Assessment of bronchial reactivity by forced oscillation admittance avoids the upper airway artefact

R. Farré*, M. Rotger*, F. Marchal[+], R. Peslin[‡], D. Navajas*

Assessment of bronchial reactivity by forced oscillation admittance avoids the upper airway artefact. R. Farré, M. Rotger, F. Marchal, R. Peslin, D. Navajas. ©ERS Journals Ltd 1999.
ABSTRACT: The forced oscillation technique (FOT) allows easy assessment of bronchial reactivity. The use of a standard FOT generator (SG) results in changes in respiratory system resistance (ΔRrs,SG) which are affected by an artefact caused by the extrathoracic upper airway (EUA). The aim was to improve the FOT assessment of bronchial reactivity with the SG by computing the change in FOT admittance (ΔArs,SG), which is theoretically unaffected by this artefact.

ΔRrs,SG and ΔArs,SG after bronchial challenge in 17 children were compared with the values measured with a head generator (HG) FOT setup (ΔRrs,HG and ΔArs,HG, respectively), which were taken as a reference, since HG provides data virtually freed from the EUA artefact.

At 10 Hz, the SG significantly underestimated the resistance change: ΔRrs,SG= 1.77±0.62 *versus* ΔRrs,HG=6.09±1.23 hPa·L^{-1}·s. ΔRrs,SG and ΔRrs,HG did not show a significant correlation. By contrast, the amplitude of the change in admittance measured by SG was close to the one obtained with the reference HG: |ΔArs,SG|=29.5±4.6 *versus* |ΔArs,HG|=32.7±3.9 mL·hPa^{-1}·s^{-1}. |ΔArs,SG| and |ΔArs,HG| showed a significant correlation (r=0.65, p>0.01). Similar results were found up to 20 Hz.

The extrathoracic upper airway artefact was minimized when computing the change in admittance with the standard generator. This forced oscillation technique index may improve the sensitivity in assessing bronchial reactivity with the standard generator setup, which is the most common and easiest to use method for routine lung function testing.
Eur Respir J 1999; 13: 761–766.

*Laboratori de Biofisica i Bioenginyeria, Facultat de Medicina, Institut d'Investigacions Biomediques Agusti Pi Sunyer (IDIBAPS), Universitat de Barcelona, Spain. [+]Lab. Explorations Fonctionnelles Pediatriques, Hôpital d'Enfants, Centre Hospitalier Universitaire, Nancy, France. [‡]Unité 14 de Physio-pathologie Respiratoire, INSERM, Nancy, France.

Correspondence: R. Farré, Laboratori de Biofisica i Bioenginyeria, Facultat de Medicina, Casanova 143, E-08036 Barcelona, Spain, Fax: 34 934035260

The forced oscillation technique (FOT) allows a non-invasive assessment of respiratory mechanics with minimal cooperation from the patient. This is particularly useful when assessing respiratory function in patients who are unable to cooperate in performing forced spirometry according to the standard criteria, *e.g.* in patients with severe breathing impairment or in children. An additional feature of FOT, which contrasts with forced spirometry, is that it does not modify the bronchial tone since it is applied while the patient is breathing spontaneously, obviating the need for deep inspirations. This is of special relevance in the assessment of bronchial reactivity [1] given that in such a test, a series of several consecutive forced expirations are required to quantify the effects of increasing doses of the inhaled agent.

The suitability of FOT for evaluating the effects of different bronchial challenge agents (histamine [2–4], methacholine [5–11], carbachol [12], hyperventilation with cold air [13, 14]) has been substantiated by comparison with reference techniques such as forced spirometry or body plethysmography both in children and in adults. Most of the studies analysing the adequacy of FOT for assessing bronchial reactivity have been carried out by using the more common and simplest FOT setup, the standard generator (SG). This setup has the advantage of being comfortable for the patient since forced oscillation is simply applied through a mouthpiece. Nevertheless, it has been

reported that the results obtained with the SG are affected by an artefact due to the shunt of the extrathoracic upper airways [15–18]. This artefact can be minimized, both in adults and in children, by using a variant of the FOT technique which consists in applying oscillation with a head generator (HG) [18, 19]. In particular, it has been shown that the sensitivity and specificity of the technique in detecting changes in respiratory impedance is greater for the HG than for the SG [16, 20]. However, this advantage of the HG is offset to a certain extent by the fact that this setup is less easily applicable to the clinical routine since it is necessary to surround the patient's head with a canopy sealed with a neck collar.

