Sabine Krueger-Ziolek*, Bo Gong, Hanna Zimmermann, Ullrich Müller-Lisse and Knut Möller

Regional analysis of airway abnormalities in cystic fibrosis employing Electrical Impedance Tomography

Abstract: To estimate the severity of airway abnormalities in cystic fibrosis (CF) Brody et al. developed a computed tomography (CT) scoring system. Each pulmonary lobe is analyzed separately considering various morphological defects. A study from Zhao et al. demonstrates that this CT-based score correlates with regional airway obstruction (RAO) measured by the real-time imaging method Electrical Impedance Tomography (EIT). Zhao et al. performed EIT measurements at the 5th intercostal space (ICS) and median RAO, including both lungs, was correlated with the associated score. In the present feasibility study, it was investigated if RAO determined by EIT within the left and right lung respectively at the 3rd and 5th ICS corresponds with the scores of the left and right lobes. EIT measurements and CT-based scoring were carried out on two CF patients. RAO was identified by ratios of impedance values associated to the maximal forced expiratory flow at 25% and 75% of the forced vital capacity. Mean RAO of each lung within both thorax sections was compared with the lobar scores. Airway abnormalities within upper lobes are assigned to RAO measured within the 3rd ICS, whereas abnormalities of the right middle lobe, both lower lobes and the lingula are mainly represented by EIT images of the 5th ICS. Results show that differences in the CT-based score between the left and right lung concur with differences in EIT derived RAO. The regional information provided by EIT might be used for a more targeted therapy of CF-related lung diseases.

Keywords: Electrical Impedance Tomography, cystic fibrosis, airway abnormalities, computed tomography

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1 Introduction

Cystic fibrosis (CF) is a congenital metabolic disorder caused by mutations of the cystic fibrosis transmembrane conductance regulator (CFTR) gene [1]. CFTR proteins are involved in the transport of salt ions through the membrane of epithelial cells. Defects of the CFTR protein entail an impaired water and salt metabolism resulting in viscous secretions. Organs like the lung, the pancreas, the liver or genitalia are primarily affected [2]. In consequence, digestive and pulmonary disorders are common symptoms. However, respiratory failure is considered as the leading cause of death in CF [1]. Viscous mucus is causing airway obstruction and flavouring bacterial inflammations. Inflammatory processes within the lung in turn could lead to morphological defects within the airways.

Follow-ups of CF-related lung diseases are usually performed by spirometry and computed tomography (CT) to detect changes in lung function and structure. For instance, Brody and colleagues [3] developed a scoring system allowing the assessment of the degree of the severity of airway abnormalities within each pulmonary lobe utilizing CT scans. Various morphological abnormalities, such as bronchiectasis or peribronchial thickening, are detected, weighted and summed up to a total score for each lobe. The sum of all lobe scores defines the Total Brody Score, which enables an estimation of the severity of CF-related lung diseases.

Recently, it has been demonstrated that regional airway obstruction (RAO) in patients with CF can also be detected by Electrical Impedance Tomography (EIT), a relatively new real-time imaging method [4-6]. EIT imaging is based on the injections of small currents and voltage measurements via electrodes on the thorax surface [7]. Thus, it is non-invasive and works without radiation. Impedance variations of the lung tissue caused by respiration are calculated from the measured thoracic voltage changes and used to assess regional ventilation distribution.

In a previous EIT study from Zhao et al., it was presented that EIT derived parameters indicating RAO can be correlated with the score obtained by the CT-based scoring system of Brody et al. [8]. In this mentioned study, EIT measurements were performed at one thorax section (5th intercostal space (ICS)) and the median RAO of both lungs within this section was correlated with the score of the corresponding lung regions.

In the present feasibility study, it should be evaluated if RAO determined by EIT within the left and right lung respectively corresponds with the CT-based score of the left and right lobes. Since upper lung areas are frequently more affected by airway abnormalities in patients with CF [6], EIT measurements were performed at the 5th and the 3rd ICS. The regional information derived by EIT might be used to make CF-related lung disease therapies more targeted and more patient-specific.

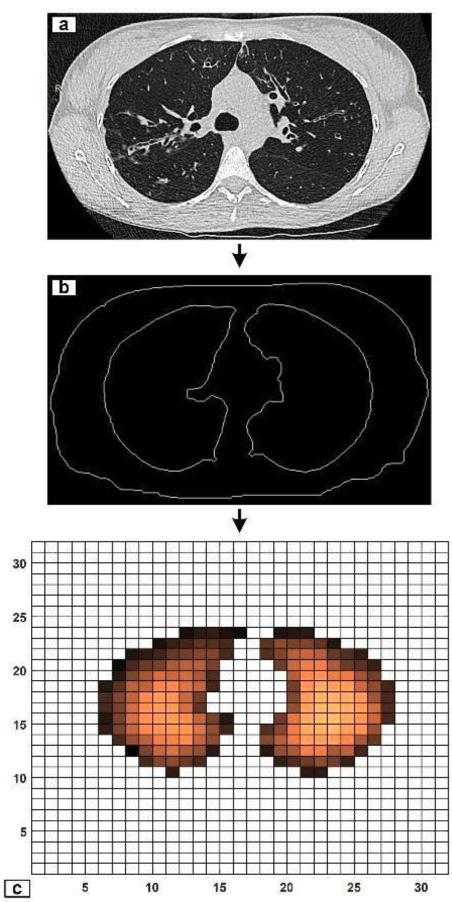

Figure 1: (a) CT image of CF patient B. (b) Extracted thorax and lung contours for EIT image reconstruction. (c) Generated EIT image.

