AN ALTERNATIVE METHOD FOR MEASURING HUMAN RESPIRATORY IMPEDANCE

Robin De Keyser and Clara M. Ionescu
Ghent University, Faculty of Engineering and Architecture, Department of Electrical Energy, Systems and Automation, Technologiepark 913, B9052, Gent-Zwijnaarde, Belgium

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Abstract: The Forced Oscillation Technique (FOT) denotes a non-invasive lung function test which serves as a medical diagnostic tool to measure human respiratory impedance. The FOT principle is based on superimposing air pressure oscillations onto the normal breathing waves of the subject, measuring both air flow and air pressure at the mouth and analyzing the data with signal processing techniques which apply to linear systems. The motivation to eliminate the need for flow measurement arises from i) economic reasons, because measurement of air flow in this case requires the presence of an expensive component, the pneumotachograph, in the FOT device and ii) innovative aspects. The present work assessed the possibility that the requirement to measure flow could be eliminated if the transformation from excitation signal to measured pressure in the FOT device (given by the internal impedances of the device) is known. This conceptual solution was theoretically proven by analyzing the electrical circuit which models these transformations. Measurements were conceived and performed in order to estimate these quantities.

1 INTRODUCTION

Non-invasive lung function tests are broadly used for assessing respiratory mechanics (Northrop, 2002; Oostveen *et al.,* 2003). Contrary to the forced manoeuvres from patient side and special training for the technical medical staff necessary in spirometry and in body plethysmography (Northrop, 2002), the technique of superimposing air pressure oscillations is simple and requires minimal cooperation from the patient, during tidal breathing. Among the air pressure oscillation techniques for lung function testing, the most popular one is that of Forced Oscillation Technique (FOT) (Smith *et al*, 2005). FOT uses a multisine signal to excite the respiratory mechanical properties over a wide range of frequencies, usually between 4-48Hz (Oostveen *et al.,* 2003).

The FOT principle is based on superimposing air pressure oscillations onto the normal breathing waves of the subject, measuring both air flow and air pressure at the mouth and analyzing the data with signal processing techniques which apply to linear systems. The attempt to eliminate the flow measurement is justified from i) economic reasons, because measurement of air flow in this case requires the presence of an expensive component, the pneumotachograph, in the FOT device and ii) innovative aspects. The present work assessed the possibility that the requirement to measure flow could be eliminated if the transformation from excitation signal to measured pressure in the FOT device (given by the internal impedances of the device) is known.

The paper is organized as follows: the traditional measuring method and device is described in the next section. The third section presents the theoretical basis for eliminating the flow measurement and the fourth section gives an overview of the possible measurements, which can be performed on such a commercially available FOT device. The results of the proposed method are given in the fifth section. A measurement on a healthy subject is used to illustrate the usefulness of the novel approach for measuring the respiratory impedance. Finally, a conclusion section summarizes the main outcome of this work.

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2 STANDARD IMPEDANCE MEASUREMENT

The impedance was measured using a modified FOT setup, able to assess the respiratory mechanics from 4-50 Hz. The specifications of the device are: 11kg, 50x50x60 cm, 40 seconds measurement time, European Directive 93/42 on Medical devices and safety standards EN60601-1.

Typically for lung function testing purposes, the subject is connected to the setup from figure 1 via a mouthpiece, suitably designed to avoid flow leakage at the mouth and dental resistance artefact. The oscillatory pressure is generated by a loudspeaker (LS), which is connected to a chamber. The LS is driven by a power amplifier, which is fed with the oscillatory signal generated by a computer (denoted by **U** in figure 1-A and by $\mathbf{U_g}$ in figure 1-B). The movement of the LS cone generates a pressure oscillation inside the chamber, which is applied to the patient's respiratory system by means of a tube connecting the LS chamber and the bacterial filter (bf). A side opening of the main tubing (BT) allows the patient to have fresh air circulation. Ideally, this BT pipeline will have high impedance at the excitation frequencies to avoid the loss of power from the LS pressure chamber. It is advisable that during the measurements, the patient wears a nose clip and keeps the cheeks firmly supported. Before starting the measurements, the frequency response of the transducers (PT for pressure measurement) and of the pneumotachograph (PN for flow measurement) is calibrated.

