

# The Impact of Breathing Pattern and Lung Size on the Alcohol Breath Test

MICHAEL P. HLASTALA<sup>1,2</sup> and JOSEPH C. ANDERSON<sup>3</sup>

<sup>1</sup>Department of Physiology and Biophysics, University of Washington, Box 356522, Seattle, WA 98195-6522, USA; <sup>2</sup>Department of Medicine, University of Washington, Box 356522, Seattle, WA 98195-6522, USA; and <sup>3</sup>Department of Bioengineering, University of Washington, Seattle, WA 98195-5061, USA

(Received 21 March 2006; accepted 29 September 2006; published online: 14 December 2006)

**Abstract**—Highly soluble gases exchange primarily with the bronchial circulation through pulmonary airway tissue. Because of this airway exchange, the assumption that end-exhaled alcohol concentration (EEAC) is equal to alveolar alcohol concentration (AAC) cannot be true. During exhalation, breath alcohol concentration (BrAC) decreases due to uptake of ethanol by the airway tissue. It is therefore impossible to deliver alveolar gas to the mouth during a single exhalation without losing alcohol to the airway mucosa. A consequence of airway alcohol exchange is that EEAC is always less than AAC. In this study, we use a mathematical model of the human lung to determine the influence of subject lung size on the relative reduction of BrAC from AAC. We find that failure to inspire a full inspiration reduces the BrAC at full exhalation, but increases the BrAC at minimum exhalation. In addition, a reduced inhaled volume and can lead to an inability to provide an adequate breath volume. We conclude that alcohol exchange with the airways during the single-exhalation breath test is dependent on lung size of the subject with a bias against subjects with smaller lung size.

**Keywords**—Ethyl alcohol, Modelling, Bronchial circulation, Airway gas exchange.

## INTRODUCTION

An assumption used in the development of the alcohol breath test (ABT) is that the ethanol concentration in the last part of the exhaled breath is equal to that in the alveolar gas. This long-held assumption is

the basis for justifying the ABT<sup>1</sup> as an accurate measure of blood alcohol concentration (BAC).

However, under normal circumstances, a single-exhalation alcohol breath test shows a gradually and continually increasing breath alcohol concentration (BrAC) if the subject exhales at a constant rate (Fig. 1). The end-exhaled alcohol concentration (EEAC) is always lower than the alveolar alcohol concentration (AAC). As more volume is exhaled the BrAC continues to increase. It has recently been shown that EEAC is less than AAC due to the exchange of alcohol in the airways during both inspiration and expiration.<sup>2,3,8</sup>

Earlier studies have examined the assumption of equality between end-exhaled and AAC by comparing ABT values with blood measurements and found a considerable amount of variation in the ratio of EEAC to BAC. For further evidence regarding the lack of end-exhaled and alveolar equality, two studies<sup>10,13</sup> have shown that EEAC is approximately 15–20% lower than AAC on average (obtained using isothermal rebreathing). The explanation for this variation has been discussed before.<sup>2,8</sup> The physiological importance of the discrepancy between EEAC and AAC are the subject of this study.

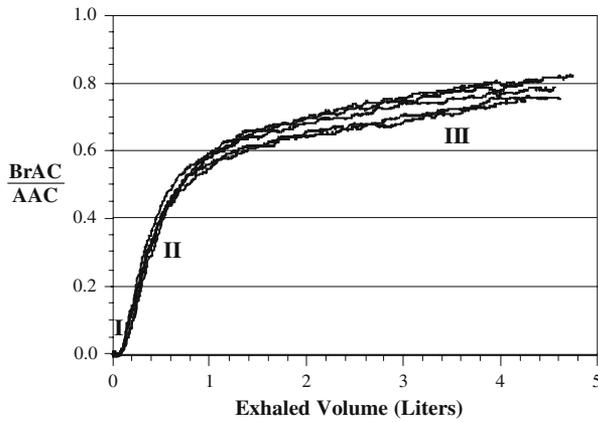
Two recent studies have demonstrated a relationship between the blood:breath<sup>2</sup> ratio (BBR) for alcohol and body weight<sup>14</sup> or gender<sup>11</sup> in normal subjects. Thus, it may be possible that the BBR for alcohol is dependent on physiological or anatomic differences among individual subjects.<sup>9</sup> One anatomical feature, lung size, depends on body size, age, gender and ethnicity.

When an ABT is performed, subjects are not required to control either the volume inhaled or the

Address correspondence to Michael P. Hlastala, Division of Pulmonary and Critical Care Medicine, University of Washington, Box 356522, Seattle, WA 98195-6522, USA. Electronic mail: hlastala@u.washington.edu

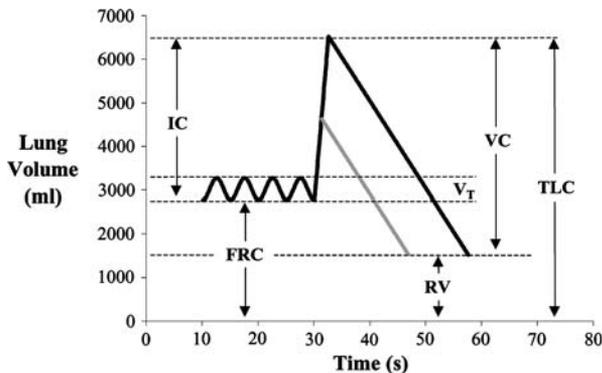
<sup>1</sup> A list of abbreviations used in this paper is shown in Table 1.

