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Interrupter technique for assessing respiratory resistance: a review

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Abstract. The use of interrupter resistance (R_{int}) is a feasible method of measuring respiratory resistance during bronchodilator and bronchial hyperresponsiveness testing in preschool children. In addition to a single value of R_{int}, it has been suggested that analysis of recorded oscillations of the mouth pressure may provide additional indices of changes in airway mechanics. This paper reviews the studies concerning analysis of those pressure oscillations, as well as modelling of the respiratory system in order to understand how different structures in this system can influence interrupter measurements.

Key words: interrupter resistance, asthma, amplitude analysis, modelling.

1. INTRODUCTION

There are several lung function tests for diagnosing and monitoring pulmonary diseases. An objective measure that would describe some specific aspect in the functioning of the lungs has been of interest to physicians for centuries, but it was not until the middle of the 19th century that systematic studies of the respiratory mechanics began [1]. A major change in objective measurements was produced by describing a spirometer by Hutchinson in 1846 [2], which together with pneumotachography, introduced by Fleisch in the 1920s, created a basis for future volume and flow measurements. Hutchinson's water sealed spirometer is still in use today with a few alterations since the original device (e.g. the reduction of the mass of the bell and the addition of graphic and timing devices), and the Fleisch pneumotachograph is also widely used in modern commercial analysers.

Probably owing to the fact that Alfred Fleisch was a professor in the Department of Physiology during 1926–1932 at the University of Tartu [3], different methods of lung function measurements have been one of the areas of interest in that department ever since. In addition to the cooperation with physicians during the last decades, there have also been several projects in cooperation with biomedical engineers (e.g. developing a new type of pneumotachograph, assessing its quality, automatization of total lung capacity measurement by the helium-dilution method, etc.) [4–6]. This paper reviews some problems our department has studied and that could be of interest to biomedical engineers, concerning another lung function test, measurement of the respiratory resistance, which has been used in our department during the last decade.

2. OVERVIEW OF THE INTERRUPTER TECHNIQUE AND ITS CLINICAL USE

Spirometry is definitely the most widely used lung function test nowadays. It can help to decide whether the patient has some obstructive changes in the airways and also whether we can rule out restriction of the lungs. However, for measuring maximal flows, the patient has to perform the manoeuvers of forced expiration or inspiration, which can be difficult for small children or patients with limited cooperation.

If we want to find out how much the diameter of the airways has diminished in an asthmatic patient, we need to measure the airway resistance. To measure the resistance of a tube, one has to know the pressure at both ends of the tube. Since direct measurement of alveolar pressure is not possible, a number of methods have been

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developed in the 20th century that have enabled indirect estimates of alveolar pressure. One of the possibilities, the interrupter technique, was first described in 1927 by von Neergaard and Wirz [1]. The technique is based on the assumption that when during the tidal breathing the airway is suddenly occluded, there is a pressure change in the mouth, which equals the resistive pressure drop across the airways. Interrupter resistance (R_{int}) can be calculated by dividing this pressure difference by the pre-occlusion flow. Originally, the rapid occlusion was done manually and this limited the accuracy of the measurement and could be a reason why it did not become popular for a long time. Only at the beginning of the 1990s, study groups started to use combined apparatuses consisting of a pneumotachograph with a pressure transducer, and a shutter, connected in series. Automated commercial devices became available later, and because R_{int} measurement requires only passive cooperation and measurements can be performed in children down to the age of two years, the method has come into use more widely, either in assessing the decrease in R_{int} during bronchodilatation (BD) or the increase in R_{int} during bronchial hyperresponsiveness (BHR) testing.

Several commercial devices are available and the measurement procedure can slightly vary between devices. Our group uses MicroRint devices (MicroMedical, UK); measurements are made using a filter and a cardboard mouthpiece with the nose clipped and the cheeks supported. During normal and quiet breathing, up to 10 interruptions are made on the peak flow of expiration. The valve closes within 10 ms and remains closed for 100 ms. Sampling frequency of the pressure signal is 2000 Hz, and the accuracy for flow and pressure measurement is ±3% according to the manufacturer. Before the analysis, all mouth pressure graphs are checked using specific software from the manufacturer. The mean of 5–10 acceptable readings is taken as a measurement.

