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Variations in airways impedance during respiratory cycle derived from combined measurements of input and transfer impedances

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Variations in airways impedance during respiratory cycle derived from combined measurements of input and transfer impedances. W. Tomalak, R. Peslin, C. Duvivier. ©ERS Journals Ltd 1998.

ABSTRACT: Simultaneous measurement of input (Z_{in}) and transfer impedances (Z_{tr}) allows separation of airway and tissue properties at a single frequency, without making assumptions concerning the structure of the two compartments. This approach offers the possibility of studying the variation in airway impedance (Z_{aw}) during the respiratory cycle.

Z_{in} and Z_{tr} were measured at frequencies of 10, 20, 30 and 40 Hz in eight healthy subjects to study the variations in Z_{aw} according to a modification of the Rohrer's equation: $X=K_1+K_2(V'_{ao})-K_3V$, where V is volume and V'_{ao} the flow at the airway opening.

The results showed that Z_{aw} could be modelled as a simple resistance–inertance pathway. Variations in airway resistance (R_{aw}) with flow were greater during expiration than during inspiration with K_2 values varying from 0.76–0.90 hPa·s^2·L^{-2} during inspiration and 0.84–1.47 hPa·s^2·L^{-2} during expiration, independently of frequency. R_{aw} was negative volume dependent; it decreased more with increasing volume during inspiration than during expiration. Airways inertance calculated from the imaginary part of Z_{aw} also underwent systematic variations during the respiratory cycle, but, in contrast to R_{aw}, flow dependence was negative during both phases.

In conclusion, the approach used in this study allows flow and volume dependencies of airways mechanical properties to be studied and can also provide indices of airway patency independently of flow, which is of great potential interest for studying variations in airway resistance during bronchomotor tests.

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The forced oscillations technique, described by DuBois *et al.* [1] in 1956 can be used to explore the mechanical properties of the respiratory system in various ways. The most common measurement is the relationship between pressure (P_{ao}) and flow (V'_{ao}) at the airway opening (input impedance (Z_{in}) = P_{ao}/V'_{ao}), when pressure oscillations are applied at the mouth. Another approach consists of relating the pressure applied at one point of the system, either the body surface or the airway opening, to the flow measured at the other point; this provides respiratory system transfer impedance (Z_{tr}), which has been shown to be the same whether the pressure is applied at the mouth and flow measured at the body surface (V'_{bs}) or *vice versa* [2]. Both Z_{in} and Z_{tr} are related to the mechanical properties of the airways and of the tissues, and, for many physiological and clinical applications, it would be of interest to separate these two components. While this cannot be achieved by analysing Z_{in} data in humans, whatever the frequency range over which it is measured [3], the separation may be done reliably by analysing Z_{tr} data over a wide enough frequency range [4, 5] using a six-coefficient model proposed by DuBois *et al.* [1]. An alternative approach is to measure simultaneously Z_{in} and Z_{tr}, which may be done by recording both V'_{ao} and V'_{bs} when pressure oscillations are applied at the airway opening [6, 7]. Indeed, based on the T-network model of DuBois *et al.* [1] (fig. 1) which features airways impedance (Z_{aw}) and tissue impedance (Z_t) separated by the shunt impedance of the alveolar gas (Z_g), it may be shown that:

$$Z_t = Z_g\,(Z_{tr}/Z_{in} - 1) \quad (1)$$

$$Z_{aw} = Z_{in} - Z_g\,(1 - Z_{in}/Z_{tr}) \quad (2)$$

As Z_g may easily be computed from thoracic gas volume (TGV):

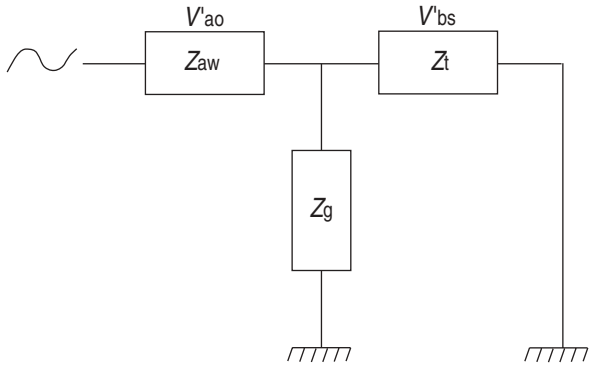

Fig. 1. – DuBois T-network model of the respiratory system. V'_{ao}, V'_{bs}: flow at airway opening and body surface, respectively; Z_{aw}: airway impedance; Z_t: tissue impedance; Z_g: alveolar gas impedance.

