Respiratory mechanics in ventilated COPD patients: forced oscillation versus occlusion techniques

R. Farré*, M. Ferrer*, M. Rotger*, A. Torres*, D. Navajas*

ABSTRACT: The respiratory mechanics of artificially ventilated chronic obstructive pulmonary disease (COPD) patients were investigated by means of the forced oscillation (FOT) and the end-inspiratory airway occlusion (AOT) techniques. FOT was applied to measure respiratory resistance ($R_{rs}$) and reactance ($X_{rs}$) from 0.25–16 Hz. Maximum ($R_{max}$) and minimum ($R_{min}$) resistances, static elastance ($E_{s}$) and time constant ($\tau$) were computed by AOT. FOT and AOT data were interpreted with models featuring airway wall shunt, tissue viscoelasticity and parallel inhomogeneity. $R_{rs}$ and $X_{rs}$, predicted from the AOT data, were computed and compared with $R_{rs}$ and $X_{rs}$ measured by FOT.

$R_{rs}$ and $X_{rs}$ (hPa·L·1) decreased from 31.2±10.3 to 5.9±4.6 and increased from -20.3±7.1 to -8.0±4.4 from 0.25–16 Hz, respectively. Central resistance ($R_{c}$) and peripheral resistance ($R_{p}$) (in hPa·L·1), and shunt elastance ($E_{sh}$) and tissue elastance ($E_{t}$) (in hPa·s·L·1) were 4.4±5.4, 28.4±15.3, 723±393 and 31.8±10.1, respectively. $R_{min}$, $R_{max}$ and $E_{t}$ were 18.4±5.9, 28.4±12.8 and 18.1±4.2 respectively, and $\tau$=0.76±0.25 s. The frequency dependence of predicted $R_{rs}$* and $X_{rs}$* differed markedly from that of measured $R_{rs}$ and $X_{rs}$.

The use of different models to interpret the measured data suggests that both airway and tissue properties determined the frequency dependence of respiratory resistance and respiratory reactance in ventilated chronic obstructive pulmonary disease patients at the investigated frequencies (0.25–16 Hz).

Optimization of the ventilator settings in mechanical ventilation is a key issue in minimizing the risk of barotrauma and hemodynamic compromise, in avoiding hyperinflation and in reducing the work of breathing [1]. Improvement in the ventilator variables may be facilitated by better understanding of the role played by the different mechanical properties of airways and tissue in determining the dynamic relationships among the pressure, flow and volume excursions applied to the patient's respiratory system [2, 3]. The use of a mechanical model to mimic respiratory mechanics as realistically as possible for each pathological situation may be helpful in predicting the outcome variables of clinical interest in response to the applied ventilator waveform. In the case of mechanically ventilated chronic obstructive pulmonary disease (COPD) patients, the conventional simple model consisting of a resistance and an elastance is not able to describe adequately the behaviour of the respiratory system [4]. In these patients, respiratory mechanics has been interpreted in terms of the viscoelastic tissue properties and/or the gas redistribution phenomena due to airways inhomogeneity [5–7].

Published works devoted to analysing in detail the dynamic response of the respiratory system in artificially ventilated COPD patients report conflicting results. Indeed, when the technique of end-inspiratory airway occlusion with a constant flow inflation was applied, the effective resistance and elastance of the respiratory system could be interpreted in terms of a homogeneous resistance and a viscoelastic tissue compartment [5]. By contrast, data obtained by means of the forced oscillation technique (FOT) in COPD patients suggested that airway inhomogeneity plays a major role in determining the frequency dependence of respiratory resistance and reactance over a wide frequency range [7]. Nevertheless, it is difficult to compare the results from these works since the two techniques applied differ in both the frequency domain and the amplitude range of excursions and were applied to patients with possibly different degrees of COPD. Therefore, the aim of this work was to characterize better the mechanics of the respiratory system in artificially ventilated COPD patients by applying the FOT and the end-inspiratory airway occlusion technique (AOT) to the same patients. A key point in making the comparison between the two techniques was to extend the FOT measurements to the low frequencies typical of the occlusion technique. To this end, a modified FOT device [8] was used which, in contrast to the set-ups used in previous measurements in mechanically ventilated patients [7, 9], allowed FOT to be applied for frequencies down to 0.25 Hz. The results obtained by means of both techniques were interpreted in terms of models featuring tissue and airway properties.
Subjects and methods

