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Fractional order model parameters for the respiratory input impedance in healthy and in asthmatic children

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ABSTRACT

This paper provides an evaluation of a fractional order model for the respiratory input impedance, using two groups of subjects, respectively healthy and asthmatic children. The purpose is to verify if the model is able to deliver statistically meaningful parameter values in order to classify the two groups. The data are gathered with the non-invasive lung function test of forced oscillations technique, by means of a multisine signal within the 4–48 Hz frequency range. Based on our previous work, a fractional order model for this range of frequencies is obtained. Additional parameters are proposed to evaluate the two groups. The results indicate that the model was unable to detect significant changes between the asthmatic children with normal spirometry results (as result of medication) and the healthy children. Due to medication intake during the hours prior to the exam, bronchial challenge did not modify substantially the respiratory parameters. Our findings correspond to similar studies reported in the specialized literature. Combined model parameters, such as the tissue damping and the tissue elastance were significantly different in the two groups ($p < 0.01$). Two extra indexes are introduced: the quality factor and the power factor, providing significantly different results between the two groups ($p \ll 0.01$). We conclude that the model can be used in the respective frequency range to characterize the two groups efficiently.

1. Introduction

The concept of fractional order modelling in biological systems has received significant interest in the research community [1,2]. Initial characterizations of the lung's mechanical properties have been reported in invasive animal studies, showing the necessity of a fractional order (FO) integral [3,4]. Recent studies led to the conclusion that a FO model outperforms most of the integer-order models for characterizing the frequency-dependence in human respiratory input impedance [5]. The major advantage of the FO models over the integer-order counterpart is not only their low number of parameters, but also their intrinsic capability to characterize the viscoelastic properties and the recurrent structures of biologic materials [6,7].

Fractional order models have been employed previously in both healthy subjects group [8] and various pathologies, such as asthma [9], Chronic Obstructive Pulmonary Disease (COPD) [10], during surgery [11], and animal studies [12,13]. The respiratory impedance poses several resonant frequencies [14] and the validity of one fractional order model is restricted to the frequency range where its parameters have been identified. The result is that a FO model structure is valid in a limited range of frequencies [15]. As soon as the frequency range, in which the lung function is evaluated, changes, important

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Table 1 – Biometric and spirometric parameters of the healthy and asthmatic children. Values are presented as mean ± standard deviation values; % pred: predicted values; VC: vital capacity; FEV_1: forced expiratory volume in 1 s; see text for all symbols.

	Healthy	Asthma
N	16	19
Female/male	13/3	3/16
Age (years)	9.66 ± 0.47	11.05 ± 4.7
Height (cm)	139.8 ± 7.31	140.3 ± 17.99
Weight (kg)	32.3 ± 6.34	36.25 ± 15.58
FEF/VC% pred	–	85.31 ± 31.15
FEV_1/VC% pred	–	97.75 ± 12.83
MEF75/25 (l)	–	2.12 ± 0.95

variations in the frequency-dependence of the respiratory impedance may occur and the model must be revisited.

We have shown that the FO model from literature introduced by Hantos et al. [3,4] has limitations with respect to its ability to capture the frequency dependence of the real part in the respiratory impedance in the 4–48 Hz range, hence an alternative model structure was proposed [8,15]. We have also shown that this alternative model structure is able to distinguish between healthy subjects and patients diagnosed with COPD [10]. The current study aims to verify the ability of the proposed model to detect changes in respiratory mechanics in healthy and asthmatic children. The FO model introduced by Hantos et al. [3,4] has been broadly used in various pathologies in children [16–19]. The model parameters are useful to assess respiratory mechanics, but differences between investigated groups may not always be statistically significant. Hence, we introduce combined parameters in order to gather further insight on the identified model parameters in healthy and asthmatic children.

The paper is organized as follows: the healthy group and the asthmatic group are characterized in the next section, along with a description of the measurement protocol and the identified model structure. The third section presents the results and the fourth section discusses these results from the physiological viewpoint, along with the prospective limitations. A conclusion section summarizes the main outcome of this investigation and points to future steps in this research topic.

2. Materials and methods

2.1. Patients

This study was approved by the local Ethics Committee and informed consent was obtained from all volunteers before inclusion in the study. The study involved 35 subjects, of which 16 were healthy and 19 were asthmatic children. The corresponding biometric and spirometric values are given in Table 1. No significant difference between the healthy and asthma groups were obtained for age ($p < 0.25$), weight ($p < 0.26$) and height ($p < 0.99$), suggesting that the biometrical characteristics have no influence on the results.

The healthy children had no history of pulmonary disease, and were selected using a specific questionnaire. The questionnaire verified the absence of dyspnoea, chronic cough, and wheeze in the chest.

Table 2 – Number of the asthmatic children related to various asthma parameters: ICS: inhaled corticosteroid; LABA: long acting beta agonist; LRA: leukotriene receptor antagonist; PC: partial; C: controlled.

Medication	ICS: 12	LABA: 15	LRA: 8
Level of asthma control	PC: 6	C: 8	None: 5
Asthma history	<1 Year: 9	<2 Years: 3	<5 Years: 7
Allergic asthma	Yes: 17	No: 2	–

The asthmatic patients were clinically diagnosed with asthma and referred to the clinical pulmonary function laboratory (see Table 1). The spontaneous improvement of the symptoms mentioned above, after the bronchodilator use was also an indicative of asthma (>12% improvement of forced expiratory volume for the 1 s (FEV1) predicted baseline after inhalation). For the bronchodilatation, Ventolin 100 (4 × Salbutamol 100 mg) was administered. Allergy was determined based on specific positive reaction to inhaled allergen (house dust mite, birch tree, grass pollen, weed, dog/cat dander), and further details are given in Table 2.

Exclusion criteria were the inability to perform technically adequate spirometry or FOT measurements, evidence of current airway infection, acute exacerbation and any respiratory disease other than asthma. All patients were in stable clinical condition.

2.2. Spirometry

Using a closed circuit spirometer (JAEGER MasterLab, Germany) measurements for forced vital capacity (FVC), FEV1, the ratio FEV1/FVC and the ratio of forced expiratory flow (FEF) between 25% and 75% of FVC to FVC (FEF/FVC) were obtained for the asthmatic patients in a sitting position. These parameters were presented as raw data and percentile of the predicted values (% pred) in a healthy subject with the same biometric details. Quality control of spirometry is given by the ATS (American Thoracic Society) criteria, with the software allowing detection of non-acceptable manoeuvres. From the 19 patients with clinical diagnosis of asthma, 16 presented normal respiratory response by spirometry, and will be further referred to as *normal-to-the exam* (NE) patients. The underlying reason for this was intake of specific medication in the hours prior to the lung function test (see Tables 1 and 2).

2.3. Input impedance measurement

The measurement of input impedance is done using the non-invasive lung function test of forced oscillations technique in conditions of quiet breathing [20]. Air-pressure variations P (kPa), with respect to the atmospheric pressure and corresponding air-flow Q (l/s) during the FOT lung function test can be measured either at the mouth of the patient, either endotracheal, either at body surface [21]. If the impedance is measured at the mouth of the patient, then it is called *input impedance*. In the case when the measurements are done across the body surface, this is then called *transfer impedance*. Using electrical analogy, where the P corresponds to voltage and Q corresponds to current, the respiratory impedance Z_r