$$Z_g = -j\,(BP-P_{H_2O})/(TG\times\omega) \quad (3)$$

where j is the unit imaginary number, BP the barometric pressure, P_{H_2O} is a water vapour pressure and $\omega = 2\pi f$ with f the oscillation frequency; equations 1 and 2 provide a convenient means of obtaining Z_t and Z_{aw}. This approach offers two specific advantages: 1) the separation is achieved without making assumptions about the nature of the mechanical properties of the airways and of the tissues, *i.e*. without modelling Z_{aw} and Z_t; and 2) the separation may be done from the data obtained at a single frequency, which provides the best possible time resolution, and, should the system be nonlinear, avoids the interference between frequencies which may happen with signals containing several components. Equation 2 was used recently to measure Z_t in normal subjects and it was shown that tissue elastance exhibits large variations during the respiratory cycle [8]. The aim of the present investigation was to assess the potential of that approach to study airway properties and their variations during quiet breathing.

Material and methods

The study was performed on a group of eight healthy adults (five males and three females) recruited from the laboratory staff. They were all trained in respiratory manoeuvres. Their biometric characteristics and lung volumes are shown in table 1.

Equipment

The experimental set-up has been described in detail previously [8]. In brief, the subject was seated in a 350-L flow-type body plethysmograph (Emerson, Cambridge, MA, USA) and breathed from the outside through a Fleisch 2 pneumotachograph (METABO, Switzerland). The flow element of the box was made of two layers of metal screen (area 144 cm^2, resistance 0.083 $hPa\cdot s\cdot L^{-1}$) and its time constant (screen resistance times gas compressibility) was about 18 ms. V'_{bs} was derived from box pressure measured with a Validyne MP45 ±2 cmH_2O differential transducer (Validyne, Northridge, Ca, USA). The pressure drop across the pneumotachograph, which provided V'_{ao}, as well as P_{ao}, were measured with similar transducers. Us-ing appropriate connecting tubes, all three transducers were matched within 2° of phase and 1% of amplitude up to 40 Hz. The flow channels were calibrated before each series of measurements by the integral method using a 1-L syringe and P_{ao} was calibrated using a slanted fluid mano-meter.

Table 1. – Biometric characteristics and lung volumes of the subjects

Subject No.	Sex	Age yrs	Height cm	Weight kg	FRC L	VC L
1	M	50	168	92	1.96	5.13
2	F	34	171	70	3.28	4.27
3	M	58	168	66	2.82	4.33
4	M	65	168	71	2.69	4.84
5	F	40	155	48	3.12	3.54
6	F	40	160	60	2.60	3.80
7	M	58	178	55	5.39	5.09
8	M	34	187	84	3.45	6.10

M: male; F: female; FRC: functional residual capacity; VC: vital capacity.

Pressure oscillations with a peak-to-peak amplitude of about 2 hPa were applied at the airway opening by a 100 W loudspeaker connected to the distal end of the pneumotachograph; the loudspeaker was supplied with computer-generated sinusoidal signals through a power amplifier. The subjects breathed through a low resistance–high-inertance side-tube, branched in parallel with the loudspeaker and connected to a small reservoir where the inspired gas was conditioned to body temperature and ambient pressure, and saturated with water vapour (BTPS) to eliminate any difference between Z_{in} and Z_{tr} related to differences in temperature and P_{H_2O} of the gas.

During the measurements V'_{ao}, V'_{bs} and P_{ao} were digitized at 360 Hz by a 12-bit analogue/digital conversion board (Digimetrie-PCLab, Perpignan, France) and stored on the disk of a 486-type computer for later analysis.

