Respiratory Physiology & Neurobiology 233 (2016) 25–32

Contents lists available at ScienceDirect

Respiratory Physiology & Neurobiology

journal homepage: www.elsevier.com/locate/resphysiol

Multi-layer ventilation inhomogeneity in cystic fibrosis

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ARTICLE INFO

Article history:
Received 12 July 2016
Received in revised form 27 July 2016
Accepted 28 July 2016
Available online 28 July 2016

Keywords:
Electrical impedance tomography
Cystic fibrosis
Regional lung function
Ventilation inhomogeneity

ABSTRACT

Differences in regional lung function between the 3rd and 5th intercostal space (ICS) were explored in 10 cystic fibrosis (CF) patients and compared to 10 lung-healthy controls by electrical impedance tomography (EIT). Regional ratios of impedance changes corresponding to the maximal volume of air exhaled within the first second of a forced expiration (ΔI_{FEV1}) and the forced vital capacity (ΔI_{FVC}) were determined. Regional airway obstruction and ventilation inhomogeneity were assessed by the frequency distribution of these ratios ($\Delta I_{FEV1}/\Delta I_{FVC}$) and an inhomogeneity index (GI_{TI}). The mean of the frequency distribution of $\Delta I_{FEV1}/\Delta I_{FVC}$ and the GI_{TI} in both thorax planes were significantly different between CF patients and controls ($p < 0.001$). CF patients exhibited a significantly lower mean of $\Delta I_{FEV1}/\Delta I_{FVC}$ frequency distribution ($p < 0.05$) and a significantly higher degree of ventilation inhomogeneity ($p < 0.01$) in the 3rd ICS compared to the 5th ICS. Results indicated that EIT measurements at more cranial thorax planes may benefit the early diagnosis in CF.

1. Introduction

Cystic fibrosis (CF) is a chronic progressive disease affecting the lung but also other organs like the pancreas or the liver. An inherited genetic defect induces changes in sweat, mucus and digestive fluid producing cells, leading to thick and sticky secretions (Buckingham, 2011). Pulmonary insufficiency is the main cause of death in 80% of people suffering from cystic fibrosis (O'Sullivan and Freedman, 2009). Mucus accumulating in the small airways causes obstructions and promotes bacterial infections. Inflammatory processes impair the function of the bronchial walls by destroying the epithelium which in turn results in bronchiectasis (Treves, 2007). Up to now, CF cannot be cured. However, diagnosis and therapy have been substantially improved over the last years, leading to a predicted median survival age for CF patients close to 40 years (Eichinger et al., 2012). Common methods for CF diagnosis and follow-up are spirometry and imaging modalities like computed tomography (CT). However, lung function testing by spirometry only provides information about the whole lung and CT, although delivering regional information, involves potentially harmful radiation.

Electrical impedance tomography (EIT), an emerging medical imaging technique, can be applied to monitor regional changes in ventilation without the exposure to radiation (Gong et al., 2015). In lung EIT, an array of electrodes is circumferentially attached around the thorax, and small alternating currents are induced between pairs of electrodes in a rotating manner, while resulting voltages occurring at the thorax surface are measured by the other electrodes. The measured voltages are used to reconstruct cross-sectional images of impedance distribution within the thorax. Thus, EIT images represent changes in the electrical impedance of the lung tissue caused by regional variations in gas and blood volumes associated with ventilation.

Several studies have already shown that EIT, due to its high temporal resolution, is suitable to measure rapid changes in ventilation during lung function testing in patients with obstructive lung diseases (Frerichs et al., 2016; Lehmann et al., 2016; Vogt et al., 2012; Vogt et al., 2016; Zhao et al., 2012). Recently, Lehmann et al., (2016) confirmed that relative impedance changes measured during forced expiration correlate with lung function parameters

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http://dx.doi.org/10.1016/j.resp.2016.07.010
1569-9048/

