

Biofeedback using electrical impedance tomography during inhalation therapy for chronic obstructive lung disease – a pilot study

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Abstract

Background

Airflow limitation and hyperinflation contribute to increased respiratory workload and dyspnea in COPD. Inhalation therapy plays a crucial role, but its effectiveness depends on correct technique. Electrical impedance tomography (EIT) offers real-time visualization of ventilation and may improve inhalation technique, when used as biofeedback.

Objectives

This study aimed to investigate the impact of biofeedback-guided inhalation using EIT on lung function, specifically targeting obstructive and hyperinflation parameters.

Methods

In this prospective, randomized, single-blinded study, 29 patients with COPD were divided into a control group (no biofeedback) and an intervention group (inhalation using visual biofeedback). Body plethysmography was performed before and after a single inhalation session. The primary outcome was the change in lung function parameters. Secondary outcomes included real-time EIT data during inhalation and a follow-up questionnaire assessing subjective benefit.

Results

No differences were observed in obstructive lung parameters (FEV1) between groups, but the intervention group showed a significant FRC reduction compared to the control group (control – 0.1 L vs. intervention – 0.4 L, $p < 0.05$). Resistance indices (sR_{tot}/sR_{eff}) tended to increase in the intervention group whereas a decrease was noted in control. No in between differences in EIT-derived data or subjective benefit at follow-up.

Conclusion

Biofeedback using lung EIT may improve inhalation technique and deposition of inhaled medication resulting in decreased hyperinflation. However, changes in breathing pattern, may also explain changes in lung parameters, highlighting the complex lung volume, ventilation and airway resistance interplay. Future research should investigate repeated EIT-biofeedback effects on lung function and disease symptoms.

Introduction

Chronic obstructive pulmonary disease (COPD) is a major global health challenge, contributing significantly to morbidity and mortality.^{1–3} Although COPD has multiple causes, the main driver is airway damage from inhaled noxious substances. Effects include chronic inflammation and airflow limitation, presenting as incompletely reversible obstruction with chronic bronchitis. Altered respiratory mechanics due to air-trapping, hyperinflation and finally the development of emphysema can contribute to a further deterioration in ventilation.

Therapeutic drug approaches, primarily inhaled, are intended to reduce obstruction and decrease inflammation by inhalation of bronchodilators and corticosteroids.^{4,5} Effective inhalation therapy requires sufficient drug deposition in the lungs. In COPD diaphragm dysfunction and hyperinflation impair ventilation and reduce inspiratory flow – a key factor for drug delivery.⁶ Incorrect inhalation technique often limits treatment success.^{7,8} Biofeedback training can improve technique, adherence and outcome.⁹ Although training can improve inhalation technique, it is not clear which method is most effective in identifying and correcting inhalation errors.¹⁰ Visually supported biofeedback, was found to be beneficial for patients with COPD in rehabilitation.^{11,12}

Electrical lung impedance tomography (EIT) is a bedside method visualizing real-time ventilation via thoracic impedance changes during ventilation. Alveolar air changes during ventilation alter lung impedance, enabling real-time 2D imaging of chest sections to show regional ventilation, the distribution of air and parameters of regional ventilation. Lung EIT is primarily applied in ventilated patients, such as in ARDS or during weaning.¹³ Lung EIT has not yet been used as biofeedback to visualize or improve inhalation in patients with COPD. This study investigated EIT as biofeedback for potential benefits of real-time visualized ventilation in inhalation therapy.

Material and methods

Study design and population

This prospective randomized, single-blinded study was performed in the Department of Internal Medicine V, Pneumology, Allergology and Critical Care Medicine of the University Hospital of Saarland and Saarland University, Homburg/Saar, Germany. Adults diagnosed with COPD who were on continuous inhalation therapy and in a stable disease stage, i.e. no sudden worsening of cough, sputum production, shortness of breath or recent hospitalization were included in this study. The protocol was approved by the local ethics review committee (No. 87/23). Written informed consent was obtained from the participants. Exclusion criteria included contraindications for EIT as specified by the manufacturer (pacemakers or ICDs, BMI > 50, unstable thorax including open chest injuries, large burns or wounds on the thorax), signs of acute exacerbation of COPD or cognitive impairments and language barriers.

Study protocol

Participants with a history of COPD were recruited during routine pulmonary clinic visits, consented, randomized into control or intervention group, and underwent body plethysmography before the study. Both groups were trained to use a pressurized metered-dose nebulizer with a short-acting beta₂-agonist (salbutamol) to avoid handling errors. All participants were connected to an EIT device (PulmoVista® 500, Dräger, Germany) via a chest belt placed at the 4th -6th intercostal space. In the control group, only the examiner saw the EIT monitor, whereas in the intervention group both examiner and participants observed real-time ventilation at the EIT monitor. The intervention group was subsequently informed that breathing would be displayed in real-time and was given a few minutes to adapt to the visualization. The control group was told that the examiner would observe their breathing in real-time. Both groups performed 10 resting breathing cycles, then inhaled 100 µg salbutamol (pressurised inhaler) with a minimum 5-second to a maximum 10 second breath hold. The procedure was repeated four times within 5 minutes. After inhalation, body plethysmography was repeated within 10 minutes to assess the effect of the biofeedback guided inhalation. During the experiment, real-time data of EIT during inhalation were recorded for further analysis. Study protocol, see supplementary Fig. 1.

