Since the aim of this study did not demand that the subjects achieved a certain level of intoxication, the subjects were not given any restrictions regarding fasting prior to the tests and were allowed to drink non-alcoholic beverage and eat during the time they waited after alcohol consumption. All subjects sat while performing the spirometry and the breath tests.

2.4. Data analysis

Vital capacity (VC), and forced expiratory volume during the first second of the exhalation (FEV_1) measured by the spirometer were used for further analysis.

From the expirograms the concentrations of ethanol, H_2O and CO_2 at 2 s of exhalation and at the end of exhalation were extracted together with the corresponding mean value during the last second of the breath test. Mean concentrations of ethanol and H_2O and partial pressure of CO_2, PCO_2 that are presented are the mean of the concentration during the last second of each breath test, in accordance with the instrument's measurement procedure.

The time interval between the start of the breath and the onset of the final phase of the expirogram was analysed for characterization purposes. The onset was defined as the point in time when the slope of the expirogram had decreased to less than half of its maximum value.

For comparison of intra-individual differences between the low and maximum volume breath tests, paired sample *t*-tests were used. For comparison of the concentration differences between the healthy subjects and the patients, one-factor analyses of variance (ANOVA) were performed. The strength of the statistical significance found is indicated with significance stars (NS $p > 0.05$; $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$). The Pearson correlation coefficient was calculated for the assessment of the strength in the relationship between parameters.

Methane found in exhaled air originates from the bacterial flora in the large intestine. Expired methane interferes with the detection of ethanol at 3.41 μm, and was thus detected as a false ethanol signal. Methane was present in the exhaled air from 13 of the 30 subjects, but it was only corrected for in eight subjects, in which the contribution constituted more than 5% of the ethanol level at any of the alcoholic breath tests. Correction for this was enabled through the similarities in characteristics of the expirograms of ethanol and methane, and that the methane concentration could be quantified from the sober breath tests where no ethanol was expired. Correction of the interference was done by subtracting the level of methane concentration found in the low and maximum volume sober breath tests, from the ethanol concentration found in the corresponding alcoholic breath tests.

3. Results

3.1. Spirometry

There were large differences in vital capacity between the healthy subjects and the patients. Spirometric data are shown in table 1. The healthy subjects had VC and FEV_1 within one standard deviation of predicted reference volumes and the patients were below two standard deviations of predicted [7, 8]. FEV_1/VC was 76 ± 7% in the healthy subjects and 60 ± 12% in the patients.

3.2. Characteristics of the breath tests

All subjects managed to perform the intended alcohol breath tests, and the low and maximum volume tests were all included for further analysis. The mean exhaled volume from the two maximum volume tests (vital capacity expiration) was strongly correlated to the vital capacity measured by spirometry ($r = 0.95$) for all subjects, indicating good participation in the tests.

The exhaled volume during the maximum volume test was significantly larger than the exhaled volume during the low volume test for the healthy subjects ($p < 0.01$), and for the patients ($p < 0.01$). During the maximum volume test the patients exhaled a significantly smaller volume than the healthy subjects ($p < 0.01$), table 1. No significant differences in duration of the expiration existed between the healthy subjects and the patients.

3.3. Ethanol concentration

The ethanol concentration measured at the maximum volume breath tests showed a large range between 0.03 and 0.31 mg l^{-1}. This is due to the fact that the subjects consumed different alcoholic beverages and were not fasting prior to the tests, which affected the time aspect of the ethanol absorption and elimination, and also the maximum BrAC reached. For all subjects, both the healthy and sick, the ethanol concentration was slightly but consistently lower at the low volume breath tests (mean ± standard deviation of 0.14 ± 0.06 mg l^{-1}) compared to the maximal volume breath tests (0.16 ± 0.05 mg l^{-1}) (individual paired *t*-test: $p < 0.001$).

Table 1. Characteristics of the healthy subject and the patient groups, and the characteristics of the low and maximum volume breath tests. The statistical significance of the difference in values measured at the low and maximum volume breath tests (tested with paired *t*-tests) is presented with stars of significance in the table. Footnotes (a–f) refer to the result of the ANOVA tests between the healthy subject and the patient groups.

