

Flow-volume loops measured with electrical impedance tomography in pediatric patients with asthma

Chuong Ngo¹  | Falk Dippel¹ | Klaus Tenbrock² | Steffen Leonhardt¹  | Sylvia Lehmann²

¹ Philips Chair for Medical Information Technology, RWTH Aachen, Aachen, Germany

² Department of Pediatric Pulmonology, RWTH Aachen University Hospital, Aachen, Germany

Correspondence

Sylvia Lehmann, Department of Pediatric Pulmonology, RWTH Aachen University Hospital, Pauwelsstrasse 30, 52074 Aachen, Germany.
Email: slehmann@ukaachen.de

Abstract

Background: Electrical impedance tomography (EIT) provides information on global and regional ventilation during tidal breathing and mechanical ventilation. During forced expiration maneuvers, the linearity of EIT and spirometric data has been documented in healthy persons. The present study investigates the potential diagnostic use of EIT in pediatric patients with asthma.

Methods: EIT and spirometry were performed in 58 children with asthma (average age $\pm$ SD: 11.86 ± 3.13 years), and 58 healthy controls (average age $\pm$ SD: 12.12 ± 2.9 years). The correlation between EIT data and simultaneously acquired spirometric data were tested for FEV₁, FEV_{0.5}, MEF₇₅, MEF₅₀, and MEF₂₅. Binary classification tests were performed for the EIT-derived Tiffeneau index FEV₁/FVC and the bronchodilator test index Δ FEV₁. Average flow-volume (FV) loops were generated for patients with pathologic spirometry to demonstrate the feasibility of EIT for graphic diagnosis of asthma.

Results: Spirometry and global EIT-based FV loops showed a strong correlation ($P < 0.001$, $r > 0.9$ in FEV₁ and FEV_{0.5}). In all criteria, the binary classification tests yielded high specificity ($>93\%$), a high positive predictive value ($\geq 75\%$) and a high negative predictive value ($>80\%$), while sensitivity was higher in Δ FEV₁ (86.67%) and lower in FEV₁/FVC (25% and 35.29%). A typical concave shape of the EIT-derived average FV loops was observed for asthmatic children with improvement after bronchospasmolysis.

Conclusions: Global FV loops derived from EIT correlate well with spirometry. Positive bronchospasmolysis can be observed in EIT-derived FV loops. Flow-volume loops originated from EIT have a potential to visualize pulmonary function.

KEYWORDS

asthma, electrical impedance tomography, flow volume loop, pulmonary function testing, spirometry, tiffeneau test

Abbreviations: Δ Z, relative EIT-impedance changes; AU, arbitrary units; BSL, bronchospasmolysis; EIT, electrical impedance tomography; FEV₁, forced expiratory volume in 1 s; FEV_{0.5}, forced expiratory volume in 0.5 s; FVC, forced vital capacity; FV loop, flow volume loop; MEF₇₅, MEF₅₀, MEF₂₅, maximum expiratory flow at 25, 50, and 75% of FVC; TI, tiffeneau index; SD, standard deviation.

1 | INTRODUCTION

Pulmonary function testing is a routine diagnostic tool for pediatric and adult patients with asthma. During spirometry, a flow volume (FV) loop is generated that provides information on obstructive, restrictive, and combined ventilation disorders. However, spirometry is dependent on the patients cooperation and provides only global information on lung function.^{1,2}

Electrical impedance tomography (EIT) is a non-invasive, highly dynamic tool that also provides regional functional information on lung ventilation. Although the high correlation between EIT and aeration of the lung during tidal breathing is well documented,^{3,4} EIT is still mainly used to provide information on lung aeration in intensive care settings to improve mechanical ventilation.^{5–8} However, preliminary studies have shown a similar correlation between EIT and aeration during forced expiration maneuvers when performing spirometry^{9–15} and during forced oscillation maneuvers.¹⁶ This implies that EIT is also of potential value for pulmonologists, as it combines functional and regional information during pulmonary function testing.

This study investigated the correlation between EIT and spirometry to evaluate the use of EIT in lung function testing. We also hypothesized that the EIT-derived Tiffeneau index (TI), the EIT-derived bronchodilator test, and the EIT-based FV loops might serve as indicators in the diagnosis of asthma. To our knowledge, this is the first EIT study on pediatric asthma patients to focus on a direct comparison between EIT and spirometry, as well as demonstrating the possible use of the EIT-derived FV loops to detect asthma.

2 | MATERIALS AND METHODS

2.1 | Subjects and examination protocol

This prospective observational study was approved by the Ethics Committee of the University Hospital RWTH Aachen (Clinical trial no. CIV-14-03-011942; Ethics Committee approval no. EK088/14). Written informed consent was obtained from all the children and/or their legal guardian(s) prior to enrolment. For this study, healthy children and children with obstructive lung diseases were examined during lung function testing at the University Hospital Aachen. From these lung tests, data were used from $n = 58$ asthmatic patients and 58 age-matched controls with healthy lungs.