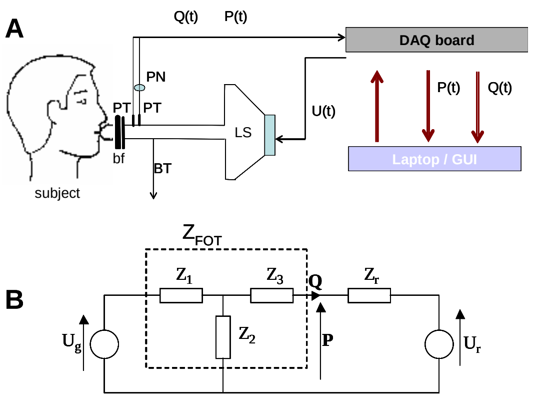

Figure 1: A schematic overview (**A**) and an electrical analogy of the FOT setup (**B**).

The measurements of air-pressure **P** and air-flow **Q** during the FOT lung function test are done at the mouth of the patient. The FOT excitation signal was kept within a peak-to-peak range of 0.1-0.3 kPa, in order to ensure optimality, patient comfort and linearity (Oostveen *et al.*, 2003). From these signals, the non-parametric representation of the patient's lung impedance Z_r is obtained assuming a linear dependence between the breathing and superimposed oscillations at the mouth of the patient (Daroczy and Hantos, 1982; Ionescu and De Keyser, 2003).

Consider the equivalent circuit for the global setup, denoted by figure 1-B, with the notations as: U_g = generator test signal – driving signal (measured); U_r = effect of spontaneous breathing (respiratory system / unknown); Z_r = impedance of interest (to be estimated): the impedance of the total respiratory system (including the airways, lung tissues and chest wall); Z_1 = impedance (unknown) describing the transformation of driving voltage (U_g) to chamber pressure; Z_2 = impedance (unknown) of both bias tubes and loud-speaker chamber; Z_3 = impedance (unknown) of tube segment between bias tube and mouth piece (effect of pneumotachograph essentially); P = (measured) pressure; Q = (measured) flow. The corresponding equation is:

$$P(s) = Z_r(s)Q(s) + U_r(s) \tag{1}$$

where s denotes the Laplace operator. Since the excitation signal is designed such that it is not correlated with the breathing of the patient, correlation analysis can be applied to the measured signals. Therefore, one can estimate the respiratory impedance as the ratio:

$$Z_r(j\omega) = \frac{S_{PU_g}(j\omega)}{S_{QU_g}(j\omega)} \tag{2}$$

where the **P** corresponds to pressure (its electrical equivalent is voltage) and **Q** corresponds to air-flow (its electrical equivalent is current), $\mathbf{U_g}$ the excitation signal, $S_{ij}(j\omega)$ the cross-correlation spectra between the various input-output signals, ω is the angular frequency and $j = (-1)^{1/2}$, resulting in the complex variable Z_r. From the point of view of the forced oscillatory experiment, the signal components of respiratory origin (U_r) have to be regarded as pure noise for the identification task (Ljung, 1999).

3 THEORETICAL BASIS

The following input-output relationship can be written based on figure 1-B (Ionescu and De Keyser, 2003):

$$\begin{bmatrix} S_{PU_g} \\ S_{QU_g} \end{bmatrix} = \begin{bmatrix} \frac{(Z_m - Z_3)Z_r}{(Z_m + Z_r)Z_1} \\ \frac{Z_m - Z_3}{(Z_m + Z_r)Z_1} \end{bmatrix} \cdot S_{U_g U_g} \tag{3}$$

with $Z_m = Z_3 + \frac{Z_1 Z_2}{Z_1 + Z_2}$. In the classical approach the two equations are divided and an expression for the impedance of the subject, Z_r, is obtained as in (2). This requires knowing the flow. Now, suppose that the flow measurement cannot be used, Z_r can be expressed from the first equation:

$$S_{PU_g} = \frac{Z_m - Z_3}{(Z_m + Z_3)Z_1} Z_r \cdot S_{U_g U_g} \tag{4}$$

The end result is:

$$Z_r = Z_m \frac{S_{PU_g}}{S_{U_g U_g} \frac{Z_2}{Z_1 + Z_2} - S_{PU_g}} \tag{5}$$

The relation (5) is in agreement with Thévenin's theorem. We conclude therefore that if one needs to measure the respiratory impedance by means of only pressure signal, the internal impedances of the FOT device need to be known. More precisely, two combinations of these internal impedances: $Z_3 + \frac{Z_1 Z_2}{Z_1 + Z_2}$ and $\frac{Z_2}{Z_2 + Z_1}$.