	Healthy subjects (*n*:21)			Patients (*n*:9)		
Age (years)						
Range	21–71			27–69		
Mean	45			57		
BMI						
Range	19.4–30.9			20.3–30		
Mean ± standard deviation	24.2 ± 3.2			25.7 ± 3.5		
VC (l)						
Range	2.8–7.0			2.5–6.1		
Mean ± standard deviation	4.9 ± 1.3			4.1 ± 1.2		
FEV_1 (l)						
Range	2.0–5.7			1.0–4.2		
Mean ± standard deviation	3.7 ± 1.0[a]			2.5 ± 1.0		
FEV_1/VC (%)						
Range	66.8–86.7			31.1–68.2		
Mean ± standard deviation	76.3 ± 6.3[b]			59.9 ± 12.0		
	Low volume		Maximal volume	Low volume		Maximal volume
Exhaled volume (l)						
Range	0.6–1.2 l		2.0–6.1 l	0.6–1.5 l		1.7–4.6 l
Mean ± standard deviation	0.9 ± 0.2 l		3.9 ± 1.2 l[c]	0.9 ± 0.2 l		2.9 ± 0.9 l
		**			**	
Exhalation time (s)						
Range	2.1–3.9 s		3.4–14.6 s	2.1–3.7 s		3.5–12.7 s
Mean ± standard deviation	2.8 ± 0.5		7.7 ± 2.7	2.7 ± 0.4 s		6.5 ± 2.9 s
		NS			NS	
Mean PCO_2 (kPa)						
Range	3.14–5.19		3.74–5.39	2.32–4.26		2.44–4.63
Mean ± standard deviation	4.08 ± 0.45[d]		4.39 ± 0.47[e]	3.51 ± 0.59		3.88 ± 0.70
		**			**	
Mean H_2O concentration (mg l^{-1})						
Range	34.7–40.5		37.8–41.9	35.1–39.7		37.4–40.2
Mean ± standard deviation	37.8 ± 1.4		40.0 ± 1.0[f]	37.7 ± 1.3		39.1 ± 1.2
		***			***	

[a] Significant difference (**) between healthy subjects and patients in FEV_1
[b] Significant difference (***) between healthy subjects and patients in FEV_1/VC.
[c] Significant difference between healthy subjects and patients in mean exhalation volume (**) during their maximum volume breath test.
[d] Significant difference (***) between healthy subjects and patients in mean PCO_2, during their low volume breath tests.
[e] Significant difference (**) between healthy subjects and patients in mean PCO_2, during their maximum volume breath tests.
[f] Significant difference (**) between healthy subjects and patients in mean H_2O concentration, during their maximum volume breath test.

3.4. Partial pressure of carbon dioxide

No significant difference in the PCO_2 could be found, neither between the two low volume tests, nor between the two maximum volume breath tests. The mean PCO_2 was significantly higher at the maximal volume than at the low volume breath tests for both the healthy subjects and the patients ($p < 0.01$, $p < 0.01$), table 1. The distribution of the subjects' PCO_2 for the maximum volume tests can be seen in figure 1. The mean PCO_2 for the healthy subjects was significantly higher than for the patients, for both the low ($p < 0.001$) and the maximum ($p < 0.01$) volume breath tests, table 1.

3.5. Water concentration

The mean concentration of H_2O for the maximum volume tests was significantly higher than for the low volume tests ($p < 0.001$), for both the healthy subjects and the patients, table 1. In the maximal volume breath tests the healthy subjects had a small but significantly higher H_2O concentration than the patients ($p < 0.01$), table 1. Figure 1 shows the distribution for the maximum volume breath tests.

3.6. Characteristics of the expirograms

Figure 2 shows a typical expirogram from a healthy subject. A characteristic feature is the late onset of CO_2 in comparison with both ethanol and H_2O. During the final phase, the concentration of each gas increases steadily with an almost constant slope. The slope is smaller for H_2O than for ethanol and CO_2. In the CO_2 curve the cardiac pulsations can be seen.

Figure 3 shows that the average time of the onset of the final phase occurs within 1 s for all three gases, although significantly later for the CO_2 signal. During the maximum

