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Detection of Respiration Movement Asymmetry Between the Left and Right Lungs Using Mutual Information and Transfer Entropy

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ABSTRACT Using diagnostic imaging, asymmetry in the mechanic of the left and right lungs has been discovered in unilateral lung disease. Unilateral lung disease might affect information interaction between two lungs, which is often neglected in the study of lung function. In this paper, twenty-one subjects were recruited to collect bio-impedance respiratory signals of the left and right lungs. The differences of correlation and amplitude between the two respiratory signals were combined to verify three types of respiration movement: respiration symmetry (RS), respiration asymmetry type I (T1RA), and respiration asymmetry type II (T2RA). We extracted the correlation coefficient, mutual information (MI), and transfer entropy (TE) to evaluate lung function in these three types of lung respiration. Results showed that MI was significantly larger in RS than in T1RA and T2RA. TE in both directions (TE(L→R) and TE(R→L)) were significantly different in RS, T1RA, and T2RA. TE(R→L) increased progressively when shifting RS to T1RA and then to T2RA. The prominent direction of transferred information in two lungs was significantly different for T1RA and T2RA. The results indicate that MI is suitable parameters for detecting respiration symmetry and asymmetry. TE is a useful tool for detecting two respiration movement asymmetry. The results provide a better understanding of the mechanisms underlying responsible for pulmonary ventilation redistribution and could provide novel clinical markers to evaluate asymmetry of two lungs effectively.

INDEX TERMS Bio-impedance technique, information interaction, mutual information (MI), respiration, transfer entropy (TE).

I. INTRODUCTION

Unilateral lung disease (ULD) is a disease condition characterized by pathology changes in unilateral lung tissue. Common ULD include unilateral pulmonary edema, lobar pneumonia, pneumothorax, and so on. Research indicated that ULD results in asymmetry in the mechanic of two lungs [1]. The asymmetry leads to poor therapy efficacy of mechanical ventilation that may has potential for further deteriorating lung [2], [3].

The diagnosis of ULD requires medical imaging such as chest radiography, computed tomography and digital radiography [4]. However, the above-mention medical imaging cannot be implemented frequently because of the ionizing radiation and the larger expense involved [5]. Besides, the above-mention medical imaging cannot provide diagnostic information in real time. Recently, the bio-impedance technique has been a popular method to retrieve information about lung at low cost and without ionizing radiation. It has been developed to monitor lung volume changes by measuring a voltage developed via an applied electrical current [6]. There are two approaches in adapting this technique for lung monitoring. One is transthoracic measurement and the other is electrical impedance tomography (EIT) [7].

Given its advantages, bio-impedance technique has been gaining popularity as a powerful tool for characterizing pulmonary ventilation (function). Brown *et al.* [8] used

EIT technique to measure the absolute resistivity of lung tissue, with a global mean value of 5.7 ± 1.7 Ωm. Zlochiver *et al.* [7] improved a bio-impedance system to obtain mean left and right lung resistivity values (12.05 Ωm and 12.0 Ωm, respectively) and reflected the symmetry of two lungs in healthy people. Kurth *et al.* [9] succeeded in calculating accurate tidal volumes based on quadrant impedance measurement. Although great attention has been placed on applying bio-impedance technique to obtain lung information, there is few study about the asymmetry of two lungs [10].

In previous study, evidence of the influence of body postures on pulmonary function was observed [11]. Liu *et al.* [12] proved that body postures could influence the respiratory coordination between the left and right lungs and found that respiratory coordination between two lungs was best in the supine posture. Pulmonary capillary wedge pressure decreased in both lateral positions compared to the supine position, which interfered with gas exchange and the ability to store gases [13], [14]. It is well documented the importance of recumbent body position on optimizing ventilator function and gas exchange for unilateral lung disease patients with their normal lung [15]. Thus, we intend to obtain the asymmetry of two lungs by utilizing different body postures, and find powerful indices to evaluate the asymmetry between two lungs in our study.

