Ventilation inhomogeneity in obstructive lung diseases measured by electrical impedance tomography: a simulation study

B. Schullcke^{1,2} · S. Krueger-Ziolek^{1,2} · B. Gong^{1,2} · R. A. Jörres³ · U. Mueller-Lisse² · K. Moeller¹

Received: 3 February 2017 / Accepted: 23 September 2017 / Published online: 10 October 2017
© Springer Science+Business Media B.V. 2017

Abstract Electrical impedance tomography (EIT) has mostly been used in the Intensive Care Unit (ICU) to monitor ventilation distribution but is also promising for the diagnosis in spontaneously breathing patients with obstructive lung diseases. Beside tomographic images, several numerical measures have been proposed to quantitatively assess the lung state. In this study two common measures, the ‘Global Inhomogeneity Index’ and the ‘Coefficient of Variation’ were compared regarding their capability to reflect the severity of lung obstruction. A three-dimensional simulation model was used to simulate obstructed lungs, whereby images were reconstructed on a two-dimensional domain. Simulations revealed that minor obstructions are not adequately recognized in the reconstructed images and that obstruction above and below the electrode plane may result in misleading values of inhomogeneity measures. EIT measurements on several electrode planes are necessary to apply these measures in patients with obstructive lung diseases in a promising manner.

Keywords Electrical impedance tomography · Ventilation inhomogeneity · Obstructive lung diseases · Simulation study

1 Introduction

Electrical impedance tomography (EIT) is an imaging modality that is used in clinical settings to visualize the ventilation distribution of the lungs. The most common application occurs in the Intensive Care Unit (ICU), where the ability to get real-time insight into the ventilation distribution is valuable to adjust ventilator settings or change the posture of mechanically ventilated patients [1, 2]. The measuring principle of EIT is to estimate regional impedance changes in the thorax from electrical current injection and corresponding voltage measurements at the boundary. For this purpose, an array of electrodes (typically 16–32) is placed around the patient’s chest. The electrodes are used for both the injection of small alternating currents and the measurement of voltage differences between the electrodes.

The obvious advantages of this type of measurement are that there is no radiation burden, and that the instrumental effort is relatively small, compared to other medical imaging techniques. Additionally, EIT is capable of real-time imaging, which is a major reason for its use as a tool to optimize ventilator settings. EIT is currently the only commercially available technique that allows real-time and bedside monitoring of ventilation distribution.

Besides the ICU application, EIT has recently also been used in spontaneously breathing patients with obstructive lung diseases, such as asthma [3], cystic fibrosis (CF) [4–6], or chronic obstructive pulmonary disease (COPD) [7]. Common approaches for diagnosis and monitoring of the disease state in these patient groups

Partial results of this study will be presented at the 20th World Congress of the International Federation of Automatic Control (IFAC), Toulouse, France.

✉ B. Schullcke
sben@hs-furtwangen.de

¹ Institute of Technical Medicine, Furtwangen University, VS-Schwenningen, Germany

² Department of Radiology, Ludwig-Maximilians-Universität, Munich, Germany

³ Institute and Outpatient Clinic for Occupational, Social and Environmental Medicine, Ludwig-Maximilians-Universität, Munich, Germany

are based on clinical history, clinical signs and symptoms, and lung function, as well as occasional scans with X-ray computed tomography (CT). While CT-scans are costly and bare a risk due to the exposure to radiation, lung function tests are more feasible but provide only global parameters representing the disease state of the entire lung without spatial information on inhomogeneous ventilation. EIT could add valuable information through its ability to provide regional information and to be applied in real time without risk from radiation.

Beyond the images visualizing ventilation, a number of quantitative measures can be derived from EIT data to characterize ventilation distribution [8]. One set of these measures aims to describe ventilation inhomogeneity within the lungs and comprises the ‘Global Inhomogeneity-Index’ (*GI*) [9, 10] and the ‘Coefficient of Variation’ (*CV*) [7, 11]. Increased values in *GI* and *CV* indicate higher heterogeneity within the set of reconstructed pixels. It has been shown that the *GI* is capable of reflecting the disease state in spontaneously breathing patients suffering from CF [4, 5], but it can also be used to adjust the positive end-expiratory pressure (PEEP) in mechanically ventilated patients [12]. Likewise, *CV* has been used in spontaneously breathing patients with obstructive lung disease [7] and also in mechanically ventilated patients with acute respiratory distress syndrome (ARDS) [11].