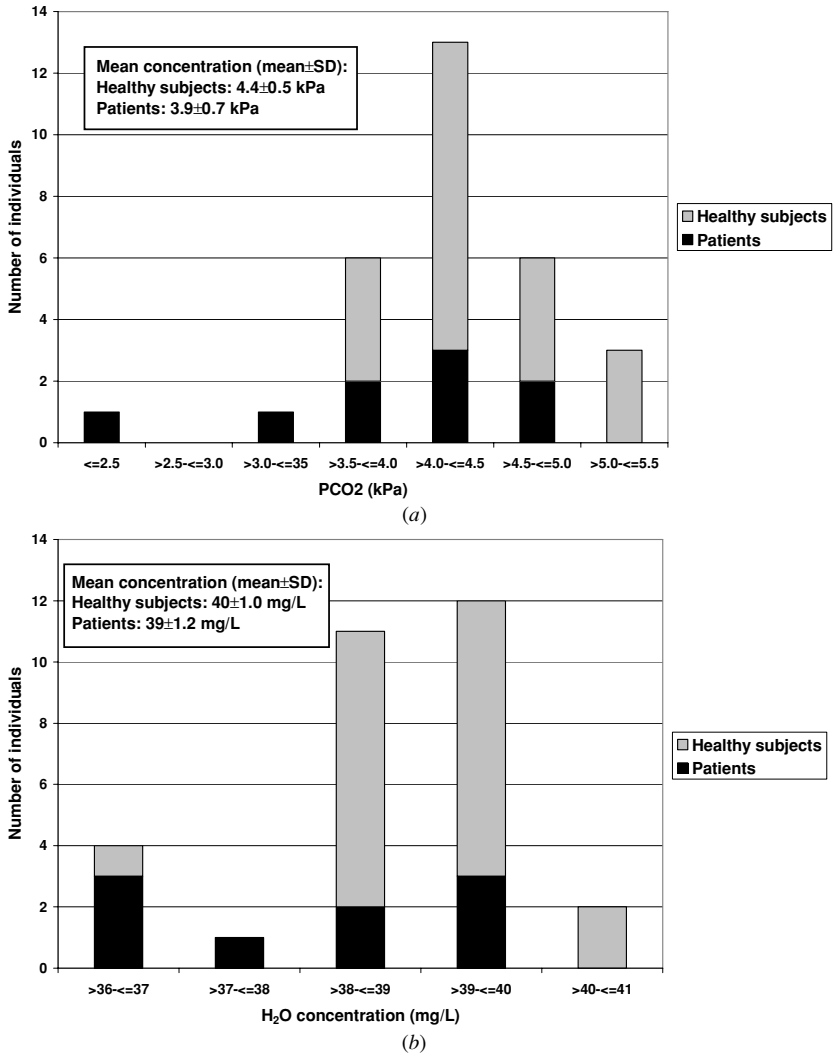


Figure 1. Distribution of the individuals' (*a*) mean PCO_2 and (*b*) mean H_2O concentrations for the maximum volume breath tests. The value is the mean concentration during the last second, for the two breath tests.

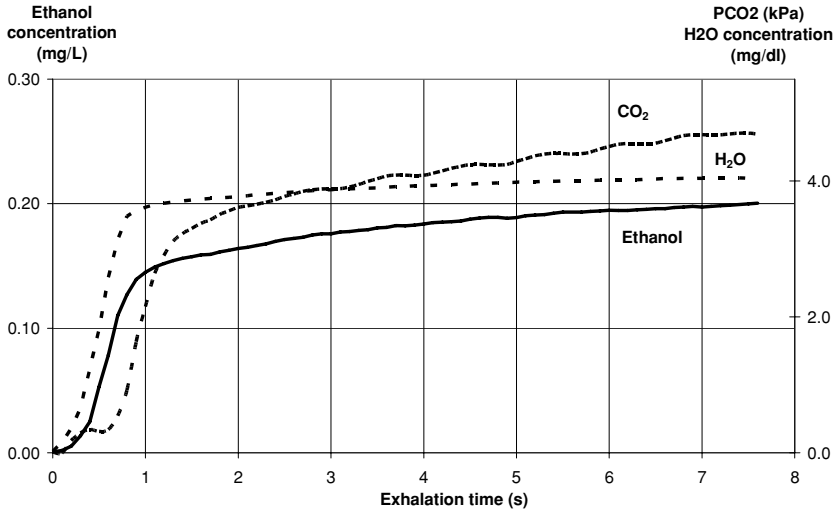


Figure 2. The ethanol, CO_2 and H_2O expirograms during a maximum volume breath test performed by a healthy test subject.