Spirometry was performed with a MasterLab device (Care Fusion Inc., Hoechberg, Germany) and included performance and evaluation, including positive bronchospasmolysis (BSL), in accordance with the ATS/ERS guidelines.^{1,2} EIT data were acquired with a PulmoVista 500 EIT device (Dräger, Lübeck, Germany) with the attached electrode belt (size 70 cm), or with the prototype belt of the EIT Evaluation Kit 2 (size 53 cm) (Dräger, Lübeck, Germany) (see Figure 1). The EIT belt with 16 electrodes was fixed at the 5th–6th intercostal space and the patient was seated. After taking the history and detection of vital parameters and lung auscultation, EIT and spirometry were performed simultaneously. In the asthmatic children, measurements were performed before and after BSL. Only the asthmatic group underwent BSL. This

was performed in accordance to ATS/ERS guidelines^{1,2} by inhaling 200 µg of salbutamol, followed by a repeated spirometry after ≥ 10 min. For ethical reason, the control group with healthy lungs did not undergo BSL.

2.2 | EIT data acquisition and offline analysis

To generate an EIT frame, the PulmoVista500 applies an alternating current (IEC 60601-1-2, 80–130 Hz, automatic adjustment of current amplitude) and measures the impedance changes for detailed offline analysis. A total of 16 consecutive current injections and 13 adjacent electrode pairs results in 208 voltages measured during each cycle. An integrated finite-element-method-based, linearized Newton-Raphson reconstruction algorithm for ellipsoid EIT images was used. For this study, the EIT data were converted to MATLAB file format (MATLAB 2015b, The MathWorks Inc., Natick, MA).

Spirometric parameters were provided by the MasterLab device with automatic selection of the best forced expiration maneuver from three maneuvers, displaying the following parameters: forced vital capacity (FVC), forced expiratory volume in 1 s (FEV₁), forced expiratory volume in 0.5 s (FEV_{0.5}), and maximum expiratory flow at 25%, 50%, and 75% of FVC (MEF₇₅, MEF₅₀, and MEF₂₅).

EIT scans displayed 32×32 pixels in temporal connection of each slice $\left(\Delta Z_{\text{global}}(t) = \sum_{i=1}^{1024} \Delta Z_i(t) \right)$. The global EIT flow was depicted as the derivation of the global impedance index $\left(\dot{V}_{\Delta Z_{\text{global}}}(t) = \frac{d(\Delta Z_{\text{global}}(t))}{dt} \right)$. Similar to spirometry, we manually chose the best EIT-derived forced expiratory maneuver from three maneuvers, regarding the maximum change in $\dot{V}_{\Delta Z_{\text{global}}}(t)$ during forced expiration. Subsequent data analysis required a manual separation of this forced breathing cycle, starting with the beginning of inspiration and stopping at the end of expiration. Maximum impedance change during forced expiration $\text{FVC}_{\text{EIT}}[\text{AU}]$, as well as impedance changes in the first 1 s and 0.5 s of the forced expiration $\text{FEV}_{1,\text{EIT}}[\text{AU}]$ and $\text{FEV}_{0.5,\text{EIT}}[\text{AU}]$ were computed. Calculation of EIT-derived flow parameters, $\text{MEF}_{75,\text{EIT}}[\text{AU/s}]$, $\text{MEF}_{50,\text{EIT}}[\text{AU/s}]$, and $\text{MEF}_{25,\text{EIT}}[\text{AU/s}]$ required the creation of an EIT-derived global $\dot{V}_{\Delta Z_{\text{global}}}(t)$ FV loop. The conventional curve of an FV loop was achieved by plotting $\dot{V}_{\Delta Z_{\text{global}}}(t)$ over $\Delta Z_{\text{global}}(t)$, reflecting both signals and shifting the loop to the origin. Therefore, we called the $\dot{V}_{\Delta Z_{\text{global}}}(t)/\Delta Z_{\text{global}}(t)$ loop the “EIT-derived FV loop.”

For the subsequent analysis, it was necessary to make a direct comparison of spirometry and EIT-derived lung function parameters, as well as comparison of the form of each FV loop. Therefore, a scaling between these two data were required. In an earlier study in healthy adults, we showed that spirometric volumes $V_{\text{spiro}}(t)$ and impedance changes $\Delta Z_{\text{global}}(t)$ correlate well during spontaneous breathing and forced expiration maneuvers.¹⁴ In detail, this is described as:

$$V_{\text{spiro}}(t) = a \cdot \Delta Z_{\text{global}}(t) + b, \quad (1)$$

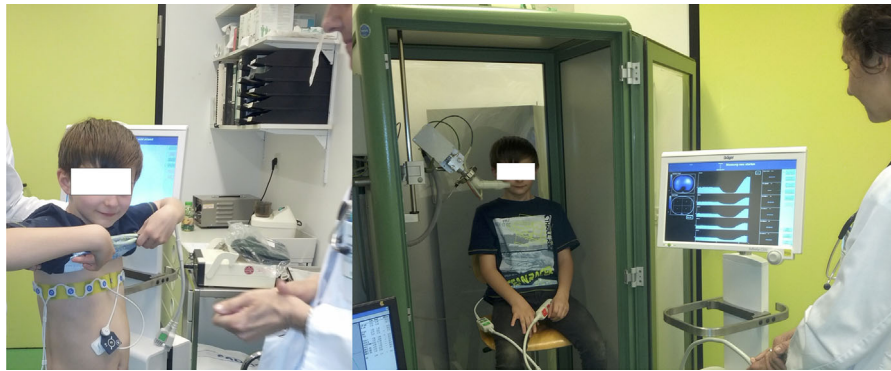


FIGURE 1 EIT measurement during a lung function test of one child (with permission)