<sup>2</sup> The blood:breath ratio is equal to the ratio of end-exhaled alcohol concentration divided by blood alcohol concentration (EEAC/BAC).



**FIGURE 1.** Exhaled ethanol concentration, normalized by alveolar alcohol concentration, over a full exhalation at a constant flow (From<sup>4</sup>).

volume exhaled. Under normal resting conditions, a subject inhales and exhales a tidal volume ( $V_T$ ) beginning from a functional residual capacity (FRC) (Fig. 2). When administering an ABT, the subject is asked to inhale ambient air and exhale into the breath test instrument as far as possible. Although the subject is asked to take a full inhalation, he/she is not required to inhale to total lung capacity (TLC). Because it takes some effort to inhale from FRC to TLC, a volume known as inspiratory capacity (IC), it is most likely that a subject's lung size is less than TLC at the time exhalation is initiated (gray line in Fig. 2). Some subjects may exhale after inhaling only a very small volume. The expiratory volume also varies naturally between tests. To obtain a valid ABT, a subject can exhale any amount between the minimum exhaled volume required by the particular breath test instru-



**FIGURE 2.** Lung volume tracing for a single exhalation maneuver. A subject breathes tidal volumes ( $V_T$ ) at functional residual capacity (FRC) and then expands his lungs to total lung capacity (TLC) by inhaling a volume equal to the inspiratory capacity (IC). The subject exhales his vital capacity (VC) at a constant flow rate, which causes his lung volume to approach residual volume (RV). The gray tracing shows the lung volume dimensions if the subject only inhales 50% of IC during the prolonged inhalation.

**TABLE 1.** Glossary of abbreviations.

AAC	Alveolar alcohol concentration
ABT	Alcohol breath test
ATS	American Thoracic Society
BAC	Blood alcohol concentration
BBR	Blood:breath ratio
BrAC	Breath alcohol concentration
EEAC	End-exhaled alcohol concentration
FRC	Functional residual capacity
IC	Inspiratory capacity
RR	Respiratory rate
RV	Residual volume
TLC	Total lung capacity
VC	Vital capacity
VI	Volume of inspiration
$V_T$	Tidal volume

ment (usually either 1.1 or 1.5 l)<sup>5</sup> and the maximum exhaled volume of the lungs, which is limited by the vital capacity (VC), the difference between TLC and residual volume (RV). The exhaled volume depends on the mechanical limitations of the lungs and the relative effort of the subject, which may vary from time to time. For the calculations below, we assume that an average exhaled volume is the average of the minimum volume (1.5l) and the VC.

Lung volume varies substantially among individual human subjects (both normal and with lung disease). In 1991, the American Thoracic Society (ATS) compiled data from three international societies (the ATS, the European Community for Coal and Steel, and the European Society for Clinical Respiratory Research) and published a summary document of lung volumes in normal, non-smoking, human subjects for clinical use in interpretation of pulmonary function tests.<sup>1</sup> Collectively, the summary of data (Table 2) shows that, in adults, lung volume increases with body height and decreases with age. Lung volumes are smaller in African Americans, both males and females, than their Caucasian height-, age-, and gender- matched counterparts. For either racial group, females have smaller vital capacities than males. Because individuals with smaller lung size must exhale a greater fraction of their lung volume to fulfill any minimum volume requirement for a valid sample, we reasoned that a subject with a smaller lung volume would exhale farther along the increasing exhaled partial pressure profile before an end-exhaled sample is taken (see Fig. 3). Consequently, the alcohol breath test would tend to overpredict the BAC for individuals with small lung volumes.

We use a mathematical model<sup>2</sup> to explore the dependence of BrAC on lung size (a function of height, age, gender, and race), inspiratory volume, and expiratory volume. We hypothesize that BBR will depend on the subject physical characteristics as well as the level of cooperation.

**TABLE 2. Predicted forced vital capacity for healthy, Non-smoking subjects: Caucasian and African American, male and female.**