Although these indices of inhomogeneity are widely used in EIT research, a systematic evaluation of these measures has not yet been conducted. This evaluation has two aspects, first the comparison with data obtained in patients using independent assessments of the heterogeneity of ventilation, and second, an analysis of the principal technical capabilities and limitations of the EIT method and the indices proposed. The present analysis addresses the second question. This question should be clarified before addressing the first topic, since evaluation of the first aspect is limited by the fact that all alternative methods that can be reasonably used for comparison in patients also require the validity of model assumptions. The methodological aspect can be investigated via simulated data bearing the advantage that the characteristics of the lung put into the analysis are known. Especially the effect of the inherent blurring of reconstructed EIT images and the low spatial resolution compared to morphological imaging modalities (e.g. CT) appears to be important and has not been examined until now. Since EIT might have a wide applicability beyond the ICU in patients with obstructive lung disease, the present study specifically compared the applicability of *GI* and *CV* indices in this patient group. Two static conditions (end-expiration and end-inspiration) were used to simulate the effect of heterogeneous ventilation.

2 Methods

All calculations in this work were carried out using MATLAB 2015a (Mathworks, Natick, USA) and the EIDORS toolbox [13]. Finite element models (FEM) were generated with the meshing software NETGEN [14].

2.1 Forward calculations

Electrode voltages were simulated based on a CT-Dataset of a human subject (male, age 59 years), using a 3D FEM model (185841 elements) which was generated by extrusion of the thorax shape at the position of the electrode plane in the cranio-caudal direction using NETGEN and a custom-made MATLAB function. The lateral dimension of the thorax in the 512×512 pixel CT scan comprised 476 pixels and the anterior-posterior dimension 333 pixels. Considering the height of the lung, this resulted in a FEM model with a height of 303, lateral dimension of 476 and anterior-posterior dimension of 333, respectively. A set of 16 rectangular electrodes, modeled with the ‘Complete Electrode Model’ [15], were placed equidistantly around the boundary of the mesh. The electrodes were placed at a height of 120, corresponding to the 5th intercostal space, which is assumed to be the thoracic section least sensitive to movements of the lung during tidal breathing [16]. The lungs were incorporated into the FEM model by assigning respective FEM elements as ‘lung tissue’, based on their centroid positions and the underlying CT dataset.

The ‘adjacent pattern’ was used for current injection and voltage measurement. Thus, neighboring electrodes were used for current injection and voltage measurement and switched in a rotating manner. Voltages were only measured on electrodes not used for current injection. For the 16-electrode EIT-system ($n_{elec} = 16$) considered here, this led to $n_{meas} = n_{elec} \times (n_{elec} - 3) = 208$ voltage measurements.

Different lung conditions and structures were modeled to simulate heterogeneous ventilation distribution. Therefore, two static lung conditions were modeled; the first condition represents the lung at end-expiration, and the second condition represents the lung at end-inspiration. This was realized by setting FEM elements, assigned as ‘lung tissue’, to different conductivity values.

The condition at end-expiration was modeled by setting the conductivity of respective FEM elements to $\sigma_{exp} = 120$ mS/m. Inspiration leads to a decrease of lung conductivity. Accordingly, the state at end-inspiration was modeled by setting the elements to $\sigma_{insp} = 60$ mS/m. FEM elements not attributed to the lung were kept at a conductivity of $\sigma_{bkg} = 480$ mS/m. These conductivity values were taken from previously published studies [17].

