Evaluation of lung ventilation distribution in chronic obstructive pulmonary disease patients using the global inhomogeneity index

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Abstract— The global inhomogeneity (GI) index is a electrical impedance tomography (EIT) parameter that quantifies the tidal volume distribution within the lung. In this work the global inhomogeneity index was computed for twenty subjects in order to evaluate his potential use in the detection and follow up of chronic obstructive pulmonary disease (COPD) patients.

EIT data of 17 subjects were acquired: 14 patients with the main diagnoses of COPD and 3 healthy subjects which served as a control group. Two or three datasets of around 30 seconds were acquired at 33 scans/s and analysed for each subject. After reconstruction, a tidal EIT image was computed for each breathing cycle and a GI index calculated from it.

Results have shown significant differences in GI values between the two groups (0.745 ± 0.007 for COPD and 0.668 ± 0.006 for lung-healthy subject, $p < 0.005$). The GI values obtained for each subject have shown small variance between them, which is a good indication of stability. The results suggested that the GI may be useful for the identification and follow up of ventilation problems in patients with COPD.

I. INTRODUCTION

Pulmonary air flow is less than normal in certain lung areas of chronic obstructive pulmonary disease (COPD) patients. This leads to a higher ventilation inhomogeneity than in healthy subjects. Therefore, parameters that quantify the degree of this inhomogeneity provide useful information about the lung condition.

Several methods are able to detect this inhomogeneity in ventilation in the lung such as computed tomography [1] and the multibreath washout technique [2]. However, these methods are not suitable for continuous monitoring.

Electrical Impedance Tomography (EIT), while having a lower spatial resolution than CT, can provide a non-invasive, radiation-free and continuous image of pulmonary impedance [3]. This is because lung resistivity is around five times higher when compared to most other soft tissues within the thorax, and its value increases and decreases significantly between inspiration and expiration [4]. Furthermore, due to having high temporal resolution, EIT quickly detects changes in lung ventilation. The reliability of EIT for lung ventilation

monitoring has already been confirmed by various studies [5]. However, EIT images obtained from different subjects are hard to compare directly without prior calibration, since the resulting image does not display absolute impedance values.

In this paper we aim to evaluate the lung condition of COPD patients by calculating the global inhomogeneity (GI) index, a parameter that quantifies ventilation inhomogeneity with a single number [6]. This parameter is calculated from tidal EIT images that represent differences in impedance between end inspiration and end expiration. The GI index has been used mainly with patients under mechanical ventilation in mind, in particular acute respiratory distress syndrome (ARDS) patients [7][8][9], and has shown to be reliable and interpatient comparable [7]. To the best of our knowledge this is the first work that evaluates the viability of this parameter for COPD patients during tidal breathing.

II. METHODS AND DATA

A. Database

Datasets from 17 adult subjects were examined, each around 30 seconds long. Three healthy subjects (37.7 ± 4.6 years old, mean age $\pm$ SD; female/male: 1/2) and 14 patients (72.8 ± 8.3 years old; female/male: 2/12) with diagnosis of COPD were examined using EIT. All data was acquired during tidal breathing.

Sixteen self-adhesive electrodes (Blue Sensor L-00-S, Ambu, Ballerup, Denmark) were attached on the chest circumference in the 5-6th intercostal space and one reference electrode on the abdomen in each studied subject.

Measurements involved application of a current (50 kHz, 5 mA$_{rms}$) between two adjacent electrodes, while the voltage is measured by the rest of the electrodes. This process is repeated for current applied between all the adjacent electrode pairs around the body in a sequential process. The EIT data were acquired using the Goe-MF II EIT device (CareFusion, Höchberg, Germany) at around 33 images/s.

This study was approved by the institutional ethics committee and informed written consent was obtained from each study participant.