The study was conducted on five (four males and one female) COPD patients who were admitted to the respiratory intensive care unit (ICU) of the hospital owing to an acute exacerbation of their underlying disease. The COPD diagnosis was established according to the forced expiration indices determined after or before the admission of the patient into the ICU. The study protocol was approved by the Ethics Committee of the hospital and informed consent was obtained from the next of kin of the patients. The study was carried out 12–36 h after the admission of the patient to the ICU. The patients, in a supine position and intubated with a cuffed orotracheal tube (8 mm internal diameter (ID)), were mechanically ventilated with a Siemens Servoventilator 900-C (Siemens, Solna, Sweden) in the constant flow volume-controlled mode. The ventilator settings (table 1) were established by the attending physician. To carry out the study, which lasted for ~20 min, the patients were sedated (i.v. infusion of 5–10 mg of midazolam, Dormicum®; Roche SA, Madrid, Spain) and paralysed (i.v. infusion of 2 mg of pancuronium bromide, Pavulon®; Organon-Hermes SA, Sant Boi de Llobregat, Spain). At the start of the study, tracheal secretions were conventionally aspirated and external positive end-expiratory pressure (PEEP), if any, was removed. The inflating pressure of the endotracheal tube cuff was checked periodically and care was taken to avoid leaks in the connections.

Flow was measured by means of a heated Fleisch-II type pneumotachograph (Metabo, Epalinges, Switzerland) placed between the Y-piece of the ventilator and the endotracheal tube. The pressure drop across the pneumotachograph was recorded with a differential transducer (±2 hPa, LCVR; Celesco, Canoga Park, CA, USA). Tracheal pressure was measured with a piezo-resistive pressure transducer (176PC14; Honeywell, Freeport, IL, USA) connected to a catheter (50 cm in length and 0.12 cm ID) with a lateral pressure port at its tip placed 2 cm beyond the outlet of the endotracheal tube [10]. This catheter was periodically cleaned by injecting a bolus of 3 mL of air through it. Pressure and flow signals were low-pass filtered (Butterworth, eight poles, 32 Hz), sampled at 128 Hz and stored in a microcomputer. A FOT generator especially designed for low-frequency measurements in mechanical ventilated patients [8] was placed in parallel with the ventilator in the inspiratory line. The FOT generator was connected to the inspiratory line by means of a flexible tube (2 mm ID, 80 cm) and a Y-valve. This valve, which was closed during the normal ventilator cycling, was connected directly to the Y-piece to increase minimally the air volume, and hence the compliance, in the ventilation line when the valve was closed. The compliance of the system connecting the ventilator to the patient was decreased by omitting the humidifier and reducing the length of the standard low-compliance tubing of the ventilator (2 cm ID, 60 cm) [5]. Four end-inspiratory occlusion manoeuvres and four FOT measurements were carried out in a random order in each patient, allowing at least 10 normal ventilation cycles between measurements.

To measure respiratory system resistance ($R_s$) and reactance ($X_s$) by FOT the expiratory valve of the ventilator was occluded by pressing the corresponding button and the valve connecting the FOT generator to the patient was manually opened. The forced oscillation signal ($±3$ hPa, ±80 mL·s$^{-1}$) contained power at 0.25, 0.5, 1, 2, 4, 8 and 16 Hz and the amplitudes of the low-frequency components were enhanced. FOT was applied for ~12 s of end-expiratory pause at the intrinsic PEEP (PEEPi) corresponding to the ventilator settings in each patient (table 1). After application of FOT the normal ventilator cycle was resumed. $R_s$ and $X_s$ were computed from the last 8 s of the recorded pressure and flow. These signals were divided into three blocks of 4 s each (50% overlapping). After subtraction of the mean value, each block was multiplied by a Hannings window and its fast Fourier transform (FFT) was computed. $R_s$ and $X_s$ were computed by averaging in the frequency domain (12 blocks) the data from the four FOT measurements. The frequency responses of the pressure and flow measuring systems were digitally corrected.