The aim of this work was to optimize the analysis of the data obtained with the most conventional and simplest SG in order to eliminate the upper airway artefact when FOT is employed to assess bronchial reactivity. The rationale behind this procedure is that in a bronchial challenge the patient is their own control and also that the mechanical properties of the extrathoracic upper airway are not modified by the bronchial challenge. Accordingly, the change in the oscillatory admittance measured by the SG was computed. The practical improvement in the assessment of bronchial challenge expected from the theoretical background was substantiated by applying the method to the FOT data measured with the SG before and after bronchial challenge in children. The results were compared with

those obtained with the HG, which were taken as the reference, since they are virtually free of the upper airway artefact [18].

Methods

Rationale

The conventional method of assessing respiratory system impedance (Z_{rs}) is based on applying a forced oscillation through a mouthpiece by means of an SG and computing $Z_{rs,SG}$ from the oscillatory pressure (P) and flow (V') signals recorded at the mouth. As illustrated in figure 1, measured $Z_{rs,SG} = P/V'$ does not coincide with actual Z_{rs} due to the shunt induced by the parallel impedance of the extrathoracic upper airway (Z_{eua}) [21, 22]:

$$Z_{rs,SG} = Z_{rs} \times (1 + Z_{rs}/Z_{eua})^{-1} \qquad (1)$$

Accordingly, the error induced by Z_{eua} is higher as Z_{rs}/Z_{eua} increases. A bronchial challenge induces a change of impedance from the basal value Z_{rs} to $Z_{rs}*$ and the values measured with the SG vary from baseline $Z_{rs,SG}$ to $Z_{rs}*,SG$. It may be shown from equation 1 that the measured change in impedance ($\Delta Z_{rs,SG} = Z_{rs}*,SG - Z_{rs,SG}$) is related to the actual change ($\Delta Z_{rs} = Z_{rs}* - Z_{rs}$) according to:

$$\Delta Z_{rs,SG} = \Delta Z_{rs} \times (1 + Z_{rs}*/Z_{uaw})^{-1} \times (1 + Z_{rs}/Z_{uaw})^{-1} \qquad (2)$$

Consequently, the change in impedance measured with the SG ($\Delta Z_{rs,SG}$) is also affected by the upper airway artefact. This is illustrated in figure 2a, which shows a representative example of the different impedances, represented as respiratory system resistance (R_{rs}) and reactance (X_{rs}) ($Z_{rs} = R_{rs} + j \times X_{rs}$; where $j = (-1)^{1/2}$), involved in a FOT measurement before and after bronchial challenge in adults [3]. From the mean measured values with the SG at 6 Hz ($Z_{rs,SG} = 2.9 - j \times 0.6$ hPa·L^{-1}·s and $Z_{rs}*,SG$ $= 5.7 - j \times 1.8$ hPa·L^{-1}·s), the actual pre- and postchallenge impedances were estimated (equation 1) assuming a value of $Z_{eua} = 20 - j \times 15$ hPa·L^{-1}·s at this frequency [16]: $Z_{rs} = 3.3 - j \times 0.5$ hPa·L^{-1}·s and $Z_{rs}* = 7.7 - j \cdot 2.9$ hPa·L^{-1}·s. As expected, the change from pre- to postchallenge impedances measured by the SG effectively underestimated the actual value (equation 2).

To improve the detection of the changes induced by a bronchial challenge when using the SG it was proposed to compute the change in respiratory admittance (A_{rs}), which is the reciprocal of Z_{rs}. According to figure 1, the admittances measured with the SG before and after challenge
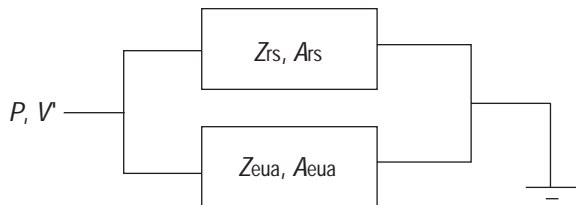