where “a” is the scaling factor from arbitrary unit [AU] to liter [L] and “b” corresponds to a shift of the ordinate. Here, we calculated the parameter “a” regarding the forced expiratory volume measured by pneumotachography FVC_{spiro} and by $EITFVC_{\text{EIT}}[AU]$:

$$a = \frac{FVC_{\text{spiro}}}{\Delta Z_{\text{ex,max}} - \Delta Z_{\text{ex,min}}} [L/AU]. \quad (2)$$

Assuming the same linearity in patients in the present study, EIT data (in [AU]) were scaled to equivalent data in [L] regarding the parameter “a.” As a result, EIT-derived parameters were scaled from [AU] and [AU/s] to [L] and [L/s], respectively.

2.3 | Statistical analysis

T-test was performed for the demographic data between the two patient groups. Pearson's correlation tests between spirometry and EIT were performed for the parameters FEV_1 , $FEV_{0.5}$, MEF_{75} , MEF_{50} , and MEF_{25} . A P -value <0.05 was considered statistically significant. Statistical analyses included mean values and standard deviation (SD). Statistics were performed with Excel 2013 and MATLAB 2015b.

According to the 2017 updated report of the Global Initiative for Asthma,¹⁷ a spirometry test result was considered pathological in terms of asthma (confirmed variable expiratory limitation) if the Tiffeneau index FEV_1/FVC was reduced ($FEV_1/FVC < 90\%$ for

children aged <12 years old and $FEV_1/FVC < 80\%$ for children aged 12–18 years) and a positive bronchodilator test was present ($\Delta FEV_1 > 12\%$). For the Tiffeneau index and the bronchodilator results measured with EIT, we performed a binary classification test, assuming the spirometric measurements to be the gold standard (Figure 2).

A direct graphical comparison of asthmatic patients and healthy controls may be clinically useful, since the FV loops of the asthmatics show a typical concave form.¹ However, since a large number of our asthmatic patients had a stable course of their disease during medical treatment and exhibited normal lung function parameters, a graphical comparison for $n = 58$ patients would not allow to discriminate between the asthmatic and healthy FV loops. Therefore, for better graphical comparisons, we selected only those patients who fulfilled the above-mentioned criteria of a confirmed variable expiratory limitation and compared them with the age-matched healthy controls. Average EIT-based FV loops of the asthmatic group and the control group were derived and presented in the same figure.

3 | RESULTS

3.1 | Demographic data

The group of asthmatics (32 male, 26 female) had an average age of 11.86 ± 3.13 years, height 152.6 ± 17.7 cm, weight of 50.6 ± 19.6 kg,

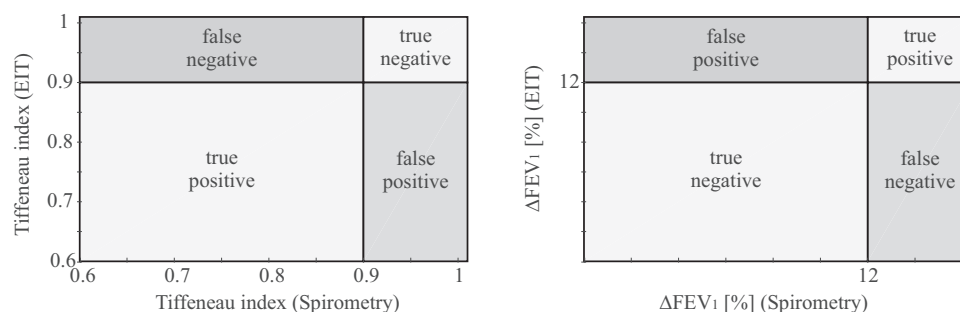


FIGURE 2 Binary classification test for the Tiffeneau index and the bronchodilator results measured by EIT in comparison with spirometry. Inclusion criteria: Tiffeneau index $FEV_1/FVC < 90\%$ for children aged <12 years and $<80\%$ for children aged 12–18 years; positive bronchodilator test ($\Delta FEV_1 > 12\%$)

TABLE 1 Mean values $\pm$ SD of lung function parameters, measured by pneumotachography and EIT