Protocol

The measurements were made in triplicate at oscillation frequencies of 10, 20, 30 and 40 Hz in random order. The subjects supported their cheeks firmly with their palms. V'_{ao} and lung volume (V; obtained on-line by digital integration of V'_{ao}) were displayed on the computer screen to help the subject perform the manoeuvres. The measurements consisted of recording 4–8 tidal breaths followed by a slow vital capacity (VC) manoeuvre serving to provide a volume reference. At the beginning and at the end of each measurement, zero flow offsets were recorded to correct the flow signal for any drift. The flows were also measured while the subject was off the mouthpiece for several seconds; the corresponding relationship between V'_{ao} and V'_{bs} (V'_{ao}/V'_{bs}) represented the equipment flow transfer function (FTF_{eq}) and was used to correct the data for the relative frequency responses of the pneumotachograph and of the plethysmograph.

Since the vibrations of upper airway walls may be responsible for errors in both Z_{in} and Z_{tr}, upper airway wall shunt impedance (Z_{uaw}) was also measured in all subjects during Valsalva manoeuvres [9] at the same four frequencies; this was performed using the same equipment as above to record P_{ao} and V'_{ao}. Total lung capacity was also measured in each subject using a constant-volume body plethysmograph which, in conjunction with the above-mentioned VC manoeuvres, permitted the calculation of TGV and Z_g (equation 3) at any time during breathing.

Data analysis

To correct for any departure from BTPS conditions of inspired air or for any small difference in gain between the flow channels, the slope of the relationship between V'_{ao} and V'_{bs} during the slow VC manoeuvres was computed by linear regression and the V'_{ao} data were divided by this value. The correction factor ranged 0.996–1.040. After elimination of their low-frequency component [10], the Fourier coefficients of the signals at the frequency of interest were computed on a cycle-by-cycle basis and combined to obtain Z_{in} and Z_{in}/Z_{tr}. Z_{in} was corrected for the 2.1 ms time constant of the pneumotachograph [10] and

Z_{in}/Z_{tr} for FTF_{eq}. Both were also corrected for the flow shunted through upper airway walls according to:

$$Z_{in,c} = Z_{in} \times Z_{auw}/(Z_{uaw}-Z_{in}) \quad (4)$$

$$(Z_{in}/Z_{tr})_c = (Z_{in}/Z_{tr}-H)/(1-H) \quad (5)$$

where $H=Z_{in}/Z_{auw}$ and c refers to corrected values. Finally, Z_{aw} was computed according to equation 2, using values of Z_g computed from the instantaneous TGV (equation 3).

Results

A time plot of V'_{ao}, V, the real (R_{aw}) and the imaginary ($Z_{aw,im}$) parts of Z_{aw} obtained with an oscillation frequency of 20 Hz in a representative subject is shown in figure 2. The four curves have been low-pass filtered at 1 Hz to eliminate the high frequency components of V'_{ao} and V and smooth the impedance data. It can be seen that both R_{aw} and $Z_{aw,im}$ undergo systematic variations during the respiratory cycle. R_{aw} increases during the early part of both inspiration and expiration and decreases during the latter part. R_{aw} was usually slightly greater at end-expiration than at end-inspiration. That pattern was similar in all subjects. The variations of $Z_{aw,im}$ almost mirrored those in R_{aw}, exhibiting a decrease in the early part of both phases and an increase in the latter part.

Using similar time plots, ensemble-averaged cycles were built for all variables and for all subjects with 32 points per respiratory cycle (16 for each phase). The mean values of R_{aw} and $Z_{aw,im}$ over the whole cycle in the eight subjects at the four oscillation frequencies are shown in figure 3. R_{aw} tended to increase slightly with increasing frequency, rising from 1.51±0.79 hPa·s·L^{-1} at 10 Hz to 1.80±1.10 hPa·s·L^{-1} at 40 Hz; that trend, however, was not statistically significant by one-way analysis of variance. In contrast, $Z_{aw,im}$ increased almost linearly with increasing frequency, rising from a mean value of 0.81±0.13 hPa·s·L^{-1} at 10 Hz to 3.59±0.57 hPa·s·L^{-1} at 40 Hz ($p<0.001$). This increase is consistent with the usual assumption that the airways may be modelled as a resistance–inertance pathway [1], so that $Z_{aw,im}=I_{aw}\times\omega$, with I_{aw} the airway inertance. I_{aw}, as obtained from that relationship, did not vary significantly with increasing frequency; it averaged 1.29±0.21 Pa·s^2·L^{-1} at 10 Hz and 1.40±0.23 Pa·s^2·L^{-1} at 40 Hz.