B. EIT Reconstruction

Raw EIT images were reconstructed from the EIT data using the GREIT algorithm [10]. Reconstruction was done using the EIDORS software: an adult thorax shaped model with a single plane of 16 electrodes and adjacent stimulation pattern was selected from the model library [11]. Each

obtained EIT image consists of 32×32 pixels, but only 912 of those are pixels of interest, representing the inside of the thorax. The values on these pixels are equal to the normalised difference between the instantaneous and the average pixel impedance for that data set. End-inspiration and end-expiration moments were identified by analysing the global impedance value evolution over time. This value was obtained by calculating the sum of all pixels for each image. At end-inspiration the lungs are filled with air, increasing the measured resistivity on that region, and the total sum of all pixels reaches a maximum. At end-expiration the opposite occurs (step 3 of Figure 2).

A tidal EIT image, showing the impedance difference between end-inspiration and end-expiration, was calculated for each breathing cycle (Figure 1). The higher the volume of air reaching the area represented by each pixel during inspiration, the higher will the value of impedance difference on that pixel be.

C. GI calculation

For each tidal image, the lung area was identified. The lung areas were estimated using functional EIT with a predefined threshold of 35%, i.e., pixels with values larger than 35% of the maximum value in that image were identified as lung area. Since the lungs are expected to be relatively symmetric, the lung area identified was mirrored from left to right and from right to left and combined by a logical OR operation. The final resulting lung area was used to calculate the GI index.

The median value of the pixels in the identified lung area is calculated. The sum of the absolute difference between the median value and every pixel value is considered to represent the variation in tidal volume distribution in the whole lung region [6]. To make the GI index universal and interpatient comparable, it is normalized to the sum of the impedance values within the lung area:

$$ GI = \frac{\sum_{x,y\in lung} |DI_{x,y} - Median(DI_{lung})|}{\sum_{x,y\in lung} DI_{xy}} \quad (1) $$

where $DI_{x,y}$ is the value of the differential impedance for the pixel at x,y in the tidal image and DI_{lung} represents all the pixels considered to be part of the lung area.

D. Statistical analysis

Data analysis was performed using MATLAB 8.3 (The Mathworks, Natick, MA, USA). The obtained results were compared using the Kruskal-Wallis test. A p value <0.05 was considered to reject the null hypothesis "GIs from the control and from the COPD group are drawn from the same distribution". Data are presented as mean and standard deviation (SD). An overview of the methodology can be found on Figure 2.

III. RESULTS

Table I shows: the mean GI and number of breathing cycles analysed for each subject; the average GI and SD for each group; and the total weighted mean for each group.

TABLE I

MEAN OF THE GI VALUES OBTAINED FOR EACH OF THE THREE SUBJECTS OF THE CONTROL GROUP AND THE 14 PATIENTS.

Group	GI values (mean ± SD)	# of breathing cycles analyzed
Control Group	0.664 ± 0.009	21
	0.677 ± 0.010	17
	0.661 ± 0.016	19
	Weighted average 0.668 ± 0.006	
COPD Group	0.977 ± 0.035	30
	0.843 ± 0.033	20
	0.660 ± 0.034	19
	0.907 ± 0.041	14
	0.748 ± 0.027	16
	0.732 ± 0.018	22
	0.740 ± 0.022	17
	0.558 ± 0.027	20
	0.795 ± 0.025	27
	1.176 ± 0.049	29
	0.818 ± 0.040	36
	0.581 ± 0.024	31
	1.048 ± 0.037	35
	0.677 ± 0.017	27
	Weighted average 0.745 ± 0.007	

A consistently lower GI value was obtained for the control group (0.668 ± 0.006) compared to the COPD group (0.745 ± 0.007). The standard deviation for the GI index for each subject is relatively small (SD average of 0.012 for control group and 0.030 for COPD patients), which indicates there is little variance between different data sets of each patient.

The GI values obtained for the COPD patients were compared to the control group using the Krustal-Wallis test. The returned p value ($p = 2.10 \times 10^{-11}$) is lower than the significance level, thus rejecting the null hypothesis. Figure 3 compares the obtained GI values for those two groups.

There are significantly more subjects for our COPD group than for the control group. Due to the existence of unbalanced groups, a cross validation was done, by selecting 100 times 57 random GI values from the COPD group and comparing them with the 57 GI values from the control group using the Kruskal-Wallis test. The 100 p values obtained are represented in Figure 4, with all of them being lower than the significance level. These results support the conclusion that there is a consistent difference between the GI values obtained from the COPD group and the control group.