The end-inspiratory occlusion manoeuvre was applied first by pushing (~3 s) the end-expiratory button of the ventilator to reach PEEPi, then by releasing the button to allow for the inspiratory inflation and then by pressing the end-inspiratory pause button for ~6 s before resuming normal ventilation [5, 11–13]. For each occlusion manoeuvre the closing time was defined as the time at which flow decreased by 50%. The four occlusion manoeuvres in each patient were averaged after being synchronized in accordance with the closing time. The effect of the finite closure time of the ventilator valve was reduced as suggested [14]. Pressure immediately before flow interruption ($P_i$) was determined by extrapolating the preocclusion increasing pressure to the closing time. Pressure immediately after flow interruption ($P_2$) was determined by backextrapolation of the postocclusion decreasing pressure to the closing time. The plateau pressure at 3 s after the occlusion ($P_3$) and the time constant ($\tau$) of the pressure relaxation immediately after the flow interruption were computed. The resistances and elastances commonly used to characterize the occlusion manoeuvre were computed as $R_{min}=(P_1-P_2)/V'$, $R_{max}=(P_1-P_3)/V'$, $E_{stat}=(P_4-P_3)/V'T$, and $\Delta E=(P_2-P_1)/V'T$ [5, 11–13], where $R_{min}$ = minimum resistance, $R_{max}$ = maximum resistance, $V'$ = gas flow, $E_{stat}$ = static elastance, $V_T$ = tidal volume, and $\Delta E$ = differences in elastance.

Data measured by FOT and by the occlusion technique were interpreted in terms of the models A, B and C in figure 1. Model A, which was initially proposed by MEAD [15] and recently used to interpret FOT data in ventilated COPD patients [7], consists of a central resistance ($R_c$), a shunt elastance ($E_{sh}$) accounting for airway wall compliance, a peripheral resistance ($R_p$) and a tissue elastance ($E_t$). Model B, usually employed to interpret respiratory

Table 1. – Ventilation parameters

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>$f_b$ (beats·min$^{-1}$)</th>
<th>$n$</th>
<th>$V_T$ (L)</th>
<th>$V'$ (L·s$^{-1}$)</th>
<th>$F_{O_2}$ (%</th>
<th>PEEP (hPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11.2</td>
<td>1.29</td>
<td>0.512</td>
<td>0.397</td>
<td>0.40</td>
<td>10.6</td>
</tr>
<tr>
<td>2</td>
<td>11.3</td>
<td>1.37</td>
<td>0.423</td>
<td>0.308</td>
<td>0.30</td>
<td>10.9</td>
</tr>
<tr>
<td>3</td>
<td>1.5</td>
<td>0.95</td>
<td>0.539</td>
<td>0.367</td>
<td>0.35</td>
<td>10.3</td>
</tr>
<tr>
<td>4</td>
<td>11.2</td>
<td>1.15</td>
<td>0.556</td>
<td>0.483</td>
<td>0.40</td>
<td>10.1</td>
</tr>
<tr>
<td>5</td>
<td>11.3</td>
<td>1.33</td>
<td>0.589</td>
<td>0.443</td>
<td>0.32</td>
<td>10.8</td>
</tr>
<tr>
<td>Mean</td>
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<td>1.22</td>
<td>0.524</td>
<td>0.440</td>
<td>0.35</td>
<td>10.5</td>
</tr>
</tbody>
</table>

$\Delta$: standard deviation; $f_b$: ventilator frequency; $n$: inspiratory time; $V_T$: tidal volume; $V'$: constant flow inflation; $F_{O_2}$: oxygen inspiratory fraction; PEEP: intrinsic positive end-expiratory pressure.
system mechanics by means of the occlusion technique [16], consists of an airway resistance ($R_1$) and a viscoelastic compartment of the respiratory tissues ($R_a$, $E_a$, $R_b$, $E_b$) pathways. Model C corresponds to a respiratory system inhomogeneity characterized by two parallel resistance-elastance ($R_r$-$E_a$, $R_t$-$E_b$) pathways. The concept of parallel inhomogeneity was initially proposed by Oms et al. [17] and has more recently been employed to interpret the frequency dependence of resistance and elastance [18–20].

As these models (A, B and C) are described by the same general equation of motion, they exhibit the same frequency dependence of resistance and reactance and the same response when subjected to the occlusion manoeuvre [6, 21]. Consequently, the parameters of one of the models can be computed from the parameters of any of the other models. $R_{rs}$ and $X_{rs}$ measured by FOT were used to compute the $R_c$, $E_{sh}$, $R_p$ and $E_1$ of model A by minimizing the distance ($ε$) between the model and the data [7] for positive values of the parameters $R_1$, $E_1$, $R_2$ and $E_2$ of model B and $R_a$, $E_a$, $R_b$ and $E_b$ of model C were computed from the parameters derived from model A. The data obtained by the occlusion technique were used to compute the parameters $R_1$, $R_2$, $E_1$ and $E_2$ of model B ($R_1=R_{min}$, $E_1=E_{sh}$, $R_2=(R_{max}-R_{min})(1-\exp(-n/τ))$ and $E_2=R_2/τ$ [5, 11–13, 21–23]) and these values were used to compute $R_c$, $E_{sh}$, $R_p$ and $E_1$ of model A and $R_a$, $E_a$, $R_b$ and $E_b$ of model C. The frequency dependence of respiratory resistance ($R_{rs^*}$) and reactance ($X_{rs^*}$) estimated for each patient from the occlusion technique was computed ($R_{rs^*}=R_1+R_2/(1+(2πfτ)^2)$ and $X_{rs^*}=E_{sh}+2πfτ^2E_2/(1+(2πfτ)^2)$ [21]).

