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Determination of regional lung function in cystic fibrosis using electrical impedance tomography

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Abstract: Electrical impedance tomography (EIT) can be used to monitor regional lung ventilation. Due to its relatively high temporal resolution, EIT has already been applied during lung function tests in spontaneously breathing subjects with obstructive lung diseases like chronic obstructive pulmonary disease (COPD) or cystic fibrosis (CF). In our study, ratios of the maximal volume exhaled in 1 s during forced expiration and forced vital capacity (FEV_1/FVC) were calculated in predefined lung regions for five CF patients and five lung healthy subjects. The degree of FEV_1/FVC homogeneity was assessed by using a slightly modified version of the global inhomogeneity index ($GI_{FEV_1/FVC}$). CF patients showed a higher degree of inhomogeneity in pixel FEV_1/FVC than lung healthy subjects. Since EIT is able to deliver regional information to assess airway obstruction in CF patients, it might represent a promising supplement to existing methods like spirometry providing global lung parameters.

Keywords: cystic fibrosis; electrical impedance tomography; obstructive lung disease; regional lung function.

1 Introduction

Electrical impedance tomography (EIT) is a non-invasive, radiation-free imaging technique which can be applied to visualize regional lung dynamics. Variations in blood and gas volumes due to breathing result in impedance changes of the lung tissue. Changes in electrical potentials at the skin during breathing, measured by surface electrodes attached at the human thorax, are used to reconstruct a 2-dimesional image of impedance distribution within the thorax. Up to now, EIT is mainly used at the bedside e.g. to trace ventilation distribution during mechanical ventilation [1, 2] or to optimize ventilator settings [3, 4].

However, it was already demonstrated that EIT is also able to measure volume changes during lung function testing in spontaneously breathing COPD (chronic obstructive pulmonary disease) and CF (cystic fibrosis) patients due to its relatively high temporal resolution [5, 6]. In 2013, Zhao et al. showed that regional airway obstructions determined in CF patients by EIT correlated with obstructions identified by CT [7]. Since EIT works without radiation and provides regional information of the lung, it might depict a promising supplementary tool to well-established methods like CT or spirometry for the diagnosis of obstructive lung diseases.

A typical parameter to evaluate airway obstruction is the ratio of the maximal volume exhaled in 1 s during a forced expiration and the forced vital capacity (FEV_1/FVC) determined during lung function testing. In the present study, we investigated ratios of regional impedance changes corresponding to FEV_1/FVC in CF patients and lung healthy volunteers using EIT. Identifying differences in impedance ratios of FEV_1 and FVC between CF patients and lung healthy subjects might improve the diagnosis and assessment of obstructive lung diseases.

2 Methods

2.1 Data acquisition

EIT and spirometry measurements were carried out simultaneously on five CF patients [two male and three female, age 34.0 $\pm$ 5.5 years (mean $\pm$ SD)] and five lung healthy subjects [five male, age 24.2 $\pm$ 2.7 years (mean $\pm$ SD)], respectively. EIT measurements were conducted in the 5^{th} intercostal space using an electrode belt comprising 16 electrodes (PulmoVista 500, Dräger, Germany). EIT data were gathered with a frame rate of 30–40 Hz. Subjects

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were performing normal tidal breathing followed by an inspiratory vital capacity (IVC) manoeuvre and a FVC manoeuvre according to the guideline [8] to determine FEV_1 and FVC (SpiroScout, Ganshorn Medizin Electronic, Germany). Spirometry and EIT measurements were repeated up to three times per subject depending on their health status.

2.2 EIT data processing

EIT data were reconstructed with a linearized Newton-Raphson algorithm provided by the EIT manufacturer (Dräger EIT Data Analysis Tool 6.1, Dräger, Germany) obtaining EIT images with a resolution of 32×32 pixels. To filter out the cardiac activity, a low-pass filter with a cut-off frequency of 50 min^{-1} was applied. Lung regions included in further analyses were defined by generating functional EIT images using a linear regression fit [9]. Pixel values smaller than 20% of the maximum value of the functional image [10] were not assigned to respiration and therefore excluded from analyses.

2.3 Data analysis

EIT data measured during the FVC manoeuvre leading to the highest FVC value were analysed for each subject. Relative impedance changes corresponding to FEV_1 and FVC were determined for each pixel of the predefined lung regions. FEV_1/FVC images were generated by calculating the ratio of FEV_1 and FVC in each pixel. A slightly modified version of the inhomogeneity index (GI) introduced by Zhao et al. in 2009 [11], was applied to evaluate the distribution of FEV_1/FVC within the predefined lung regions (see eq. 1).

$$GI_{\frac{FEV_1}{FVC}} = \frac{\sum_{x,y \in lung} \left| \frac{FEV_1}{FVC}_{xy} - \text{Median}\left(\frac{FEV_1}{FVC}_{lung}\right) \right|}{\sum_{x,y \in lung} \frac{FEV_1}{FVC}_{xy}} \quad (1)$$

where FEV_1/FVC depicts the ratio of the relative impedance changes corresponding to FEV_1 and FVC, FEV_1/FVC_{xy} represents a pixel in the predefined lung region and FEV_1/FVC_{lung} comprises all pixels belonging to the lung region.

$GI_{FEV_1/FVC}$ was calculated for the CF patients and the lung healthy volunteers, respectively.

Ratios of FEV_1 and FVC determined by spirometry were stated as mean $\pm$ standard deviation.

