A new FOT set-up for the assessment of respiratory system mechanics in mechanically ventilated infants

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Abstract—The assessment of respiratory system mechanics in mechanically ventilated newborns would help in tailoring the ventilatory settings. The Forced Oscillations Technique (FOT) is a non-invasive method for the measurement of the mechanical properties of the respiratory system. The aim of the present work was to develop a measurement set-up suitable to apply FOT in mechanically ventilated newborns. Forced oscillations were generated by a servo-controlled linear motor connected to the inspiratory line of the ventilator. Pressure and flow were measured at the inlet of the tracheal tube and used to compute impedance. The set-up was tested on a mechanical analog of the infant's respiratory system showing good agreement with a traditional FOT set-up. The performance of the system was not influenced by the positive pressures generated by the ventilator. Finally, the system was well tolerated by 5 preterm babies and the measurements allowed to track changes in respiratory mechanics associated to changes in the pressure delivered by the ventilator.

Forced oscillations technique; infants; mechanical ventilation

I. INTRODUCTION

The assessment of the mechanical properties of the respiratory system would be very useful in order to optimize the ventilatory strategy in mechanically ventilated infants.

Unfortunately none of the traditional techniques used for the evaluation of lung function is suitable for this application, because they either require the cooperation of the subject or they are affected by respiratory muscles activity or by non-linearities of the system.

The forced oscillation technique (FOT) is a noninvasive tool for the investigation of respiratory mechanics introduced by DuBois et al. in 1956 [1]. The most attractive feature of FOT is that it is not affected by spontaneous breathing activity and it does not require particular respiratory maneuvers because external driving signals (the forced oscillations) are applied and overimposed on the normal breathing. The mechanical response of the respiratory system to the stimulus is evaluated in terms of respiratory system impedance (Zrs). Zrs is composed of resistance (Rrs) and reactance (Xrs), which accounts for the compliance and inertance of the system. Zrs is computed by the principles of linear systems analysis. Since the respiratory system, especially in diseased conditions, may be strongly non-linear the requirement of linearity is satisfied by the use of small-amplitude oscillations.

The aim of the present work was to develop and validate a measurement set-up suitable for the application of FOT in mechanically ventilated infants.

II. MATERIALS AND METHODS

A. Forced oscillations generator

Traditionally in FOT set-ups used during mechanical ventilation the oscillations are generated by a loudspeaker enclosed in a rigid box. The limitation of this solution is that the loudspeaker and the gas enclosed in the box and in the additional tubing represents an additional compliance to the inspiratory line of the ventilator. So, if the inspiratory pressure rise is too slow because it is smoothed through the complaint circuit, there will be a delay between the patient’s respiratory effort and the ventilation. Preliminary measurements on preterm babies showed that this delay induces respiratory fatigue, as demonstrated by an increased Silverman score.

For the present application the forced oscillations generator has to meet the following requirements:

1. It should generate oscillations in the frequency range of 5-20 Hz.
2. Its behavior should not be influenced by the pressures delivered by the ventilator.
3. It should add the lowest possible compliance to the patient circuit, in order to be well tolerated even by very low birth weight preterm infants (gestational age (GA) < 37 weeks; weight < 1500 g).
4. It should be suitable for the application in the neonatal intensive care environment.

In order to achieve this result we generated the oscillations using a 20 ml glass syringe, the piston of which was moved by a servocontrolled linear motor. The position of the motor was controlled in closed loop, using a PID controller, the parameters of which were tuned using Zigler and Nicolson...
A digital-to-analog board (NI-DAQ USB-6221, National Instruments, Austin, TX) mounted on a personal computer was used to generate the signal which, amplified, controlled the motor. The oscillations generator is a modified version of that used by Dellacà et al [2] to study the development of edema in rats. However there is a relevant difference between the two set-ups: in the present study the oscillator is placed in parallel to the mechanical ventilator, in the other one it was used both to ventilate and stimulate the animal. In the present study measurements were performed at three stimulating frequencies: 5, 11 and 19 Hz. The amplitude of the driving signal was adjusted in order to have a peak-to-peak amplitude of the pressure swing of ~2 cmH$_2$O.

Fig. 1 is a schematic representation of the FOT set-up.

![Fig. 1. Schematic representation of the set-up](image)

**B. Measurements**

The pressure signal was measured by a differential pressure transducer (PXLA0075DN, Sensym, Milpitas, CA). The flow signal was measured by a mesh-type heated pneumotachograph (Hans Rudolph 8410A, resistance = 0.6 cmH$_2$O/l s at 0.27 l/s, deadspace volume = 1.3 ml) coupled with a differential pressure transducer (PXLA02X5DN, Sensym, Milpitas, CA). The common mode rejection ratio of the flow channel, which may be critical with high impedances, like those of the infants, was ≥ 50 dB up to 20 Hz. All the signals were sampled at 600 Hz by the same A/D-D/A board used to control the motor and recorded on a personal computer.