Obstruction of the lung, e.g. due to mucus plugging in CF patients, was simulated by fixing the conductivity of selected FEM elements to for both end-expiration and

end-inspiration. Specifically, FEM elements corresponding to randomly assigned spheres were defined as ‘obstructed lung tissue’, and for each simulation 500 spheres were placed inside a $512 \times 512 \times 333$ pixel grid. FEM elements with centroid positions covered by the spheres were considered as ‘obstructed lung tissue’. The radius of the spheres was randomly chosen, and different severities of obstruction were modeled by limiting the maximum radius of the spheres. The maximum radius of the spheres for mildly affected lungs was set to 10 grid units, whereas the most severe obstruction was modeled by a maximum radius of 70 grid units. Overall, 10 different levels of severity were simulated, with the maximum radius of the spheres uniformly distributed between 10 and 70 grid units. For each severity level, 10 random patterns with different locations and sizes of the spheres were simulated. Figure 1 (left panel) depicts the model used for simulation of boundary voltages at end-expiration and two models with arbitrary obstructions of different severity (Fig. 1, middle and right panels) that were used to simulate the conditions at end-inspiration. The approach using the spheres was employed to model both the heterogeneity of ventilation and the amount of airway obstruction, which in most patients with obstructive lung disease is heterogeneous throughout the lung and varies during the breathing cycle.

The model with the lowest obstruction severity was associated with a mean ratio of non-ventilated obstructed tissue to overall lung tissue of $\eta_{obstr} = 0.3\%$. The models used to describe the most severe obstruction implied a mean fraction of $\eta_{obstr} = 72\%$.

2.2 Inverse calculations

EIT aims to reconstruct changes in internal impedance distribution from changes in boundary voltages. This problem is mathematically ill-posed, which means that arbitrarily small perturbations in the measured voltages can lead to large

perturbations in the resulting images of impedance distribution [18]. The most common method employed in clinical applications is ‘time-difference EIT’, which has turned out to be more robust to variations in electrode contact impedance, movements of patients and general measurement noise than ‘absolute EIT’. In this study, we focus on ‘normalized time-difference EIT’, which is designed to reconstruct relative changes in conductivity distribution rather than absolute values of conductivity.

Changes in conductivity are denoted as $\mathbf{x} = \boldsymbol{\sigma} - \boldsymbol{\sigma}_{ref}$, where $\boldsymbol{\sigma}$ contains the present conductivity values and $\boldsymbol{\sigma}_{ref}$ is the vector of reference conductivity. The respective vectors of measured voltages are denoted $\mathbf{v}$ and $\mathbf{v}_{ref}$. Throughout this paper $\boldsymbol{\sigma}_{ref}$ is considered to be the conductivity distribution at end-expiration of the patient, while $\boldsymbol{\sigma}$ represents the conductivity at end-inspiration. The relative change in the measured voltage is denoted by $\mathbf{z}$. Correspondingly, the elements of $\mathbf{z}$ are $z_i = (v_i - v_{ref,i})/v_{ref,i}$, where the index i denotes the i th vector element.

Equation (1) shows a general formulation of the EIT problem to estimate changes in impedance $\hat{\mathbf{x}}$ from a set of changes in boundary voltages $\mathbf{z}$ using a minimization approach

$$\hat{\mathbf{x}} = \underset{\mathbf{x}}{\operatorname{argmin}} \left\{ \frac{1}{2} \|F(\mathbf{x}) - \mathbf{z}\|_2^2 + \lambda^2 \|\mathbf{R}\mathbf{x}\|_2^2 \right\} \quad (1)$$

$F(\mathbf{x})$ is a forward model that maps changes in conductivity $\mathbf{x}$ to changes in measured voltages. The second term in Eq. (1) is the regularization term and is necessary to solve the ill-posed problem by introducing a sort of controllable bias that helps to reduce the sensitivity to noise. The hyperparameter λ is used to control the level of regularization. Prior information is incorporated into the solution using the regularization matrix $\mathbf{R}$. Depending on the choice of $\mathbf{R}$ the solution $\hat{\mathbf{x}}$ is either smooth, small or slowly changing. In this study the Tikhonov prior and the Laplace prior [19] were used to penalize large

Fig. 1 Simulation models. Left: Simulation model used to compute voltages at end-expiration. Middle: Model used to compute voltages at end-inspiration with moderate airway obstruction. Right: Model used to compute voltages at end-inspiration with severe airway obstruction

changes in the reconstructed conductivity and favor smooth solutions, respectively.