Measurements and data recording

Static and dynamic lung volumes were measured by using body plethysmography (FEV₁, FEV₁/FVC, FVC, TLC, RV, FRC, sR_{tot}, sR_{eff}) under supervision by trained medical-technical assistants. Pre- and post-inhalation plethysmography values were recorded and compared between groups. Differences in lung function before and after the experiment were calculated for each patient separately before calculating and comparing group values. Baseline labs and CAT scores were recorded. After three months, follow-up included a repeated CAT score and an ordinal questionnaire on subjective biofeedback benefit. Recorded EIT data was sampled at 30 Hz, transferred to an external computer and analyzed using dedicated software (PulmoVista SW 1.30 and EITDiag V1.7), both supplied by Dräger. The following EIT-derived indices were calculated:

Global tidal volume image (TID):

The number of pixels corresponding to a defined surface. Since there is no absolute reference for measuring EIT ventilation, we quantified the relative change in tidal impedance. TID was analysed during 3–5 resting breathing cycles before inhalation (baseline) and during medication inhalation (changes in TID compared to baseline). The relative changes in pixel counts between baseline and during inhalation was interpreted as marker of the vital capacity available for inhalation. These changes in TID were compared between control and intervention group.

Global inhomogeneity index (GI):

The GI is derived from a global tidal volume image. GI is calculated as the difference between the median value of all pixels within a tidal volume image and the corresponding value of each individual pixel. The GI reflects the variability of ventilation distribution. Similar to TID, GI was analysed before

inhalation (baseline) and during inhalation (changes in GI) and compared between control and intervention group. A lower GI indicates a more homogeneous distribution of ventilation, while a higher GI index suggests a more inhomogeneous ventilation. Calculation of GI is displayed in Fig. 1.

Figure 1:

Left: TID, Tidal impedance difference; **Middle:** GI, Global inhomogeneity index; **Right:** RVD, Regional ventilation delay index; Examples of a patient from the intervention group during normal breathing cycles (1) and during inhalation (2). TID values during inhalation are expressed relative to the normal breathing cycle (set at 100%). Ventilation (TID) is color-coded from dark blue (low ventilation) to white (high ventilation). In this example, difference between tidal breathing and inhalation is 38%. GI is color-coded from dark red (homogeneous) to bright red (inhomogeneous). In this example GI increases from 48% before inhalation to 53% (indicating less homogeneous ventilation) during inhalation. Regional ventilation delay (RVD40), color-coded in orange, shows a reduction in ventilation delay from 8.19% to 2.84% during inhalation

GI: Global inhomogeneity index; **DI:** Value of the differential impedance in the tidal images; DI_{xy} : Pixel in the identified lung area; DI_{lung} : Total pixels representing the lung area

RVD40

Regional ventilation delay inhomogeneity; time difference between initiation of inspiration and 40% ventilation achieved, $t_{max} - t_{min}$ = Inspiration time

Regional ventilation delay inhomogeneity (RVDI):

Regional ventilation delay (RVD) was defined as the time interval between the onset of inspiration and the time point at which 40% of the maximal regional impedance change during tidal inspiration was reached. RVD was calculated for each pixel, and RVDI was defined as the standard deviation of RVD across all lung pixels, reflecting spatial inhomogeneity of regional filling. Lower RVDI values indicate more homogeneous and synchronous ventilation, whereas higher values reflect increased regional delay and inhomogeneity. Differences between resting breathing and the inhalation were analysed to assess changes in regional ventilation timing during inhalation. Calculation of RVDI is displayed in Fig. 1.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics (version 29.0.1.0.) Figures in the results section was generated with Python (version 3.12.4.) and randomization was conducted using R (version 4.2.2.) Normal distribution was assessed with Shapiro-Wilk test. As data were not normally distributed, between-group comparison of unpaired continuous variables was performed using the Mann-Whitney test, and categorical variables from follow-up surveys were analysed using the chi-square test. Results are reported as control versus intervention, due to non-normal distribution data is presented as median, unless stated otherwise. Lung function results are reported in liters (L) and as height-adjusted percent of

predicted reference values (% pred.). Predicted reference values are based on a healthy reference population.^{18,19} The response of lung function parameters was determined for each individual patient by calculating the difference between post- and pre-inhalation values. These derived variables were then used for further statistical analysis between groups, in this case using a Mann-Whitney test. P-value < 0.05 was considered statistically significant.