In addition to the simple models A, B and C, $R_{rs}$ and $X_{rs}$, measured by FOT were interpreted by a more general model (fig. 1D) which includes compliant airways and a viscoelastic tissue compartment. The airway compartment consisted of $R_c$ and $R_p$ separated by $E_{sh}$, as in model A. The tissue compartment was characterized by a Newtonian tissue resistance ($R_1$), an elastance ($E_1$) and an element with a time constant ($R_2/E_2$), as in model B. In this model, $R_1$ and $R_p$ play the same role in determining its mechanical properties and are, therefore, indistinguishable.

**Results**

Figure 2a plots the $R_{rs}$ and $X_{rs}$ from 0.25–16 Hz measured by FOT in a representative patient (no. 1). Figure 3a shows that, on average, $R_{rs}$ (mean±SE) decreased progressively over the frequency bands from 31.2±4.6 hPa·s·L-1 at 0.25 Hz to 5.9±2.1 hPa·s·L-1 at 16 Hz. $X_{rs}$ (mean±SE) increased markedly from -20.3±3.2 hPa·s·L-1 at 0.25 Hz to -10.1±1.8 hPa·s·L-1 at 2 Hz and from then on slightly increased to -8.0±2.0 hPa·s·L-1 at 16 Hz. Respiratory elastance ($E_{rs}$; $E_{rs^*}=-2π/X_{rs}$) increased progressively with frequency in all patients (fig. 4). The use of models A, B and C to interpret the measured $R_{rs}$ and $X_{rs}$ resulted in...
the parameters shown in table 2. The quality of the fit achieved (ε) is shown in table 2 and is illustrated in the representative example of figure 2a. The use of the more complex model D to fit the Rs and Xs measured by FOT resulted in the parameter values shown in table 3. This model was able to fit the data better than models A, B and C: on average, the fitting error ∆ε decreased markedly from 2.35 hPa·s·L⁻¹ (table 2, fig. 2a) to 0.83 hPa·s·L⁻¹ (table 3, fig. 2b).

The values of the resistances (Rmin, Rmax) and elastances (Emin, Emax) describing the end-inspiratory occlusion manoeuvre are shown in table 4. Rmax was systematically higher than Rmin and on average their difference (ΔR), which is an indirect index of the frequency dependence of resistance, was considerable: ΔR=10.0 hPa·s·L⁻¹ (35% of Rmax). ∆E was systematically positive and on average was ∆E=8.0 hPa·L⁻¹ (44% of Emin). The time constant (τ) corresponding to the slow decrease in pressure after the airway occlusion was in the order of 1 s (0.76±0.25 s). The parameters of models A, B and C computed from the occlusion data are shown in table 5. Rs* and Xs* corresponding to the models (A, B and C) used to interpret the occlusion manoeuvres in patient no. 1 are shown in figure

Table 2. – Resistances and elastances derived by fitting models A, B and C of figure 1 to forced oscillation technique data