The time dependence of R_{aw} and I_{aw} was analysed by studying their relationship to V'_{ao} and V. This was done by fitting the data from the block-averaged cycles to the following equation by multiple linear regression:

$$X = K_1 + K_2 \times \mathrm{abs}(V'_{ao}) + K_3 \times V \quad (6)$$

where X stands for either R_{aw} or I_{aw}, abs(V'_{ao}) is the absolute value of V'_{ao}, K_2 and K_3 express the dependence of X over the absolute flow and lung volume, respectively, and K_1 is the value of X at zero flow and zero volume (arbitrarily taken at midtidal volume). The analysis was made separately for the inspiratory and expiratory phases and the results are presented in tables 2 and 3.

Equation 6 usually gave a good fit to R_{aw} data; the residuals averaged 0.03–0.07 hPa·s·L^{-1} and the multiple r^2 0.94–0.98. R_{aw} was slightly, but not significantly, larger during expiration than during inspiration at 10–30 Hz; this was not due to any difference in K_1, but to a substantially

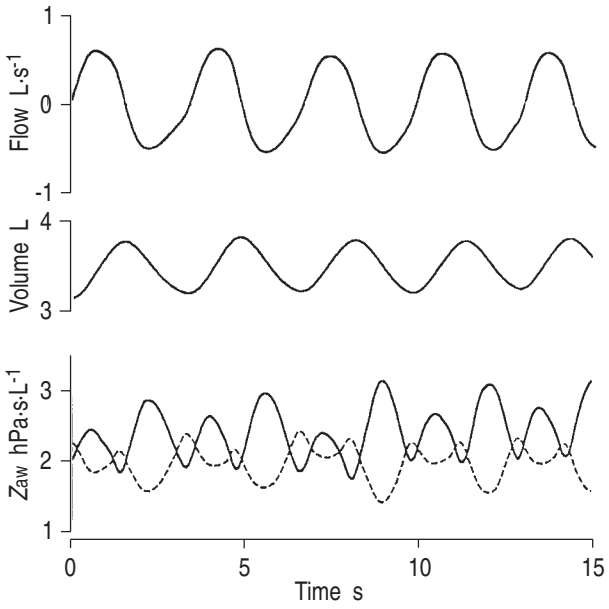

Fig. 2. – Time plots of flow, volume, real (R_{aw}; ——) and imaginary ($Z_{aw,im}$; - - - -) parts of airway impedance (Z_{aw}) at 20 Hz in a representative subject.

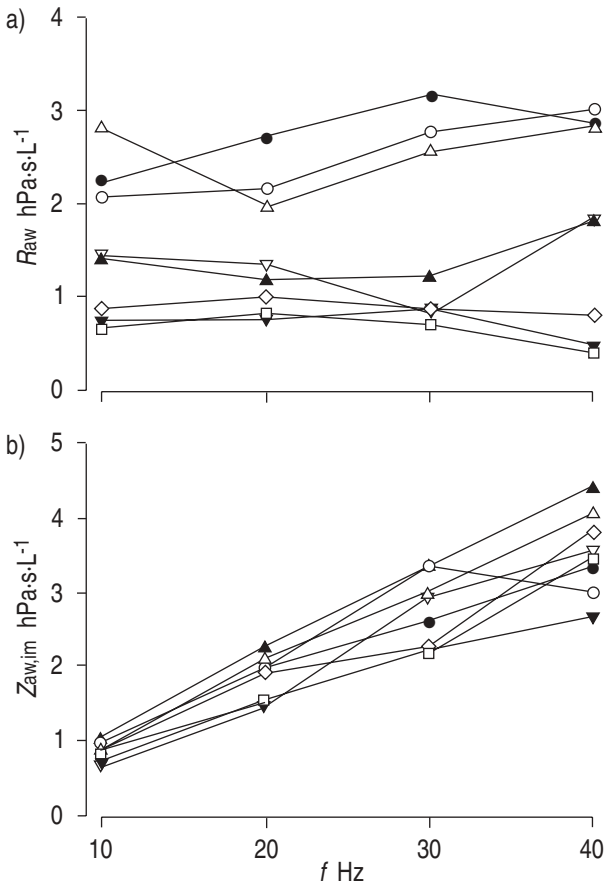

Fig. 3. – Frequency (f) dependence of a) airway resistance (R_{aw}) and b) imaginary airway impedance ($Z_{aw,im}$) in eight subjects. Subjects are represented by the same symbols in both graphs. Values are means calculated over the entire respiratory cycle.