3 Results

Averaged FEV_1/FVC ascertained by spirometry was 83.7 $\pm$ 2.5% for the healthy subjects and 63.8 $\pm$ 6.8% for the CF patients.

EIT measurements revealed that FEV_1/FVC images of the CF patients were more inhomogeneous compared to the FEV_1/FVC images of the healthy subjects. Figure 1 exemplarily shows one FEV_1/FVC image of a healthy subject and one FEV_1/FVC image of a CF patient.

The boxplot in Figure 2 represents a comparison of the $GI_{FEV_1/FVC}$ obtained from the lung healthy subjects and the CF patients. All CF patients exhibited a higher $GI_{FEV_1/FVC}$ compared to the lung healthy subjects [CF: 0.103 (0.045), lung healthy subjects: 0.049 (0.017), median (interquartile range)]. Furthermore, the CF patients showed a higher variation in $GI_{FEV_1/FVC}$ than the healthy subjects.

4 Discussion

Global ratios of FEV_1 and FVC measured by spirometry were distinctly higher in the lung healthy subjects compared to the CF patients confirming airway obstructions in the CF patients.

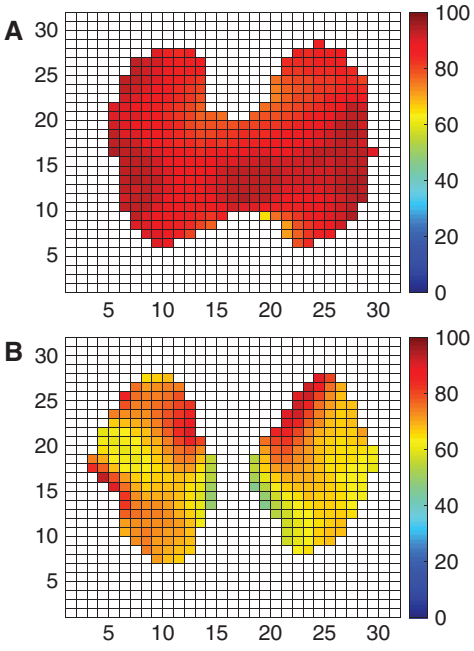

Figure 1: Regional FEV_1/FVC images of (A) one lung healthy subject and (B) one CF patient. EIT measurements were performed in the 5th intercostal space. The colour bars indicate the ratio values in each pixel.

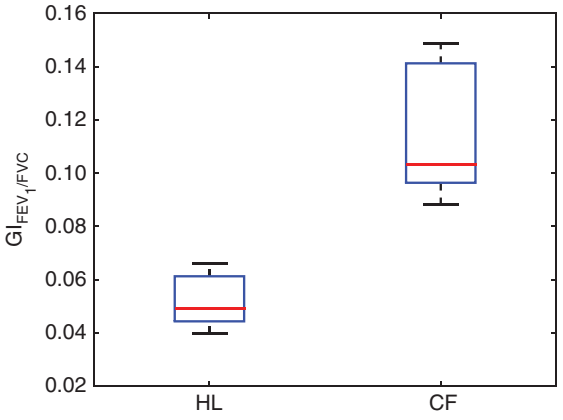

Figure 2: Modified global inhomogeneity index ($GI_{FEV_1/FVC}$) of the lung healthy subjects (HL) and the cystic fibrosis patients (CF). Box: 25% percentile, median and 75% percentile. Whiskers: minimum and maximum values.

Differences in the FEV_1/FVC images between the CF patients and the lung healthy subjects could be visualized. In 2012 Zhao et al. showed that the ratio of maximum expiratory flow at 25% and 75% of vital capacity (MEF_{25}/MEF_{75}) could be used to identify regional airway obstruction in CF [6]. Since the CF patients in our study showed a more inhomogenous distribution of FEV_1/FVC compared to the lung healthy subjects, FEV_1/FVC images might also be applicable to identify regional airway obstructions. Differences within a FEV_1/FVC image might indicate that some lung regions are more affected than others. In 2012 Vogt et al. presented that COPD patients exhibited a higher degree of heterogeneity and a flatter frequency distribution of pixel FEV_1/FVC ratios compared to lung healthy subjects [5]. These findings coincide with the results of our study. To characterize the heterogeneity of the spatial distribution of regional FEV_1 and FVC within a chest cross section, Vogt et al. calculated the coefficient of variation (CV) of all pixel values.

In our study, we utilized a modified global inhomogeneity index $GI_{FEV_1/FVC}$ to assess the inhomogeneity degree of the regional FEV_1/FVC. $GI_{FEV_1/FVC}$ indicated a more homogenous distribution of FEV_1/FVC in the lung healthy subjects than in the CF patients. Determining $GI_{FEV_1/FVC}$ might benefit the diagnosis but also the follow-up of obstructive lung diseases. $GI_{FEV_1/FVC}$ could possibly help the physicians to evaluate the progress of the diseases or the effectiveness of therapy.

One limitation of the study is the limited number of subjects. To confirm results statistically, additional trials with more subjects are necessary. Additionally, the regional information obtained by EIT was restricted to a certain thorax plane. Further measurements in different thorax planes are needed to investigate the influence of the belt position on our results. To verify the results obtained by EIT, a comparison with structural imaging modalities such as CT is required.

5 Conclusion

Results of our study revealed that CF patients showed a higher degree of inhomogeneity in pixel FEV_1/FCV ratios compared to lung healthy subjects. FEV_1/FVC images might depict a promising tool to identify regional airway obstructions in CF patients benefitting diagnosis and therapy.

Author's Statement

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