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# Modelling respiratory impedance in patients with kyphoscoliosis

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ABSTRACT

When a nonlinear biological system is under analysis, one may employ linear and nonlinear tools. Linear tools such as fractional order lumped impedance models have not been previously employed to characterize difference between healthy volunteers and patients diagnosed with kyphoscoliosis (KS). Nonlinear tools such as detection lines from nonlinear contributions in frequency domain have also not been employed previously on KS patient data. KS is an irreversible restrictive disease, of genetic origin, which manifests by deformation of the spine and thorax. The forced oscillation technique (FOT) is a non-invasive, simple lung function test suitable for this class of patients with breathing difficulties, since it does not require any special maneuvre. In this work we show that the FOT method combined with both linear and nonlinear tools reveals important information which may be used as complementary to the standardized lung function tests (i.e. spirometry).



## 1. Introduction

When extracting information from complex nonlinear biological systems, it is important to decide whether a linear or a nonlinear analysis is envisaged. The respiratory system is a complex nonlinear system, which changes properties with disease, i.e. the nonlinear behaviour may become more pronounced. A combination of both linear and nonlinear tools may be beneficial for the extraction of most information. In this work, we employ linear impedance extraction and detection of nonlinear distortions in the impedance data from patients diagnosed with kyphoscoliosis. Additionally, we employ a parametric model of fractional order which is directly linked to mechanical properties in the lungs, to identify quantitative differences between healthy volunteers and KS patients.

Biological systems modelled by fractional order impedance models have received significant interest in the research community [35,7,6,22]. Initial characterizations of the lung's mechanical properties have been reported in several invasive animal studies, showing the necessity of a fractional order (FO) integral [9,10]. 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 [11]. 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 [1,15,16,33,4].

Fractional order models have been employed previously in both healthy subjects group [14] and various pathologies, such as asthma [18], Chronic Obstructive Pulmonary Disease (COPD) [17]. The respiratory impedance poses several resonant frequencies [21] and the validity of one fractional order model is restricted to the frequency range where its parameters have been identified [27]. As soon as the frequency range, in which the lung function is evaluated, changes, important variations in the frequency-dependence of the respiratory impedance may occur and the structure of the model must be revisited.

Hitherto, to our knowledge, there is a lack of information on KS patients from the linear and nonlinear tools employed in this work. As such, the restrictive properties arise not from a lung parenchyma itself, but from the sub-optimal shape and anatomy of the thorax. The forced oscillation technique is a non-invasive, simple lung function test suitable for this class of patients with breathing difficulties, since it does not require any special maneuvre. In this work we show that the forced oscillation technique (FOT) combined with both linear and nonlinear tools revels important information which may be used as complementary to the standardized (spirometry) lung function tests. The only work which uses FOT in KS patients is that of Van Noord et al. [34]. There, the authors showed the ability of FOT to distinguish between various forms of restrictive and obstructive patterns.

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**Table 1**
Biometric parameters of the healthy subjects and KS patients. Values are presented as mean ± standard deviation.

| | Healthy (80) | KS (11) |
|---|---|---|
| Female/male | 31/49 | 4/7 |
| Age (years) | 27 ± 5 | 62.25 ± 10.12 |
| Height (m) | 1.73 ± 0.17 | 1.55 ± 0.08 |
| Weight (kg) | 69 ± 9.6 | 63.25 ± 15.62 |
| *VC* % pred | | 33.25 ± 14.15 |
| $FEV_1$ % pred | | 31.62 ± 11.30 |
| *FVC* % pred | | 34.62 ± 12.12 |
| Cobb angle (°) | | 75 ± 19.63 |
| $R_{aw}$ (kPa/l/s) | | 0.51 ± 0.12 |
| $C_{cw}$ pred* (l/kPa) | | 0.98 ± 0.29 |
| *VC* % pred* | | 65.06 ± 10.48 |

The work presented in this paper aims to provide the reader with a proof of concept on the added value of using FOT as a complementary lung function test to the standardized spirometry test. The added value is shown by means of linear non-parametric identification of the respiratory impedance, further parameterization with a FO model. The FOT data is also processed for the detection of nonlinear contributions from the lungs in the measured air-pressure.

The paper is organized as follows: the methods, patients and measurement protocol are described in the next section. Third section presents the results and a fourth section discusses these results. A conclusion section summarizes the main ideas of this paper.