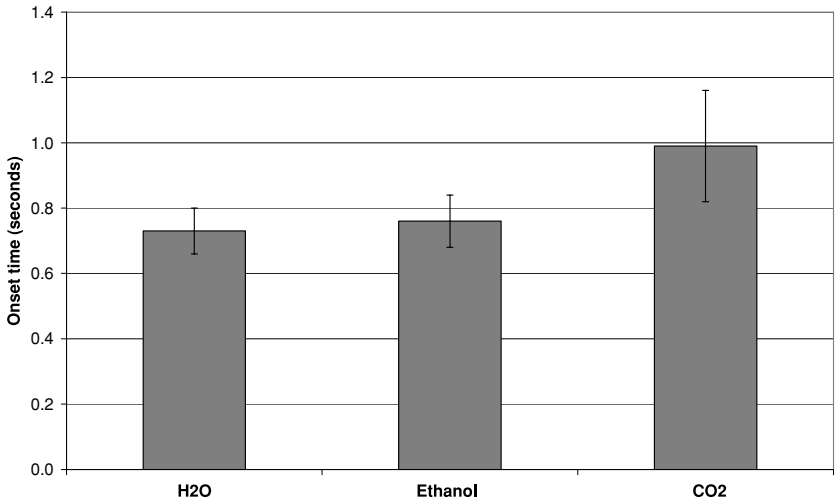


Figure 3. The mean and standard deviation of the time of onset for the ethanol, CO_2 and H_2O expirograms during the two maximum volume breath tests.

volume breath tests, the onset of the final phase for the CO_2 signal occurred on average 0.26 ± 0.14 s later than for H_2O ($p < 0.001$) and the ethanol ($p < 0.001$) signals which occurred almost simultaneously. After 2 s of a maximum volume expiration, the average ethanol concentration of all subjects had reached 85 ± 7% and PCO_2 78 ± 8% of the end value, whereas the average H_2O had reached 95 ± 2% of its end value.

Figures 4(*a*) and (*b*) show the relation between BrAC determined after 2 s compared to the end BrAC of the maximum volume breaths. In figure 4(*a*), the actual instantaneous concentrations at 2 s are plotted versus the end value measured with the reference instrument. As expected, most of the 2 s concentrations are lower than the end concentration, and a strong linear correlation is found, as presented in table 2. The measurements in patients exhibit larger scatter than the healthy subjects.

In figure 4(*b*) the BrAC determined by using the 2 s ratio in equation (1), with either CO_2 or H_2O as tracer gas, is plotted versus the end BrAC measured with the reference instrument. The ratio of the measured concentration of ethanol and the tracer gas was multiplied with the average end-expiratory values according to table 1 for each group. With CO_2 as tracer gas, most BrAC values were overestimated (located above the identity line), whereas the opposite behaviour was observed for the corresponding H_2O values. As in figure 4(*a*) the scatter is larger in patients than in the healthy subjects, and larger for the CO_2 determinations than for H_2O. This is shown in table 2.

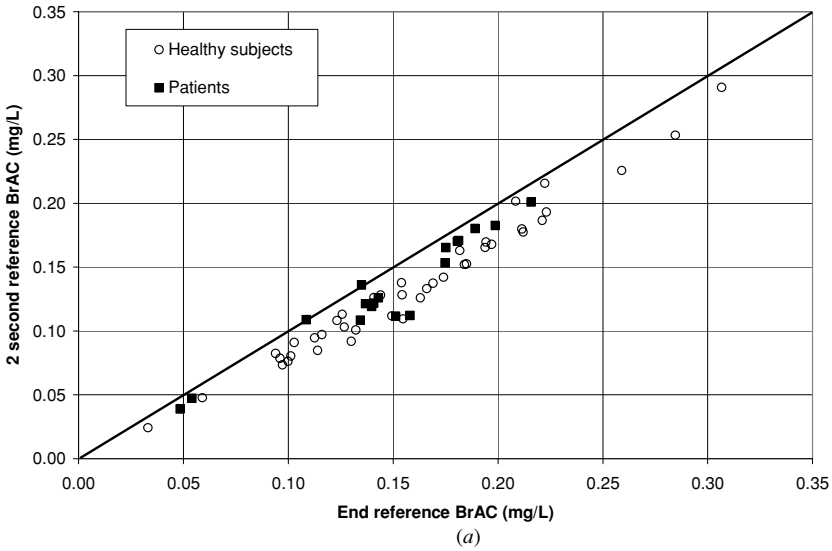
4. Discussion

Our results concerning the magnitude and distribution of end-expiratory CO_2 concentrations are consistent with values reported in the literature. It is generally taught that the mean arterial partial pressure of CO_2 is 5.1–5.3 kPa in healthy individuals, with a standard deviation of about 0.4–0.5 kPa [4, 12, 16–19]. It may be lower in patients with pulmonary embolism, normal or low in moderate COPD and asthma, and increased in more severe obstructive airway diseases. The difference between arterial and end-expiratory CO_2 concentration at rest is normally small, but larger in patients with chronic pulmonary disease [5, 15] and acute pulmonary embolism [5]. Modest inter-individual variations in end tidal PCO_2 in healthy subjects [2], and small variations over time for both arterial [18] and end tidal PCO_2 [2, 12] have been reported.