	Healthy controls		Asthmatics: before BSL		Asthmatics: after BSL	
	Mean $\pm$ SD	Mean % reference prediction $\pm$ SD	Mean $\pm$ SD	Mean % reference prediction $\pm$ SD	Mean $\pm$ SD	Mean % reference prediction $\pm$ SD
Spirometric parameters (pneumotachography)						
FVC [L]	2.48 $\pm$ 0.93	78 $\pm$ 15.9	2.37 $\pm$ 0.92	77.3 $\pm$ 15	2.42 $\pm$ 0.93	79.7 $\pm$ 14.7
FVC ₁ [L]	2.38 $\pm$ 0.87	90.3 $\pm$ 13.7	2.16 $\pm$ 0.83	83.7 $\pm$ 16.9	2.29 $\pm$ 0.86	88.9 $\pm$ 16
FEV _{0.5} [L/s]	1.86 $\pm$ 0.63	93.1 $\pm$ 16.9	1.64 $\pm$ 0.61	83.7 $\pm$ 20.5	1.80 $\pm$ 0.63	92.7 $\pm$ 19.9
MEF ₇₅ [L/s]	4.62 $\pm$ 1.61	93.4 $\pm$ 18.9	4.03 $\pm$ 1.6	80.1 $\pm$ 23.3	4.63 $\pm$ 1.67	92.1 $\pm$ 21.1
MEF ₅₀ [L/s]	3.5 $\pm$ 1.18	98 $\pm$ 21.6	2.75 $\pm$ 1.09	77.4 $\pm$ 23.3	3.37 $\pm$ 1.24	95.0 $\pm$ 24.6
MEF ₂₅ [L/s]	2.02 $\pm$ 0.77	109.3 $\pm$ 28.7	1.52 $\pm$ 0.67	82.7 $\pm$ 28.5	1.95 $\pm$ 0.81	106.3 $\pm$ 32.4
FEV ₁ /FVC [%]	95.97 $\pm$ 4.56	115.2 $\pm$ 12.5	91.36 $\pm$ 7.62	108.8 $\pm$ 9.72	94.89 $\pm$ 5.68	112.6 $\pm$ 6.9
Δ FEV ₁ [%]	-	-	-	-	7.44 $\pm$ 12.94	-
EIT-derived spirometry parameters						
FVC [L]	2.48 $\pm$ 0.93	-	2.38 $\pm$ 0.92	-	2.42 $\pm$ 0.93	-
FVC ₁ [L]	2.36 $\pm$ 0.87	-	2.24 $\pm$ 0.85	-	2.36 $\pm$ 0.89	-
FEV _{0.5} [L/s]	1.90 $\pm$ 0.73	-	1.79 $\pm$ 0.69	-	1.90 $\pm$ 0.73	-
MEF ₇₅ [L/s]	6.16 $\pm$ 2.77	-	5.24 $\pm$ 2.98	-	6.68 $\pm$ 3.51	-
MEF ₅₀ [L/s]	4.23 $\pm$ 1.89	-	3.84 $\pm$ 1.78	-	4.52 $\pm$ 2.17	-
MEF ₂₅ [L/s]	2.25 $\pm$ 0.97	-	1.99 $\pm$ 0.92	-	2.34 $\pm$ 1.07	-
FEV ₁ /FVC [%]	95.28 $\pm$ 5.93	-	94.22 $\pm$ 5.99	-	97.73 $\pm$ 3.67	-
Δ FEV ₁ [%]	-	-	-	-	4.79 $\pm$ 12.93	-

and a body mass index (BMI) of 20.89 ± 4.73 . The healthy controls (29 male, 29 female) had an average age of 12.12 ± 2.90 years, height 153.8 ± 17.1 cm, weight 46.9 ± 18.9 kg, and a BMI of 19.04 ± 4.35 . There is no statistically significant difference between the two groups in age ($P = 0.65$), height ($P = 0.71$), and weight ($P = 0.30$).

3.2 | Correlation between spirometry and EIT-based measurements

Table 1 presents the mean values and SD of the parameters FVC, FEV₁, FEV_{0.5}, MEF₇₅, MEF₅₀, MEF₂₅ as well as the Tiffeneau index FEV₁/FVC and the bronchodilator test index Δ FEV₁. With regard to spirometry, for the controls the mean FVC value was 2.48 ± 0.93 L, and for the asthmatics this was 2.37 ± 0.92 L before BSL and 2.42 ± 0.93 L after BSL. In the asthmatic group, all lung function parameters increased after BSL. FEV₁ increased from 2.16 ± 0.83 L (2.24 ± 0.85 L measured with EIT) to 2.29 ± 0.86 L (2.36 ± 0.89 L measured with EIT), which resulted in a positive Δ FEV₁ [%] of 7.44 ± 12.94 (4.79 ± 12.93 measured with EIT). The positive effect of BSL was also observed in the increase of MEF₇₅, MEF₅₀, and MEF₂₅.

Figure 3 presents the boxplot and Pearson's correlation between spirometry and EIT-based measurements for FEV₁, FEV_{0.5}, MEF₇₅, MEF₅₀, and MEF₂₅. Comparison of the spirometry and EIT measurements showed that FEV₁ and FEV_{0.5} correlated well for all groups of

patients (all P -values < 0.05 , all r -values > 0.9). MEF₇₅, MEF₅₀, and MEF₂₅ values also correlated well (all P -values < 0.05 , r -values ranging from 0.673-0.805). Deviations in the maximum expiratory flows were documented being strongest at higher flows. The mean MEF₇₅ values of the controls were 4.62 ± 1.61 L/s in spirometry and 6.16 ± 2.77 L/s (EIT), with an r -value of 0.673. For MEF₅₀ ($r = 0.792$) and MEF₂₅ ($r = 0.805$), a better correlation was found between EIT and spirometry. Similar data were derived from the asthmatic children, both before and after BSL (Figure 3).