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>ε</th>
<th>Rc</th>
<th>Esh</th>
<th>Rp</th>
<th>Ei</th>
<th>R1</th>
<th>E1</th>
<th>R2</th>
<th>E2</th>
<th>Rs</th>
<th>Ea</th>
<th>Rb</th>
<th>Eb</th>
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<tr>
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<td>13.6</td>
<td>702</td>
<td>24.0</td>
<td>42.2</td>
<td>13.6</td>
<td>39.8</td>
<td>21.4</td>
<td>662</td>
<td>23.3</td>
<td>1814</td>
<td>36.5</td>
<td>40.7</td>
</tr>
<tr>
<td>2</td>
<td>1.99</td>
<td>3.9</td>
<td>264</td>
<td>51.2</td>
<td>43.3</td>
<td>3.9</td>
<td>37.2</td>
<td>37.8</td>
<td>227</td>
<td>5.7</td>
<td>313</td>
<td>53.6</td>
<td>42.2</td>
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<tr>
<td>3</td>
<td>1.63</td>
<td>0.4</td>
<td>850</td>
<td>11.7</td>
<td>26.2</td>
<td>0.4</td>
<td>25.4</td>
<td>11.0</td>
<td>825</td>
<td>0.4</td>
<td>911</td>
<td>12.1</td>
<td>26.1</td>
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<tr>
<td>4</td>
<td>3.78</td>
<td>3.3</td>
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<td>35.2</td>
<td>25.4</td>
<td>3.3</td>
<td>24.9</td>
<td>33.9</td>
<td>1280</td>
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<td>38.4</td>
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<tr>
<td>5</td>
<td>1.76</td>
<td>0.8</td>
<td>496</td>
<td>20.0</td>
<td>21.9</td>
<td>0.8</td>
<td>21.0</td>
<td>18.3</td>
<td>475</td>
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<td>723</td>
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<td>4.4</td>
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<td>SD</td>
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<td>396</td>
<td>9.5</td>
<td>647</td>
<td>16.2</td>
<td>9.5</td>
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Resistances are in hPa·s·L⁻¹ and elastances in hPa·L⁻¹: fitting error. See figure 1 for definitions of resistances and reactances.

Table 3. – Resistances and elastances derived by fitting model D of figure 1 to forced oscillation technique data

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>ε</th>
<th>Rs</th>
<th>Ers</th>
<th>Rp</th>
<th>Ei</th>
<th>R1</th>
<th>E1</th>
<th>R2</th>
<th>E2</th>
<th>Rs*</th>
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<th>Rp+R1</th>
<th>E1</th>
<th>R2</th>
<th>E2</th>
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<td>39.8</td>
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<td>40.9</td>
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<tr>
<td>2</td>
<td>0.53</td>
<td>2.14</td>
<td>374</td>
<td>29.5</td>
<td>38.2</td>
<td>20.4</td>
<td>119</td>
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<tr>
<td>3</td>
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<td>6.4</td>
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<td></td>
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<tr>
<td>Mean</td>
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<td>917</td>
<td>22.4</td>
<td>27.2</td>
<td>16.5</td>
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<tr>
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Resistances are in hPa·s·L⁻¹ and elastances in hPa·L⁻¹: ε (in hPa·s·L⁻¹): fitting error. See figure 1 for definitions of resistances and reactances.

The frequency dependence of respiratory elastance (Ers) measured by forced oscillation technique in the five patients with chronic obstructive pulmonary disease. Labels indicate the patient number. The use of the more complex model D to fit the Rs and Xs measured by FOT resulted in the parameter values shown in table 3. This model was able to fit the data better than models A, B and C: on average, the fitting error ε decreased markedly from 2.35 hPa·s·L⁻¹ (table 2, fig. 2a) to 0.83 hPa·s·L⁻¹ (table 3, fig. 2b).

Fig. 3. – a) Respiratory resistance (Rrs; ●) and reactance (Xrs; ▼) measured by the forced oscillation technique. b) Rrs* (●) and Xrs* (▼) derived from the airway occlusion technique data. Values are shown as means±SE.

Fig. 4. – Frequency dependance of respiratory elastance (Ers) measured by forced oscillation technique data. Values are shown as mean±SE.
No. Patient from the end-inspiratory occlusion manoeuvres

tance frequencies (above ~1 Hz). Moreover, the effective elas-

ting the frequency dependence of

to account for the dynamic response (0.25–16 Hz) of

ting the models (A, B and C) used to interpret the

dots (dashed lines). The mean±SE of \( r_s^* \) and \( X_s^* \) corre-

ding to the models (A, B and C) featured only

A considerable discrepancy was found when compar-

ing the frequency dependence of \( r_s \) and \( X_s \) measured by

The first result obtained when applying FOT to mec-

anically ventilated COPD patients over a frequency band

tending down to spontaneous breathing rates was that
\( r_s \) and \( X_s \) exhibited a marked frequency dependence