Our group has had several projects using R_{int} measurements, one in cooperation with Sheffield Children's Hospital, UK, and the others with Tartu Children's Hospital. Our UK study [7,8] analysed R_{int} as a potential method of assessing bronchial hyperresponsiveness during a methacholine (Mch) challenge in young children and compared the results with other similar studies [9–11]. The Asthma UK Collaborative Initiative was established to collate lung function data from healthy young children in order to produce reference equations. Data from 1090 children (from six centres, including Tartu) aged 3–13 years were collated to construct sex-specific reference equations for R_{int} [12]. The European Respiratory Society and American Thoracic Society have combined their experts to compile the standards for R_{int} measurements [13,14].

3. ALGORITHMS TO FIND THE CHANGE IN PRESSURE

Whereas flow and mouth pressure (Pmo) are easily measured at the mouth, alveolar pressure is derived from the mouth pressure–time transient Pmo(t) during a brief interruption of tidal breathing. Immediately after occlusion, there is a very rapid change in pressure, followed by damped pressure oscillations, and finally, there is a relatively slow rise in pressure (Fig. 1).

Traditionally, R_{int} is calculated when dividing back-extrapolated pressure, derived from the slow rise of the Pmo(t) signal by pre-occlusion flow. However, it has been stated that pressure equilibration between alveoli and mouth can be incomplete in case of severe airway obstruction and therefore the interrupter technique may underestimate airway resistance [15].

Pmo(t) curves, obtained from asthmatic children, are different from those of normal adults. The curves, especially from obstructed children, are considerably more concave with respect to the x axis than in adults and this can represent a difficulty when back-extrapolation is used [9,15]. Different techniques to analyse the mouth pressure curve after the flow interruption have been proposed and compared in BD or BHR testing (e.g. back-extrapolating a fitted smooth curve, using an end-oscillation or end-interruption pressure, etc.) [9,11,16,17]. However, in spite of attempts to standardize the R_{int} measurement, there is still no agreement as to which is the recommended method to assess pressure change during occlusion [14].

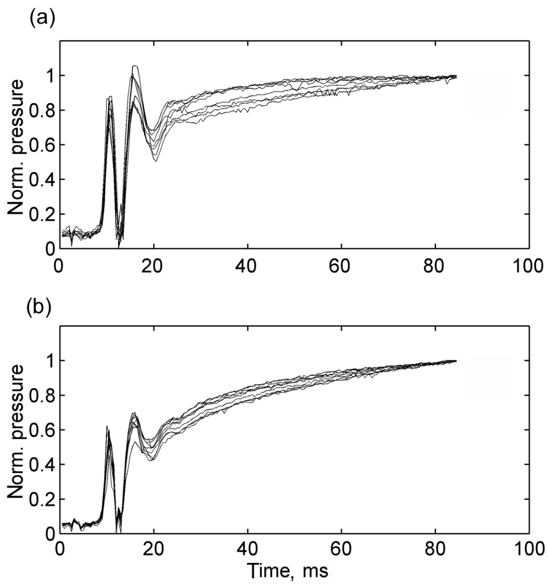

Fig. 1. Mouth pressure curves from one child, normalized to the last recorded pressure: (a) at the baseline, (b) after assessing bronchial hyperresponsiveness with methacholine.

4. ANALYSIS OF PRESSURE OSCILLATIONS

Attempts have been made to pay more attention to the dynamic behaviour of pressure equilibration between the mouth and alveoli seen as pressure oscillations on Pmo(t). Studies in schoolchildren and adults concluded that different amplitudes or damping factors, derived from post-occlusion oscillations, are even more sensitive than R_{int} in assessing changes in airway mechanics during BHR testing [18–20]. Bridge et al. [21] studied pre-school children and used three different characteristics to describe the changes in pressure oscillations after administering a bronchodilator.

Our group decided to test the hypothesis that amplitude analysis of pressure oscillations on Pmo(t), obtained by a commercial device, can detect changes during BHR testing in preschool children, and to compare the relative sensitivities of amplitude or damping properties of those oscillations and R_{int} to measure changes in response to a bronchoconstriction.