**C. In vitro study**

The validation of the measuring set-up was performed on a mechanical analogue of the infant’s respiratory system by comparison with a traditional loudspeaker-based set-up. The mechanical model consisted in a tube (length = 6.1 cm, ID = 1.5 mm) and a 0.5 l rigid bottle. This model resulted in a simple R-L-C series ($R = 92$ cmH$_2$O/s/l, $C = 0.35$ ml/cmH$_2$O, $L = 0.42$ cmH$_2$O s$^{-2}$/l).

In order to enhance the S/N ratio we used single frequency oscillations at 5, 11 and 19 Hz to stimulate the system.

Since the performance of the motor can vary depending on the pressure that it has to stand, the measurements were performed at three different levels of positive end-expiratory pressure (PEEP): the lowest, the average and the highest values used in the clinical practice (2 cmH$_2$O, 6 cmH$_2$O, 10 cmH$_2$O).

**D. In vivo study**

The measurements were performed in a neonatal intensive care unit. The study was approved by the institutional ethical committee and informed consent was obtained by the parents. 5 infants were enrolled. Patients’ characteristics are reported in Table I.

**TABLE I

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>GA</th>
<th>PNA</th>
<th>BW</th>
<th>WM</th>
<th>RP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 F</td>
<td>24</td>
<td>30</td>
<td>810</td>
<td>650</td>
<td>810</td>
<td>BPD</td>
</tr>
<tr>
<td>2 M</td>
<td>29</td>
<td>1</td>
<td>1490</td>
<td>1400</td>
<td>RDS</td>
<td></td>
</tr>
<tr>
<td>3 M</td>
<td>31</td>
<td>1</td>
<td>1630</td>
<td>1640</td>
<td>RDS</td>
<td></td>
</tr>
<tr>
<td>4 M</td>
<td>26</td>
<td>4</td>
<td>845</td>
<td>755</td>
<td>RDS</td>
<td></td>
</tr>
<tr>
<td>5 M</td>
<td>33</td>
<td>1</td>
<td>2310</td>
<td>2310</td>
<td>RDS</td>
<td></td>
</tr>
</tbody>
</table>

GA: Gestational Age (weeks); PNA: Post-Natal Age (days); BW: Birth Weight (g); WM: Weight at Measure (g); RP: Respiratory Pathology; BPD: Broncho-Pulmonary Dysplasia; RDS: Respiratory Distress Syndrome.

Measurements were performed while PEEP was decreased from 10 to 2 cmH$_2$O in one minute steps of 2 cmH$_2$O. To be sure that measurements at different frequencies were performed in the same condition and to minimize the duration of the measurement for the in vivo study we used a composite stimulating signal containing 5, 11 and 19 Hz.

**E. Data processing**

Taking advantage of the a priori knowledge of the frequency components of the forcing signal, impedance was computed using the least squared method [3].

In the in vivo study, in order to separate the different stimulus frequencies, the pressure and flow signals were filtered with a 2nd order band-pass butterworth filter with a bandwidth of 2Hz centered on each stimulating frequency. As insufficient electro-mechanical characteristics of the generator, fast respiratory flow transients, strong non-linearities of the respiratory system, poor S/N ratio and other factors can distort the flow signal, we used the Flow Shape Index (FSI) to identify inaccurate sinusoidal fitting. Briefly, FSI is the mean sign-less difference between the observed flow oscillation and the ideal sine wave having the same Fourier coefficients, expressed as a fraction of the amplitude of the oscillation. The sinusoidal fitting was considered accurate only for FSI values lower that 0.2 as previously suggested [4].

During inspiration, the FSI overcomes the threshold of 0.2 because the frequency content of the ventilatory waveform includes the stimulating frequencies. In order to avoid this artifact, only the end-expiratory values of impedance were considered.
III. RESULTS

Fig. 2 shows an example of pressure and flow tracings acquired in vivo over which single frequency forced oscillations at 5Hz are superimposed during conventional mechanical ventilation. The corresponding traces of FSI, resistance and reactance are also reported.

A. In vitro study

Table II shows Rs and Xs measured using the two different set-ups at 0 PEEP. Data are expressed as average ± SD of 5 consecutive breaths.

<table>
<thead>
<tr>
<th>PEEP</th>
<th>2 cmH2O</th>
<th>6 cmH2O</th>
<th>10 cmH2O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rs5Hz</td>
<td>114.84 ± 3.78</td>
<td>112.72 ± 4.41</td>
<td>108.21 ± 3.21</td>
</tr>
<tr>
<td>Xs5Hz</td>
<td>-75.21 ± 7.59</td>
<td>-73.62 ± 6.28</td>
<td>-70.56 ± 4.38</td>
</tr>
<tr>
<td>Rs11Hz</td>
<td>121.90 ± 1.95</td>
<td>116.94 ± 1.49</td>
<td>112.10 ± 1.38</td>
</tr>
<tr>
<td>Xs11Hz</td>
<td>-10.75 ± 2.14</td>
<td>-9.13 ± 2.28</td>
<td>-8.02 ± 1.97</td>
</tr>
<tr>
<td>Rs19Hz</td>
<td>128.74 ± 2.04</td>
<td>123.26 ± 1.24</td>
<td>116.69 ± 0.67</td>
</tr>
<tr>
<td>Xs19Hz</td>
<td>25.60 ± 2.40</td>
<td>29.32 ± 1.09</td>
<td>31.12 ± 0.49</td>
</tr>
</tbody>
</table>

Rs5Hz: R measured at 5 Hz, Xs5Hz: X measured at 5 Hz, Rs11Hz: R measured at 11 Hz, Xs11Hz: X measured at 11 Hz, Rs19Hz: R measured at 19 Hz, Xs19Hz: X measured at 19 Hz. R and X are in cmH2O*s/l.