2 Methods

2.1 Patients

Two patients (one male: 43 years, 73 kg, 183 cm; and one female: 35 years, 44 kg, 156 cm) having CF were enrolled in this feasibility study. Both patients exhibited an impaired lung function showing a spirometric ratio of the volume exhaled within one second of a forced expiration and the forced vital capacity (FEV_1/FVC) of approximately 70%. Written informed consent was given by both patients.

2.2 EIT and CT data recording

EIT data were recorded successively at the 3rd and 5th ICS during the performance of FVC manoeuvres [9]. For this purpose, 16 electrodes were attached around the thorax at the corresponding heights in a transversal plane. EIT data were collected with a frame rate of 30 Hz and a stimulation frequency of around 98 kHz (Pulmovista 500®, Dräger Medical, Lübeck, Germany).

CT images were received from a routine check. Thereby, CT image acquisition was performed during inspiration to make the lung structure more visible in the images. A period of 0.8 to 3.2 years was inbetween EIT and CT data recording.

2.3 EIT image reconstruction

Patient-specific CT images (axial direction) at the thoracic level of the 3rd and 5th ICS have been used to get structural information for the EIT image reconstruction (Figure 1, a). The EIT model was built by using the thorax and lung contours extracted from the CT images (Figure 1, b). Since impedance changes within the thorax are mainly caused by varying air volume within the lungs, EIT data reconstruction was restricted to the lung regions (Figure 1, c). A canonical One-Step Gauss-Newton solver with Laplacian regularization was employed to reconstruct the data.

2.4 EIT and CT image analysis

2.4.1 EIT derived ‘obstruction maps’

EIT based ‘obstruction maps’ were calculated for each thorax section by using the method of Zhao et al. introduced in 2012 [4]. Regional ratios of impedance values corresponding to the

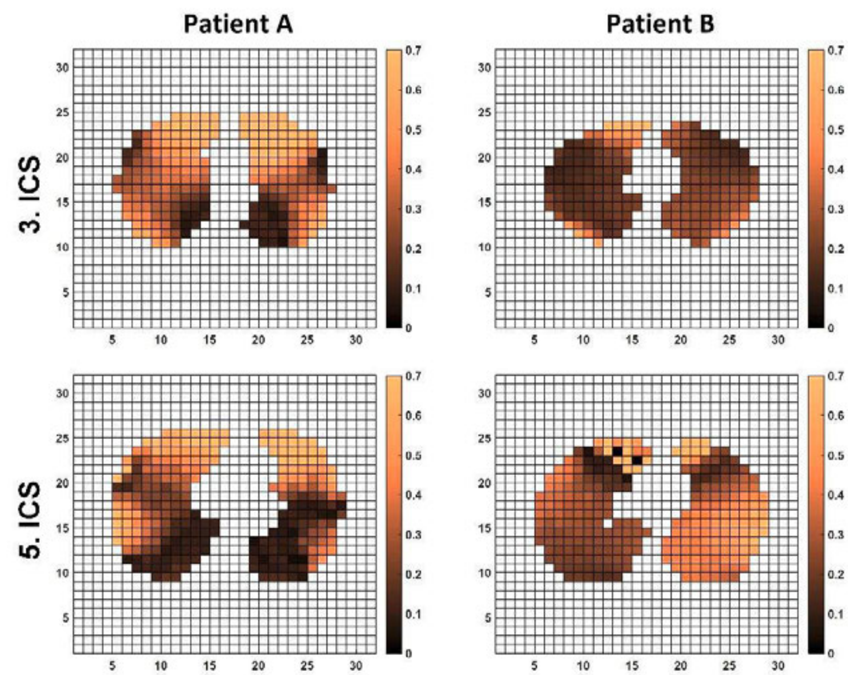

Figure 2: Regional ratios of impedance values corresponding to the maximal forced expiratory flow at 25% and 75% of the forced vital capacity ($\Delta I_{MEF25}/\Delta I_{MEF75}$) within the 3rd and 5th intercostal space (ICS) of two cystic fibrosis patients.

maximal forced expiratory flow at 25% and 75% of the forced vital capacity ($\Delta I_{MEF25}/\Delta I_{MEF75}$) were determined for the left and the right lung respectively. Low $\Delta I_{MEF25}/\Delta I_{MEF75}$ values indicate affected lung regions. The mean values of regional $\Delta I_{MEF25}/\Delta I_{MEF75}$ were calculated for both lungs within the 3rd and 5th ICS.