Table 2. – Mean values of airway resistance (R_{aw}), K_1, K_2 and K_3 for inspiration and expiration at four oscillating frequencies (f_{os})

	Inspiration				Expiration			
f_{os} Hz	10	20	30	40	10	20	30	40
Mean R_{aw} hPa·s·L^{-1}	1.43±0.65	1.44±0.63	1.60±0.99	1.80±1.07	1.60±0.96	1.57±0.96	1.70±1.09	1.80±1.13
K_1 Pa·s^2·L^{-1}	1.10±0.52	1.06±0.52	1.27±0.90	1.48±1.05	1.12±0.52	1.05±0.50	1.28±0.90	1.52±1.07
K_2 Pa·s^3·L^{-2}	0.82±0.38	0.90±0.40	0.83±0.44	0.76±0.36	1.39±1.25	1.47±1.13*	1.30±0.87	0.84±0.76
K_3 Pa·s^2·L^{-2}	-0.35±0.22	-0.34±0.24	-0.39±0.32	-0.35±0.30	-0.20±0.47	-0.03±0.32*	-0.17±0.42*	-0.18±0.40

Values are means±SD. K_1: value of R_{aw} at zero flow and zero volume; K_2 and K_3: dependence of R_{aw} over the absolute flow and lung volume, respectively. *: $p<0.05$ for difference between inspiration and expiration (paired t-test).

larger flow dependence during the expiratory phase ($p<0.05$ at 20 Hz). K_2 did not vary significantly with the oscillation frequency; it was statistically significant in all subjects and at all frequencies, except in one subject at 10 Hz during expiration. K_3 was also significant in most instances; on average, it was negative at all frequencies, *i.e.* R_{aw} tended to decrease with increasing lung volume, and this trend was stronger during the inspiratory phase.

Equation 6 also gave a good fit to I_{aw} data; the residuals averaged 0.01–0.04 Pa·s^{-2}·L^{-1} and the multiple r^2 0.96–0.99. The mean I_{aw} and K_1 were similar during inspiration and expiration. As for R_{aw}, the flow dependence was stronger during the expiratory phase but, in contrast to R_{aw}, I_{aw} decreased with increasing absolute flow; K_2 was significant in all instances during both phases. Although statistically significant in most instances, the volume dependence was weak except at 10 Hz during inspiration.

Discussion

The data presented in this study show that airway impedance varies during the respiratory cycle; thus, it is possible to distinguish between its flow-dependent and flow-independent portions, which is of great potential interest.