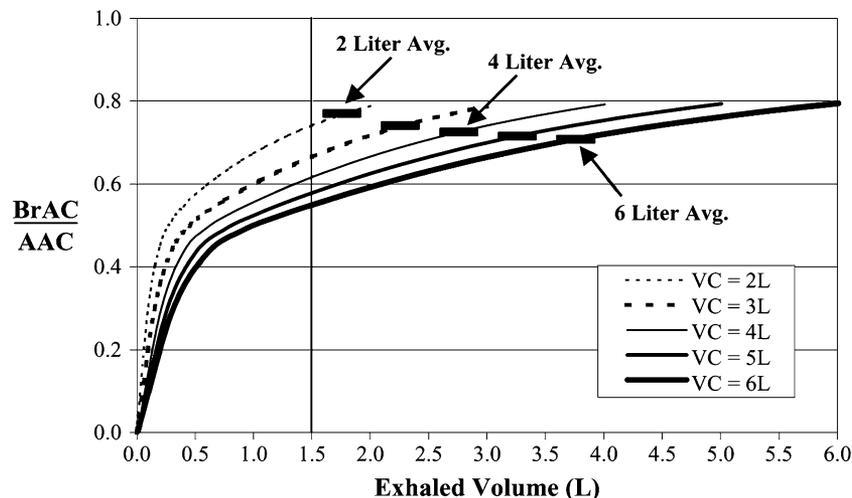
Height (in)	Height (m)	Age (Year)	Predicted vital capacity (l)			
			Caucasian		African-American	
			Male	Female	Male	Female
51	1.30	20	2.587	2.137	2.866	2.244
51	1.30	40	2.195	1.721	2.430	1.810
51	1.30	60	1.803	1.305	1.994	1.376
55	1.40	20	3.178	2.560	3.191	2.541
55	1.40	40	2.786	2.144	2.755	2.107
55	1.40	60	2.394	1.728	2.319	1.673
59	1.50	20	3.770	2.984	3.517	2.838
59	1.50	40	3.378	2.568	3.081	2.404
59	1.50	60	2.986	2.152	2.645	1.970
63	1.60	20	4.361	3.407	3.842	3.135
63	1.60	40	3.969	2.991	3.406	2.701
63	1.60	60	3.577	2.575	2.970	2.267
67	1.70	20	4.952	3.830	4.167	3.432
67	1.70	40	4.560	3.414	3.731	2.998
67	1.70	60	4.168	2.998	3.295	2.564
71	1.80	20	5.544	4.254	4.493	3.729
71	1.80	40	5.152	3.838	4.057	3.295
71	1.80	60	4.760	3.422	3.621	2.861
75	1.90	20	6.135	4.677	4.818	4.026
75	1.90	40	5.743	4.261	4.382	3.592
75	1.90	60	5.351	3.845	3.946	3.158
79	2.00	20	6.727	5.100	5.144	4.323
79	2.00	40	6.335	4.684	4.708	3.889
79	2.00	60	5.943	4.268	4.272	3.455

## METHODS

### *Mathematical Model*

A detailed description of the model has been published previously.<sup>2,4,15</sup> Only the essential features will

be described here. The airway tree has a symmetric bifurcating structure through 18 generations. The respiratory bronchioles and alveoli are lumped together into a single well-mixed alveolar unit. Axially, the airways are divided into 480 control volumes.



**FIGURE 3.** Effect of lung size (as represented by vital capacity) on the exhalation profile. At a given exhaled volume (e.g., 1.5 l), BrAC/AAC is inversely related to lung size. The model simulated a lung performing an IC inhalation ( $IC = 0.75 \cdot VC$ ) and a VC exhalation at a rate of  $200 \text{ ml s}^{-1}$ . The horizontal solid bars indicate the end-exhaled normalized BrAC at an average exhaled volume. The relative average end-exhaled breath to alveolar concentration ratios are 0.767, 0.722 and 0.705 for subject vital capacities of 2.0, 4.0, and 6.0 l, respectively.

Radially, the airways are divided into six concentric layers: (1) the airway lumen, (2) a thin mucous layer, (3) connective tissue (epithelium and mucosal tissue), (4) the bronchial circulation, (5) the adventitia, and (6) the pulmonary circulation. Functionally, the upper respiratory tract and cartilaginous airways (generation  $< 10$ ) only have the first four layers. Within each radial layer, concentration and temperature values are bulk averages for the entire layer. Mass and energy are transported between luminal control volumes by bulk convection and axial diffusion. Radial transport between the gas phase and mucous layer is described with heat and mass transfer coefficients. Radial transport of water and soluble gas between concentric layers occurs via filtration (from bronchial circulation to mucus) and diffusion (Fick's law). In the alveolar unit, the concentration of soluble gas is allowed to vary with time and depends on the pulmonary blood flow, ventilation, blood solubility, and concentration of soluble gas in the incoming blood as described by a mass balance on the alveolar compartment.

Because airway volume increases with increasing lung size, the lengths and diameter of the intraparenchymal airways were scaled to ensure the ratio of the airway volume to the VC was constant. Since the VC of the Weibel lung model is  $\sim 5000$  ml, these dimensions were scaled by the factor  $(VC/5000)^{1/3}$ . None of these airway dimensions changed dynamically during the breathing cycle. The dimensions of the airway wall compartments were calculated using data and a method outlined previously.<sup>2</sup>

Mass and energy balances around a control volume produce three partial-differential equations in time,  $t$ , and space,  $z$  and nine ordinary differential equations. The equations are solved simultaneously for the following 12 dependent variables: the mole fraction of soluble gas in the air, mucous, connective tissue, bronchial bed, and adventitial tissue layers; the temperature of the air, mucous, connective tissue, bronchial bed, and adventitial tissue layers; the mole fraction of water in the air; and the mucous thickness. The 12 differential equations are solved numerically using previously published boundary conditions.<sup>2</sup> The spatial derivatives are approximated by upwind finite difference while the time derivatives are solved using LSODE, an integrating software package developed by Hindmarsh.<sup>7</sup>