To solve Eq. (1) the domain was discretized using a FEM-Model and the forward model was linearized around a pre-selected conductivity distribution σ_0 . This simplification led to the following formulation of the forward model in the image reconstruction process

$$F(\mathbf{x}) \approx \mathbf{J}\mathbf{x} + \mathbf{n} \quad (2)$$

where $\mathbf{J}$ is the Jacobian or Sensitivity Matrix that maps changes in conductivity $\mathbf{x}$ to voltage changes. Each element $J_{ij} = \frac{\partial z_i}{\partial x_j} \bigg|_{\sigma_0}$ relates a small change in conductivity in the j th

FEM element to the i th element of the voltage change vector $\mathbf{z}$. Throughout this paper the initial conductivity distribution σ_0 was set to the vector $\mathbf{1}$, containing 1 at each location. This is common in EIT literature, since the actual distribution of conductivity is usually not known. To prevent the ‘inverse crime’ [20] in the image reconstruction, a coarser 3D-FEM model (comprising 141,931 elements) was used for the calculation of $\mathbf{J}$ than the model used for simulation of boundary voltages. The vector $\mathbf{n}$ represents the measurement noise, which is assumed to be uncorrelated white Gaussian.

Due to the diffuse current propagation in the thorax the depicted ventilation distribution is a projection of a lens-shaped volume, which is smaller at the boundary of the thorax and extends to approximately 1/2 of the body diameter above and below the electrode plane [21]. This inherent extension into the cranio-caudal direction has been considered by using a ‘dual model 2.5D’ approach [22] for image reconstruction by calculation of the Jacobian $\mathbf{J}$ on the basis of a 3D FEM model and projection to a 2D reconstruction model. This approach is described by the following equation:

$$\mathbf{J}_{2D} = \mathbf{J}\mathbf{P} \quad (3)$$

where the elements P_{ij} represent the fraction of the i th 3D finite element enclosed in the extrusion of the j th 2D finite element in cranio-caudal direction.

Applying these simplifications and assumptions, Eq. (1) can be solved in a closed form, resulting in

$$\hat{\mathbf{x}} = (\mathbf{J}_{2D}^T \mathbf{J}_{2D} + \lambda^2 \mathbf{R}^T \mathbf{R})^{-1} \mathbf{J}_{2D}^T \mathbf{z} = \mathbf{B}\mathbf{z} \quad (4)$$

The reconstruction matrix $\mathbf{B}$ can be generated e.g. during the start-up phase of the EIT-device. Once $\mathbf{B}$ has been calculated, the reconstruction process can be realized as an efficient matrix multiplication as shown in Eq. (4), which is one of the reasons for the real-time capability of EIT.

The hyperparameter λ was chosen utilizing the ‘noise amplification measure’ (NF) [23], which is defined as

$$NF = \frac{SNR_{in}}{SNR_{out}} = \frac{\text{mean}(|\mathbf{z}|)}{\sqrt{\text{var}(\mathbf{n})}} \bigg/ \frac{\text{mean}(|\mathbf{B}\mathbf{z}|)}{\sqrt{\text{var}(\mathbf{B}\mathbf{n})}} \quad (5)$$

Using a bisection search the hyperparameter λ was taken to achieve ‘noise amplifications’ of 0.6, 1.0 and 1.4. By comparing the results based on these choices the stability of the solutions was estimated.

2.3 Evaluation of ventilation inhomogeneity

To evaluate the inhomogeneity of the lungs used in the simulations and the reconstructed EIT images, a slightly modified version of the *GI*-Index [9] was used.

$$GI = \frac{\sum |\hat{\mathbf{x}}_{lung} - \text{mean}(\hat{\mathbf{x}}_{lung})|}{\sum |\hat{\mathbf{x}}_{lung}|} \quad (6)$$

The originally introduced *GI*-Index uses the estimated median value in the numerator of Eq. (6). To calculate the inhomogeneity in simulated lungs, applying the mean value over the regions with known values seems more appropriate, in which the impedance change is either $x = 0$ mS/m (for obstructed regions) or $x = -60$ mS/m (for non-obstructed regions).