Results

General

A total of 30 participants were recruited; 29 were analyzed (n = 15 control group vs. n = 14 intervention group). One control participant was excluded due to incomplete plethysmography. Intervention or intervention group refers to EIT-Biofeedback.

Baseline demographics and laboratory findings

The study population comprised 29 patients, including 15 female and 14 male participants, with an age of 64 years vs. 65.5 years ($p > 0.05$) and a BMI of 27 kg/m² vs. 24.3 kg/m² ($p > 0.05$), and Pack-years of 40 vs. 40 ($p > 0.05$). The median CAT score at inclusion was 26 / 40 points vs. 24.3 / 40 points with no significant difference between groups ($p > 0.05$). Spirometric GOLD classification (FEV₁) was comparable between groups (Table 1). Inflammation markers, including leukocytes, C-reactive protein, eosinophils, were within normal range in median and showed no significant group differences, except for C-reactive protein (which was within normal range). The basic laboratory values are listed in Table 1.

Table 1

Baseline characteristics and laboratory findings of COPD patients in the control group (n = 15) compared to the intervention group (n = 14).

Age [years]	Control; N = 15	Intervention; N = 14	p-value
	median (IQR)	median (IQR)	
	64 (60.5–76)	65.5 (60.3–69.5)	.847
Sex [male, N; %]	8/15; 53.3%	6/14; 42.9%	.853
Body mass index [kg/m ²]	27 (26.2–33.1)	24.3 (21.3–32.8)	.425
Pack Years	40 (30–50)	40 (18.8–50)	.533
CAT score	26 (12.8–29)	24.5 (21.3–30.8)	.949
GOLD grade [N]			.400
I	3	0	
II	2	3	
III	6	7	
IV	4	4	
Leukocytes [g/l]	9.0 (8–11.3)	8.2 (6.5–11)	.339
CRP [mg/dl]	4.4 (1.5–8.6)	1.2 (0.6–2.2)	.046
Eosinophils [/μl]	114.3 (83.1–345) N = 13/15	115 (69.1–185.8) N = 12/15	.027
CAT: COPD assessment test; GOLD: Global Initiative for Chronic Obstructive Lung Disease; Hb: Haemoglobin; CRP: C-reactive protein;			

Body plethysmography results control group vs. intervention group

Lung function results before the experiment (inhalation) are listed in Table 2.

Table 2

Pulmonary function before inhalation in control group (n = 15) and intervention group (n = 14). Absolute measurements are supplemented by values normalized to the expected values of a healthy population [%].

FEV₁ [L]	Control; N = 15	Intervention; N = 14	p-value
	median (IQR)	median (IQR)	
	1.2 (0.6–1.7)	0.9 (0.7–1.2)	.451
FEV ₁ [%]	42 (22–65)	33.5 (27–42)	.451
FEV₁/FVC	50.7 (43.1–66.9)	49.6 (38.5–73)	.914
PEF [L]	3.1 (2.2–4.7)	3.0 (1.7–3.6)	.451
PEF [%]	44 (33–72)	44.5 (29–52.5)	.377
FVC [L]	2.0 (1.7–2.8)	1.7 (1.5–2.1)	.252
FVC [%]	58 (48–77)	52 (47–61)	.172
TLC [L]	6.7 (6.2–8.1)	6.5 (5.5–8.9)	.983
TLC [%]	123 (107–139)	126.5 (93–141)	.949
RV [L]	4.8 (3–5)	4.7 (3.6–6.5)	.621
RV [%]	208 (144–242)	228.5 (146–253)	.533
FRC [L]	5.0 (3.5–5.8)	5.3 (4–7.5)	.621
FRC [%]	176 (123–195)	189.5 (118–209)	.533
sRtot [kPa*s]	5.3 (1.6–8.1)	4.0 (2–7.8)	.914
sRtot [%]	448 (161–840)	384.5 (167–747)	.847
sReff [kPa*s]	4.7 (1.5–5.8)	3.3 (1.7–7.2)	.780
sReff [%]	400 (154–606)	310 (153–644)	.914
FEV₁ : Forced Expiratory Volume in one second; FEV₁/FVC : Ratio of Forced Expiratory Volume in one second to Forced Vital Capacity; PEF : Peak Expiratory Flow; FVC : Forced Vital Capacity; TLC : Total Lung Capacity; RV : Residual Volume; FRC : Functional Residual Capacity; sRtot : Specific Total Airway Resistance; sReff : Specific Effective Airway Resistance;			

Results after the experiment (inhalation) are listed in Table 3.

Table 3

Pulmonary function after inhalation in control group (n = 15) and intervention group (n = 14). Absolute measurements are supplemented by values normalized to the expected values of a healthy population [%].