4 PROPOSED METHOD

As shown in the previous section, one can estimate the impedance of a load without measuring the air-flow signal explicitly. However, a pre-requisite condition is that the internal impedances of the lung function testing device have to be known. The content of this section will give a mathematical background of the possible measurement protocols.

The measurements have to be made on each FOT device on which the pressure-only estimation technique is applied. This would mean that these measurements will have to be done after a device is built. This can be omitted in the case of mass-production if the manufacturer can guarantee that the parameters of the device which play a role in these values are the same, with a certain tolerance, for each of the devices produced. However, if these parameters are found to be varying with time or with other parameters (ageing, temperature, etc.) the measurements will have to be renewed periodically.

The fact that the location of the sensors are fixed reduces the freedom in measuring the internal impedances of the device. The various parts of the FOT device cannot be disassembled and measured separately since measurement errors will accumulate. Additionally, the behaviour of the elements acting together cannot be captured. In consequence, methods have to be developed which allow measurement of these impedances using available fixed instrumentation.

The final objective is that once the internal impedances of the device are known, no flow measurement is necessary to perform measurements of the respiratory impedance in subjects.

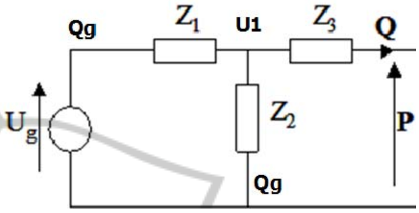

Figure 2: Equivalent circuit for measurement M1.

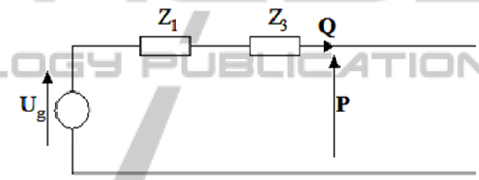

Figure 3: Equivalent circuit for measurement M2.

4.1 M1: Measuring Pressure with a Sealed Mouthpiece

The equivalent circuit in this setup is given in figure 2; notice that it ends in an open circuit. This implies no flow going out from the device (through mouthpiece) $Q = 0$. The flow will only travel through the bias tube $Qbias = Qgenerator$. In this case

$$U_1 = \frac{Z_2}{Z_1 + Z_2} U_g \tag{6}$$

where $P = U_1$ because Q is zero and in consequence Z_3 does not play a role. Therefore:

$$\frac{Z_2}{Z_1 + Z_2} = \frac{P}{U_g} = a \tag{7}$$

is the first set of measurement that we can apply.

4.2 M2: Measuring Flow with a Sealed Bias Tube and Open Mouthpiece

The equivalent circuit in this measurement protocol is given in figure 3. For this measurement the pressure is theoretically zero, because the pressure sensor is directly connected to the atmosphere. In order to perform this test, the bias tube has to be sealed. Without disassembling the device, this is only possible at the outer end. There is no flow across the bias tube, so the associated impedance, Z_2 does not play a role. All the generated flow leaves through the mouthpiece and is measured. This is a simple series structure, which gives that flow is:

$$Q = \frac{U_g}{Z_1 + Z_3} \quad (8)$$

and the impedances of interest can be estimated as:

$$Z_1 + Z_3 = \frac{U_g}{Q} = b \quad (9)$$

4.3 M3: Measuring Flow, Both Bias Tube and Mouthpiece Open

The equivalent circuit in this setup is given in figure 4. Here we also have pressure almost zero (pressure sensor directly connected to atmosphere).

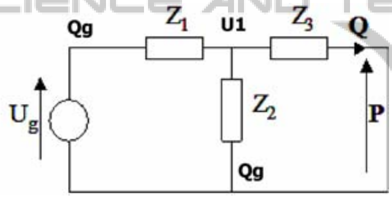

Figure 4: Equivalent circuit for measurement M3.

Flow is measured by

$$Q = \frac{U1}{Z_3} = \frac{Z_2}{Z_1(Z_2+Z_3)+Z_2 Z_3} U_g \quad (10)$$

from where we extract the third relationship for estimating internal impedances in the device:

$$\frac{Q}{U_g} = \frac{Z_2}{Z_1(Z_2+Z_3)+Z_2 Z_3} = c \quad (11)$$

4.4 M4: Measuring Pressure with a Known Load (Calibration Tube)

The equivalent circuit in this setup is given in figure 5, where Z_r is in fact the known impedance of the calibration tube.