The values of the *CV* were calculated as usual according to the following formula:

$$CV = \frac{SD(\hat{\mathbf{x}}_{lung})}{\text{mean}(\hat{\mathbf{x}}_{lung})} \quad (7)$$

The *GI*-Index and the *CV* values were normalized to range from 0 (mildly affected lung) to 1 (severe obstruction), in order to facilitate the comparison between the different reconstruction methods. In the subsequent parts of this paper, their values are denoted as GI_{norm} and CV_{norm} , respectively.

In principle, the values of GI_{norm} and CV_{norm} could be calculated in the simulation runs using all FEM elements assigned as ‘lung tissue’. However, to avoid the effect of artifacts in the reconstructed EIT images, their values were calculated only in a defined region of interest and not in all reconstructed FEM elements. In this analysis, the set of relevant elements $\hat{\mathbf{x}}_{lung}$ was derived from the reconstructed conductivity change $\hat{\mathbf{x}}$ as follows:

$$lung = \{i | \hat{x}_i \leq \alpha \cdot \min(\hat{\mathbf{x}})\} \quad (8)$$

This means that only elements with a reconstructed conductivity smaller than a certain threshold value were considered in the calculation of the inhomogeneity measures. For this purpose, the parameter α was used. Its value was chosen to achieve a fraction of ‘lung tissue’ to ‘overall tissue’ in the reconstruction of 40%, which was about the fraction visible in the CT-slice of the electrode plane that was used to construct the simulation model. For the selection of

α a simulated lung without obstruction was used in the EIT reconstruction (see Fig. 2).

3 Results

3.1 Difference of inhomogeneity measures

The mean values of GI_{norm} and CV_{norm} for different amounts of lung obstruction η_{obstr} in the simulation model are plotted in Fig. 3. A linear regression analysis of GI_{norm} and η_{obstr} revealed a coefficient of determination $R^2 = 1$ for GI_{norm} . This high correlation was the immediate result of the definition of GI_{norm} and η_{obstr} . The CV_{norm} slightly overestimated the inhomogeneity for $\eta_{obstr} < 0.22$ and underestimated the inhomogeneity for $\eta_{obstr} > 0.22$, which is reflected by a coefficient of determination $R^2 = 0.98$.

Figure 4 illustrates the differences in the measures of inhomogeneity in reconstructed images compared to the inhomogeneity in the simulation models (ground truth). These reconstructions were carried out with a noise amplification measure of $NF = 1$. The differences between the two priors (Tikhonov and Laplace) used for the image reconstruction were negligible, and for both measures, the values differed by less than 0.04 units.

According to these results, the sensitivity of GI_{norm} and CV_{norm} appeared to be small for lungs with low levels of obstruction η_{obstr} and to increase for a larger amount of obstruction η_{obstr} .

The standard deviation of the inhomogeneity measures for the random obstruction patterns is exemplarily depicted in Fig. 5 for images reconstructed with ‘noise amplification’ of $NF = 1.4$ using the ‘Laplace-prior’. In all reconstructions, the standard deviation increased with higher values of η_{obstr} reflecting the higher degree of heterogeneity. The highest value of the standard deviation was 0.43 and was obtained

Fig. 3 Inhomogeneity measures plotted over mean fraction of lung obstruction η_{obstr} in the simulation models. Black circle: Mean values of GI_{norm} . Red diamond: Mean values of CV_{norm}

for reconstructions using the Laplace-prior and a noise amplification of $NF = 0.6$.

3.2 Difference in reconstructed images

The following figure shows examples of images of reconstructed conductivity changes with different degrees of obstruction η_{obstr} and different priors for image reconstruction.

Although the use of different priors led to considerably different images in Fig. 6 (upper and lower row), the derived inhomogeneity indices were very similar, as illustrated in Figs. 4 and 5.