FEV1 [L]	Control; N = 15	Intervention; N = 14	p-value
	median (IQR)	median (IQR)	
	1.2 (0.8–1.7)	1 (0.7–1.2)	.377
FEV1 [%]	40 (28–65)	34.5 (28–48)	.354
FEV1/FVC	54 (43.1–68.6)	46.5 (37.7–65.7)	.505
PEF [L]	3.3 (2.1–4.8)	2.7 (2.2–3.8)	.505
PEF [%]	41 (28–74)	43 (35–51)	.683
FVC [L]	2.0 (1.6–3.1)	1.9 (1.6–2.2)	.533
FVC [%]	54 (51–83)	53 (50–66)	.400
TLC [l]	7.1 (6.4–7.9)	6.6 (5–8.3)	.561
TLC [%]	123 (104–142)	115 (91–136)	.451
RV [l]	4.5 (2.8–5.2)	4.3 (2.8–5.5)	.949
RV [%]	199 (137–271)	196.5 (127–244)	.747
FRCpl [L]	5.5 (3.4–5.9)	5.2 (3.6–7)	.652
FRCpl [%]	173 (119–215)	168 (106–207)	.983
sRtot [kPa*s]	3.9 (1.5–5.9)	4.2 (2.1–7.1)	.621
sRtot [%]	332 (160–617)	402 (193–685)	.652
sReff [kPa*s]	3.8 (1.5–5.6)	3.7 (1.8–6.1)	.652
sReff [%]	325 (152–580)	349 (166–539)	.715
FEV1: Forced Expiratory Volume in one second; FEV1/FVC: Ratio of Forced Expiratory Volume in one second to Forced Vital Capacity; PEF: Peak Expiratory Flow; FVC: Forced Vital Capacity; TLC: Total Lung Capacity; RV: Residual Volume; FRC: Functional Residual Capacity; sRtot: Specific Total Airway Resistance; sReff: Specific Effective Airway Resistance;			

Calculated differences, before-after inhalation compared between groups are displayed in Table 4.

Table 4

Calculated differences in pulmonary function before and after inhalation in control group (n = 15) and intervention group (n = 14). Group-level statistics were calculated from individual pre-post difference values.

FEV1 [L]	Control; N = 15	Intervention; N = 14	p-value
	median (IQR)	median (IQR)	
	0.1 (0.0–0.2)	0.0 (0.0–0.1)	.425
FEV1 [%]	3 (0.0–5)	0.5 (-1–4)	.468
FEV1/FVC	2.1 (-3.8–4.6)	- 1.3 (-4.6–3)	.377
PEF [L]	0.1 (-0.3–0.2)	0.0 (-0.3–0.5)	.628
PEF [%]	-1 (-4–3)	0 (-4.5–8.5)	.722
FVC [L]	0.1 (-0.1–0.2)	0.1 (-0.1–0.3)	.511
FVC [%]	2 (-3–6)	2 (-2.3–9)	.456
TLC [L]	-0.1 (-0.3–0.5)	- 0.4 (-0.7–0.1)	.149
TLC [%]	0.0 (-7–10)	-5 (-13.5–1.8)	.204
RV [L]	-0.2 (-0.5–0.4)	-0.5 (-1.1–0.1)	.230
RV [%]	-7 (-25–20)	-19 (-42.8–5.3)	.213
FRC [L]	-0.1 (-0.2–0.4)	-0.4 (-0.7 – -0.1)	.040
FRC [%]	-2 (-6–12)	-11 (-22.3 – -2.8)	.031
sRtot [kPa*s]	- 0.6 (-1.3 – -0.2)	-0.1 (-0.3–0.2)	.020
sRtot [%]	-50 (-113 – -18)	-8.5 (-29.3–17.8)	.033
sReff [kPa*s]	-0.5 (-1.1 – -0.1)	0.01 (-0.4–0.2)	.033
sReff [%]	-43 (-106 – -7)	1 (-32.5–20.3)	.046
FEV1: Forced Expiratory Volume in one second; FEV1/FVC: Ratio of Forced Expiratory Volume in one second to Forced Vital Capacity; PEF: Peak Expiratory Flow; FVC: Forced Vital Capacity; TLC: Total Lung Capacity; RV: Residual Volume; FRC: Functional Residual Capacity; sRtot: Specific Total Airway Resistance; sReff: Specific Effective Airway Resistance;			