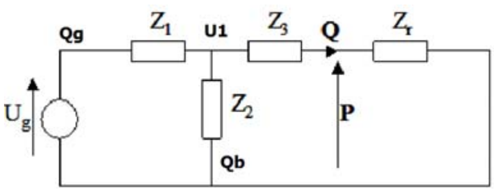

Figure 5: Equivalent circuit for measurement M4.

The measured pressure is:

$$P = \frac{Z_2 Z_r}{Z_1 Z_2 + Z_2 Z_3 + Z_2 Z_r + Z_1 Z_3 + Z_1 Z_r} U_g \quad (12)$$

However, to have information only about the internal impedances of the device, the effect of the calibration tube has to be eliminated. Consider the notation:

$$d = \frac{Z_r}{Z_q + Z_p Z_r} = \frac{P}{U_g} \quad (13)$$

where Z_p comes from the result of measurement M1, namely

$$Z_p = \frac{1}{a} = \frac{Z_1 + Z_2}{Z_2} \quad (14)$$

and, respectively

$$Z_q = Z_1 + Z_3 + \frac{Z_1 Z_3}{Z_2} \quad (15)$$

The new information is contained in Z_q. It can be expressed by:

$$Z_q = \frac{Z_r(1 - d \cdot Z_p)}{d} \quad (16)$$

Notice that Z_p was measured in measurement M1 and Z_r is known, hence (16) can be calculated.

4.5 M5: Measuring Pressure with a Known Load and Closed Bias Tube

The equivalent circuit in this setup is given in figure 6, where Z_r is in fact the known impedance of the calibration tube. The measured pressure is:

$$P = \frac{Z_r}{Z_1 + Z_3 + Z_r} U_g \quad (17)$$

from where we can extract that:

$$\frac{P}{U_g} = \frac{Z_r}{Z_1 + Z_3 + Z_r} = e \quad (18)$$

The sum of the two unknown impedances can be easily expressed as in

$$Z_1 + Z_3 = \frac{Z_r - Z_r \cdot e}{e} = Z_{sum} \quad (19)$$

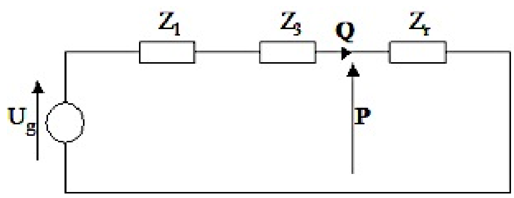

Figure 6: Equivalent circuit for measurement M5.

In consequence this is an alternative measurement, along with measurement M2, to determine the sum of the impedances Z_1 and Z_3. The reliability of this measurement is questionable because experiments show that the result is not significantly different than that of measurement M4. This may be explained by a combination of two effects, as summarized below.

a) The bias tube does not play a significant role in measurement M4, because it is designed to have high impedance on the excited frequencies. This effect is important in the case of the commercial device, because it works on frequencies significantly higher than the breathing (4-250Hz). It would be less important in the case of a custom-built device which works on lower frequencies, i.e. closer to the breathing frequency, because on these frequencies the bias tube does not have high impedance (<1Hz).

b) The bias tube is not entirely excluded in measurement M5, because it is long and has elastic walls, so it may have a capacitive role even if its outer opening is closed. This effect is more important in the case of the custom-built device, because that, working on higher pressures at lower frequencies, has the capability to push some air into the elastic bias tube, exploiting its capacitive properties.

4.6 Possible Combinations of Measurements M1...M5

4.6.1 First Combination

The first set of measurements consists of measurements M1, M2 and M3 (their results are denoted by a, b and c, respectively). With these parameters it results that the individual values of the impedances can be determined from these equations:

$$Z_1 = \frac{a-bc}{(a-1)c} \tag{20}$$

$$Z_2 = -\frac{a(a-bc)}{(a-1)^2 c} \tag{21}$$

$$Z_3 = \frac{-a+abc}{(a-1)c} \tag{22}$$

But, considering the equation (4), which gives the impedance of the patient, the following two equations become important:

$$\frac{Z_2}{Z_1+Z_2} = a = \frac{P}{U_g} \tag{23}$$

$$Z_3 + \frac{Z_1 Z_2}{Z_1+Z_2} = \frac{a}{c} = \frac{P_1/U_g}{Q_3/U_g} = \frac{P_1}{Q_3} \tag{24}$$