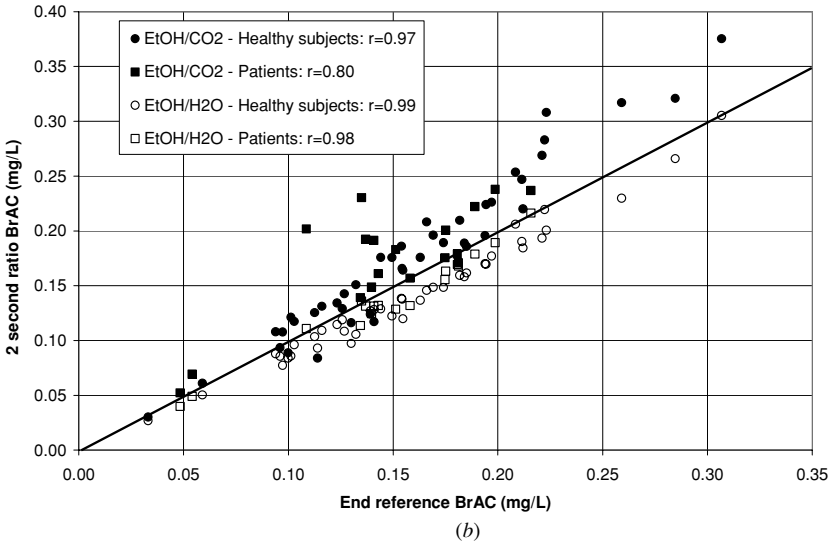
Our results show that the variability of end-expiratory H_2O is significantly smaller than that of CO_2, as expected from differences in etiology [14]. The observed variation in H_2O corresponds to a temperature variation of less than 0.5 °C, possibly partly due to significant differences in exhaled volume. The use of H_2O rather than CO_2 as tracer gas in contactless breath analysis comes logically to mind, and offers the added feature of temperature compensation when referring to (arterial) blood alcohol concentration [14]. However, other aspects should also be considered. For an instrument operating in a well-controlled indoor environment, it will be possible to accurately determine the ambient background H_2O level, but in outdoor applications, the background variations could be excessive. For comparison, the CO_2 background concentration is not expected to exceed 2% of the end-expiratory CO_2 [6].

The observed inter-individual variations in end-expiratory CO_2 and H_2O concentrations in our study are of the same order of magnitude as the tolerance for technical measurement errors of alcolocks (±15% according to EN50436-2) and evidential instruments (±5% according to OIML R126), respectively. The results of the present study thus provide support that the use of equation (1) for enabling contact-free breath alcohol analysis is feasible from this point of view.

Our study provides support for the early determination of BrAC, without compromise in accuracy. The results indicate that the random error will increase by 0.01–0.02 mg l^{-1} when taking a reading after 2 s instead of after 5 s. The designer of breath analysers is provided with the option of simply up-counting the 2 s value, or using a tracer gas ratio.



(*a*)



(*b*)

Figure 4. (*a*) The relation between the breath alcohol concentrations (BrAC) measured at 2 s and at the end of expiration, measured with the reference instrument. The identity line is shown in the graph. (*b*) The relation between the breath alcohol concentrations (BrAC) determined by using the 2 s ratio according to equation (1), using both CO_2 and H_2O as tracer gas, versus the end BrAC measured with the reference instrument. The correlation coefficients of the different series are indicated in the inset.

Table 2. Linear correlation between the 2 s BrAC (measured with the reference instrument or determined using CO_2 or H_2O as tracer gas) and the measured end reference BrAC, including correlation coefficients and residual standard deviation.

	Equation regression line	Correlation coefficient (R value)	Residual standard deviation (mg l^{-1})
2 s reference BrAC—all subjects	$y = 0.94\,x - 0.012$	0.98	0.022
2 s $EtOH/CO_2$ ratio BrAC—all subjects	$y = 1.20\,x - 0.010$	0.94	0.024
2 s $EtOH/H_2O$ ratio BrAC—all subjects	$y = 0.96\,x - 0.009$	0.99	0.009

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