The approach used in this study to separate airway and tissue properties does not imply any assumption concerning the mechanical properties of the two compartments. Thus, in contrast to the analysis of Z_{tr} data using the six-coefficient model of DuBois *et al.* [1], it is not assumed that the chest wall behaves as a resistance–elastance–inertance system and that the airways are a resistance–inertance pathway; it is only after the separation is made that modelling may be performed if one wishes to interpret the compartmental impedances in terms of specific mechanical properties. Moreover, provided alveolar pressure is homogeneous, equations 1 and 2 are still valid if the tissues are made of several parallel compartments with different properties. This is clearly of importance since the chest wall has been shown to behave inhomogeneously above a few Hertz [6, 11]. When the alveolar pressure is inhomogeneous, that is when the respiratory system is made of several T-networks (fig. 1) in parallel, the distribution of flow between the compartments depends on both their individual tissue and airway properties. It follows, for instance, that an increase in a local elastance will modify the apparent local and global resistance. In that situation, airways and tissue effective properties are interdependent and, except by making local measurements, it is not possible to separate them, whatever the approach. To evaluate the potential influence of mechanical inhomogeneity on Z_{aw}, as measured by equation 2, a system made of two T-networks in parallel, with inhomogeneous properties, was simulated numerically. Their overall Z_{in} and Z_{tr} at 20 Hz were derived and their apparent Z_{aw} computed according to equation 2. In the homogeneous case, both networks had a R_{aw} of 2 hPa·s·L^{-1} and an I_{aw} of 2 Pa·s^2·L^{-1}, a TGV of 2 L, a tissue compliance (C_t) of 0.05 L·hPa^{-1} and a tissue resistance (R_t) 1 hPa·s·L^{-1}. The data are shown in table 4. Decreasing one of the TGV by a factor of 10 increased the computed R_{aw} by 1.4% and I_{aw} by 3.1%. Varying one of the local C_t or R_t by any amount, however, did not influence at all the estimated R_{aw} and I_{aw}. Increasing one of the R_{aw} by a factor of 10 increased, as expected, the global R_{aw}, but also increased the global I_{aw}. In this situation, additional inhomogeneities of the TGV or the tissues changed little the apparent R_{aw}, but could modify the apparent I_{aw}. It was concluded that: 1) mechanical inhomogeneity of the tissues and gas distribution in the lung has little influence on the estimation of airway properties, the fact that R_{aw} and I_{aw} varied little with the oscillation frequency (tables 2 and 3) supports this conclusion; and 2) inhomogenity of R_{aw} may interfere with the estimation of I_{aw}.

The accuracy of Z_{aw}, as obtained by this approach, also depends on methodological factors. In practice, the relative frequency response of the body box and the pneumotachograph (FTF_{eq}), which was recorded after each measurement, appeared extremely reproducible in a given individual. A problem common to all forced oscillation measurements with the pressure input applied at the airway opening is the upper airway artefact [12], that is the flow shunted by

Table 3. – Mean values of airway inertance (I_{aw}), K_1, K_2 and K_3 for inspiration and expiration at four oscillating frequencies (f_{os})

	Inspiration				Expiration			
f_{os} Hz	10	20	30	40	10	20	30	40
Mean I_{aw} Pa·s^2·L^{-1}	1.34±0.22	1.51±0.27	1.52±0.28	1.49±0.25	1.26±0.23	1.42±0.22	1.41±0.26	1.38±0.21
K_1 Pa·s^2·L^{-1}	1.46±0.25	1.62±0.29	1.60±0.34	1.53±0.28	1.51±0.31	1.62±0.32	1.61±0.35	1.55±0.28
K_2 Pa·s^3·L^{-2}	-0.33±0.16	-0.25±0.19	-0.20±0.26	-0.12±0.17	-0.78±0.63	-0.60±0.44	-0.66±0.59	-0.52±0.40
K_3 Pa·s^2·L^{-2}	0.30±0.17	0.16±0.30	0.05±0.10	0.04±0.10	-0.14±0.28	-0.09±0.13	-0.07±0.12	-0.03±0.09

Values are means±SD. K_1: value of I_{aw} at zero flow and zero volume; K_2 and K_3: dependence of I_{aw} over the absolute flow and lung volume, respectively.

Table 4. – Influence of mechanical inhomogeneity on estimates of airway resistance (R_{aw}) and inertance (I_{aw}) (computer simulation)

Condition	R_{aw} hPa·s·L^{-1}	I_{aw} Pa·s^2·L^{-1}
Homogeneous	1.000	1.000
TGV2/10	1.014	1.031
C_{t2}/10	1.000	1.000
$R_{t2} \times 10$	1.000	1.000
$R_{aw2} \times 10$	2.193	1.474
$R_{aw2} \times 10$ and TGV$_2$/10	1.952	1.602
$R_{aw2} \times 10$ and TGV$_1$/10	2.533	1.435
$R_{aw2} \times 10$ and C_{t_2}/10	2.199	1.515
$R_{aw2} \times 10$ and C_{t_1}/10	2.006	1.284
$R_{aw2} \times 10$ and $R_{t_1} \times 10$	2.114	1.584
$R_{aw2} \times 10$ and $R_{t_2} \times 10$	2.173	0.729