where P_1 denotes the pressure measured during the measurement M1, and Q_3 denotes the flow measured during measurement M3. Relation (24) describes the ratio between pressure measured with an infinite load and flow measured with zero load in concordance again with Thévenin's theorem. Once more, the formula by which the impedance of a subject can be expressed from these results is:

$$Z_r = \frac{a}{c}\frac{S_{PU_g}}{a \cdot S_{U_g U_g} - S_{PU_g}} \tag{25}$$

The conclusion is that only measurements M1 and M3 have to be performed to estimate the subject's impedance. If the individual values are needed, measurement M2 needs to be added also. In any case, there is a need to measure flow at least once.

4.6.2 Second Combination

This set uses measurements M1, M4 and M5. None of them involve flow measurement so they can be done without the presence of a pneumotachograph in the system. From the results of these measurements it follows that the individual values of the impedances can be determined from these equations:

$$Z_1 = -\frac{Z_q - Z_p \cdot Z_{sum}}{Z_p - 1} \tag{26}$$

$$Z_2 = -\frac{Z_q - Z_p \cdot Z_{sum}}{(Z_p - 1)^2} \tag{27}$$

$$Z_3 = \frac{Z_q - Z_{sum}}{Z_p - 1} \tag{28}$$

where Z_p comes from M1, namely

$$Z_p = \frac{1}{a} \tag{29}$$

After performing a measurement with a patient, his/her impedance can be calculated as:

$$Z_r = Z_m \frac{S_{PU_g}}{S_{U_g U_g}\frac{Z_2}{Z_1+Z_2} - S_{PU_g}} = \frac{Z_q}{Z_p} \cdot \frac{S_{PU_g}}{S_{U_g U_g}\frac{1}{Z_p} - S_{PU_g}} = \frac{Z_q \frac{S_{PU_g}}{S_{U_g U_g}}}{1 - Z_p \frac{S_{PU_g}}{S_{U_g U_g}}} \tag{30}$$

using pressure data collected during the FOT experiment with the patient, $\frac{S_{PU_g}}{S_{U_g U_g}}$.

This is theoretically the same method as the one from section 4.6.1, in the sense that it also contains the ratio between pressure measured with an infinite load and flow measured with zero load. However, in this case, flow measurement without load has been replaced by pressure measurement with a known load and further processing of that measurement.

Yet again, measurement M5 is only needed if the individual values have to be known. **To estimate a subject's impedance there is only need for the results of measurements M1 and M4. Notice that these two experiments require only the pressure measurement.**

5 RESULTS

5.1 Characterization of the Measuring Device

We have applied the tests described in the previous section in order to extract the transfer function of the device using only the information coming from the pressure signal. We have also applied these using different types of excitation signals U_g. The underlying rationale for this was to verify the linearity of the system, since we suspected that the voltage-to-pressure conversion holds a nonlinear relationship. Indeed, the nonlinearity of the system is illustrated by the figures 7 and 8, respectively.

The lines depicted in figures 7, 8, 9, 10, 11 and 12 represent data collected with different frequencies in the excitation signal, i.e. the multisine:

- **A:** 2.5:2.5:177.5 Hz, a total of 71 frequencies, signal between -1 and 1 Volt
- **B:** 2.5:2.5:57.5 Hz, a total of 23 frequencies, signal between -1 and 1 Volt
- **C:** 2.5:5:177.5 Hz, a total of 36 frequencies, signal between -1 and 1 Volt
- **D:** 2.5:2.5:177.5 Hz, a total of 71 frequencies, signal between -0.5 and 0.5 Volt
- **E:** 82.5:2.5:177.5 Hz, a total of 39 frequencies, signal between -1 and 1 Volt

Figure 7 represents the impedance of the device in terms of its complex representation (i.e. real and imaginary parts), while Figure 8 is the equivalent Bode plot (i.e. magnitude and phase). The data presented in Figures 7 and 8 originates from the measurement M4.