For both reconstruction priors, the GI and CV values were smallest for low degree of obstruction (Fig. 6: left column) and largest for severe obstruction (Fig. 6: right column). However, the figures also suggest that the inhomogeneity indices not closely reflect the actual degree and pattern

Fig. 2 Definition of the lung area for calculation of inhomogeneity measures: Left panel: The CT image includes about 40% lung tissue: Middle panel: Reconstruction of ventilation distribution. Right panel: Lung area comprising 40% of the domain

Fig. 4 Left panel: GI_{norm} for different mean proportion of lung obstruction η_{obstr} in the simulation model (black circle) and for different image reconstruction priors (red triangle: Tikhonov prior, blue asterisk: Laplace prior). Right panel: CV_{norm} for different mean pro-

portions of lung obstruction η_{obstr} in the simulation model (black circle) and for different image reconstruction priors (red triangle: Tikhonov prior, blue asterisk: Laplace prior)

Fig. 5 Standard deviations of GI_{norm} (black circles) and CV_{norm} (red triangles) as a function of different mean fractions of lung obstruction η_{obstr}

of obstruction. Figure 6 (third column) shows reconstructions using a degree of obstruction of $\eta_{obstr} = 0.47$. For the Laplace prior the GI and CV values are only slightly increased compared to the reconstruction performed for moderate obstruction with $\eta_{obstr} = 0.25$ (Fig. 6, second column), and for the Tikhonov prior the CV values even showed a slight decrease. In contrast, Fig. 6 (right column) showing reconstructions for $\eta_{obstr} = 0.50$, illustrates a considerable increase in GI and CV , although the change in η_{obstr} was small compared to the models shown in the third column.

4 Discussion

In the present work, we show the results of a simulation study aiming to reveal, in which manner different degrees of lung obstruction and heterogeneity of ventilation are reflected by two common measures of ventilation inhomogeneity in reconstructed EIT images. The model used for simulation was constructed based on the CT-image of a patient with obstructive airway disease. It turned out that both measures GI and CV were not very sensitive to a low level of obstruction, while sensitivity increased with higher levels of obstruction. Presumably the limited spatial resolution of EIT leads to the observed behavior, especially if only a small fraction of lung tissue is affected. Regarding the methodological aspects, an important result of our study is that the amount of regularization, expressed e.g. by different ‘noise amplification’, does not influence the inhomogeneity measures, at least under the idealized conditions of a simulation study. The same was true for the choice of the Tikhonov prior versus the Laplace prior in the regularization term; both of them led to similar patterns in the inhomogeneity measures GI and CV . At average, their values were similar for the different estimation approaches. On the other hand, the simulation study revealed that the variation of these measures was relatively large (Fig. 5). This implies that small changes in the amount or distribution of obstructed lung may not be well reflected by the two measures. Figure 6 even demonstrates that more severe obstruction and inhomogeneity, corresponding to a higher proportion of affected

Fig. 6 Image reconstruction with different priors and different degrees of simulated obstruction. Upper row obtained using the Tikhonov prior, lower row using the Laplace prior. The columns refer to the different degrees of obstruction

lung tissue, can result in similar or even slightly reduced inhomogeneity measures compared to moderate obstruction. Although the applied ‘dual model 2.5D’ approach takes into account the current propagation above and below the electrode plane, it is well possible that obstructed regions at a certain distance from the electrode plane are not adequately reconstructed, which may result in misleading values of the two inhomogeneity measures.

Numerous studies used either the *GI*-Index or *CV* to describe inhomogeneity of lung ventilation. As a consequence of the most common application of EIT, which is ventilation monitoring of mechanically ventilated patients in the ICU, most of the studies examined patients in the supine position. In this position, the ventilation gradient is redistributed along the gravitational axis, which is true for patients without obstructive lung disease [24] but probably also for other conditions. Based on this a single 2D thorax slice is considered to adequately represent the ventilation condition [25] and under these standardized conditions the common measures of inhomogeneity can be used to monitor disease progression or optimize ventilator settings. Zhao et al. concluded in a study of intubated patients that the *GI*-Index provided good interpatient comparability [9], and Becher et al. suggest how the *GI*-Index could be utilized for the adjustment of PEEP and tidal volume during mechanical ventilation [12].

Interest in the application of EIT outside the ICU has resulted in studies performed in spontaneously breathing patients with various obstructive lung diseases. In this context, EIT is usually applied in the lung function laboratory in sitting position. Similarly to the ICU application, the

measures *GI* and *CV* have also been used in these patient groups. Vogt et al. (2012) performed EIT measurements in COPD patients and lung-healthy control subjects [7]. At average, *CV* values were higher in the group of COPD patients, as expected, but individual COPD patients could exhibited lower *CV* values than some individuals of the control group. This underlines that improvements are necessary to achieve a degree of reliability that enables us to clearly recognize lung disorders. The present work investigated some of the methodological and principal questions that should be answered before proceeding with more extensive studies in patients.