Currently, causal relationships in various biological systems have witnessed a rapid surge in interest in the past years. The first attempt to capture the amount of coupling (shared information) between two random variables was the feature of mutual information (MI) [16], [17]. MI quantifies the amount of information that can be obtained about a random variable from another one. However, the MI=MI(x,y)=MI(y,x) is a symmetric quantity measuring the common influence between two random variables x and y. It only obtains coupling strength between two random variables. In 2000, transfer entropy (TE) was used to quantify the information interaction between two variables in both directions [18]. Compared to model-based approaches such as Granger causality and dynamic causal modeling [19], [20], TE has an advantage in quantifying interactions without building linear model. Moreover, it is sensitive to both linear and nonlinear interactions which may be not always be known a priori. Therefore, MI and TE are useful tools for detecting coupling and causal relationships. For example, Zhu *et al.* [21] used MI with phases to investigate cardiorespiratory coupling in anesthetized rats and found that the interaction between heartbeat and respiration was reciprocal but biased toward the influence of respiration on heartbeat. MI has been used to assess quality of EIT reconstruction by calculating the mutual information between the EIT and magnetic resonance images [22]. TE was suggested and successfully applied to help elucidate cardiovascular, cardiopulmonary, and vasculopulmonary regulation through the study of simultaneously measured heart period, systolic arterial pressure, and respiratory flow spontaneous variability. Faes *et al.* [23]–[25] measured heart period, systolic arterial pressure, and respiration and assessed the directional and dynamic interaction among several physiological systems by using TE. It is all known that the left and right lung are two physiological subsystems of respiratory. We assume there are complex physiological interaction between the left and right lungs, and the interaction is affected by the asymmetry of two lungs.

In the present study, we sought to investigate the relationship of the asymmetry of two lungs and respiratory movement asymmetry, and tested physiological interaction between left and right lungs. A bio-impedance technique was used to measure the two lungs' respiratory signals. The differences of correlation and amplitude between the two respiratory signals were combined to define three types of respiration: respiration movement symmetry (RS), respiration movement asymmetry type I (T1RA), and respiration movement asymmetry type II (T2RA). We used the correlation coefficient to evaluate the changes in the similarities between two lungs for the three types of respiration. Then, using MI and TE, we investigated the coupling between two lungs. In particularly, TE quantified the transfer of information between two lungs on both directions. The analysis of interaction might provide a better understanding of lung mechanics responsible for pulmonary ventilation and fluid redistribution. In addition, these indices could be useful and effective for physicians to evaluate and diagnose the asymmetry in ULD.

II. EXPERIMENT

A. PARTICIPANTS

Twenty-one healthy male persons were recruited as subjects for this study. Their mean age was 24 years (SD = 1.46), and their average height was 170 cm (SD = 1.94). The subject selection criteria included the following: (1) no history of respiratory disorders, such as chronic bronchitis or bronchial asthma; and (2) no history of lung diseases, such as cough or emphysema. The experimental procedures were carefully explained to the subjects before the experiment. Informed consent was obtained from all subjects, and the subjects did not receive any remuneration or other benefits from the study. The study was approved by the Ethics Committee of Sun Yat-sen University.

B. STUDY PROTOCOL

The respiration bio-impedance signals of the subjects' left and right lungs were measured using a Biopac MP150 computerized system with two Biopac EBI100C electrobioimpedance amplifiers (BIOPAC, USA). All the signals were sampled at 1000 Hz and then resampled offline at 7.812 Hz. We used the tetrapolar impedance measurement obtained from four electrodes. One pair of electrodes was the stimulus electrode (I+, I−), which provided an input stimulus current to the upper side, near the intersection of

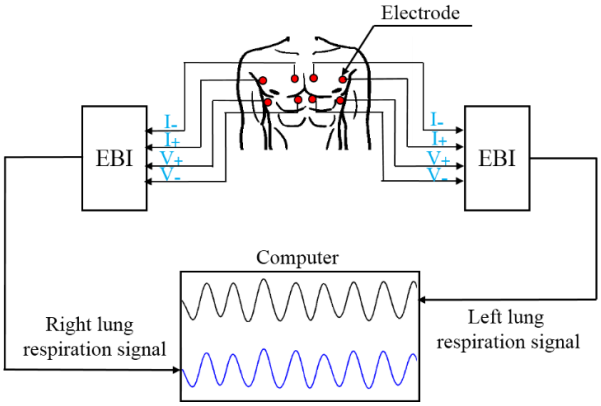

FIGURE 1. Schematic illustration of the experimental manipulation. EIB100C: electrobioimpedance amplifier.