Figures 9 and 10 depict the same experiment data when using flow as the information signal (instead of pressure). Again, we observe that different results are obtained for different input signals, suggesting that the transformation from

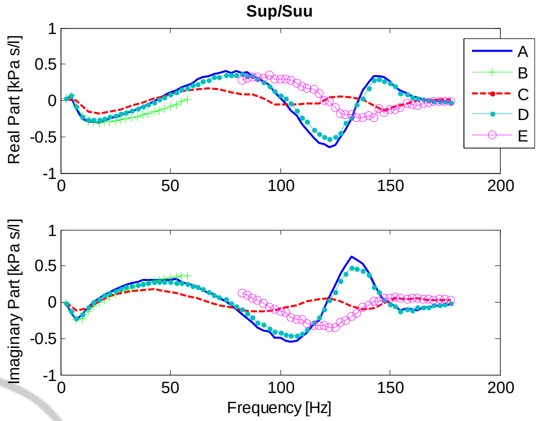

Figure 7: Real and Imaginary parts of the impedance of the lung function testing device extracted from measurement M4 for various inputs (see text for legend).

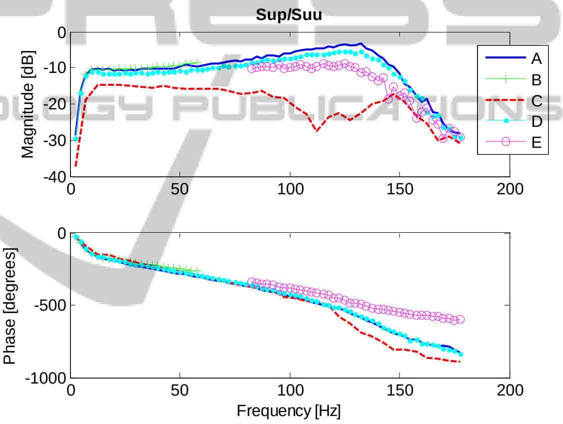

Figure 8: Magnitude and Phase of the impedance of the lung function testing device extracted from measurement M4 for various inputs (see text for legend).

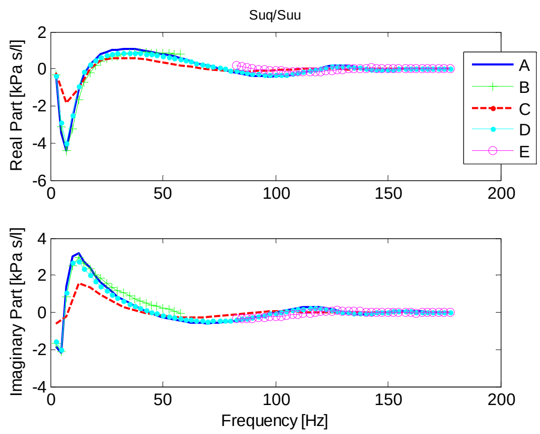

Figure 9: Real and imaginary parts of the impedance of the device using only flow information extracted from measurement M4 for various inputs (see text for legend).

voltage-to-flow is also nonlinear. Intuitively, one expects that these nonlinearities cancel out if both pressure and flow can be measured because pressure and flow are all affected in the same way. This is then illustrated by Figures 11 and 12 below, in terms

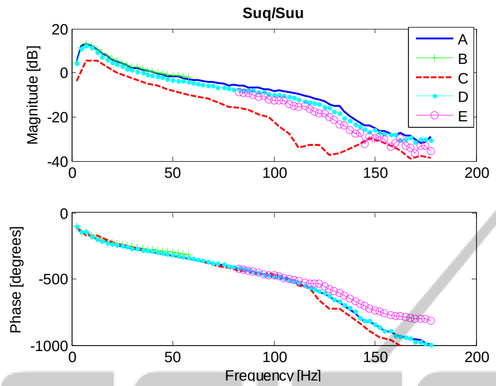

Figure 10: Bode plot of the impedance of the device using only flow information extracted from measurement M4 for various inputs (see text for legend).

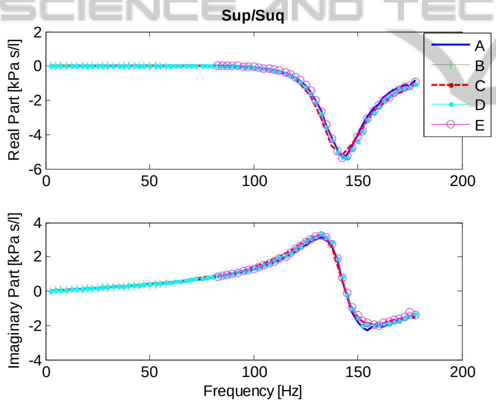

Figure 11: Real and Imaginary parts of the impedance of the device measured using both flow and pressure knowledge (see text for legend).