Fig. 1. – Diagram of the impedances and admittances in a forced oscillation measurement with the standard generator. P: oscillatory pressure at the patient's mouth; V': oscillatory flow at the patient's mouth; Z_{rs}: respiratory system impedance; A_{rs}: respiratory system admittance; Z_{eua}: impedance of the extrathoracic upper airway; A_{eua}: admittance of the extrathoracic upper airway.
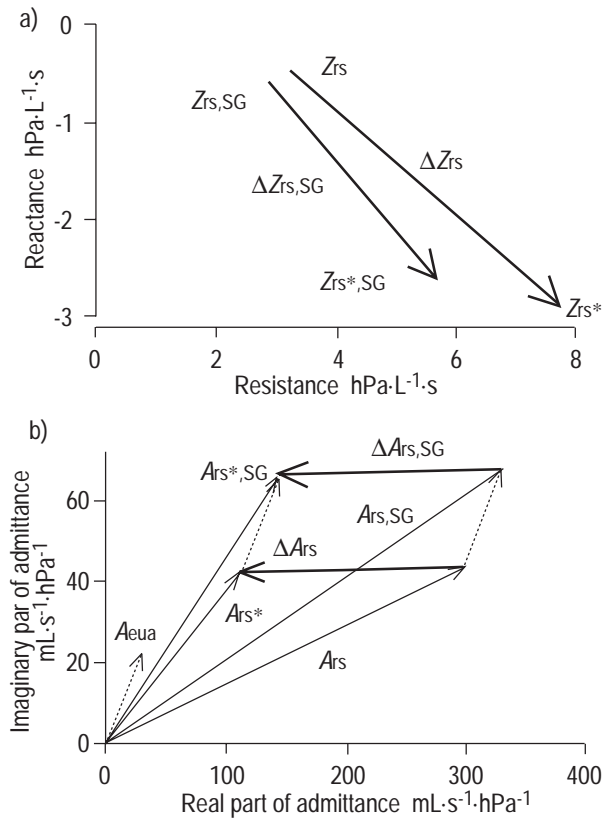

Fig. 2. – Representative values of impedances (a) and admittances (b) at 6 Hz in a forced oscillation measurement before and after a bronchial challenge with histamine. Z_{rs}: respiratory system impedance before bronchial challenge; $Z_{rs}*$: respiratory system impedance after bronchial challenge; $Z_{rs,SG}$: Z_{rs} measured with a standard generator; $Z_{rs}*,SG$: $Z_{rs}*$ measured with a standard generator; ΔZ_{rs}: actual change in impedance; $\Delta Z_{rs,SG}$: change in impedance measured with a standard generator; A_{rs}: actual respiratory system admittance before bronchial challenge; $A_{rs}*$: respiratory system admittance after bronchial challenge; $A_{rs,SG}$: A_{rs} measured with a standard generator; $A_{rs}*,SG$: $A_{rs}*$ measured with a standard generator; ΔA_{rs}: actual change in admittance; $\Delta A_{rs,SG}$: actual change in admittance measured with a standard generator; A_{eua}: admittance of the extrathoracic upper airway. Note that $\Delta Z_{rs,SG} \neq Z_{rs}$ and that $\Delta A_{rs,SG} = \Delta A_{rs}$.

($A_{rs,SG} = 1/Z_{rs,SG}$ and $A_{rs}*,SG = 1/Z_{rs}*,SG$ respectively) are the addition of the actual respiratory admittances ($A_{rs} = 1/Z_{rs}$ and $A_{rs}* = 1/Z_{rs}*$, respectively) and the admittance of the extrathoracic upper airway ($A_{eua} = 1/Z_{eua}$):

$$A_{rs,SG} = A_{rs} + A_{eua} \qquad (3)$$

$$A_{rs}*,SG = A_{rs}* + A_{eua} \qquad (4)$$

where A_{eua} is expected to be unaffected by the bronchial challenge. Consequently, the change in admittance due to the bronchial challenge measured by the SG ($\Delta A_{rs,SG} = A_{rs}* - A_{rs}$) coincides with the actual change of respiratory admittance ($\Delta A_{rs} = A_{rs}* - A_{rs}$):

$$\Delta A_{rs,SG} = \Delta A_{rs} \qquad (5)$$

as is illustrated in figure 2b. This figure shows that, in contrast to that found in impedance data (fig. 2a), the effect of the extrathoracic upper airway shunt on actual A_{rs}, and $A_{rs}*$ is additive (equations 3 and 4). Therefore, the absolute

change in admittance is not influenced by A_{eua}. Consequently, assessing the effects of the bronchial challenge by means of the change in admittance measured with the SG allows an unbiased estimation of the actual change in the mechanical properties of the respiratory system.