TGV: thoracic gas volume; C_t: tissue compliance; R_t: tissue resistance. Homogeneous case: R_{aw}: 2 hPa·s·L^{-1}; I_{aw}: 2 Pa·s^2·L^{-1}; TGV: 2 L; C_t: 0.05 L·hPa^{-1}; R_t: 1 hPa·s·L^{-1} in both compartments. Subscripts 1 and 2 identify the compartments in which the properties are altered compared to the homogeneous case.

the motion of upper airway walls (cheeks, mouth floor, pharynx). With the present set-up, this flow could modify not only Z_{in}, but also Z_{tr} because the head of the subject was inside the body box. To minimize the problem, the subjects were asked to support their cheeks firmly during the measurements; in addition, the data were corrected for the residual shunt impedance of the upper airway walls (equations 4 and 5). The correction, however, may have been incomplete because Z_{uaw}, as measured during Valsalva manoeuvres [9], has been shown to be slightly larger than during quiet breathing [13]. To evaluate this factor, the influence was tested of correcting the data with values of Z_{uaw} (real and imaginary parts) reduced by 30% at all frequencies. The influence of this overcorrection was negligible on $Z_{aw,im}$ up to 40 Hz and weak on R_{aw} up to 20 Hz. At higher frequencies, R_{aw} appeared to be substantially lower with the decreased Z_{uaw}. However, the residual error was not thought to be large in practice, because R_{aw} did not exhibit much frequency dependence.

The mean values of R_{aw} (1.62±0.88 hPa·s·L^{-1}) and I_{aw} (1.40±0.20 Pa·s^2·L^{-1}) are similar to those obtained in healthy humans by analysing transfer impedance data with the six-coefficient model of DuBois: 1.35±0.62 hPa·s·L^{-1} and 2.5±0.7 Pa·s^2·L^{-1} [14]; 2.15±1.07 hPa·s·L^{-1} and 2.2±0.5 Pa·s^2·L^{-1} [15]; 1.39±0.44 hPa·s·L^{-1} and 1.7±0.23 Pa·s^2·L^{-1} [2]; and 2.30±0.52 hPa·s·L^{-1} and 2.8±0.8 Pa·s^2·L^{-1} [4] for R_{aw} and I_{aw}, respectively. This is worth mentioning because the data were derived from measurements at a single frequency while reliable estimates of R_{aw} and I_{aw} from Z_{tr} data require measurements from 4 to at least 30 Hz [5]. It supports the validity of applying the model of DuBois over such a large frequency range.

The advantages of separating airway and tissue properties from impedance data obtained at a single frequency are many. Firstly, it avoids the crosstalk between frequencies observed with nonlinear systems when the input signal does not meet a number of very stringent criteria [16]. Secondly, it provides the best possible time resolution; indeed, while, in theory, the time resolution of data from multiple frequency inputs may be as good as the period of the lowest frequency component, the minimal duration of a data block containing an integer number of cycles of all frequency components may be much longer with inputs meeting the above-mentioned criteria. Thirdly, the signal/noise ratio is better when all of the energy is concentrated in a single frequency than when it is distributed among several components. Finally, it avoids assuming that the mechanical properties of the respiratory system are independent of frequency, which is implicit when analysing Z_{tr} data with the model of DuBois. The results shown in figure 3 suggest that R_{aw} may vary substantially with frequency in some individuals; also, as mentioned above, the effective resistance and elastance of the tissues may vary with frequency as a result of the mechanical inhomogeneity of the chest wall.

This study showed substantial variations in R_{aw} during the respiratory cycle. These variations were analysed with a descriptive model (equation 6) inspired from Rohrer's equation [17], which expresses the nonlinear pressure–flow relationship along the airways:

$$P_{ao}\text{-}P_A = K_1 \times V'_{ao} + K_2 \times V'^2_{ao} \quad (7)$$

where P_A is the alveolar pressure. From that relationship, R_{aw}, as measured by forced oscillation from small variations of pressure and flow, is expected to be proportional to flow:

$$R_{aw} = d(P_{ao}\text{-}P_A)/dV'_{ao} = K_1 + 2K_2 \times V'_{ao} \quad (8)$$

From this equation, the coefficient K_2 in equation 6 would correspond to twice Rohrer's K_2 coefficient when the pressure oscillations are infinitely small. This is not the case in practice and the expected ratio between Rohrer's K_2 and our K_2 coefficient may vary between 1 and 2, depending on the relative amplitudes of the oscillatory and respiratory flows [18]. In the present model, a third term was included to account for any variations in R_{aw} in relation to lung volume. The analysis showed a good fit of the data to the model with K_2 values around 0.8 hPa·s^2·L^{-2} during the inspiratory phase and 1.3 hPa·s^2·L^{-2} during the expiratory phase.