### *Computer Simulations*

Before an ABT was simulated, the model first must reach breath-to-breath steady-state conditions. The temperature, water concentrations, and ethanol concentrations within the mathematical model were

brought to steady-state conditions by simulating tidal breathing at FRC. A respiratory rate of  $12 \text{ br min}^{-1}$ , a sinusoidal flow waveform, and a tidal volume equal to 10% of VC were used for the case study (Table 3). For the parameter study, tidal volume was varied between 200 and 600 ml in 100 ml increments. The inspired air temperature and relative humidity were set to  $23^\circ\text{C}$  and 50%, respectively. The bronchial blood flow rate was set to  $1 \text{ ml s}^{-1}$ . The concentration of ethanol in the pulmonary arterial blood was constant and equal to  $0.10 \text{ g dl}^{-1}$  of blood. Steady-state conditions were reached when the end-exhaled water and ethanol concentrations changed by less than 0.1% between breaths. Then, the model simulated a single inhalation of a volume equal to or a fraction of IC, the volume from FRC to TLC, at a constant rate of  $1500 \text{ ml s}^{-1}$ . Inspiratory capacity was approximated to be 75% of the VC.<sup>6</sup> Then, the model simulated a prolonged exhalation; the lung was emptied at a rate of  $200 \text{ ml s}^{-1}$  until the lung volume reached RV.

## RESULTS

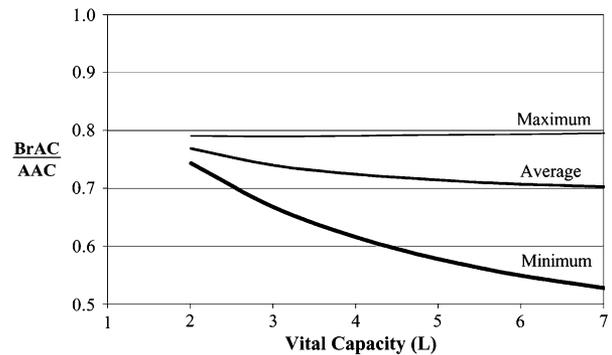
For highly soluble gas like ethyl alcohol, the exhaled concentration continues to increase with continued exhalation due to airway gas exchange. An example of an exhaled ethyl alcohol profile is shown in Fig. 1. In this example, a male subject with a BAC  $\sim 0.09 \text{ g/dl}$  inhaled quickly to TLC, exhaled at a constant flow rate, and stopped exhalation at RV.<sup>4</sup> Several different expiratory profiles for the same subject are shown. During exhalation at a constant flow rate, the exhaled ethanol concentration rises continuously during the final phase (phase III) of the ethanol profile. When the subject stops exhalation (either due to reaching RV or simply because the subject chooses to stop), the alcohol concentration plotted against time levels off because exhalation has stopped and no new air enters the breath test machine.<sup>8</sup> At this time, a sample is taken and assumed to be "alveolar" in nature. However, any breath sample is "always" lower in alcohol concentration than AAC. The classical interpretation assumes that the EEAC is related to the BAC with an average BBR of 2100. This factor neglects the exchange of alcohol with the airways of the lungs and any variability in this ratio among individuals.

From the model's predictions of exhaled ethanol profiles from human subjects,<sup>4</sup> we can describe the mechanisms underlying ethanol exchange in the airways. As fresh air is inhaled, it absorbs ethanol from the mucous layer, thereby depleting the ethanol concentration in the airway wall. Because of the small bronchial blood flow ( $Q_{br}$ ) and the significant diffusion barrier between the bronchial circulation and mucous

layer, the mucus is not replenished with ethanol before exhalation begins. During exhalation, respired air encounters a lower concentration of ethanol in the mucus and, therefore, a large driving force for the deposition of ethanol onto the mucus. This large air-to-mucus gradient promotes recovery of ethanol by the mucous layer, decreases the ethanol concentration in the air, and delays the rise in ethanol concentration at the mouth. A large (small) air-to-mucus gradient causes a slowly (rapidly) increasing phase III slope. These absorption-desorption phenomena decrease the ethanol concentration leaving the lung (relative to the alveolar concentration) throughout exhalation and are the major mechanisms of pulmonary ethanol exchange.

The mathematical model simulated the effect of lung size on the exhalation profile (Fig. 3). After a steady-state was reached during tidal breathing ( $RR = 12 \text{ br min}^{-1}$  and  $V_T = 400 \text{ ml}$ ), the model simulated a full inhalation from FRC to TLC and then a constant ( $200 \text{ ml s}^{-1}$ ) exhalation to RV. These conditions were simulated in five lung sizes as represented by the VC that varied from 2 l to 6 l. The normalized BrAC after a maximum exhalation (to RV) was  $\sim 0.79$  for all five lung sizes and appears to be unaffected by lung size (i.e., VC). However, many times subjects do not exhale their entire VC and, in addition, most alcohol breath-testing instruments only require a minimum exhaled volume (e.g., 1.5 l) before a breath test is acceptable. We examined the normalized BrAC in Fig. 3 after 1.5 l of air had been exhaled from lungs of different sizes: small ( $VC = 2 \text{ l}$ ), medium ( $VC = 4 \text{ l}$ ) and large ( $VC = 6 \text{ l}$ ). The normalized BrAC was 0.74, 0.61, and 0.55, respectively. At this exhaled volume, the ratio of change in normalized BrAC to change in lung size is  $-0.048 \text{ l}^{-1}$ . Additionally, we examined how lung size affected the normalized BrAC (Fig. 3) after an average exhalation. We assumed that, on average, an individual would exhale a volume that is the mean of the minimum (1.5 l) and maximum (VC) volume. Thus, for an individual with  $VC = 6 \text{ l}$ , an average exhaled volume (after an IC inhalation) is 3.75 l and results in a normalized BrAC of 0.705. Subjects with smaller lung size, 4 and 2 l, and providing an average exhalation have normalized BrAC of 0.722 and 0.767, respectively. For an average exhalation, individuals with smaller lung size provide BrAC samples that are greater than those with larger lung size because of the minimum exhalation volume requirement in combination with the mechanics of airway gas exchange. The effect of lung size on this average BrAC is  $-0.015 \text{ l}^{-1}$ . Thus, a one liter increase in VC decreases the normalized BrAC at this average volume by 0.015.