In addition to the fact that the measurement of the absolute change in admittance ($\Delta A_{rs,SG}$) is unbiased (equation 5), it should be pointed out that its relative change:

$$\Delta A_{rs,SG}/A_{rs,SG} = \Delta A_{rs}/A_{rs} \times (1+Z_{rs}/Z_{eua})^{-1} \qquad (6)$$

exhibits an error that depends on the baseline impedance (Z_{rs}). Consequently, the error factor $(1+Z_{rs}/Z_{eua})^{-1}$ is the same for the different successive measurements with increased dose of the challenge agent. By contrast, the magnitude of error in the relative change in impedance:

$$\Delta Z_{rs,SG}/Z_{rs,SG} = \Delta Z_{rs}/Z_{rs} \times (1+Z_{rs}*/Z_{eua})^{-1} \qquad (7)$$

depends not on the value of the baseline impedance, but on the actual impedance after each dose of bronchial challenge agent ($Z_{rs}*$). Moreover, the magnitude of the error, in the relative change in admittance (equation 6) is expected to be lower than the error in the relative change in impedance (equation 7) because the error factor, $1+Z_{rs}/Z_{eua}$, is expected to be smaller than $1+Z_{rs}*/Z_{eua}$, since a bronchoprovocation results in an increase in impedance ($Z_{rs}* > Z_{rs}$).

Patient measurements

To substantiate the practical improvement when using the change in forced oscillation admittance measured by the SG ($\Delta A_{rs,SG}$) to assess bronchial reactivity, the FOT data obtained with SG and HG during bronchial challenge in 17 children were re-analysed [18]. All the patients, aged 2–9 yrs, presented with a history of mild-to-severe asthma and were referred to the laboratory for assessment of airway reactivity. These patients had been free of respiratory symptoms for three weeks preceding the challenge, and β-agonists were withheld for at least 12 h prior to the test. The study was approved by the Regional Committee on Human Subjects Experimentation.

The FOT system and the signal processing used in the measurements have been described in detail previously [18]. Briefly, respiratory impedance was computed from at least two 16 s records of the pressure and flow signals sampled when applying a pseudorandom forced oscillation while the patient was breathing spontaneously. The experimental system could apply the forced oscillation through a mouthpiece while the patient's cheeks were supported, *i.e.* SG, and the oscillation pressure could also be applied around the head to minimize the shunt of the extrathoracic upper airway, *i.e.* HG. In each patient, SG and HG measurements were taken in a random order and the time interval between the two techniques was 2–3 min.

After baseline measurements of $Z_{rs,SG}$ and $Z_{rs,HG}$, the patient was subjected to a bronchial challenge with acetylcholine or to a specific allergen. Aerosols were delivered with a Wright nebulizer (Harlow, UK). Acetylcholine (11 patients) was given at a dose of 0.5 or 1 mg. Aerosols of allergenic extracts of house dust mites (five patients), and alternaria (Pasteur, Paris, France) (one patient) were given in cumulative doses, starting from 0.5 IR for mites, and

from a solution of 2.5% (w/v) for alternaria. FOT was applied 10 min after inhalation of the last dose of the test.

Impedance data (10–20 Hz) were first analysed according to the most conventional procedure, to quantify the changes induced by the bronchial challenge, *i.e.* by computing the change in the resistance, both for SG ($\Delta R_{rs,SG}$) and HG ($\Delta R_{rs,HG}$). To verify the improvement when using admittance for assessing bronchial challenge, the amplitude of the change in admittance measured with the SG ($|\Delta A_{rs,SG}|$) was compared with the one obtained from the reference head generator ($|\Delta A_{rs,HG}|$). This allowed us to employ a unique FOT index to quantify the change in respiratory mechanics after bronchial challenge. The same analysis was carried out for the relative changes in resistance ($\Delta R_{rs,SG}/R_{rs,SG}$ and $\Delta R_{rs,HG}/R_{rs,HG}$) and admittance ($|\Delta A_{rs,SG}|/|A_{rs,SG}|$ and $|\Delta A_{rs,HG}|/|A_{rs,HG}|$). Data are expressed as mean±SEM. Differences between means were analysed with paired Student's t-tests and were considered statistically significant at p<0.05.