2.4.2 CT-based scoring system

To estimate the severity of airway abnormalities in both CF patients, the CT scoring system suggested by Brody et al. was utilized [3]. Morphological defects were identified (subscores) and summed up for each pulmonary lobe individually (lobar total score). Thus, the total score of the right lung was defined by the right upper, middle and lower lobe score, and the total score of the left lung by the lingula, the left upper and lower lobe score.

3 Results

Figure 2 shows the $\Delta I_{MEF25}/\Delta I_{MEF75}$ images within the 3rd and 5th ICS of both CF patients. Patient A has a higher mean value of $\Delta I_{MEF25}/\Delta I_{MEF75}$ in the left lung compared to the right lung within the 3rd ICS. Within the 5th ICS, mean values are nearly the same in size. Patient B exhibited equally sized mean values of $\Delta I_{MEF25}/\Delta I_{MEF75}$ in both lungs within the 3rd ICS, but shows a greater mean value of $\Delta I_{MEF25}/\Delta I_{MEF75}$ in the left lung compared to the right lung at the 5th ICS. An overview of $\Delta I_{MEF25}/\Delta I_{MEF75}$ mean values of both patients are presented in Table 1.

Table 1: Mean $\Delta I_{MEF25}/\Delta I_{MEF75}$ values of the left and the right lung within the 3rd and the 5th ICS of both CF patients.

	Patient A		Patient B	
	Right Lung	**Left Lung**	**Right Lung**	**Left Lung**
3. ICS	0.41	0.47	0.26	0.26
5. ICS	0.37	0.35	0.36	0.47

The CT-based scoring system revealed that the right upper lobe of patient A is more affected by airway abnormalities (total lobe score of 13.50) than the remaining lobes (averaged total lobe score of 6.05). In total, the right lung of patient A was more affected than the left lung.

In patient B, both upper lobes as well as the right middle lobe (total lobe scores between 12.00 and 15.00) seemed to be more affected than both lower lobes and the lingula (total lobe scores between 6.50 and 8.50). Thus, the right lung of patient B also showed more airway defects than the left lung. Total lobe scores of both CF patients are presented in Table 2.

Table 2: Total lobe scores of both CF patients determined by the CT-based scoring system of Brody et al. [3].

	Patient A	Patient B
right upper lobe	13.50	13.00
right middle lobe	6.00	15.00
right lower lobe	5.75	8.50
Right Lung	***25.25***	***36.50***
left upper lobe	6.75	12.00
left lower lobe	5.75	6.50
lingula	6.00	7.00
Left Lung	***18.50***	***25.50***

4 Discussion

EIT derived obstruction maps and the CT-based scoring system revealed that in both CF patients the right lung was more affected by airway abnormalities than the left lung.

In patient A, the right upper lobe showed a higher total lobe score compared to the remaining lobes indicating more airway defects. Comparing $\Delta I_{MEF25}/\Delta I_{MEF75}$ mean values of the right (0.41) and left (0.47) lung within the 3rd ICS reinforced this observation. Mean $\Delta I_{MEF25}/\Delta I_{MEF75}$ values of the left (0.35) and right (0.37) lung within the 5th ICS and the similar total lobe scores of the right middle and lower lobe as well as the lingula and the left lower lobe implied no significant differences in the severity of airway abnormalities between the middle and lower lungs.

In patient B, total scores of the upper lobes and $\Delta I_{MEF25}/\Delta I_{MEF75}$ mean values of both lungs within the 3rd ICS (0.26) showed that the upper lungs seemed to be equally affected by airway abnormalities. Differences in mean values of $\Delta I_{MEF25}/\Delta I_{MEF75}$ between lungs within the 5th ICS (right lung: 0.36; left lung: 0.47) revealed that the left lower lung and the lingula are less severely affected by airway defects than the right middle and lower lung. This was confirmed by differences in the corresponding total lobe scores. Variations in the size of the mean values of $\Delta I_{MEF25}/\Delta I_{MEF75}$ between thorax sections in both patients could be based on physiological (e.g. varying respiratory flows) or methodical (e.g. another measurement situation comprising changes in belt positioning) conditions, which should be kept in mind by the data interpretation.

Limitations of this study are the small number of patients and the relatively long period between CT and EIT image acquisition. It has to be considered, that the CT-based scoring system of Brody et al. [3] includes permanent and temporary morphological abnormalities, whereas EIT provides current dynamical information of the regional lung ventilation.

5 Conclusion

This study shows that differences in the severity of airway abnormalities between the left and right lung determined by a CT-based scoring system in two CF patients coincided with differences in RAO detected by EIT. Thus, EIT may be a useful supplement to evaluate the severity of CF-related lung diseases and may support a more targeted therapy.

Author Statement
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