Among the limitations of our study it has to be mentioned that the simulation model is based on the assumption that airway obstruction is always complete for a given FEM element, which means that the affected lung regions have a complete loss of ventilation and thus no conductivity change during inspiration. We want to remark that this approach does not necessarily reflect the pathophysiology of chronic obstructive lung diseases, where obstruction leads to a marked decrease in airflow, which causes a significant prolongation of inhalation and especially exhalation, but rarely a complete loss of regional ventilation. Moreover, heterogeneous ventilation was simulated by ‘fixing’ conductivity values of selected FEM elements to those of the end-expiration model (i.e. 120 mS/m in our models). This assumption might not be valid for lung regions affected by air-trapping where the conductivity is lower at end-expiration. However, since we used difference EIT it can be disregarded if conductivity values are persistently high (e.g. due to limited airflow during inspiration) or persistently low

(e.g. due to air-trapping). Future research should address lung conductivity changes within a breath, which requires to simulate airflow in obstructive lung diseases and therefore needs a more detailed modelling of the lung structures. This would also allow to compare simulated EIT data with dynamic parameters like e.g. FEV1/FVC, which are the most important parameters in the assessment of obstructive lung diseases.

Additionally, in this study only one CT-derived thorax model was used in the simulations and that the distribution of obstruction was simulated with a rather simple model and no excursion of the thorax or movement of the lungs during breathing was incorporated in the models. Also, only linearized reconstruction methods and ‘difference-EIT’ were used in this study, which are established techniques in ventilation monitoring [26]. Further studies are necessary to investigate the effect of nonlinear reconstructions and edge-preserving regularization methods [27].

From the results of the simulations, we conclude that, even under ideal conditions, the severity of heterogeneity of ventilation and obstruction may not be adequately detected in patients with mild disorder and not be well quantified in patients with more severe disorder. This is probably due to the fact that under these conditions of lung-intrinsic heterogeneity one electrode plane is not sufficient. These results are in line with the empirical data obtained by Krueger-Ziolek et al., in which significantly different values for the *GI*-Index were obtained for cranial and caudal lung regions in CF patients [4]. We thus propose to evaluate the ventilation inhomogeneity in several thorax slices, if the common inhomogeneity measures *GI* and *CV* are used to quantify the lung condition in patients with obstructive lung diseases. Further research should address the question whether novel inhomogeneity measures are better suited to reflect the degree of heterogeneity and obstruction. Additionally, the effect of the diffuse current propagation and the low spatial resolution of EIT need to be investigated further, and how these factors influence 2D, 2.5D and 3D image reconstructions.

5 Conclusion

This simulation study addressed the application of electrical impedance tomography (EIT) in the diagnosis and monitoring of patients with obstructive airway disease outside the ICU. It demonstrated that two commonly used measures of ventilation inhomogeneity, *GI* and *CV*, are not very sensitive to mild obstruction and heterogeneity, whereby their sensitivity increases for more severe obstruction, however still can show paradoxical results. The results underline the need for more refined, e.g. 3-dimensional, methods and indices to apply EIT outside the ICU in a promising way.

Acknowledgements This work has been partially supported by the Federal Ministry of Education and Research (BMBF) under Grant No. 03FH03813 (MOSES).

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent This article does not contain any studies with human participant performed by any of the authors.