Results

The mean±SEM of baseline respiratory impedance measured by the conventional generator ($Z_{rs,SG}$) and with the head generator ($Z_{rs,HG}$) are shown in figure 3a. As expected, R_{rs} was scarcely affected by the upper airway
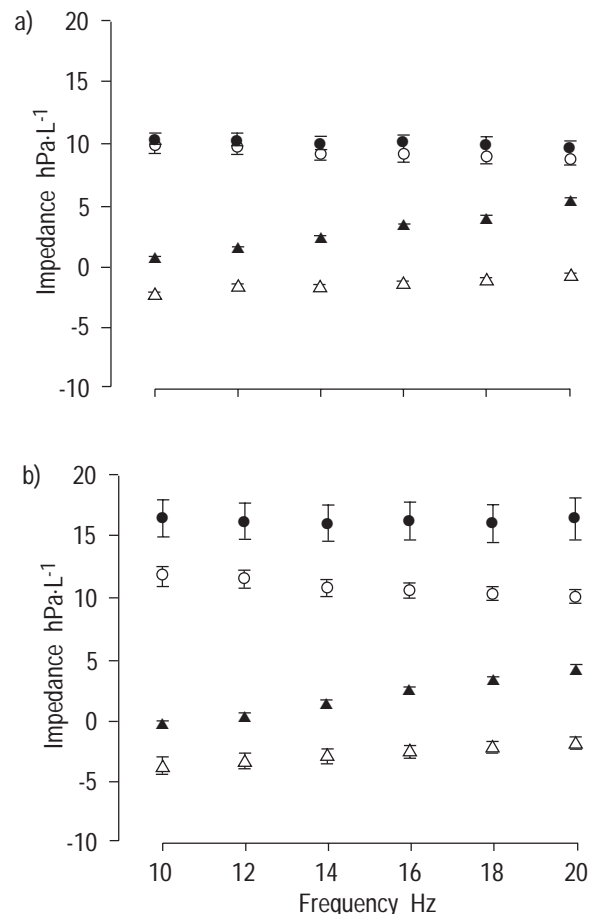
Fig. 3. – Respiratory system resistance (R_{rs}) and reactance (X_{rs}) at baseline (a) and after bronchial challenge (b), measured by the standard generator (SG) and by the head generator (HG). Values are mean±SEM. ○: $R_{rs,SG}$; △: $X_{rs,SG}$; ●: $R_{rs,HG}$; ▲: $X_{rs,HG}$.

shunt, especially at the lowest frequencies. By contrast, $X_{rs,SG}$ measured by the SG was lower and showed smaller frequency dependence than the reference $X_{rs,HG}$. Also, in accordance with previous data, figure 3b shows that the difference between the results obtained with SG and HG increased after the bronchial challenge. The discrepancies between the resistances measured with both variants of the technique increased with frequency.

Figure 4 illustrates that, at all the investigated frequencies, the increase in resistance was considerably underestimated when measured by the SG as compared with the results obtained with the reference HG. For instance, at 10 Hz, $\Delta R_{rs,SG}=1.77\pm0.62$ hPa·L^{-1}·s and $\Delta R_{rs,HG}=6.09\pm1.23$ hPa·L^{-1}·s. At this frequency, $\Delta R_{rs,SG}$ exhibited a lower statistical significance (t=2.8) than $\Delta R_{rs,HG}$ (t=5.0). The difference between $\Delta R_{rs,SG}$ and $\Delta R_{rs,HG}$ was statistically significant (p>0.01). Both changes in resistance did not show significant correlation.

The results obtained when assessing the effects of the bronchial challenge by means of the change in absolute oscillatory admittance are shown in figure 5 for all the investigated frequencies. At 10 Hz, which is a representative frequency, the change in admittance measured by the SG ($|\Delta A_{rs,SG}|=29.5\pm4.6$ mL·hPa^{-1}·s^{-1}) was very close to the one measured by the reference HG ($|\Delta A_{rs,HG}|=32.7\pm3.9$ mL·hPa^{-1}·s^{-1}), the difference being not significant. The statistical significance was similar for both SG (t=6.4) and HG (t=8.4) and the t-values were much higher than the ones corresponding to the changes in resistance. $|\Delta A_{rs,SG}|$ and $|\Delta A_{rs,HG}|$ showed a significant correlation (r=0.65, p>0.01).