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>( R_{\text{min}} ) (hPa·s·L(^{-1}))</th>
<th>( R_{\text{max}} ) (hPa·s·L(^{-1}))</th>
<th>( E_{\text{st}} ) (hPa·L(^{-1}))</th>
<th>( \Delta E ) (hPa·L(^{-1}))</th>
<th>( \tau ) (s)</th>
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<td>12.2</td>
<td>7.4</td>
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<td>28.8</td>
<td>16.1</td>
<td>3.7</td>
<td>0.81</td>
</tr>
<tr>
<td>Mean</td>
<td>18.4</td>
<td>28.4</td>
<td>18.1</td>
<td>8.0</td>
<td>0.76</td>
</tr>
<tr>
<td>SD</td>
<td>5.9</td>
<td>12.8</td>
<td>4.2</td>
<td>6.3</td>
<td>0.25</td>
</tr>
</tbody>
</table>

\( R_{\text{min}} \): minimum resistance; \( R_{\text{max}} \): maximum resistance; \( E_{\text{st}} \): static elastance; \( \Delta E \): change in elastance; \( \tau \): time constant.

2 (dashed lines). The mean±SE of \( r_s^\# \) and \( X_s^\# \) corre-

A considerable discrepancy was found when compar-

The first result obtained when applying FOT to mec-

Table 5. - Resistances and elastances derived by fitting models A, B and C of figure 1 to the occlusion manoeuvres data

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>( R_e ) (hPa·L(^{-1}))</th>
<th>( E_b ) (hPa·L(^{-1}))</th>
<th>( R_p ) (hPa·L(^{-1}))</th>
<th>( E_t ) (hPa·L(^{-1}))</th>
<th>( R_1 )</th>
<th>( E_2 )</th>
<th>( R_1 )</th>
<th>( E_2 )</th>
<th>( R_s )</th>
<th>( E_s )</th>
<th>( R_b )</th>
<th>( E_b )</th>
</tr>
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<tr>
<td>1</td>
<td>11.7</td>
<td>33.0</td>
<td>81.1</td>
<td>72.7</td>
<td>11.7</td>
<td>22.7</td>
<td>7.9</td>
<td>10.3</td>
<td>83.6</td>
<td>114</td>
<td>25.4</td>
<td>28.4</td>
</tr>
<tr>
<td>2</td>
<td>23.9</td>
<td>98.6</td>
<td>43.1</td>
<td>26.8</td>
<td>23.9</td>
<td>21.1</td>
<td>26.6</td>
<td>77.5</td>
<td>53.3</td>
<td>302</td>
<td>58.1</td>
<td>22.7</td>
</tr>
<tr>
<td>3</td>
<td>12.6</td>
<td>22.7</td>
<td>52.8</td>
<td>26.4</td>
<td>12.6</td>
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<td>4</td>
<td>20.2</td>
<td>26.8</td>
<td>77.4</td>
<td>58.7</td>
<td>20.2</td>
<td>18.4</td>
<td>7.6</td>
<td>8.4</td>
<td>126</td>
<td>156</td>
<td>33.5</td>
<td>20.9</td>
</tr>
<tr>
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<td>23.8</td>
<td>23.6</td>
<td>60.4</td>
<td>50.7</td>
<td>23.8</td>
<td>16.1</td>
<td>6.1</td>
<td>7.5</td>
<td>159</td>
<td>220</td>
<td>33.8</td>
<td>17.4</td>
</tr>
<tr>
<td>Mean</td>
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<td>40.9</td>
<td>62.9</td>
<td>47.1</td>
<td>18.4</td>
<td>18.1</td>
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<td>22.8</td>
<td>94.7</td>
<td>171</td>
<td>36.9</td>
<td>20.9</td>
</tr>
<tr>
<td>SD</td>
<td>5.9</td>
<td>32.5</td>
<td>16.1</td>
<td>20.2</td>
<td>5.9</td>
<td>4.2</td>
<td>8.4</td>
<td>30.6</td>
<td>44.7</td>
<td>92.7</td>
<td>12.4</td>
<td>5.1</td>
</tr>
</tbody>
</table>

Resistances are in hPa·s·L\(^{-1}\) and elastances in hPa·L\(^{-1}\). See figure 1 for definitions of resistances and reactances.

Discussion

The first result obtained when applying FOT to mec-
anically ventilated COPD patients over a frequency band

whereas the analysis of the occlusion manoeuvre data re-

2 at ~1 Hz and then remained constant at this value at higher frequencies.