A comparison between the COPD group and the control group for each gender was done as well. There is an high difference between the number of breathing cycles acquired, so a cross validation was done also for gender. The highest p value obtained for both cross validations was lower than the significance level (female $p_{max} = 2.79 \times 10^{-4}$; male $p_{max} = 0.013$). The obtained results are represented at Figure 5 and 6.

IV. DISCUSSION

The method used to define the lung area, while being simple and achieving reasonable results, may contain some pixels related to cardiac activity which may affect the value obtained for the GI parameter [7]. Some methods, like
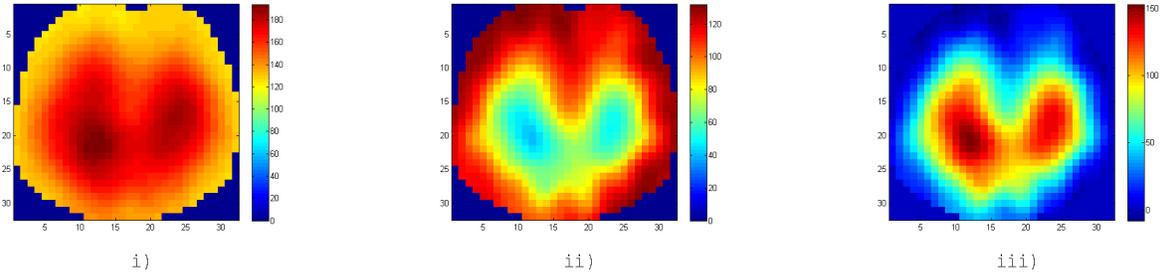
Fig. 1. Image obtained for: i) reconstruction at end-inspiration; ii) reconstruction at end-expiration; iii) the resulting tidal image, equal to the relative impedance difference between the two prior reconstructed images.
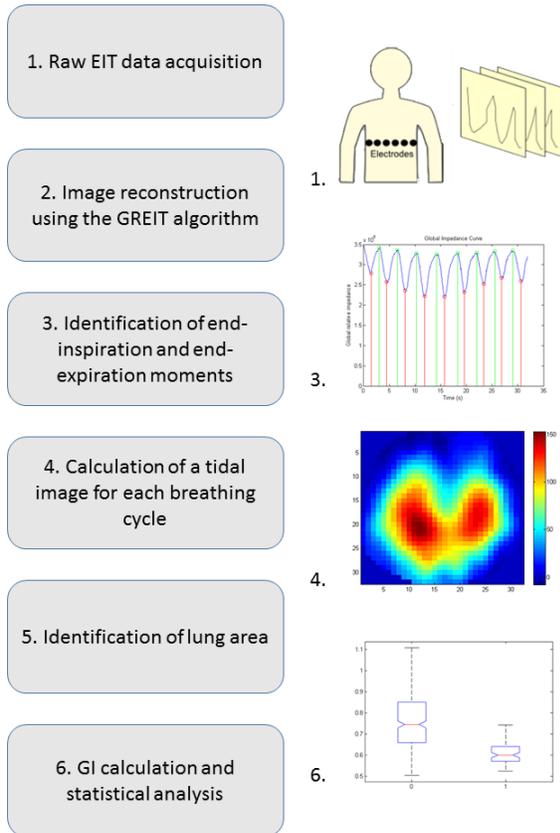

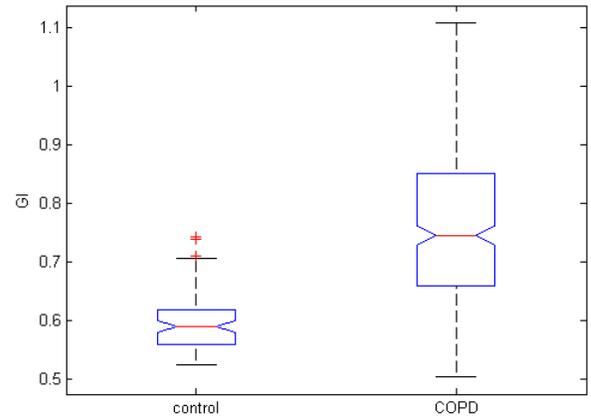Fig. 2. Diagram of the methodological steps followed for GI calculation.