Figure 6 shows the results obtained in the patients when computing the relative changes of resistance ($\Delta R_{rs,SG}/R_{rs,SG}$ and $\Delta R_{rs,HG}/R_{rs,HG}$) and admittance ($|\Delta A_{rs,SG}|/|A_{rs,SG}|$, and $|\Delta A_{rs,HG}|/|A_{rs,HG}|$). As expected (equation 6), the percentage change in resistance was underestimated by the SG, showing lower statistical significance for SG (t=3.0) than for HG (t=5.3). By contrast, the percentage change in admittance computed from the SG was only slightly, although significantly, underestimated when compared with the reference value from the HG (27±3% and 33±4%, respectively). Similarly, as found in the case of the absolute changes (figs. 4 and 5), the statistical sig-

nificances of the relative changes in admittance (t=8.7 for SG and t=8.5 for HG) were much higher than those of the relative changes in resistance.

Discussion

The theoretical prediction that computing the change in FOT admittance after a bronchial challenge from data obtained with the SG is free of the upper airway artefact (equation 5) was verified in children, in whom the FOT is

Fig. 5. – Changes in admittance ($|\Delta A_{rs}|$) after bronchial challenge measured with the standard generator (○) and with the head generator (●). Values are mean±SEM.
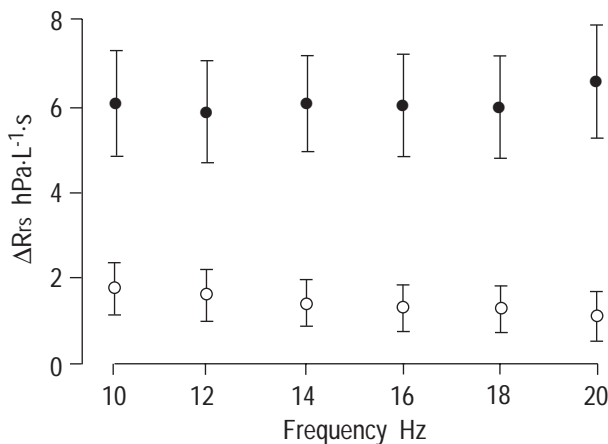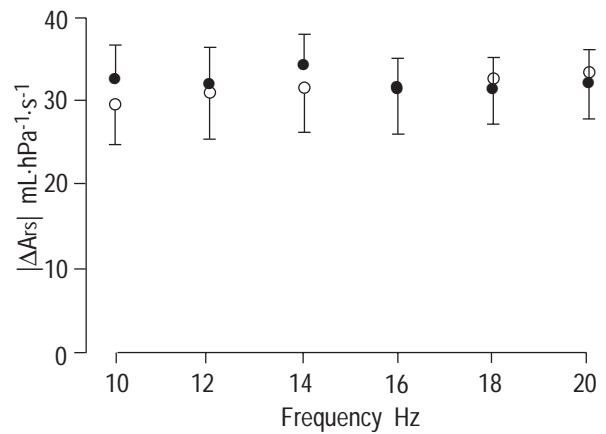

Fig. 4. – Changes in respiratory resistance (ΔR_{rs}) after bronchial challenge measured with the standard generator (○) and with the head generator (●). Values are mean±SEM.
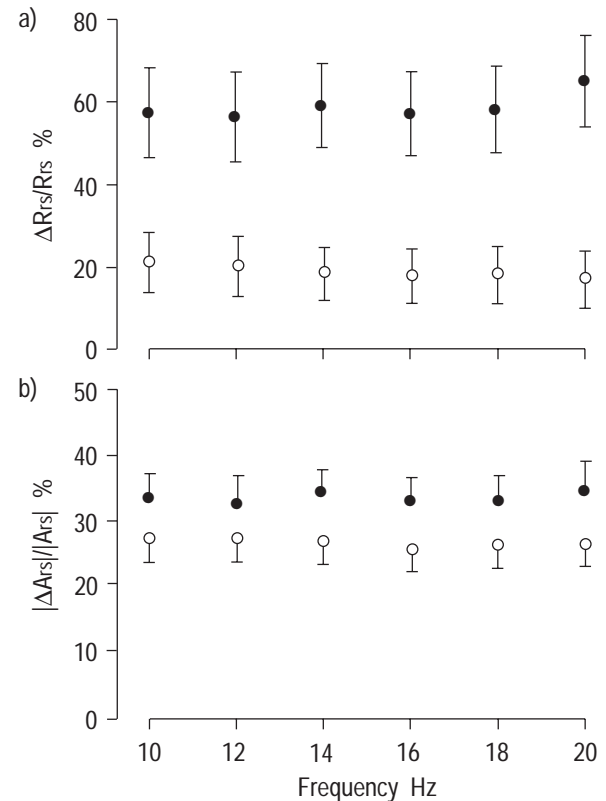