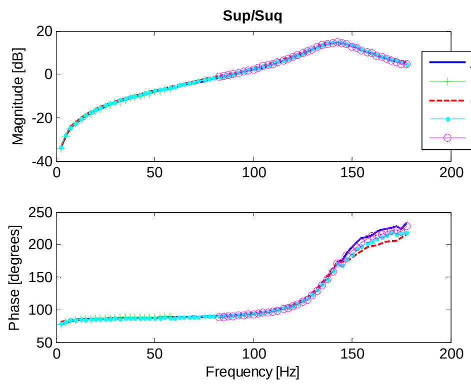

Figure 12: Real and Imaginary parts of the impedance of the device measured using both flow and pressure knowledge (see text for legend).

of the complex representation and Bode plot of the impedance. One may observe that in this case, irrespective of the excitation signal we apply, we always obtain the same frequency response.

A serious limitation, which arises from this nonlinear behaviour, is that the data collected with one range of excitation cannot be used to estimate the impedance of the patient if the patient was not measured with a signal which has the same spectral composition.

5.2 Respiratory Impedance of a Healthy Subject

In order to verify if the theoretical developments under section 4 were correct, it was necessary to test them on the respiratory impedance of a volunteer. We performed the lung function test described in section 2 on a healthy volunteer, non-caucasian male, 23 years age, 182 cm height and 70 kg weight. The protocol implied comparing the traditional method using both flow and pressure signals in relation (2) with the two combination sets described in section 4.6. Figures 13 and 14 depict the obtained results for the respiratory impedance by these three methods, in terms of complex impedance and Bode plot, respectively. One may conclude that the traditional method and the second combination set (i.e. M1 and M4) gave the same results, therefore the proposed alternative estimation concept without flow measurement may be useful in practice to evaluate correctly the respiratory impedance.

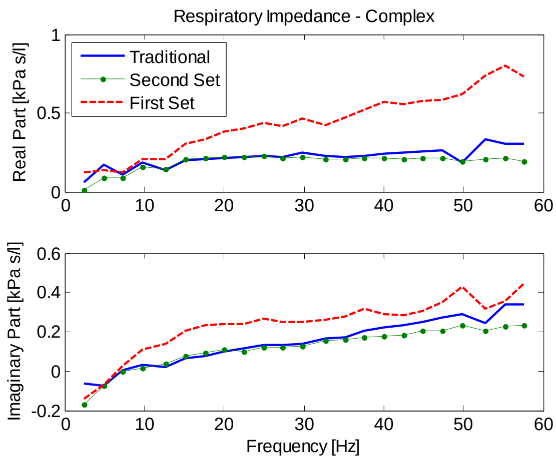

Figure 13: Complex impedance data for human respiratory impedance in a healthy volunteer.

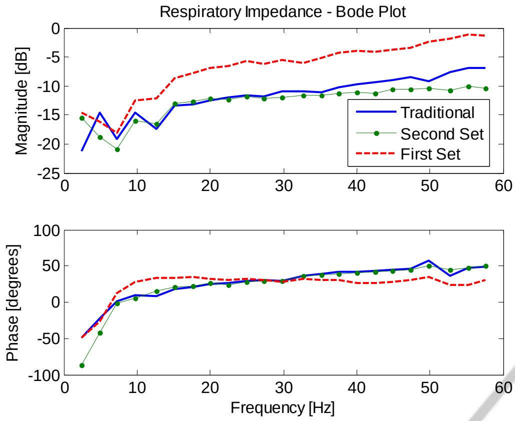

Figure 14: Magnitude and Phase for human respiratory impedance in a healthy volunteer.

6 CONCLUSIONS

The Forced Oscillations Technique (FOT) denotes a non-invasive lung function test which serves as a medical diagnostic tool to measure human respiratory impedance. A justification to eliminate the need for flow measurement arises from i) economic reasons, because measurement of air flow in this case requires the presence of an expensive component, the pneumotachograph, in the FOT device and ii) innovative aspects.

The present work assessed the possibility that the requirement to measure flow could be eliminated if the transformation from excitation signal to measured pressure in the FOT device (given by the internal impedances of the device) is known. This conceptual solution was theoretically proven by analyzing the equivalent electrical circuit, which models these transformations. Measurements were conceived and validated on a healthy volunteer, showing good agreement between the traditional method (using both flow and pressure signal information) and the proposed alternative method (using only pressure signal information).

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