3.3 | Binary classification tests

Figure 4 presents the Tiffeneau index and bronchodilator index in the binary classification tests, based on spirometry as the evaluated standard and EIT as the prediction. The data were divided into two age groups (i.e., ≥ 12 years of age and < 12 years of age) with regard to the different criteria applied for the Tiffeneau index.¹⁷ The binary classification tests yielded high specificity ($> 93\%$) in all three criteria, while sensitivity was higher in Δ FEV₁ (86.67%) and lower in FEV₁/FVC (25% and 35.29%). A high positive predictive value ($\geq 75\%$) and a high negative predictive value ($> 80\%$) were observed. There were no significant differences between the groups aged ≥ 12 years and < 12 years regarding the Tiffeneau index when evaluating the correlation between spirometry and EIT.

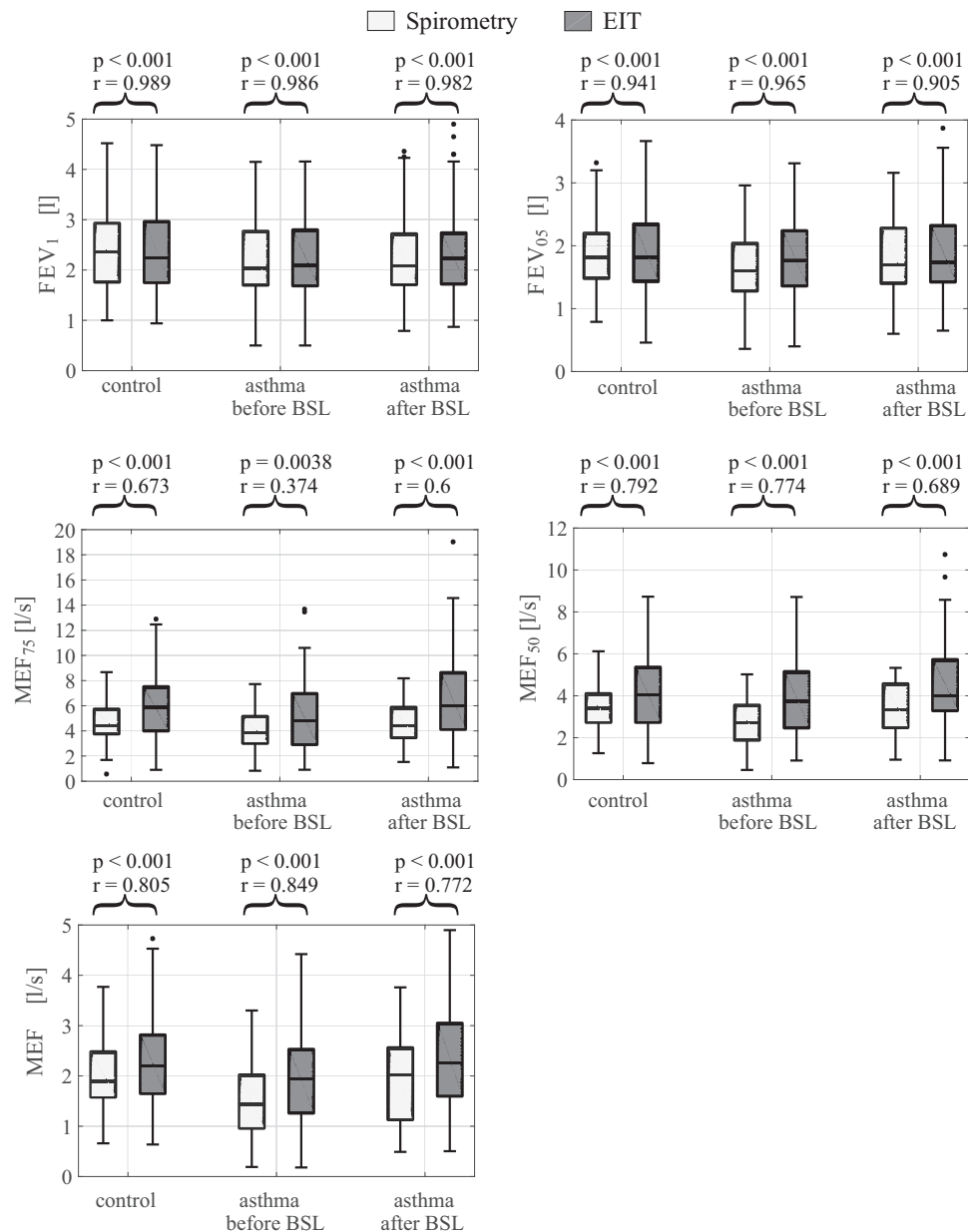


FIGURE 3 Boxplot and Pearson's correlation between spirometry and EIT-based measurements for FEV₁, FEV_{0.5}, MEF₇₅, MEF₅₀, and MEF₂₅. BSL, Bronchospasmolysis