For the same frequency band in healthy, anaesthetized, paralysed patients [25]. The most remarkable feature of \( X_s \) (fig. 3) was that it always remained negative and therefore no patient exhibited the resonant frequency within the investigated frequency band, which is also in contrast to the findings in healthy patients [25]. The only FOT data available on mechanically ventilated patients correspond to frequencies above 4–5 Hz [7, 9]. Bédon et al. [9] reported a negative frequency dependence of \( R_s \) (35% decrease from 4–16 Hz), which was smaller than that found in the present study (65% decrease) between these two relatively high frequencies. Nevertheless, data from these

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Model A</th>
<th>Model B</th>
<th>Model C</th>
</tr>
</thead>
<tbody>
<tr>
<td>( R_e ) (hPa·L(^{-1}))</td>
<td>11.7</td>
<td>33.0</td>
<td>81.1</td>
</tr>
<tr>
<td>( E_e ) (hPa·L(^{-1}))</td>
<td>22.2</td>
<td>79.7</td>
<td>10.3</td>
</tr>
<tr>
<td>( R_p ) (hPa·L(^{-1}))</td>
<td>23.9</td>
<td>98.6</td>
<td>43.1</td>
</tr>
<tr>
<td>( E_t ) (hPa·L(^{-1}))</td>
<td>21.1</td>
<td>26.6</td>
<td>77.5</td>
</tr>
<tr>
<td>( R_1 )</td>
<td>11.7</td>
<td>22.7</td>
<td>7.9</td>
</tr>
<tr>
<td>( E_2 )</td>
<td>22.7</td>
<td>79.7</td>
<td>10.3</td>
</tr>
<tr>
<td>( R_1 )</td>
<td>23.9</td>
<td>21.1</td>
<td>26.6</td>
</tr>
<tr>
<td>( E_2 )</td>
<td>21.1</td>
<td>77.5</td>
<td>10.3</td>
</tr>
</tbody>
</table>

\( R_e \) and \( E_e \) correspond to the fitted models A, B and C, respectively [21]. Data from FOT resulted in parameter sets accounting for a time constant of ~35 ms, whereas the analysis of the occlusion manoeuvre data resulted in parameter sets for models A, B and C accounting for a much greater time constant of ~0.8 s.
authors were obtained from a population including few
COPD patients (3 out of 16). By contrast, POESIN et al. [7]
reported data from a population of mechanically venti-
lated patients, most of whom (11 out of 17) suffered from
COPD. These authors analysed respiratory mechanics at
frequencies above 5 Hz during different phases of the ven-
tilation cycle and reported a frequency dependence of $R_t$
and $X_t$ consistent with that found in the patients in this
study [7]. The results obtained when using model A
(table 2) indicate that the peripheral resistance $R_p$
accounted for 87% of the total resistance ($R_t+R_p$) and the
mean elastance $E_{sh}$ partitioning central and peripheral
resistances corresponded to a compliance of 1.4 mL·hPa$^{-1}$. This
value was close to those reported by POESIN et al. [7]
(0.64–2.56 mL·hPa$^{-1}$) when using the same model to ana-
yse FOT data in ventilated COPD patients from 5–20 Hz.
Models B and C, which attribute the frequency depend-
ence of $R_t$ to tissue viscoelasticity or to parallel inhomo-
genesis, respectively, resulted in a much lower time
constant $\tau$ (<35 ms) than expected for these two mecha-
nisms, which seem to determine the frequency depend-
ence of $R_t$ mainly at the lowest frequencies [19, 20]. The
fact that the frequency dependence of $R_t$ ($E_t$) and $E_{sh}$
(fig. 4) extends to frequencies $>2$ Hz suggests that the role
played by airway wall shunting is not negligible [20].