Fig. 6. – Relative changes in respiratory system resistance ($\Delta R_{rs}/R_{rs}$) (a) and in admittance ($|\Delta A_{rs}|/|A_{rs}|$) (b) after bronchial challenge measured with the standard generator (○) and with the head generator (●). Values are mean±SEM.

most affected by this artefact. Indeed, previous data indicate that in children the ratio Z_{rs}/Z_{eua} which is the factor quantifying the amount of artefact (equation 1), is greater than in adults [17]. The results from the present study (fig. 5) confirmed that the absolute change in admittance measured with the SG was very close to the one detected with the HG, which is a measurement virtually unaffected by the artefact [18].

The rationale behind the use of the change in admittance to avoid the upper airway artefact is applicable both in bronchoprovocation and in bronchodilatation tests [20, 23]. One of the two hypotheses employed to derive equation 5 is that the effect of the extrathoracic upper airway can be modelled as a pure lumped shunt impedance (Z_{eua}). This assumption is based on data indicating that the role played by the serial component of the extrathoracic upper airway is small both in children [17] and adults [16]. The second hypothesis is that the impedance of the extrathoracic upper airway is unaffected by the bronchial challenge agent, which is a reasonable assumption since most conventional agents used in bronchial challenge, *e.g.* histamine and methacholine, have been shown to induce effects mainly at the level of central and peripheral airways [24]. As for the rationale, it should be noted that oscillatory admittance contains exactly the same information as impedance since they are reciprocal complex magnitudes. Consequently, both pre- and postchallenge admittances are affected by the upper airway artefact (equations 3 and 4). However, the key issue of the present work consists in processing the data (by computing $\Delta A_{rs,SG}$ instead of $\Delta Z_{rs,SG}$) to quantify the changes in the mechanical properties of the respiratory system with a FOT index which is theoretically free of the upper airway artefact (equation 5).

Although equations 1–5 are valid regardless of the frequency, the analysis of the FOT data was carried out taking into account the technical reliability of FOT measurements in children [25]. Indeed, at low frequencies (<10 Hz) it is difficult to obtain a satisfactory signal-to-noise ratio owing to the relatively high breathing rate of these patients. Moreover, measurements at high frequencies (>20 Hz) are more difficult in children than in adults given their higher impedance. On the one hand, the effects of possible limitations in the common-mode rejection ratio of transducers are enhanced. On the other hand, as the frequency increases the impedance of the extrathoracic upper airways, Z_{eua} may become even lower than the respiratory impedance, especially after challenge ($Z_{rs}*$), with the result that data measured with the SG may be considerably artefactual (equation 1). Accordingly, the data analysis was focused from 10 to 20 Hz, which is a frequency range similar to the one commonly employed for quantifying bronchial challenge by FOT in children and in adults.

In conclusion, it is suggested that using the absolute or relative change in oscillatory admittance as an index for assessing bronchial reactivity eliminates, or markedly reduces, the upper airway artefact when using the forced oscilation technique standard generator. Thus, this could allow us to increase the sensitivity and specificity of the forced oscillatory technique to a degree resembling that found when using the head generator [20], but with the advantage of employing the forced oscillatory technique setup which is the more common and easiest method to use for routine lung function testing.