3.4 | Individual and average flow-volume loops

For the graphical aspects of the EIT-derived FV loops for diagnosing asthma, we selected asthmatics with positive results on the Tiffeneau index and the bronchodilator tests. Three patients aged ≥ 12 years and seven aged < 12 years fulfilled these criteria; for comparison purposes, 10 age-matched controls with healthy lungs were selected. As a representative example, Figure 5, top panel shows the average FV loops of three asthmatic children. Changes in individual (numbers 1, 2, and 3) and in average FV loops after BSL are shown. Figure 5, bottom panel presents the average FV loops of 10

asthmatic and 10 control children. A typical concave shape of the EIT-derived FV loops was documented for asthmatics, but not for the controls. Moreover, the effect of BSL was graphically expressed in the asthmatics.

To present a direct comparison of global EIT and spirometry for individuals, and to demonstrate the potential use of EIT for regional pulmonary diagnostics, representative global, and regional FV loops of one patient are plotted in Figure 6. The figure shows regional FV loops obtained from EIT images for the right ventral (RiVe), left ventral (LeVe), right dorsal (RiDo), and left dorsal (LeDo) quadrant of the lung. The regional asthmatic FV loops confirmed positive bronchodilator

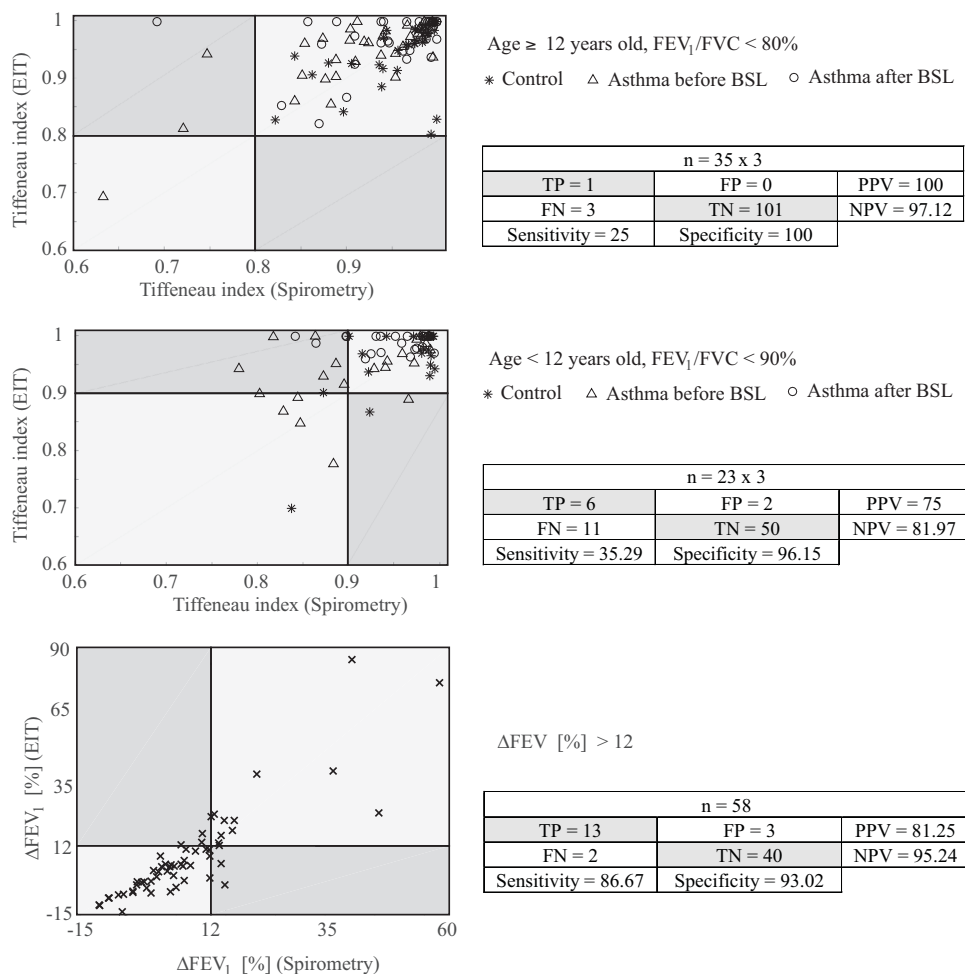


FIGURE 4 Binary classification tests of EIT-derived Tiffeneau index considering spirometry as the gold standard. Top: $FEV_1/FVC < 80\%$ for 35×3 children aged ≥ 12 years (control, asthma before and after BSL). Center: $FEV_1/FVC < 90\%$ for 23×3 children aged < 12 years (control, asthma before, and after BSL). Bottom: $\Delta FEV_1 [\%]$ aged > 12 years for 58 asthmatic children. TP, true positive; FP, false positive; TN, true negative; FN, false negative; PPV, positive predictive value; NPV, negative predictive value

test: enlargement of the regional FV loops was observed in all asthmatic patients. The patient had the largest positive bronchodilator in the LeDo quadrant.