These observations are similar to those of CAUBERGHS and VAN DE WOESTIJNE [19], who found resistance of the respiratory system (R_{rs}) values to be lower during peak tidal inspiratory flow and greater during maximal inspiratory flow. They have also shown that R_{rs} increased with increasing values of expiratory flows. The values of K_2 coefficients are similar to those obtained by PESLIN *et al*. [20], who studied Z_{in} variations during the respiratory cy-cle. Mean K_2 values in seven healthy subjects at 4–6 Hz were 0.95±0.47 and 1.49±0.55 hPa·s^2·L^{-2} for inspiration and expiration, respectively. In another work from the same laboratory [18] the analysis of Z_{in} variations measured with a head pressure generator gave values of K_2 varying from 0.65 and 1.18 at 10 Hz to 1.2 and 1.7 hPa·s^2·L^{-2} at 30 Hz for inspiration and expiration, respectively.

The analysis revealed some negative volume dependence of R_{aw}, which is consistent with previous data. OOSTVEEN *et al.* [21] reported a decrease with volume of airway resistance derived from transfer impedance during inspiratory manoeuvres. PESLIN *et al*. [18] reported values of K_3 ranging from about -0.3 to -0.7 for inspiration and -0.8 to -1.4 hPa·s·L^{-2} for expiration. These values are larger than those found in the present study, but they were calculated from Z_{in} variations during normal breathing and not from Z_{aw}, as in this study.

The study also revealed systematic variations in I_{aw} during the respiratory cycle (fig. 2) which, analysed with equation 6, corresponded mostly to negative flow dependence (table 3). This finding is in agreement with the observations of OOSTVEEN *et al*. [21] who derived I_{aw} from 4–30 Hz Z_{tr} data obtained during constant-flow inspiratory and expiratory manoeuvres. During inspiration I_{aw} decreased from 2.12 $Pa \cdot s^2 \cdot L^{-1}$ at 0.1 $L \cdot s^{-1}$ to 1.79 $hPa \cdot s^2 \cdot L^{-1}$ at 0.4 $L \cdot s^{-1}$; the changes, however, were smaller during the expiratory phase (2.15 and 1.91 $Pa \cdot s^2 \cdot L^{-1}$ at 0.1 and 0.4 $L \cdot s^{-1}$, respectively), which is at variance with the present observations. Such a negative flow dependence is consistent with a blunter velocity profile of air in the airways when the flow is larger [22].

While the possibility of separating airway and tissue mechanical properties is obviously of interest for a number of clinical and physiological applications, one may wonder about the practical usefulness of studying the variations in R_{aw} during the respiratory cycle. The flow dependence, and to a lesser extent, the volume dependence of R_{aw}, make it frequently difficult to interpret its value in patients and its variations during bronchomotor challenge. Indeed, changes in ventilation or in the respiratory pattern may modify R_{aw} and obscure the actual changes in airway patency. Moreover, most of the flow dependence of R_{aw} has been shown to be located in extra-thoracic airways [23] and it has also been observed that induced bronchoconstriction may reflexly increase extra-thoracic airway resistance [24]. Then, the flow-dependent component of R_{aw} may be largely irrelevant when studying bronchial responsiveness. When R_{aw} is measured by body plethysmography, the problem may be solved to some extent by standardizing the flow range over which the pressure is measured [25]; the data, however, still include nonlinear components. The advantage of studying the variations in R_{aw} during the cycle and analysing the data with a descriptive model, such as equation 6, is that it makes it possible to isolate its linear component, K_1. The latter should represent an index of airway patency that is much more independent of the ventilation and of the extrathoracic airways than the mean resistance or the resistance over any specific flow range.

Further studies are needed to verify that prediction and the value of this type of analysis in pulmonary function testing, especially in the evaluation of the results of bronchomotor tests.

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