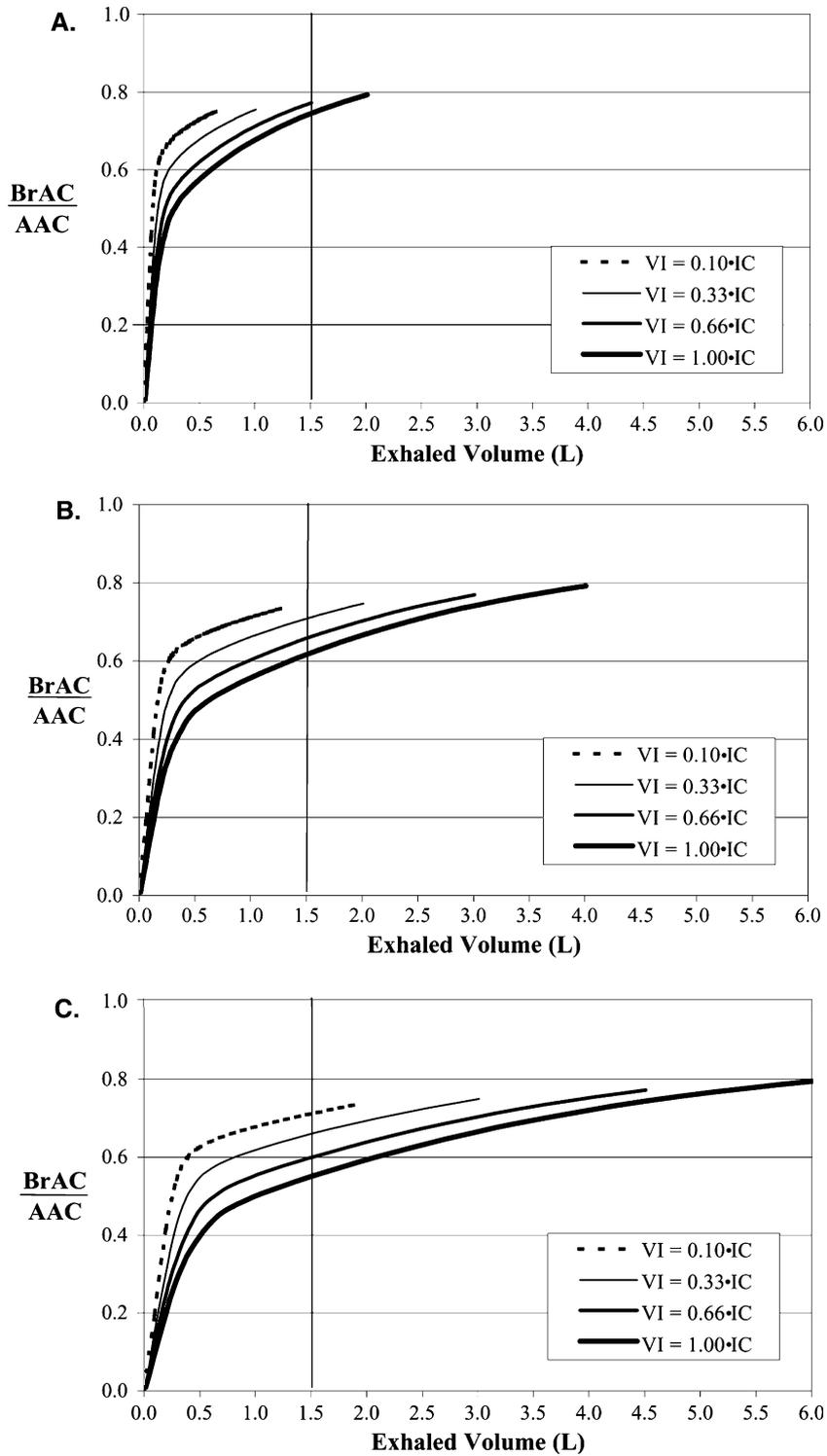
The minimum, average, and maximum BrAC values for subjects with different vital capacities are shown in



**FIGURE 4.** The relationship between normalized breath alcohol concentration and lung size (based on vital capacity) are shown for IC inhalations followed by different exhaled volumes: maximum (VC), average and minimum (1.5 l). See text for definitions.

Fig. 4. Results are shown for vital capacities varying between 2.0 and 7.0 l and for an inspiration of a full IC. As lung VC increases, the average BrAC decreases. For lungs with vital capacities less than 2.0 l, it is often difficult for the subject to fulfill the 1.5 l minimum exhalation volume.