Prior to the intervention, there was no difference between the groups, respectively in terms of FEV1 (1.2 L vs. 0.9 L, $p > 0.05$) and FVC (2 L vs. 1.7 L, $p > 0.05$). Total lung capacity (TLC) showed similar values in both groups before the intervention (6.7 L vs 6.5 L, $p > 0.05$), which exceeded 100% of the predicted TLC in both groups (123% pred. vs. 126.5% pred.). The residual volume (RV) was pathologically elevated in both groups (4.8 L, 208% pred. vs. 4.7 L, 228% pred., $p > 0.05$) indicating emphysema. Likewise, functional residual capacity (FRC) was increased indicating hyperinflation in both groups (5.0 L, 176% pred. vs. 5.3 L, 189% pred., $p > 0.05$). After the intervention, both groups showed a similar median

increase in FVC (+ 0.1 L, + 2% pred. control vs. intervention, $p > 0.05$). Regarding FEV1, the control group exhibited a slight median increase while the intervention group showed no relevant change (+ 0.1 L, + 3% pred. vs. ± 0.0 L, + 0.5% pred., $p > 0.05$). A reduction in TLC (-0.1 L, 0.0% pred. vs. -0.4 L, -0.4% pred.) and RV (-0.2 L, - 7% pred. vs. -0.5 L, - 19% pred.) was observed, more in the intervention group than in the control group, without reaching statistical significance ($p > 0.05$). Notably, FRC showed a significant improvement in the intervention group. A reduction in FRC of -0.4 L (-11% pred.) was observed, compared to a reduction of -0.1 L (-2% pred.) in the control group, reaching a significant difference ($p < 0.05$). Of note, the parameters for specific airway resistance (sR_{tot} , sR_{eff}) were significantly lower in the control group compared to the intervention group. Total airway resistance decreased by a median of 50% pred. in the control group versus 8.5% pred. in the intervention group ($p < 0.05$). Similarly, the sR_{eff} decreased by -43% pred. in the control group compared to an increase of + 1% pred. in the intervention group ($p < 0.05$). Significant see Fig. 2.

EIT-derived parameters TID, GI and RVDI

EIT-derived parameters included three key parameters: TID (Tidal Impedance Difference), GI (Global Inhomogeneity Index), and RVDI (Regional Ventilation Delay Standard Deviation). In the control group, data from 15 patients were evaluable for analyzation, whereas in the intervention group, EIT data were evaluable for only 11 patients because of artefacts during recording. Tidal Impedance Difference showed no significant group difference during inhalation (+ 237 vs. +277, $p > 0.05$). Global Inhomogeneity Index showed decreased values in both groups indicating more homogeneity during inhalation in both groups. The control group had a median GI of 48.9 pre-inhalation vs. 42.81 (-4) during inhalation ($p > 0.05$), the intervention group showed a median decrease in GI from 53.9 pre-inhalation to 45.3 (-8.3) during-inhalation, level of significance was not reached ($p > 0.05$). Regional Ventilation Delay (RVDI) differed slightly between groups. While the control group presented a RVDI with a median of 7.4 before and 7.6 during inhalation, the intervention group demonstrated a RVDI with median of 8.1 before and higher RVDI of 11.5 during inhalation ($p = 0.071$) indicating more delay during inhalation. The median difference of RVDI between pre- and inhalation was 0.2 vs. - 0.2 ($p > 0.05$). Parameters are shown in supplementary Table 5, example of EIT data is visualised in Fig. 1.

Follow-up CAT-score and subjective assessment of participants

Follow-up interview was completed in 26 of 29 enrolled patients. Two patients passed away during the follow-up period, one withdrew consent for a phone interview. 12 /14 patients in the intervention group and 14 / 15 patients in the control group completed the follow-up. Patients without follow-up interview were excluded from CAT-analysis. The mean time between study participation and follow-up was 4.8 months. Patients without follow-up CAT were excluded from analysis. At follow-up, the mean CAT score across all participants was 23.5 points, representing a mean reduction of 1.9 points compared to baseline. In the control group, the CAT score decreased by a mean of 2.4 points, whereas in the intervention group, the mean reduction was 1.4 points, see suppl. Table 5. Supplementary Table 6

summarizes quantitative results in the intervention group, values are ordered from 1 = strongly disagree, to 5 = strongly agree. The Results indicate that the EIT image was generally perceived as helpful (Question 1; mean: 3.6). Additionally, most patients found the EIT image to be understandable (Question 2; mean: 4.1), with no participants rating their understanding as "disagree" or "strongly disagree." The guidance and feedback were rated as highly helpful (Question 4; mean = 4.6). No patient rated the guidance or feedback below "3 = neutral." No clear trend was seen in perceived inhalation effectiveness (Question 5; mean: 3.0). During the follow-up, all participants were asked whether they perceived any benefit from participating in the study. Responses were categorized into three groups: "No benefit or new insights," "Subjective benefit from the EIT intervention," and "Subjective benefit from inhalation training." None of the participants in the control group reported deriving any benefit from the study. In the intervention group, the responses of three patients fell into the category "No benefit or new insights." Four patients reported benefiting from inhalation training but not from biofeedback. Five patients described a subjective benefit specifically attributed to the EIT-biofeedback.