Fig. 3. Comparison of the GI values for the COPD patients and the control group. The boxes represent the quartiles while the whiskers extend from the box out to the most extreme data value within 1.5x the interquartile range of the sample. The red crosses represent outliers.
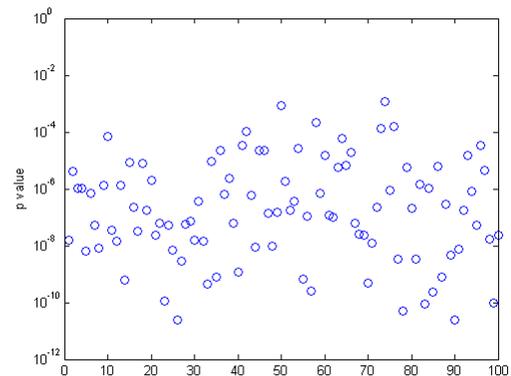

Fig. 4. Representation of the obtained p values during cross validation. Highest p value obtained: 0.0011.

the Lung Area Estimation (LAE) [12] subtract the cardiac related area from the lung area by analysing the energy distribution of every pixel of the tidal EIT image in frequency domain. Cardiac related pixels should have peaks at an higher frequency than lung related pixels.

An important aspect to keep in mind is that the value obtained for the GI index depends on the threshold value used. Higher threshold values in the fEIT method lead to smaller lung area sizes, which lead to different GI values [7]. To keep the GI values interpatient comparable, the chosen threshold value on this study is the same for all subjects of both the COPD patients group and the control group. Another limitation of the GI index is that it only gives a global view
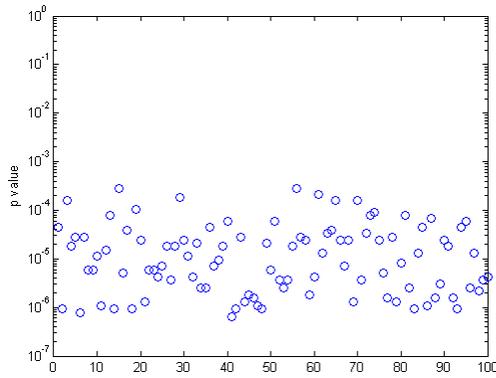
Fig. 5. Representation of the obtained p values during cross validation between female patients and our female control group. Highest p value obtained: 2.79×10^{-4}.
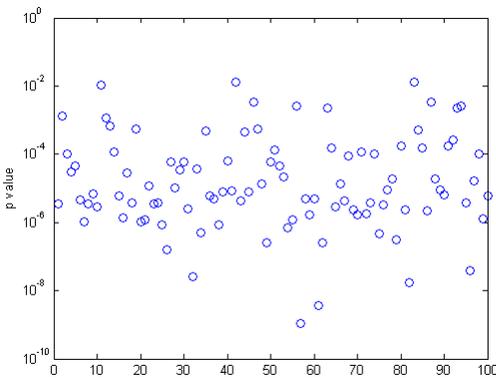

Fig. 6. Representation of the obtained p values during cross validation between male patients and our male control group. Highest p value obtained: 0.013.

of lung ventilation distribution, not considering the local inhomogeneity. We therefore recommend that it should be tested and used with other parameters that emphasize in inhomogeneity on a local level, like the local inhomogeneity (LI) index [6], which quantifies differences among neighbour pixels.

Due to the small sample size available the authors emphasize that the results of this study must be validated with more data.

V. CONCLUSIONS

The GI index is a reliable measure of ventilation heterogeneity. Results have shown significant differences in GI values between COPD patients and the control group. Since the GI index enables interpatient comparison it has great potential. The results suggest that the GI may have potential to be part of a group of parameters that identify and follow the evaluation of COPD patients under spontaneous respiration.

The control group and the COPD group in this study have high age differences. Future work should test if age by itself is a factor that influences the GI index.

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