We used data from 44 children aged 3–6 years who had successful R_{int} measurements at the baseline and after at least one Mch dose; the subjects and the test were described in detail in previous papers [22,23]. Analysis of Pmo(t) tracings was performed using MATLAB (MathWorks Inc., USA). Prior to all oscillation analyses, Pmo(t) data were normalized to the last recorded pressure in order to avoid the possible effect of interruptions, occurring at different flows [18–21]. After that, the following parameters were found in the time domain (see more details in [22,23]):

- the difference between the first Pmo maximum and minimum (Amp) (Fig. 2);
- the damping factor estimated from the first and second minimum of the differentiated pressure signal;
- the maximum instantaneous amplitude (Ainst);
- the amplitude, frequency and damping factor of the curve.

Furthermore, after applying the fast Fourier analysis of the oscillatory component, we calculated 2 parameters in the frequency domain:

- amplitude of the dominant frequency;
- the sum of frequency component amplitudes.

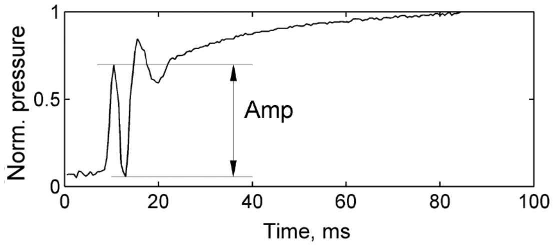

Fig. 2. Finding the oscillation amplitude (Amp) as the difference between the first pressure maximum and minimum.

All amplitude parameters decreased significantly after the Mch challenge. In order to find the most sensitive measure for describing changes in airway mechanics during a Mch challenge, we have to compare the increase in R_{int} with the decrease in amplitude parameters; quite the opposite happens during BD testing: airway resistance decreases and amplitudes increase. Measurement sensitivity is often expressed as the sensitivity index (SI), which is the absolute change after intervention divided by the standard deviation of the baseline readings. Several authors have compared absolute values of sensitivity indices of parameters changing in different directions [9,21]. Since the SI-s of two parameters, having similar variability, tend to depend on the direction of change, we calculated SI values also for reciprocals of decreasing amplitude indices. We found that 1/Ainst and 1/Amp were the most sensitive indices to describe the change (with median SI of 6.29 and 6.28, respectively). R_{int} had a median SI of 5.13. Frequency and damping factors were less sensitive, with median SI values less than 1.0 [23].

5. REPEATABILITY OF PRESSURE OSCILLATION AMPLITUDES

R_{int} measurements are most often combined with BD testing, which creates a need for a cut-off value to decide whether a change in R_{int} is caused by a pharmacological intervention or it is within the limits of short-term repeatability, reflecting the variability of the measuring instrument and the biological variability of the disease. Short-term repeatability of R_{int} has been studied by several groups; however, we decided to establish the repeatability of pressure oscillation amplitudes [24]. Analysis was based on data from 92 young children (aged 3 to 7 years); they were patients who attended the respiratory outpatients' clinic in Tartu Children's Clinic, healthy siblings or those who came in response to the invitation sent to local kindergartens. During normal and quiet breathing, children performed two sets of R_{int} measurements (15 min apart). One set consisted of up to 10 interruptions on the peak flow of expiration.

Intra-measurement repeatability was assessed by the coefficient of variation, which was calculated for all parameters as the ratio of the standard deviation to the mean of the 5–10 individual readings (in %). Median coefficients of variation for both measurements were 14% and 15% for interrupter resistance (with a range from 5% to 48%), and 14% and 13% for the oscillation amplitude (with a range from 3% to 36%).

Between-test repeatability was assessed by the coefficient of repeatability (CR): twice the standard deviation of the mean difference between two sets of values. To compare CR for R_{int} and Amp, we also expressed it as a percentage of the baseline value. Our mean CR for R_{int} was 0.23 kPa L^{-1} s or 33.3% of the baseline value. In previous studies, the coefficient of repeatability for R_{int} in pre-school children has been found to range from 0.15 to 0.28 kPa L^{-1} s [13], i.e. in line with our results. The mean CR for Amp was 0.24 or 27.6% of the baseline value.

Within- and between-test repeatability of the most simple oscillation amplitude from this study showed a good concordance with the repeatability of R_{int}; therefore, according to our data, an increase in the oscillation amplitude for more than 30% would be a significant bronchodilator response.

6. MODELLING OF THE R_{int} TECHNIQUE

Most findings, concerning different analyses of Pmo(t) curves, are specific to a particular commercially available device with its mechanical properties. Modelling of the interrupter measurements could help us to understand better how different parts of the airflow system (human + device) can determine the character of those curves.