Discussion

The present study investigated the use of electrical impedance tomography (EIT) as biofeedback in patients with COPD. The aim was to improve inhalation via real-time visual biofeedback (EIT) with expectation that optimized inhalation might enhance lung function, reduce hyperinflation and improve subjective disease burden. The primary outcome was whether inhalation with EIT biofeedback alters lung function parameters when used during inhalation. The secondary outcome was to explore whether subjective benefits could be detected and whether EIT-derived parameters could quantify differences in inhalation efficiency. While lung function parameters like FEV1 and FVC showed no between-group differences, FRC significantly decreased in the intervention group ($p < 0.05$). Despite no significant changes in EIT-derived ventilation parameters, some intervention participants reported subjective benefits from inhalation training and visual biofeedback. Thus, real-time EIT biofeedback may reduce FRC, while other spirometry values and regional ventilation remained largely unchanged. Notably, specific airway resistance improved significantly in the control group.

Interpreting the main finding, FRC reduction, requires considering static and dynamic hyperinflation, which is mainly induced by destruction of the lung parenchyma with diminished inward-directed elastic fibers. This results in a pressure-volume curve shifted upward and to the left.¹⁴ Clinically, hyperinflation increases inspiratory workload, impairs gas exchange and alters cardiopulmonary interaction contributing to dyspnea and reduced performance.^{14,15} Previous studies show that bronchodilation response does not always correlate with expiratory flow measure. Symptomatic improvement, such as reduced dyspnea often aligns with decreased FRC, rather than increased FEV1.¹⁶ Importantly, the absence of FEV1 changes does not always imply a lack of bronchodilator effect. In COPD, acute improvements in expiratory flow are often small, while changes in hyperinflation more accurately reflect physiological benefit. Consequently, FRC might represent a more sensitive parameter than FEV1 to detect short-term physiological effects of improved inhalation technique in COPD. In our experiment, we

were unable to detect any changes in FEV1; however, a significant change in FRC was observed in the intervention group, with a decrease of 0.4 L in median (– 11% pred). In the literature, an increase in FRC is generally considered clinically relevant when it exceeds approximately 120% of predicted value, corresponding to the upper limit of normal in a healthy population.^{17,18,19} However, several reports suggest that a reduction in dynamic hyperinflation is associated with clinically meaningful improvements in exercise capacity and reduction in dyspnea symptoms.^{20,21,22,23} The observed reduction in FRC in the intervention group may reflect more effective inhalation facilitated by real-time biofeedback, potentially resulting in reduced hyperinflation. Alternatively, this reduction may indicate improved breathing mechanics, particularly during exhalation, mediated by biofeedback-guided respiratory control. In the future, this effect could potentially be enhanced through structured respiratory training incorporating biofeedback. As demonstrated in previous studies in context of lung volume reduction, a decrease in FRC is associated with improved diaphragm mechanics.²⁴ In our study, the observed reduction in FRC was comparable in magnitude and direction to reductions reported after lung volume reduction interventions, such as endobronchial valve implantation²⁵. These findings raise the possibility that specific patient subgroups may derive greater benefit from biofeedback-based interventions, analogous to the heterogeneous response observed in lung volume reduction therapies. The observed decrease in specific airway resistance (sRaw) in the control group, compared with the intervention group need careful interpretation. As specific airway resistance is defined as the product of airway resistance and lung volume ($sRaw = Raw \times FRC$), one possible interpretation is that a reduction in sRaw with stable FRC suggests decreased airway resistance.²⁶ Conversely, in the intervention group, reduced FRC may have altered airway mechanics. Reduced lung volumes can decrease radial traction on the airways, potentially leading to relative airway narrowing and thereby attenuating expected reductions in sRaw despite improvements in hyperinflation.^{26, 27} However, sRaw is known to be highly dependent on breathing pattern and patient cooperation during body plethysmography. In patients with COPD, tidal expiratory flow limitation (tEFL) is common and may affect the accuracy and reproducibility of plethysmographic resistance measurements. As a result, changes in sRaw may reflect a combination of altered breathing mechanics, lung volume changes, and measurement-related factors, rather than isolated changes in airway calibre. Given these physiological and methodological considerations, sRaw should be interpreted cautiously, and may be of limited value as a primary physiological endpoint in this context. The degree of hyperinflation in COPD is closely linked to symptom burden and functional limitation²³. Reductions in hyperinflation have been associated with improvements in dyspnoea and overall symptom perception. Accordingly, subjective improvements might have been anticipated. However, in the present study, no significant changes in CAT scores were observed, and subjective assessments showed no consistent trend. A single biofeedback intervention may be insufficient to induce sustained changes in breathing behaviour. Durable improvements in respiratory mechanics and symptom perception likely require repeated training and reinforcement over time. Most existing inhalation training studies employed repeated sessions to consolidate technique over time. François and colleagues²⁸ for example, used graphical breathing feedback over 20–35 sessions, yielding improvements in FEV1 and FVC. Unlike their protocol, our single-session approach may have been