We simulated the effect of inspiratory volume on the exhalation profile for a given lung size (Fig. 5). Once a periodic steady-state was achieved ( $V_T = 400 \text{ ml}$ ), the model simulated an inhalation from FRC. The inhaled volume depended on the simulation. For a maximum IC inhalation, the inhaled volume was assumed to be 0.75·VC. Smaller inhaled volumes of 66%, 33%, and 10% of IC were simulated. After inhalation, a constant ( $200 \text{ ml s}^{-1}$ ) exhalation to RV was simulated. Figure 5 shows the effect of inhaled volume on normalized BrAC from three lungs of varying size,  $VC = 2 \text{ l}$  (panel A), 4 l (panel B) and 6 l (panel C). For every VC studied, a decrease in inhaled volume causes: (1) an increase in normalized BrAC at a given exhaled volume; (2) an increase in the normalized BrAC from a minimum (1.5 l) and average exhalation; and (3) a decrease in the normalized BrAC after a maximum exhalation to RV. Specifically, a decrease in inspired volume in a lung with  $VC = 4 \text{ l}$  causes the normalized BrAC after a minimum exhalation to increase by  $0.048 \text{ l}^{-1}$ , the normalized BrAC after an average exhalation to increase  $0.004 \text{ l}^{-1}$ , and the normalized BrAC after a maximum exhalation to decrease  $0.022 \text{ l}^{-1}$ . These rates of change of normalized BrAC per inspired volume are a function of VC. A two liter increase (decrease) in VC causes these rates to decrease (increase) by 15%. As compared with individuals with small VC, subjects with large VC can choose from more possible inspired volumes that will result in a minimum exhaled volume and an acceptable breath test. We examined the effect of tidal volume on BrAC and found that a 100 ml increase in tidal volume



**FIGURE 5.** Effect of inspiratory volume on the exhalation profile for a given lung size. At a given exhaled volume (e.g., 1.5 l), BrAC/AAC is inversely related to volume of gas inhaled (VI). The model simulated a lung inhaling a volume, VI, from FRC and exhaling to RV at a rate of  $200 \text{ ml s}^{-1}$ . VC represents lung size. For each panel, VC is 2 l (panel A), 4 l (panel B), and 6 l (panel C).

decreased all three measures (minimum, average, and maximum exhalation) of normalized BrAC by  $\sim 0.01$ .

The variation of lung volume among individuals of differing gender, body height and age are shown in

Table 2. Typical values are presented in Table 2 for normal Caucasian and African American male and female adults. Lung volumes are greater in equally sized and aged males compared with females, in Caucasians

compared with African Americans and in younger adults compared with older adults. Table 3 shows the predicted BrAC normalized by AAC taken from Fig. 4. The predictions of the mathematical model show a greater BrAC (relative to AAC) in all cases comparing a smaller lung volume with a larger lung volume.

## DISCUSSION

Alcohol breath testing-instruments require a minimum exhaled volume before a breath sample is taken at the end of an exhalation. For a subject with a small lung size, a greater fraction of the VC must be exhaled before the sample criteria are fulfilled. Most breath test instruments require a minimum exhalation pressure (or flow) for a minimal duration of time (4–6 s and a minimal exhalation volume (between 1.1 l and 1.5 l). For our calculations, we chose 1.5 l as the minimum exhaled volume. Once the minimum criteria are fulfilled, a sample will be taken when the change in exhaled alcohol partial pressure levels off (always achievable when the exhaled flow is stopped). For a subject with a VC of 6 l using a BAC Verifier Datamaster (minimum volume is 1.5 l), a sample can be obtained any where between 1.5 and 6.0 l of exhalation because the subject may choose to stop exhalation any where between 1.5 l and VC. For a subject with a VC of 2 l, a sample can be obtained using a BAC Verifier Datamaster anywhere between 1.5 and 2.0 l of exhalation. A subject with a small lung size will proceed further up the increasing BrAC exhaled profile before a sample is taken (Fig. 3).

One of the fundamental assumptions of the ABT is that during exhalation, the BrAC continues to increase until alveolar air reaches the mouth. At this point the BrAC levels off. This observation has been assumed to indicate that EEAC is equal to AAC. However, breath alcohol always increases during exhalation as air moves out of the mouth,<sup>4</sup> never reaching AAC. The flatness of the slope of the exhaled alcohol profile simply means that exhalation has stopped. It is not an indication of alveolar air. Additional support of this idea follows from two studies using isothermal rebreathing in human subjects,<sup>10,13</sup> which showed that EEAC (with a single-exhalation maneuver) is always less than AAC. The difference, on average, is approximately 15%<sup>8</sup> and consistent with the ideas described in this paper. Individuals with smaller lung size are predicted to have a smaller difference between EEAC and AAC such that an individual with a smaller lung size, would have an ABT that is greater than an individual with a larger lung size.

The major thesis of this paper is that lung size and breathing pattern influence the BrAC reading determined with a breath-testing instrument. Figure 3 shows exhaled alcohol profiles for subjects taking a full inspiration followed by a full expiration. For each lung size (represented by VC), the end exhaled BrAC is the same. In other words, if a subject takes a full inspiration followed by a full exhalation, there would be no size dependence. If these subjects were to exhale just to the minimum volume requirement (1.5 l), the greatest discrepancy is predicted between subjects with differing lung size. Every thing else being equal (including BAC), the subject with the smallest lung size would

TABLE 3. Relative BrAC comparisons.