The mean difference between the values of resistance is 0.38±0.17 (0.4±0.2%) at 5Hz, 3.88±0.10 (3.7±0.1%) at 11Hz, and 3.87±0.12 (3.3±0.1%) at 19Hz. The mean difference between the values of reactance is -1.53±0.11 (2.3±0.2%) at 5Hz, -0.82±0.10 (11.4±1.4%) at 11Hz, and -1.61±0.14 (-5.3±0.5%) at 19 Hz.

Table III shows Rs and Xs measured by our FOT set-up at different PEEP levels. The percentage differences with respect to the values obtained using the reference set-up are also reported.

B. In vivo study

Fig. 3. Respiratory system resistance and reactance at 5 Hz (closed circles, solid line), 11 Hz (open triangles, dashed line), and 19 Hz (open circles, dotted line). Panel A shows data from 1 BPD infant, panel B is the average of 4 RDS infants.
Fig. 3 shows $R_{rs}$ and $X_{rs}$ measured at 5, 11 and 19 Hz as a function of pressure. Panel A reports data for the BPD infant, panel B reports the average data of the 4 RDS infants.

At low pressure levels the BPD infant displays much higher $R_{rs}$ than the others. This can be related to his pathophysiology which is characterized by airways obstruction, which can be reversed by increasing PEEP. In all infants $X_{rs}$ increased with increasing frequency. This is expected because the respiratory system roughly behaves like a R-L-C series. In the BPD infant $X_{rs}$ increased with PEEP, which can be explained by the opening of small airways that are collapsed when the pressure delivered by the ventilator is too low. In the other infants $X_{rs}$ remained constant with pressure or slightly decreased, suggesting that if the lung is already aerated overdistension may occur at high pressure levels.

IV. DISCUSSION

The aim of the present study was to develop and validate a measurement set-up to apply FOT to mechanically ventilated infants.

We have already demonstrated that FOT can be easily applied during invasive and non-invasive mechanical ventilation and that respiratory reactance can provide useful information about lung function that could help the clinician in tailoring the ventilatory settings to the needs of each individual patient [5], [6].

Optimizing the ventilatory settings is particularly critical in mechanically ventilated infants because an improper ventilation strategy can cause a secondary ventilation induced lung injury (VILI) [7], that may impair lung maturation and lead to chronic lung disease.

Only one study was carried out in infants without disconnecting the patients from the ventilator and without altering the ventilatory pattern. In this study forced oscillations were generated using a loudspeaker enclosed in a rigid box, placed in parallel to the inspiratory line of the ventilator [8]. This study was performed on a population with an average GA $> 37$ and an average weight $> 3300$ g. However this set-up adds a high compliance to the patient circuit and could induce respiratory fatigue to very small and diseased infants, as arisen from preliminary measurements.

In the present work we developed a measurement set-up in which forced oscillations are generated by a servocontrolled linear motor, with a closed loop control of the position of the piston.

The accuracy of the system was tested on a mechanical analogue of the infant respiratory system compared to a standard and validated loudspeaker-based set-up. The mean difference between the measurements performed using the two different systems was $2.05$ cmH$_2$O/s/l for $R_{rs}$ and $-0.94$ cmH$_2$O/s/l for $X_{rs}$. The resulting accuracy is $1.7 \pm 3.8\%$ for $R_{rs}$ which is far below the limit accepted by the international guidelines and recommendation for FOT systems [9] in the whole range of frequencies of interest (5-20 Hz). Since $X_{rs}$ is frequency dependent, the percentage difference between the two measurements depends on frequency. The percentage difference between $X_{rs}$ measured using the two systems is very good at 5 Hz (2.3%). The percentage difference is maximum at 11 Hz (11.4%) because at this oscillatory frequency $X_{rs}$ is close to 0 (7.20 cmH$_2$O*s/l).

The performance of the system was tested at increasing PEEP levels and proved to be stable up to 10 cmH$_2$O, which is the highest value used in the clinical practice.

Finally, the in vivo feasibility trial showed that the set-up was well tolerated even by very small infants. FOT has the potentials to assess changes of the mechanical properties of the respiratory system in response to the development of the pathology, to changes in the ventilatory settings, or to other treatments and interventions aiming to improve lung function.

Once the clinical usefulness of FOT will be established using this experimental set-up, forced oscillations could be easily delivered by any commercial mechanical ventilator so that no additional equipment will be required to perform the measurements.

REFERENCES