The results obtained by means of the end-inspiratory
AOT (table 4) were in keeping with the few data on COPD
patients available in the literature. Resistances and elas-
tances reported by POESLE et al. [5] were smaller than those
in the present patients (by ~16% in $E_s$ and $\Delta E$ and by
~42% in $R_{min}$ and $R_{max}$), probably owing to a greater
severity in the obstructive pathology and/or a higher deg-
ree of hyperinflation in the patients in this study, as sug-
gested by the fact that the measured PEEP ($\tau$) was
44% greater than the value reported by POESLE et al. [5].
However, a remarkable agreement was found in the ratios
$R_{min}/R_{max}$ (0.64 from our data and 0.65 in [5]) and $(E_s+
\Delta E)/E_s$ (0.70 both from our data and in [5]), which are
representative of the frequency dependence of the respira-
tory system. The time constant $\tau$ ~0.8 s found in this
study, which could not be confirmed with data on COPD
patients since it was not reported in [5], was of the same
order of magnitude, although smaller than in normal sub-
jects (~1.3 s [11]). As expected, interpretation of the oc-
closure technique data with model B, which is commonly
employed with this technique, provides tissue parameters
(table 5) consistent with the values reported previously.
From the results obtained by using model A, shunt elas-
tance ($E_{sh}$) would be similar to tissue elastance ($E_t$) (table
5). According to the parameters for model C, the two par-
allel compartments would be characterized by time con-
stants with a ratio, $(R_d/E_d)/(R_t/E_t)$, of about 1/3. The more
complex model D was not fitted to the occlusion data
since the model interpretation of these data is limited by
the relatively narrow effective band width of the signals
recorded. Indeed, the occlusion technique, which is a for-
ced excitation with a pulse of flow of ~1 s of duration, has
its main frequency components restricted to the lowest
frequencies (d.c. ~2 Hz). Moreover, the actual closure
time of the valve limits the practical applicability of the
technique for detecting short time constants and, hence,
reduces the reliability of parameter estimates when ana-
ysing high frequencies [26]. In this regard, it should be
noted that the occlusion data obtained in this study, and
in others in the literature where the interruption is per-
formed with the valve of a conventional ventilator, are
affected by the finite closure time of the valve. Conse-
quently, owing to the practical limitations arising from
occluding the airway with the valve of a conventional
ventilator, this technique does not allow an exploration of
respiratory system mechanics for a frequency band as
wide as the FOT. However, the use of a more rapidly clos-
ing valve could improve the high frequency sensitivity of
the occlusion technique.

The FOT data measured from 0.25–16 Hz and their
model interpretation suggest that simple models such as
A, B or C (fig. 1), which are associated with a unique time
constant, are not able to describe adequately the frequency
dependence of $R_t$ and $X_t$ in ventilated COPD patients.
By contrast, a model (D in fig. 1) featuring more than one
mechanism, i.e. airway wall shunt and tissue viscoelastic-
ity, significantly improved the quality of fitting (table 3,
fig. 2). This model suggested that, on the one hand, the
viscoelastic tissue compartment was characterized by a
relatively long time constant ($R_t/E_t$ was 0.45 s on average,
table 3) similar to that obtained from the occlusion tech-
nique (table 5). On the other hand, airway wall shunt was
characterized by a much shorter time constant (~$R_t/R_p$
$E_{sh}$ on average ~30 ms; table 5) explaining the frequency
dependence observed at high frequencies. Nevertheless, it
should be noted that the fact that model D provided a
reasonable description of $R_t$ and $X_t$ does not exclude the
suitability of other models allowing for more than one
time constant, e.g. models that, as expected in ventilated
COPD patients, include parallel inhomogeneities [19, 20]
in addition to airway wall shunting and tissue viscoelastic-
ity. Consequently, the FOT applied for a frequency band
such as the one in this work (0.25–16 Hz), which is wide
enough to cover several time constants, is a potentially
useful tool for exploring respiratory system properties in
artificially ventilated COPD patients. Comparing the res-
ults of the FOT and AOT is of interest since the respira-
tory system is subjected to considerably different volume
excursions with the two techniques. Therefore, the results
obtained from tidal volume excursions (AOT) and from
small-amplitude FOT measurements at end-inspiratory
and end-expiratory pauses could provide information about
nonlinearities and may be useful in elucidating the mech-
anism involved in inhomogeneous airway constriction
[27, 28].

The potential clinical interest of the above results and
modelling is enhanced by the fact that the two techniques
are noninvasive and easily applicable with minimal distur-
bance of the artificial ventilation. On the one hand, the air-
way occlusion technique has been extensively used in the
literature to analyse respiratory mechanics in ventilated
healthy subjects and in patients with different pathologies.
On the other hand, the interest in the forced oscillation
 technique for monitoring respiratory mechanics in intu-
bated patients has recently been pointed out [29]. Its feasi-
bility has been facilitated by the solution of the main
methodological problems concerning this technique (gen-
erators capable of operating in parallel with the ventilator
[7, 8, 10] and ways of overcoming the nonlinearity of the
endotracheal tube [7, 30–32]. An additional feature of the
forced oscillation technique is that it may provide auto-
matic and on-line assessment of respiratory mechanics
over the breathing cycle [7, 33–35]. As the forced oscilla-
tion technique allows practical assessment of respiratory
mechanics over a frequency band wider than the occlusion
technique, its application in ventilated patients with chronic obstructive pulmonary disease may provide data for monitoring the patient’s status and progress and, therefore, may be useful in optimizing the ventilator settings.

Acknowledgements: The authors wish to thank M.A. Rodríguez for his technical assistance.

References
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