	Predicted VC (l)	BrAC/AAC		
		Min	Avg	Max
55" vs. 75" – Male 40 Years				
55" Male – 40 Years	2.786	0.681	0.747	0.794
75" Male – 40 Years	5.743	0.509	0.675	0.770
BrAC Ratio of small to large volume		1.34	1.11	1.03
67" Female vs. 67" Male – 40 Years				
67" Female – 40 Years	3.414	0.629	0.723	0.785
67" Male – 40 Years	4.560	0.560	0.696	0.776
BrAC Ratio of small to large volume		1.12	1.04	1.01
67" AA Male vs. 67" Caucasian Male – 40 Years				
67" AA Male – 40 Years	3.731	0.607	0.714	0.782
67" Caucasian Male – 40 Years	4.560	0.560	0.696	0.776
BrAC Ratio of small to large volume		1.08	1.03	1.01
75" Male – 60 Years vs. 20 Years				
75" Male – 60 Years	5.544	0.516	0.678	0.771
75" Male – 20 Years	6.351	0.487	0.667	0.767
BrAC Ratio of small to large volume		1.06	1.02	1.00

have the greatest BrAC. Table 3 summarizes this effect by comparing the relative ratio of BrAC between two hypothetical subjects that differ in height, gender, race, or age. Comparing a male and female of the same height, the female has a minimum exhalation BrAC that is approximately 12% greater than the male. Comparing a 55-inch tall male with a 75-inch tall male, at minimum exhalation, the smaller male has a 34% greater BrAC than the taller male. With a minimum exhalation, the overestimate for the smaller lung individual is substantial.

On the average, a subject with a valid breath test can exhale to any point between the minimum volume and the maximum exhalation. When the subject stops exhaling, new breath is no longer being delivered for analysis. Therefore, the BrAC levels off when plotted against time. An average of the different exhalation volumes would be approximately equal to the mean of the volumes exhaled at 1.5 l and the maximum exhalation. For hypothetical subjects that differ in either their height, gender, race or age, the ratios of average BrAC between matched subjects are shown in Column 4 of Table 3. Comparing a 67-inch tall 40-year-old male and with a female of the same height and age, the female has an average exhaled BrAC that is approximately 4% greater than the male. Comparing a 55-inch tall 40-year-old male with a 75-inch tall 40-year-old male, at average exhalation, the smaller male has an 11% greater BrAC than the taller male. Comparing a 67-inch tall 40-year-old African American male with a 67-inch tall 40-year-old Caucasian male, at average exhalation, the African American male has a 3% greater BrAC than the Caucasian male. Comparing a 75-inch tall 20-year-old Caucasian male with a 75-inch tall 60-year-old Caucasian male, at average exhalation, the African American male has a 2% greater BrAC than the Caucasian male. With an average exhalation, the bias for the smaller lung individual is less than the bias predicted for the minimum exhalation. The largest discrepancy is related to body height because of the greatest difference in relative lung size.

The mechanism of airway gas exchange has been described briefly above and used previously to explain how ethanol exchanges in the lung.<sup>2-4</sup> Based on this mechanism of ethanol exchange, the effect of changes in inspired volume on BrAC can be understood. A small inhaled volume will reduce the ethanol concentration in the airway mucus and tissue layers to a lesser extent than a large inhaled volume. During exhalation, the former case will have a smaller air-to-mucus gradient than the latter case. A smaller gradient causes less ethanol to be deposited to the airway surface and, as a result, the BrAC rises more rapidly when the inhaled volume is small than when it is large (Fig. 5). The maximum BrAC/AAC depends on the ratio of

inspiratory-to-expiratory time, but because the flow rates are prescribed, inhaled volumes are defined by percent of VC and exhalation always proceeds to RV, the maximum BrAC/AAC only depends on inhaled volume (VI) as shown in Fig. 5.

The ability to fulfill the minimum exhalation criteria for a breath test instrument is limited in individuals with smaller lungs and less than full inhalations. Figure 5 illustrates the combined impact lung size and inspiratory volume have on the ability to provide a minimum sample volume. As the size of the individual's lungs decrease, it becomes more important to inspire a greater volume before exhalation. This finding is consistent with the observations of Jones and Andersson<sup>12</sup> showing the probability of failing to provide a minimum sample is greater in females than males. Both genders show an increase in the probability of an insufficient sample with increasing age.

There are two recent studies that can be used to compare with our model predictions. Skåle *et al.*<sup>14</sup> and Jones and Andersson<sup>11</sup> determined the blood-breath ratio (or partition ratio) for several subjects (male and female) with varying heights, ages and body weight. Jones studied 9 male and 9 female subjects and found average BBRs of  $2553 \pm 576$  for males and  $2417 \pm 494$  for females. Although not statistically significant, the trend agrees with our predictions. The ratio of females to males is 1.056. The smaller lung size females had a 5.6% greater BrAC than the males. Skåle *et al.* studied 9 male and 15 female subjects and found that the blood-breath ratio was dependent on body weight. The average BBR for subjects with body weights of 50–70 kg was approximately 2250 while the BBR for subjects with body weights of 90–100 kg was approximately 2476. The ratio is 1.10. The BrAC for the smaller subjects was 10% greater than the larger subjects. Neither of these two papers measured lung VC as this was not part of their hypotheses. So we cannot directly compare our data. However the trends are consistent with the hypothesis put forward in this paper that individuals with smaller lung size have greater BrAC in comparison to the BAC<sup>3</sup>.