References

1. Gong B, et al. Electrical impedance tomography: functional lung imaging on its way to clinical practice? Expert review of respiratory medicine. 2015;9(6):721–37.
2. Frerichs I. Electrical impedance tomography (EIT) in applications related to lung and ventilation: a review of experimental and clinical activities. *Physiol Meas*. 2000;21(2):R1–21.
3. Pikkemaat R, et al. Electrical impedance tomography: New diagnostic possibilities using regional time constant maps. *Appl Cardiopul P (ACP)*. 2012;16:212–25.
4. Krueger-Ziolek S, et al. Multi-layer ventilation inhomogeneity in cystic fibrosis. *Respir Physiol Neurobiol*. 2016;233:25–32.
5. Zhao Z, et al. Regional ventilation in cystic fibrosis measured by electrical impedance tomography. *J Cyst Fibros*. 2012;11(5):412–8.
6. Zhao Z, et al. Regional airway obstruction in cystic fibrosis determined by electrical impedance tomography in comparison with high resolution CT. *Physiol Meas*. 2013;34(11):N107–14.
7. Vogt B, et al. Spatial and temporal heterogeneity of regional lung ventilation determined by electrical impedance tomography during pulmonary function testing. *J Appl Physiol*. 2012;113(7):1154–61.
8. Frerichs I, et al. Chest electrical impedance tomography examination, data analysis, terminology, clinical use and recommendations: consensus statement of the Translational EIT development study group. *Thorax* 2017;72:83–93.
9. Zhao Z, et al. Evaluation of an electrical impedance tomography-based global inhomogeneity index for pulmonary ventilation distribution. *Intensive Care Med*. 2009;35(11):1900–6.
10. Zhao Z, et al. The EIT-based global inhomogeneity index is highly correlated with regional lung opening in patients with acute respiratory distress syndrome. *BMC Res Notes*. 2014;7:82.
11. Becher T, et al. Functional regions of interest in electrical impedance tomography: a secondary analysis of two clinical studies. *PLoS ONE*. 2016;11(3):e0152267.
12. Becher T, et al. Influence of tidal volume on ventilation inhomogeneity assessed by electrical impedance tomography during controlled mechanical ventilation. *Physiol Meas*. 2015;36(6):1137.
13. Adler A, Lionheart WR. Uses and abuses of EIDORS: an extensible software base for EIT. *Physiol Meas*. 2006;27(5):S25–42.
14. Schöberl J. NETGEN an advancing front 2D/3D-mesh generator based on abstract rules. *Comput Visual Sci*. 1997;1(1):41–52.
15. Cheng K-S, et al. Electrode models for electric current computed tomography. *Biomed Eng IEEE Trans*. 1989;36(9):918–24.

16. Krueger-Ziolek S, et al. Positioning of electrode plane systematically influences EIT imaging. *Physiol Meas*. 2015;36(6):1109–18.
17. Adler A, Guardo R, Berthiaume Y. Impedance imaging of lung ventilation: do we need to account for chest expansion? *IEEE Trans Biomed Eng*. 1996;43(4):414–20.
18. Soleimani M. Computational aspects of low frequency electrical and electromagnetic tomography: a review study. *Int J Numer Anal Model*. 2008;5(3):407–40.
19. Polydorides N, Lionheart WR. A Matlab toolkit for three-dimensional electrical impedance tomography: a contribution to the Electrical Impedance and Diffuse Optical Reconstruction Software project. *Meas Sci Technol*. 2002;13(12):1871.
20. Graham BM, Adler A. Objective selection of hyperparameter for EIT. *Physiol Meas*. 2006;27(5):S65–79.
21. Putensen C, Zinserling J, Wrigge H. Electrical impedance tomography for monitoring of regional ventilation in critically ill patients. In: Vincent JL, editor. *Intensive care medicine*. New York, NY: Springer; 2006.
22. Adler A, et al. Simple FEMs aren't as good as we thought: experiences developing EIDORS v3. 3. *Proc. Conf. EIT (Hannover, NH, USA)*, 2008.
23. Adler A, Guardo R. Electrical impedance tomography: regularized imaging and contrast detection. *IEEE Trans Med Imaging*. 1996;15(2):170–9.
24. Grychtol B, Müller B, Adler A. 3D EIT image reconstruction with GREIT. *Physiol Meas*. 2016;37(6):785.
25. Adler A, et al. Whither lung EIT: where are we, where do we want to go and what do we need to get there? *Physiol Meas*. 2012;33(5):679–94.
26. Bayford RH. Bioimpedance tomography (electrical impedance tomography). *Annu Rev Biomed Eng*. 2006;8:63–91.
27. Borsic A, et al. In vivo impedance imaging with total variation regularization. *IEEE Trans Med Imaging*. 2010;29(1):44–54.