The frequency and damping properties of the mouth pressure oscillations were described already 50 years ago; however, these oscillations did not occur in patients with elevated airway resistance nor in normal subjects with added external resistances [25]. Since these oscillations were affected by changes in airway parameters they had to originate in the airways. The physiological explanation of the origin of these oscillations could be summarized as follows: the interrupter valve brings a moving column of air suddenly to a rest, causing the conversion of kinetic energy to potential energy and then back to kinetic energy, resulting in back and forth flow and oscillations in the mouth pressure signal [21]. Depending on the damping factor of the system, consisting of the lungs, thorax, upper airways, and equipment, these oscillations are damped to a greater or lesser extent [18–21]. The mechanical characteristics of this system can be correlated with models, consisting of electrical components that are analogous to the respiratory system's mechanical components.

We decided to develop an electrical circuit model, capable of simulating the main changes observed in the pressure signal from the interrupter technique and to investigate the influence of the model circuit elements on that signal [26]. Our model of the respiratory system with a flow interrupter is relatively simple (Fig. 3), consisting of two sections, one of them oscillating quite rapidly and the other having a lower time constant. The interrupter switch (Sw) is presented as a variable resistor with increasing resistance during interrupter closure, typically taking 5–10 ms. As a response to this, the pressure curve shows a rapid rise, followed by damped

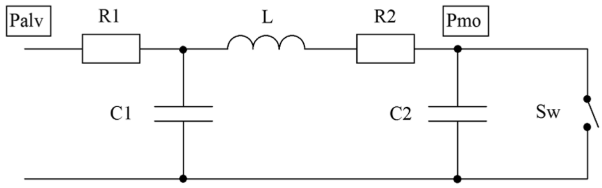

Fig. 3. Electrical model for interrupter measurements consisting of two resistors (R), an inductor (L), and two capacitors (C). Pmo – mouth pressure, Palv – alveolar pressure, Sw – interrupter switch.

pressure oscillations. These oscillations can be modelled by an RLC circuit, where the values of resistance (R), inductance (L), and capacitance (C) determine the frequency and damping of oscillations [19]. Finally, there is a relatively slow rise in the pressure curve, which cannot be described by the abovementioned RLC circuit alone, and hence, an additional RC section must be included.

All simulations were conducted in the MATLAB software environment. Mouth pressure (Pmo) curves were generated by numerical integration. An assumption was made that during the short interruption (100 ms), the alveolar pressure (Palv) has a constant value of 500 Pa. First, we fixed one set of element values as a baseline condition (see more details in [26]), and later, in order to find out how the changes in different elements of the model influence the pressure transient, we changed the values for R1, R2, and C2 separately to 200, 125, and 200% of their baseline value, respectively. Additionally, the closing time of the interrupter was doubled in one simulation.

Using this model, we generated different waveforms according to specified conditions. For example, the increased airway resistance in the peripheral part of the respiratory system corresponds to a greater value of R1 (Fig. 4a). The slightly enlarged value of R2 (the resistance of central airways and the device) caused damping of oscillations to a greater extent, as can be seen in Fig. 4b.

Our modelling showed that the pressure oscillations and the later rise in pressure can be influenced by different parts of the airway/measuring system. BHR testing often causes changes in the phase of the slow rise of the pressure signal. This corresponds to the increase of R1 in the model. The oscillation amplitude depends on different factors, such as the resistance and volume of the mouthpiece and central airways and the closing time of the shutter. Since the mouthpiece remains constant during the repeated measurements of BD or BHR testing, relative changes during the testing should not be influenced, but there is no certainty regarding changes in the lung volume.