The present hypothesis is consistent with published data and with the mechanisms of pulmonary gas exchange. We encourage future investigators to include

<sup>3</sup> The Blood-Breath Ratio (BBR) is a commonly used term in forensic science. Because alcohol is a very highly soluble gas, the ratio of concentration in the blood normalized by that in the breath is a very large number (typically around 2000). For a given Blood Alcohol Concentration (BAC), the Breath Alcohol Concentration (BrAC) is about  $1/2000 \times \text{BAC}$ . With smaller lung volumes, the BrAC is greater, hence the BBR ( $= \text{BAC}/\text{BrAC}$ ) is lesser. In one case the BrAC is in the numerator (BrAC/AAC). In the other case, the BrAC is in the denominator. So a greater BBR is the same as a lesser BrAC/AAC.

the measurement of lung VC with the measurements of BBR in order to provide data to test our hypothesis. Surely, if there is anatomically dependent variation in the alcohol breath test, it is important to make corrections for the bias of the test. Once these data are obtained, several possible alternative solutions can be used: appropriate corrections to the BrAC values can be made; adjustable legal limits can be used for individuals of differing lung size; or rebreathing can be used to obtain a better sample of AAC.

In conclusion, alcohol exchanges between the respired air and the airway tissue during both inspiration and expiration. This airway gas exchange causes the exhaled alcohol concentration to always be less than the AAC. A consequence of this airway exchange is that BrAC depends on lung size and the amount of effort provided by the subject.

#### ACKNOWLEDGMENTS

This work was supported, in part, by National Institute for Biomedical Imaging and Bioengineering Grant T32 EB001650 and by National Heart, Lung, and Blood Institute Grants HL24163 and HL073598.

#### REFERENCES

- <sup>1</sup>American Thoracic Society. Lung function testing: Selection of reference values and interpretative strategies. *Am. Rev. Respir. Dis.* 144:1202–1218, 1991.
- <sup>2</sup>Anderson, J. C., A. L. Babb, and M. P. Hlastala. Modeling soluble gas exchange in the airways and alveoli. *Ann. Biomed. Eng.* 31:1402–1422, 2003.
- <sup>3</sup>Anderson, J. C. and M. P. Hlastala. Breath tests and airway gas exchange. *Pulm. Pharmacol. Ther.* in press, 2006.
- <sup>4</sup>George, S. C., A. L. Babb, and M. P. Hlastala. Dynamics of soluble gas exchange in the airways. III. Single-exhalation breathing maneuver. *J. Appl. Physiol.* 75:2439–2449, 1993.
- <sup>5</sup>Harding, P. Methods for breath analysis. In: *Medical–Legal Aspects of Alcohol* (4th ed.), edited by Garriott J. C. Tucson: Lawyers & Judges Publishing Co., 2003, pp. 185–211.
- <sup>6</sup>Hildebrandt, J. Structural and mechanical aspects of respiration. In: *Textbook of physiology*, edited by Patton H. D., Fuchs A. F., Hille B., Scher A. M., and Steiner R. Philadelphia: W.B. Saunders Co., 1989, pp. 991–1011.
- <sup>7</sup>Hindmarsh, A. L. SODE (computer software). Laurence Livermore Laboratory, Livermore, CA.
- <sup>8</sup>Hlastala, M. P. The alcohol breath test – a review. *J. Appl. Physiol.* 84:401–408, 1998.
- <sup>9</sup>Hlastala, M. P. Invited editorial on “the alcohol breath test”. *J. Appl. Physiol.* 93:405–406, 2002.
- <sup>10</sup>Jones, A. W. Role of rebreathing in determination of the blood–breath ratio of expired ethanol. *J. Appl. Physiol.* 55:1237–1241, 1983.
- <sup>11</sup>Jones, A. W. and L. Andersson. Comparison of ethanol concentrations in venous blood and end-expired breath during a controlled drinking study. *Forensic Sci. Int.* 132:18–25, 2003.
- <sup>12</sup>Jones, A. W. and L. Andersson. Variability of the blood/breath alcohol ratio in drinking drivers. *J. Forensic. Sci.* 41:916–921, 1996.
- <sup>13</sup>Ohlsson, J., D. D. Ralph, M. A. Mandelkorn, A. L. Babb, and M. P. Hlastala. Accurate measurement of blood alcohol concentration with isothermal rebreathing. *J. Stud. Alcohol* 51:6–13, 1990.
- <sup>14</sup>Skåle, A. G., L. Slørdal, G. Wethe, and J. Mørland. Blood/breath ratio at low alcohol levels: A controlled study. *Ann. Toxicol. Analytique.* XIV:41.
- <sup>15</sup>Tsu, M. E., A. L. Babb, D. D. Ralph, and M. P. Hlastala. Dynamics of heat, water, and soluble gas exchange in the human airways: 1. A model study. *Ann. Biomed. Eng.* 16:547–571, 1988.