4 | DISCUSSION

This study investigated the EIT-derived FV loops during spirometric lung function testing in 58 pediatric patients with asthma and 58 age-matched controls with healthy lungs. EIT data were scaled from arbitrary units (AU) to liter (L) according to the linearity factor calculating FVC [L] in accordance with the maximum impedance change of EIT during a forced expiration maneuver.¹³ Based on this, other parameters, such as FEV_1 , $FEV_{0.5}$, MEF_{75} , MEF_{50} , and MEF_{25} were determined and the correlations between EIT and spirometric data were computed.

Our earlier study on healthy adults showed a good correlation between EIT and spirometric pneumotachography measurements in volume, but a small deviation in flow during forced expiration

maneuvers.¹⁴ Also in the present study, there was good correlation between spirometry and EIT for the asthmatic patients and controls ($P < 0.001$ for FEV_1 , $FEV_{0.5}$, MEF_{75} , MEF_{50} , and MEF_{25} in all groups, except $P = 0.0038$, for MEF_{75} in the asthmatics before BSL).

The deviation in MEF_{75} may indicate a moderately lower linearity between EIT and spirometry at the start of the forced expiration maneuver, which adjusts toward the end of expiration. There are two possible causes for this deviation. First, at the beginning of the maneuver, the respiratory effort of the patient generates a high intra-thoracic pressure (approximately 120 cm H_2O in a healthy adult¹⁸), which causes a rapid reduction in intra-thoracic blood volume at the start of the maneuver. Thus, in addition to the impedance change caused by the expiratory gas, there is an additional impedance change due to the change in intra-thoracic blood volume. Second, the deviation might be attributed to the properties of the PulmoVista 500, that is, this device was originally designed to monitor patients undergoing mechanical ventilation in an intensive care unit. The ventilation flow in normal tidal breathing is significantly smaller than during a forced expiration maneuver, where a large amount of air is

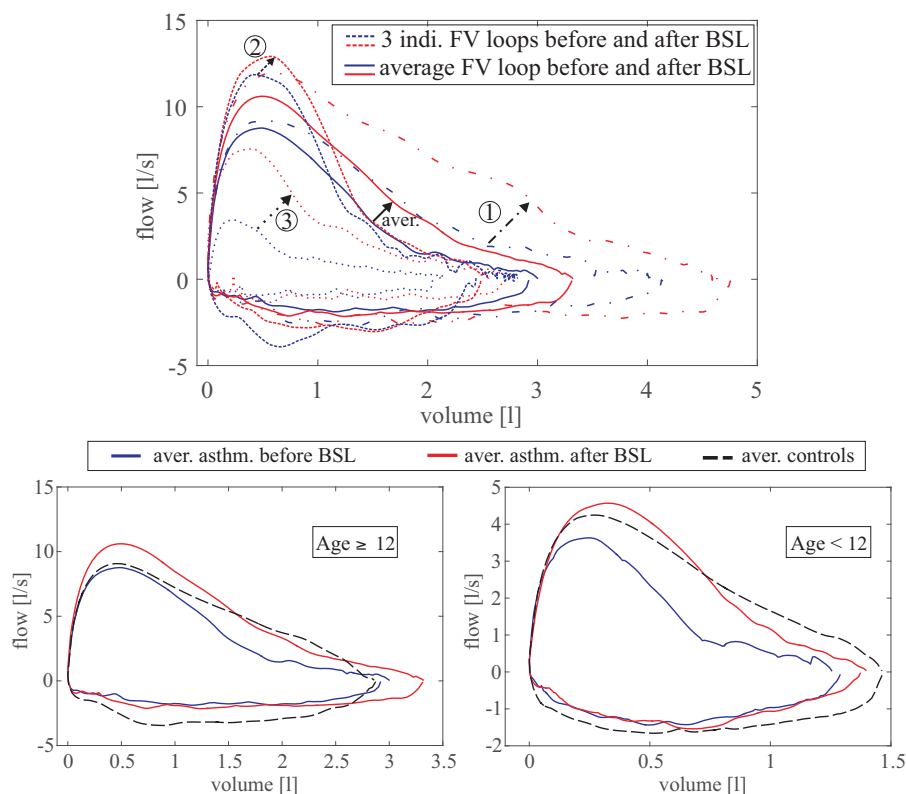


FIGURE 5 Top panel: Creation of individual (numbers 1, 2, and 3) and average FV loops before and after bronchospasmolysis (BSL, measured with EIT). Selection criteria of these three patients: age ≥ 12 years, Tiffeneau index < 0.8 , and $\Delta FEV_1 > 12\%$. Blue indicates the individual (dotted) and average (drawn) FV loops before BSL. Red indicates the individual (dotted) and average (drawn) FV loops after BSL. Bottom panel: Average FV loops of controls with healthy lungs (black, dotted), asthmatics before BSL (blue, drawn) and 10 asthmatics (red, drawn) after BSL. Left: three individuals aged ≥ 12 years, Selection criteria of asthmatics: age ≥ 12 years: Tiffeneau index < 0.8 , and $\Delta FEV_1 > 12\%$. Right: 7 individuals aged < 12 years. Selection criteria of asthmatics: age < 12 years: Tiffeneau index < 0.9 and $\Delta FEV_1 > 12\%$

pushed out of the lung in a short period of time. In the present study, the EIT reconstruction matrix used is based on a linear approach, which was developed for normal tidal volumes. Thus, for pulmonology applications, a special model-based reconstruction algorithm might be required which considers non-linear aspects such as the change of

thorax circumference, the position of the electrodes, and the change of the air/tissue volume within the thorax during the measurements.^{19,20}