References

1. Gayrard P, Orekek J, Grimaud C, Charpin J. Bronchoconstrictor effects of a deep inspiration in patients with asthma. *Am Rev Respir Dis* 1975; 111: 433–439.
2. Wouters EFM, Polko AH, Schouten HJA, Visser BF. Contribution of impedance measurement of the respiratory system to bronchial challenge tests. *J Asthma* 1988; 25: 259–267.
3. Van Noord JA, Clement J, Van de Woestijne KP, Demedts M. Total respiratory resistance and reactance as a measurement of response to bronchial challenge with histamine. *Am Rev Respir Dis* 1989; 139: 921–926.
4. Snashall PD, Parker S, Phil M, Ten Haave P, Simmons D, Noble MIM. Use of an impedance meter for measuring airways responsiveness to histamine. *Chest* 1991; 99: 1183–1185.
5. Phagoo SB, Watson RA, Silverman M, Pride NB. Comparison of four methods of assessing airflow resistance before and after induced airway narrowing in normal subjects. *J Appl Physiol* 1995; 79: 518–525.
6. Sekizawa K, Sasaki H, Shimizu Y, Takishima T. Dose-response effects of methacholine in normal and in asthmatic subjects. Relationship between the site of airway response and overall airway hyperresponsiveness. *Am Rev Respir Dis* 1986; 133: 593–599.
7. Duiverman EJ, Neijens HJ, Van der Snee-van Smaalen M, Kerrebijn KF. Comparison of forced oscillometry and forced expirations for measuring dose-related responses to inhaled methacholine in asthmatic children. *Bull Eur Physiopathol Respir* 1986; 22: 433–436.
8. Rodríguez-Roisin R, Ferrer A, Navajas D, Agusti AGN, Wagner PD, Roca J. Ventilation–perfusion mismatch after methacholine challenge in patients with mild bronchial asthma. *Am Rev Respir Dis* 1991; 144: 88–94.
9. Pairon JC, Iwatsubo Y, Hubert C, *et al*. Measurement of bronchial responsiveness by forced oscillation technique in occupational epidemiology. *Eur Respir J* 1994; 7: 484–489.
10. Klug B, Bisgaard H. Measurement of lung function in awake 2–4 year old asthmatic children during methacholine challenge and acute asthma: a comparison of the impulse oscillation technique, the interrupter technique, and transcutaneous measurement of oxygen *versus* whole-body plesthysmography. *Pediatr Pulmonol* 1996; 21: 290–300.
11. Bouaziz N, Beyaert C, Gauthier R, Monin P, Peslin R, Marchal F. Respiratory system reactance as an indicator of intrathoracic airway response to methacholine in children. *Pediatr Pulmonol* 1996; 22: 7–13.
12. Chinet T, Pelle G, Macquin-Mavier I, Lorino H, Harf A. Comparison of the dose-response curves obtained by forced oscillation and plethysmography during carbachol inhalation. *Eur Respir J* 1988; 1: 600–605.
13. Decramer M, Demedts M, Van de Woestijne KP. Isocapnic hyperventilation with cold air in healthy non-smokers, smokers and asthmatic subjects. *Bull Eur Physiopathol Respir* 1984; 20: 237–243.
14. Wesseling GJ, Wouters EFM. Respiratory impedance measurements in a dose-response study of isocapnic hyperventilation with cold air. *Respiration* 1992; 59: 259–264.

15. Peslin R, Duvivier C, Gallina C, Cervantes P. Upper airway artifact in respiratory impedance measurements. *Am Rev Respir Dis* 1985; 132: 712–714.

16. Cauberghs M, Van de Woestijne KP. Effect of upper airway shunt and series properties on respiratory impedance measurements. *J Appl Physiol* 1989; 66: 2274–2279.

17. Marchal F, Haouzi P, Peslin R, Duvivier C, Gallina C. Mechanical properties of the upper airway wall in children and their influence on respiratory impedance measurements. *Pedriatr Pulmonol* 1992; 13: 28–33.

18. Marchal F, Mazurek H, Habib M, Duvivier C, Derelle J, Peslin R. Input respiratory impedance to estimate airway hyperreactivity in children: standard method *versus* head generator. *Eur Respir J* 1994; 7: 601–607.

19. Peslin R, Duvivier C, Didelon J, Gallina C. Respiratory impedance measured with head generator to minimize upper airway shunt. *J Appl Physiol* 1985; 59: 1790–1795.

20. Mazurek HK, Marchal F. Specificity and sensitivity of respiratory impedance in assessing reversibility of airway obstruction in children. *Chest* 1995; 107: 996–1002.

21. Cauberghs M, Van de Woestijne KP. Mechanical properties of the upper airway. *J Appl Physiol* 1983; 55: 335–342.

22. Peslin R, Duvivier C, Jardin P. Upper airway walls impedance measured with head plethysmograph. *J Appl Physiol* 1984; 57: 596–600.

23. Van Noord JA, Smeets J, Clement J, Van de Woestijne KP, Demedts M. Assessment of reversibility of airflow obstruction. *Am J Respir Crit Care Med* 1994; 150: 551–554.

24. Shindoh C, Sekizawa K, Hida W, Sasaki H, Takishima T. Upper airway response during bronchoprovocation and asthma attack. *Am Rev Respir Dis* 1985; 132: 671–678.

25. Marchal F, Loos N. Respiratory oscillation mechanics in infants and preschool children. *Eur Respir Mon* 1997; 5: 58–87.