insufficient to affect subjective outcomes, suggesting that repeated training with EIT-guided biofeedback may yield greater clinical benefit. Nonetheless, to our knowledge, only one other study has explored the role of EIT as a biofeedback tool. Yang and colleagues²⁹ demonstrated that single-session EIT feedback improved breathing technique during pursed-lip breathing and led to more homogeneous ventilation distribution. In contrast, our study focused primarily on inhalation mechanics and their immediate physiological effects on lung function. EIT-derived parameters (TID, GI, RVDI) were measured during the inhalation manoeuvre to assess inhalation depth, regional distribution and timing. No significant between-group differences were observed. However, RVDI increased in the intervention group from 8.1 to 11.5 indicating more delayed ventilation during inhalation compared with the control group. This may be explained by more conscious inhalation as participants in the intervention group were able to view their ventilation status in real-time. The absence of significant EIT differences does not contradict an improved inhalation deposition with EIT as biofeedback. The EIT device used displayed only a two-dimensional cross-sectional image of the lung. Thus, the lack of EIT differences may reflect the methodological boundary of the tool rather than the absence of a real effect on inhalation. A limiting factor that may have affected the statistical power of EIT-derived parameters is the number of patients eligible for analysis. In the intervention group, only 11 patients had data of sufficient quality of inclusion. This limited sample size may have affected not only EIT-derived parameters but also other study endpoints. Larger cohorts will be required in future studies to improve statistical power and allow more robust evaluation of physiological effects. Future studies should therefore examine whether repeated EIT-guided inhalation training can lead to sustained improvements in regional ventilation distribution or clinical outcomes and further examine, which EIT features, if any, capture inhalation quality. Although COPD stages were comparable between groups, most participants were in GOLD stages III-IV. Future studies may benefit from more balanced inclusion across disease severity and from targeting patients with a pronounced hyperinflation phenotype, who may derive the greatest benefit from biofeedback-guided inhalation strategies.

Conclusion

An essential aspect of inhalation therapy for COPD is the precise application and effective deposition of medication, which can be optimized through regular training and education. Implementing a feedback system, such as visual real-time feedback via lung EIT, may further enhance training effectiveness and improve inhalation and breathing mechanics. In this study, a single training session using EIT significantly reduced hyperinflation. Future research should explore the impact of regular training on lung function and patients' subjective disease perception.

Declarations

Clinical Trial Registration Number: DRKS-IDDRKS00037626

Registration Date: 11.08.2025

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Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Availability of data and materials

Data can be provided on reasonable request addressed to the corresponding author. All data sharing statements are subject to conformity with German data protection legislation and rules (Datenschutzgrundverordnung - DSGVO).

Ethics approval and consent to participate/publication

Informed consent for conducting the study and publication of results was obtained by the patient or legal representative. The ethics committee of the Ärztekammer des Saarlandes (87/23) approved this study. Informed consent for the analysis of data is waived by the institutional review board due to the anonymous and prospective analysis of data. Study was conducted in accordance with the Declaration of Helsinki.

Use of AI

AI-assisted tools were used (Chat GPT, Version 5.1) only for language editing (grammar and readability). No AI tools were used for study design, data analysis, interpretation, or generation of scientific content. All intellectual contributions and verification of the manuscript were performed by the authors.

Author's Contribution

S.S., R.M. and A.B. contributed to the collection, review, and/or analysis of the data; S.S. and A.B. drafted the manuscript, A.B. and P.L. developed the study concept, wrote final drafts of the manuscript, and contributed to the interpretation of results. T.R. and R.B. revised the manuscript for important intellectual content. All authors have seen and approved the final version of the manuscript. A.B. is the guarantor of the manuscript.

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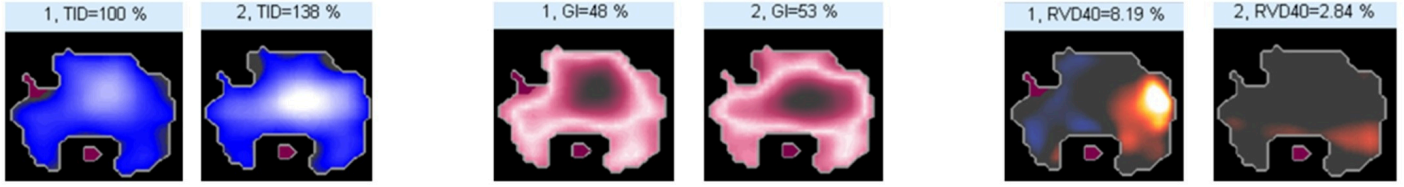
Not applicable

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Figures



Left: TID, Tidal impedance difference; **Middle:** GI, Global inhomogeneity index; **Right:** RVD, Regional ventilation delay index; Examples of a patient from the intervention group during normal breathing cycles (1) and during inhalation (2). TID values during inhalation are expressed relative to the normal breathing cycle (set at 100%). Ventilation (TID) is color-coded from dark blue (low ventilation) to white (high ventilation). In this example, difference between tidal breathing and inhalation is 38%. GI is color-coded from dark red (homogeneous) to bright red (inhomogeneous). In this example GI increases from 48 % before inhalation to 53 % (indicating less homogeneous ventilation) during inhalation. Regional ventilation delay (RVD40), color-coded in orange, shows a reduction in ventilation delay from 8.19 % to 2.84 % during inhalation.