the horizontal line formed by the nipples and the left (right) mid-axillary line and the upper side near the intersection of the horizontal line formed by nipples and the left (right) side of the sternal line. The other pair of electrodes measured the voltage (V+, V−) produced by changes in tissue conductivity on the lower side, near the intersection of the horizontal line formed by the nipples and the left (right) mid-axillary line and the lower side near the intersection of the horizontal line formed by the nipples and the left (right) side of the sternal line. A more detailed explanation of the electrode placement is provided in reference 11. A schematic illustration is shown in Fig. 1.

In order to avoid external noise interference, the experimental environment was keeping quiet when the subjects carried out experimental tasks. Each subject was instructed to breath spontaneously in the supine position for 6 minutes. Then, each subject was instructed to breath spontaneously in the right lateral position for 6 min. Finally, each subject was instructed to breathe spontaneously in the left lateral position for 6 min. The bio-impedance signals of the left and right lungs were measured simultaneously. A rest period of 2 min was provided between each trial to restore physical condition in supine position. The procedure was conducted one time per subject.

III. METHODS

After collecting the bio-impedance signals from the left and right lungs for the three postures, the bio-impedance signals were passed through band pass filtering and then were normalized. The bio-impedance signals were then analyzed to determine the similarities between the respiration of the left and right lungs, as indicated by the correlation coefficient (CC); the coupling between the respiration of the left and right lungs, as indicated by the mutual information (MI); and the interaction between the respiration of the left and right lungs, as indicated by the transfer entropy (TE). These measures were used to assess the complex physiological interactions between the two lungs. A flow diagram of the analysis is shown in Fig. 2.

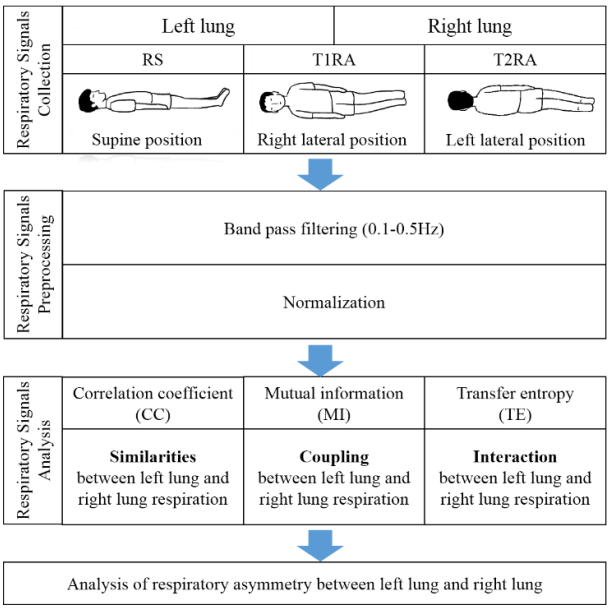

FIGURE 2. Flow diagram of analysis. RS: Respiration movement symmetry; T1RA: Respiration movement asymmetry type I; T2RA: Respiration movement asymmetry type II. Typical signals for the three types of respiration movement are illustrated in Fig. 3.

A. RESPIRATORY MOVEMENT BIO-IMPEDANCE SIGNAL PREPROCESSING

The respiratory bio-impedance signals were trimmed by 30 s at the beginning of each trial and by 30 s at the end of each trial to account for unbalanced physical condition. The signals were then segmented into 30-s intervals [26], and a sixth-order IIR Butterworth passband filter with a passband frequency between 0.1 Hz and 0.5 Hz was used to filter the bio-impedance signals to improve the signal-to-noise ratio [27]. Finally, the respiratory signals were normalized to eliminate differences between individual subjects.

The bio-impedance signals of left and right lungs were represented by two time series $X = \{x(n), n = 1, \cdots, N$ and $Y = \{y(n), n = 1, \cdots, N$, where N is the length of the bio-impedance signals and n is a progressive counter. The series were first normalized to have a zero mean and unit variance by subtracting the mean from each sample and dividing the result by the standard deviation, as shown in (1) and (2) below:

$$Z_x = \frac{X - mean(X)}{std(X)} \tag{1}$$

$$Z_y = \frac{Y - mean(Y)}{std(X)} \tag{2}$$

where Z_x and Z_y are the normalized bio-impedance signals of left and right lungs, respectively.