## 2. Methods

### 2.1. Patients

This study was approved by the local Ethics Committee of Ghent University Hospital and informed consent was obtained from all volunteers before inclusion in the study. The study involved subjects, of which were healthy and were adults diagnosed with kyphoscoliosis. 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 KS. All patients were in stable clinical condition at the moment of measurement.

The *healthy* adult group evaluated in this study consists of 80 Caucasian volunteers (students) without a history of respiratory disease, whose lung function tests were performed in our laboratory, and Table 1 presents their biometric parameters. The measurements were performed over the 2005–2009 time interval. The healthy group of adults has been verified using the reference values from [29]. Although the age groups are significantly different, the lung volumes are similar, therefore providing similar conditions.

The second group of adult patients was diagnosed with *kyphoscoliosis*. Kyphoscoliosis is a disease of the spine and its articulations, mostly beginning in childhood [8,3,30]. The deformation of the spine characteristically consists of a lateral displacement or curvature (scoliosis) or an antero-posterior angulation (kyphosis) or both (kyphoscoliosis). The angle of the spinal curvature called *the angle of Cobb* determines the degree of the deformity and consequently the severity of the restriction. Severe kyphoscoliosis may lead to respiratory failure, which often needs to be treated with non-invasive nocturnal ventilation. The study involved 11 adults diagnosed with kyphoscoliosis and their corresponding biometric and spirometric values are given in Table 1. In this table, the following notations apply: % pred: predicted values; VC: vital capacity; FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; Cobb angle: the angle of spinal deformity (one patient was excluded for it has outlier value for Cobb angle, i.e. 178°; $C_{cw}$: chest wall compliance; *pred**: denotes values predicted from the Cobb angle, according to [23,34]; $R_{aw}$: airway resistance from bodybox lung function test. All KS patients were on nocturnal ventilation. The measurements were performed during the June–August 2009 time interval.

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 KS 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 criteria (American Thoracic Society), with the software allowing detection of non-acceptable maneuvres. The details from the KS patients are given in Table 1.

### 2.2. Input impedance measurement

The impedance was measured using the Forced Oscillation Technique (FOT) setup, commercially available, assessing respiratory mechanics in two range of frequencies: 0.1–10 Hz and 4–48 Hz. Due to the fact that two distinct frequency ranges are used, two separate FOT devices were used, each optimized for the respective frequency interval. Both devices are based on standard FOT guidelines [28]. The subject is connected to the setup via a mouthpiece. The oscillation pressure is generated by an air fan (for the lower frequencies), respectively by a loudspeaker (for the higher frequencies). Both elements are moving according the fed voltage from a computer, which generates a multisine signal, creating air pressure oscillations. Opening of the main tubing allows the patient to have fresh air circulation, designed carefully not to lose significant air pressure power. During the measurements, the patient wears a nose clip and keeps the cheeks firmly supported. The FOT lung function tests were performed according to the recommendations described in [28].

The multisine signal was kept within a range of a peak-to-peak size of 0.1–0.3 kPa. All patients were tested in the sitting position, with cheeks firmly supported and elbows resting on the table. Each and every group of patients and volunteers has been tested in its unique location, using the same FOT devices, and under the supervision of the same FOT team.

### 2.3. Respiratory impedance

The spectral representation of the respiratory impedance $Z_r$ is a fast, simple and fairly reliable evaluation [28,24]. Since the multisine signal is optimized such that it does not contain components of the breathing frequency of the patient, one can calculate the respiratory impedance as in:

$$Z_r(j\omega) = \frac{S_{PU_g}(j\omega)}{S_{QU_g}(j\omega)} \quad (1)$$

whereas $U_g$ is the input signal send to the patient (i.e. sinusoidal variations in the air-pressure), the $P$ corresponds to pressure (its electrical equivalent is voltage) and $Q$ corresponds to air-flow (its electrical equivalent is current), the respiratory impedance $Z_r$ can be defined as their spectral (frequency domain) ratio relationship, with $S_{ij}(j\omega)$ the cross-correlation spectra between the various input–output signals, $\omega$ is the angular frequency and $j = (-1)^{1/2}$ [19,20].

### 2.4. Parametric model and relation to lung properties

In our previous work, we had shown that anatomical and morphological models of the respiratory tract [13] lead to ladder