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

GI: Global inhomogeneity index; DI: Value of the differential impedance in the tidal images; DI_{xy} : Pixel in the identified lung area; DI_{lung} : Total pixels representing the lung area

$$RVD40 = \frac{\Delta t_{40\%}}{t_{max} - t_{min}} * 100\%$$

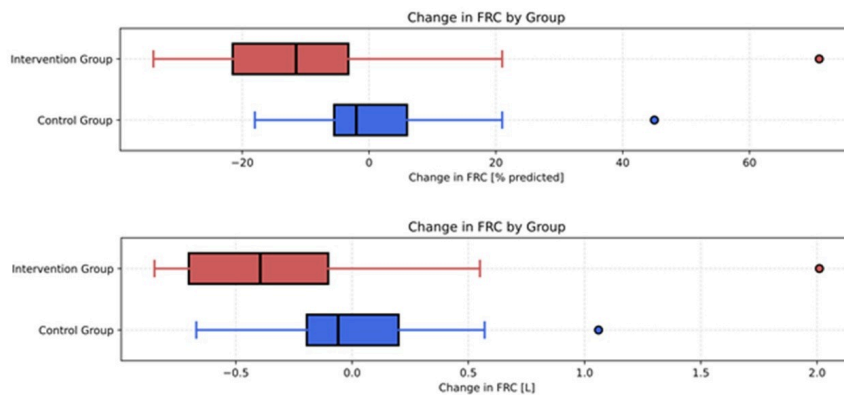
RVD40: Regional ventilation delay inhomogeneity; time difference between initiation of inspiration and 40 % ventilation achieved, $t_{max} - t_{min}$ = Inspiration time;

Figure 1

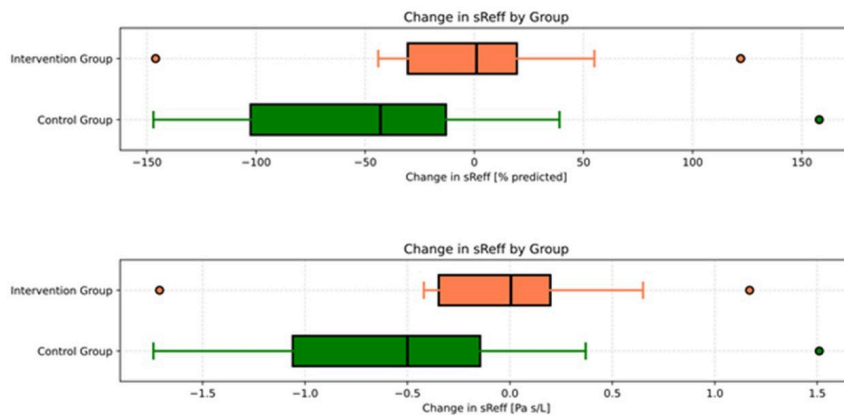
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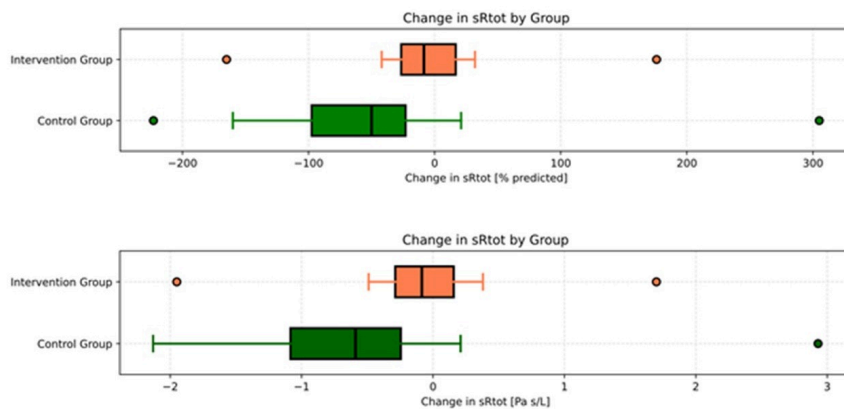
RVD40: Regional ventilation delay inhomogeneity; time difference between initiation of inspiration and 40 % ventilation achieved, $t_{max} - t_{min}$ = Inspiration time



Top: Change in FRC [% predicted] between groups after inhalation and change in FRC [L] between groups after inhalation;



Middle: Change in sR_{eff} [% predicted] between groups after inhalation and change in sR_{eff} [Pa*s/L] between groups after inhalation;



Bottom: Change in sR_{tot} [% predicted] between groups after inhalation and change in sR_{tot} [Pa*s/L] between groups after inhalation;

Figure 2

Legend not included with this version

Supplementary Files

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