B. RESPIRATORY MOVEMENT BIO-IMPEDANCE SIGNAL ANALYSIS

The complex physiological interactions of each subject were evaluated in terms of the correlation coefficient (CC), mutual information (MI) and transfer entropy (TE).

1) CORRELATION COEFFICIENT

CC was used to assess the linear dependence between the normalized respiratory signals of right lung and left lung. The correlation coefficient was computed as shown in (3) and (4):

$$CC = \frac{\mathrm{Cov}(Z_x, Z_y)}{std\,(Z_x)\,std(Z_y)} = mean[Z_x * Z_y] \quad (3)$$

$$Cov\,(Z_x, Z_y) = mean\,\{[Z_x - mean\,(Z_x)][Z_y - mean\,(Z_y)]\} \quad (4)$$

where Z_x is the normalized respiratory signal of the left lung, Z_y is the normalized respiratory signal of the right lung, and $Cov\,(Z_x, Z_y)$ is the covariance of the time series Z_x and Z_y.

2) MUTUAL INFORMATION

MI is a measure of the relationship between two normalized respiratory signals. Specifically, it measures how much information is communicated between two systems. The formula for MI is given in [16]:

$$\mathrm{MI} = \sum_{\mathrm{i}=1}^{\mathrm{N}} \sum_{\mathrm{j}=1}^{\mathrm{N}} \mathrm{p}(\mathrm{Z_x\,(i)}\,,\mathrm{Z_y(j)}) \log \frac{\mathrm{p}(\mathrm{Z_x\,(i)}\,,\mathrm{Z_y(j)})}{\mathrm{p}\,(\mathrm{Z_x\,(i)})\,\mathrm{p}(\mathrm{Z_y\,(j)})} \quad (5)$$

where $p(Z_x\,(i)\,, Z_y(j))$ is the joint probability distribution. $p\,(Z_x\,(i))$ and $p(Z_y\,(j))$ are the marginal probability distributions of Z_x and Z_y, respectively.

It can be seen from (5) that if Z_x and Z_y are independent, then MI = 0. It should also be noted that MI is symmetric with respect to the interaction of Z_x and Z_y. Therefore, it does not have any directional sense.

3) TRANSFER ENTROPY

TE is a measure of the directed interaction between two normalized respiratory signals. In other words, it is an asymmetric measure that detects the coupling strength and directional information [28]. The transfer entropy from Z_x to Z_y is defined as follows:

$$TE_{x\to y} = \sum_{Z_y(i), Z_y(i-1), Z_x(i-1)} p(Z_y(i), Z_y\,(i-1)\,, Z_x\,(i-1)) \times log \frac{p(Z_y(i)/Z_y\,(i-1)\,, Z_x\,(i-1))}{p(Z_y(i)/Z_y(i-1))} \quad (6)$$

where $p(Z_y(i), Z_y 1), Z_x\,(-1))$ is the joint probability. $p(Z_y(i)/Z_y\,(i-1)\,, Z_x\,(i-1))$ and $p(Z_y(i)/Z_y(i-1))$ are conditional probabilities.

The fixed-bins approach was used to estimate the probability in (6), which was used to allocate data points to fixed, equally spaced bins. The following step was performed to rearrange the normalized respiratory signals Z_x and Z_y transform them into $U = \{u_1, u_2, \cdots, u_N, \}$ and $V = \{v_1, v_2, \cdots, v_N, \}$. The vector U and V were ranged from smallest value to largest value of Z_x and Z_y.