The criteria for confirmed variable expiration limitation are a reduction of the Tiffeneau index ($FEV_1/FEV_0 < 90\%$ for children aged < 12 years and $FEV_1/FEV_0 < 80\%$ for children aged 12–18 years) and a

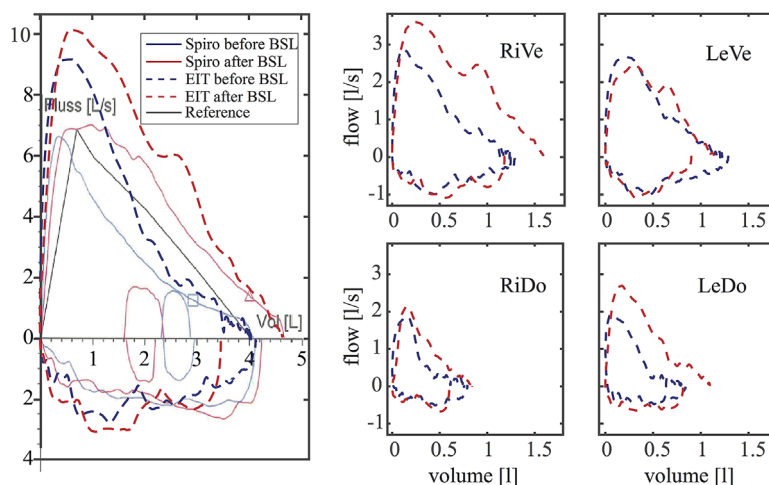


FIGURE 6 Spirometric and EIT-derived FV loop of one representative asthmatic patient. Left: global FV loops, right: regional FV loops obtained from EIT images for right ventral (RiVe), left ventral (LeVe), right dorsal (RiDo), and left dorsal (LeDo) quadrant of the lungs. BSL, bronchospasmolysis

significant positive bronchodilator test ($\Delta FEV_1 > 12\%$).¹⁷ A binary classification test between EIT and standard spirometry was performed. Very high specificity, as well as positive predictive values and negative predictive values were observed for both criteria. Sensitivity is high in ΔFEV_1 and low in FEV_1/FEV . The reason for this low sensitivity might be due to the deviation of flow between EIT and spirometry at the beginning of the forced expiration maneuvers, which causes a higher Tiffeneau index in the EIT-derived data.

In Figure 6, the differences in the global EIT-derived average FV loops for the three patient groups indicates the ability of EIT to differentiate between healthy controls and asthmatics. The FV loops of the asthmatics with pathologic spirometry yielded a concave form which improved after BSL. Note, that the form of the FV loops, as well as the Tiffeneau index and the bronchodilator test result ΔFEV_1 , did not change by scaling EIT data from AU to liters. Thus, the EIT-derived FV loops might be used in EIT standalone applications without pneumotachography. Or, in other words, EIT might become a pneumotachograph by itself.

Currently, clinical lung function tests do not provide regional information, although this would be useful for the treatment of regional inhomogeneity of lung diseases.^{14,21,22} In the present study, the statistical analyses were also solely based on global characteristics, as there is no established gold standard for regional ventilation for comparison purposes. However, EIT may also prove to be a feasible tool for regional pulmonary diagnostics. Again, there is no existing reference for regional lung function, since no functional non-invasive radiological technique (e.g., hyperpolarized He-magnetic resonance imaging) was made for comparison purposes due to both non-availability and ethical reasons. Thus, there may be some difficulty in evaluating and interpreting the regional FV loops quantitatively. A more detailed investigation of the regional FV loops is needed for a better understanding of ventilation distribution during a Tiffeneau maneuver. EIT-based FV loops might be feasible as a tool to monitor not only regional ventilation changes in diagnostic procedures, but also to determine the efficacy of the effects of local therapeutic drugs.

5 | CONCLUSION

EIT shows a high potential for pulmonary function testing for pediatric patients. Global flow-volume loops (FEV_1 , $FEV_{0.5}$, MEF_{75} , MEF_{50} , MEF_{25}) obtained by EIT correlate with spirometric findings in asthmatic children and in controls with healthy lungs. EIT-derived Tiffeneau index and the bronchodilator test index can be used to assess asthma. The typical concave shape of the EIT-derived average FV loops of asthmatics (with improvement of the FV loops after BSL) were observed. EIT has the potential to be an effective diagnostic tool for asthma in pediatric patients.

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CONFLICTS OF INTEREST

All authors declare that there are no conflicts of interest.

ORCID

Chuong Ngo  <http://orcid.org/0000-0002-3961-2173>

Steffen Leonhardt  <http://orcid.org/0000-0002-6898-6887>

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