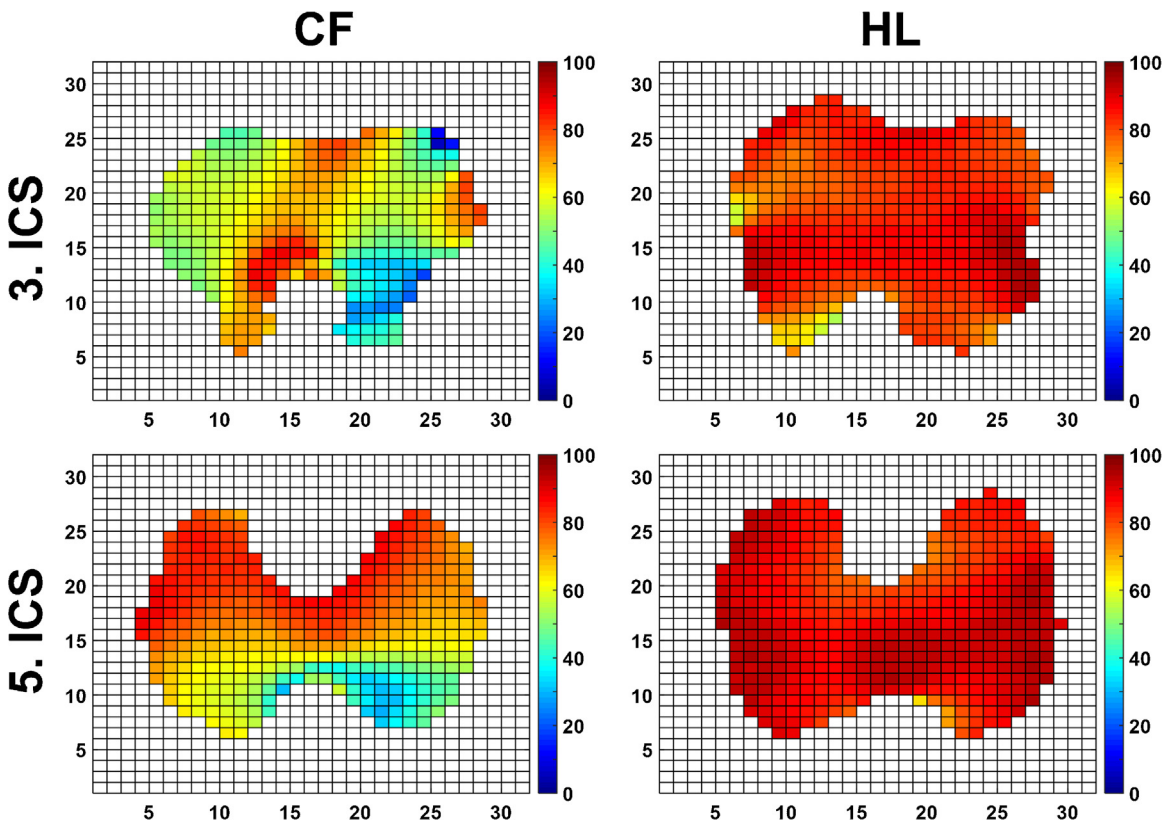

Fig. 1. EIT images of a cystic fibrosis patient (CF) and a lung-healthy control (HL) recorded at the 3rd and 5th intercostal space (ICS), respectively. Each pixel of an image depicts the regional ratio of impedance changes corresponding to the maximal volume of air exhaled within the first second of the forced expiration of a forced vital capacity maneuver and the forced vital capacity ($\Delta I_{FEV1}/\Delta I_{FVC}$). Color bars indicate the magnitude of $\Delta I_{FEV1}/\Delta I_{FVC}$ in each pixel.

and radiology in children with CF. Furthermore, Zhao et al. (2012, 2013) presented that ratios of impedance changes corresponding to maximum expiratory flow at 25% and 75% of vital capacity (MEF_{25}/MEF_{75}) can be used to identify regional airway obstruction in CF patients.

However, in all these studies EIT measurements were performed at the 5th–6th intercostal space (ICS) and did not provide information on ventilation distribution in more cranial or caudal thorax planes. Previous studies have demonstrated that regional ventilation distribution varies in cranio-caudal direction during mechanical ventilation as well as during spontaneous breathing (Bikker et al., 2011; Frerichs et al., 1999; Krueger-Ziolek et al., 2015; Reifferscheid et al., 2011). Thus, conducting EIT measurements at only one thorax plane may lead to incomplete information and, potentially, to misinterpretation of the lung condition. Since it is assumed in CF that the upper lung regions are affected earlier and more severely than the lower lung regions (Puderbach et al., 2007; Treves, 2007), information on regional ventilation distribution in more cranial thorax planes may be beneficial for the diagnosis and therapy of CF.

The aim of the present study was to investigate differences in regional lung function between two thorax planes (3rd and 5th ICS, respectively) in 10 CF patients and in 10 lung-healthy subjects (controls) to potentially extend the application range of EIT in CF. Since the ratio of the maximal volume of air exhaled within the first second of a forced expiration and the forced vital capacity (FEV_1/FVC), the so called Tiffeneau-index (TI), is typically used in lung function testing to diagnose and estimate obstructive lung disease, we evaluated regional ratios of relative impedance changes corresponding to FEV_1 and FVC to assess regional airway obstruction and ventilation inhomogeneity in the different thorax planes.

2. Methods

2.1. Study protocol and data acquisition

EIT measurements (Pulmovista 500®, Dräger Medical, Lübeck, Germany) were conducted on 10 CF patients (2 female and 8 male, weight 65.2 ± 13.4 kg; height 175.3 ± 11.4 cm; age 35.8 ± 9.0 years; body mass index 21.0 ± 2.6 kg/m^2 (mean ± SD)) and 10 lung-healthy subjects (controls, male, weight 76.8 ± 12.6 kg; height 179.2 ± 9.2 cm; age 25.6 ± 3.7 years; body mass index 23.8 ± 2.3 kg/m^2 (mean ± SD)). Exclusion criteria were age < 18 years, pregnancy and lactation period as well as contraindications for EIT, such as, e.g., a cardiac pacemaker, an implantable cardioverter-defibrillator or other active implants. The study was approved by the ethics committee of the University of Munich and written informed consent was obtained from each subject. EIT data were acquired with an electrode belt of 16 electrodes at the 3rd and 5th ICS, respectively, with a frame rate of 30–40 Hz during pulmonary function testing. The subjects were performing normal tidal breathing followed by a slow inspiratory vital capacity (IVC) maneuver and a forced vital capacity (FVC) maneuver, in accordance with pertinent clinical guidelines (Miller et al., 2005), to determine the ratio of the maximal volume of air exhaled within the first second of the forced expiration and the forced vital capacity (FEV_1/FVC). Spirometry (SpiroScout®, Ganshorn Medizin Electronic, Niederlauer, Germany) was carried out as a reference method to trace the breathing efforts of subjects