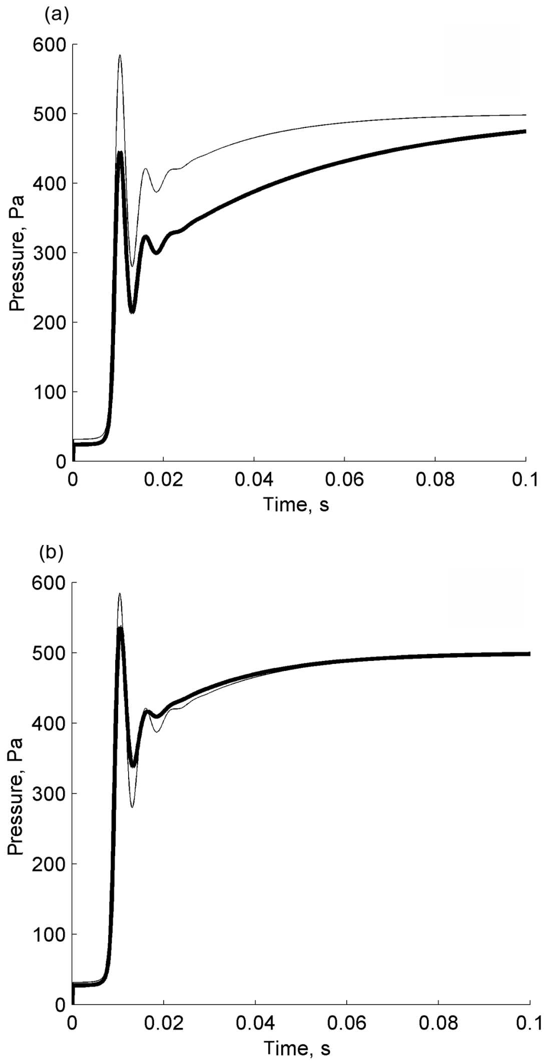

Fig. 4. Simulated pressure waveforms: (a) for baseline conditions (thin) and for increased R1 (bold), (b) for baseline conditions (thin) and for increased R2 (bold).

There are also some publications about more sophisticated modelling of the interrupter technique. Jabłoński and Mroczka [27] have proposed a methodological transformation from the real physiological system, through its linear complex model (forward model) to the reduced metrological form (inverse model). Using a complex model, consisting of six submodels, representing different components of the respiratory system and the shutter used for interruption, the flow and pressure were simulated and then used to calculate the respiratory impedance in three different states of respiratory mechanics [28]. The same group has also implemented their models in studying functional characteristics of shutters used in commercial R_{int} devices (e.g., the speed of the valve closure, the time of occlusion duration, and the valve tightness) [29,30]. Authors hope that if it were possible to supplement the equipment with numerical algorithms appropriately processing flow and pressure data, and to design more optimal shutter-transducer solutions, this could be used when developing a telemedical system for the monitoring of patients, suffering from lung diseases.

7. CONCLUSIONS

Spirometry is the most common lung function test, but not every patient is able to perform a forced expiratory manoeuver during this measurement. Interrupter resistance R_{int} measurement has numerous advantages, as low hardware requirements, easy procedure, short time of the test and need for tidal breathing only. In addition to only one R_{int} value, there has been an interest to find additional parameters from the post-interrupter pressure oscillations that could describe changes in airway mechanics. Cooperation between engineers, physiologists, and physicians will hopefully provide us with improved algorithms and also with better solutions for the construction of the devices so that we could broaden the functionality and reliability of R_{int} measurement and incorporate it into routine clinical practice.

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Hingamisteede takistuse mõõtmine katkestusmeetodil

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Suurel hulgal hingamishaigustega patsientidest esineb hingamisteede valendiku ahenemine. Forsseeritud hingamise voolu-mahu lingu registreerimisel hinnatakse kaudselt hingamisteede voolutakistuse muutusi, aga osa patsiente ei ole võimelised nõutud hingamismanöövreid sooritama. Sellistel juhtudel sobib paremini tavalise hingamise ajal teostatav katkestustakistuse (R_{int}, ingl *interrupter resistance*) määramine. Mõõtmise eelduseks on, et kui hingamisteed spetsiaalse klapiga umbes 100 millisekundiks suletakse, võrdsustuvad rõhud suuõõnes ja alveoolides. Vahetult enne klapi sulgumist registreeritakse õhuvoolu väärtus ja alveolaarrõhu ning vastava õhuvoolu jagatis võimaldabki hinnata hingamisteede takistust. Käesolevas ülevaateartiklis tutvustame lisavõimalusi, mida annaks R_{int} mõõtmisel tekkivate rõhuvõnkumiste detailsem analüüsimine, ja kirjeldame hingamissüsteemi modelleerimise abil tehtud töid, mis selgitavad, millised struktuurid hingamiselunditest ning analüsaatorist koosnevas süsteemis mõjutavad mõõtmise eri etappe.