Then, equation (6) can be expressed as follows:

$$TE_{x\to y} = \sum_{v_i, v_{i-1}, u_{i-1}} p(v_i, v_{i-1}, u_{i-1}) log \frac{p(v_i, v_{i-1}, u_{i-1}) p(v_{i-1})}{p(v_{i-1}, u_{i-1}) p(v_i, v_{i-1})} \quad (7)$$

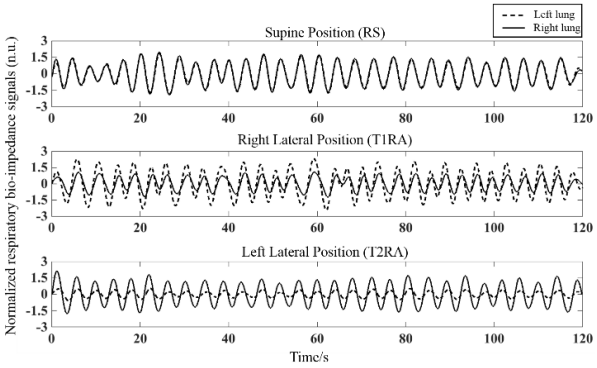

FIGURE 3. Example of a subject's normalized bio-impedance signals for the left and right lungs in the supine posture, right lateral posture, and left lateral posture. RS: Respiration movement symmetry indicated by the amplitudes of the left and right lung signals being similar; T1RA: Respiration movement symmetry type I, the amplitude of the left lung's signal is significantly higher than that of the right lung's signal; T2RA: Respiration movement symmetry type II, the amplitude of the left lung's signal is significantly lower than that of the right lung's signal.

Using the unified number of bins, Q = 8, in each dimension, (7) can be simplified as follows:

$$TE_{x\to y} = \sum_{a=1,b=1,c=1}^{Q} \frac{m_{a,b,c}}{P} log \frac{m_{a,b,c} m_b}{m_{b,c} m_{a,b}} \quad (8)$$

where$a$, b, and c are the indices of bins along v_i, v_{i-1}, and u_{i-1}, respectively; P is the total number of triplets of v_i, v_{i-1}, and u_{i-1}; $m_{a,b,c}$, $m_{b,c}$ and $m_{a,b}$, indexed by their subscripts, are the number of data points in the intersections of the one-dimensional bins; and the number of data points in the b^{th} bin in the v_{i-1} dimension is denoted by m_b.

C. STATISTICAL ANALYSIS

All of the data analyses were performed by offline processing in MATLAB (version 7, R2010b, MathWorks, USA). The data were expressed in terms of mean + SD. All of the statistical analyses were conducted using the SPSS software package (version 22, IBM). One-way ANOVAs were used to test for differences between the different sleep postures. The one-way ANOVA results were adjusted using a Bonferroni post hoc test. In all of the analyses, we considered p values $<$ 0.05 to be significant.

IV. RESULTS

A. THREE TYPES OF LEFT AND RIGHT LUNG RESPIRATION MOVEMENT

Fig. 3 shows an example of a subject's normalized bio-impedance signals from the left and right lung in the supine posture, right lateral posture, and left lateral posture. As illustrated in the upper panel of Fig. 3, the amplitude of the right lung bio-impedance signal was close to that of the left lung in the supine position. And the correlation between two lung bio-impedance signals was usually greater than 0.95. As illustrated in the middle panel of Fig. 3, the right lung bio-impedance signal had a lower amplitude than the left lung bio-impedance signal in the right lateral position. And

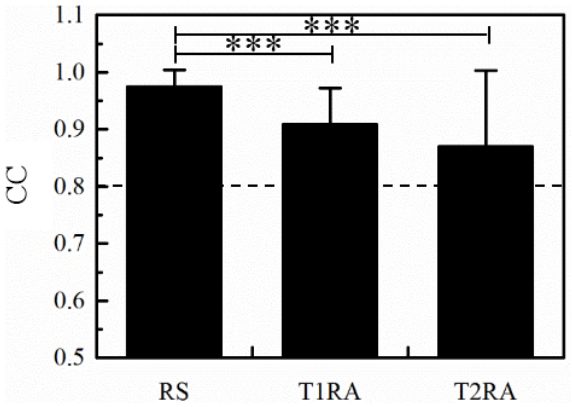

FIGURE 4. Correlation coefficient between left and right lung bio-impedance signal for respiration movement symmetry (RS), respiration movement asymmetry type I (T1RA), and respiration movement asymmetry type II (T2RA). The three types of respiration movement signal are illustrated in Fig. 3. CC: correlation coefficient; *** indicates a statistically extremely significant difference ($p < 0.001$). Dotted line indicates CC = 0.8.

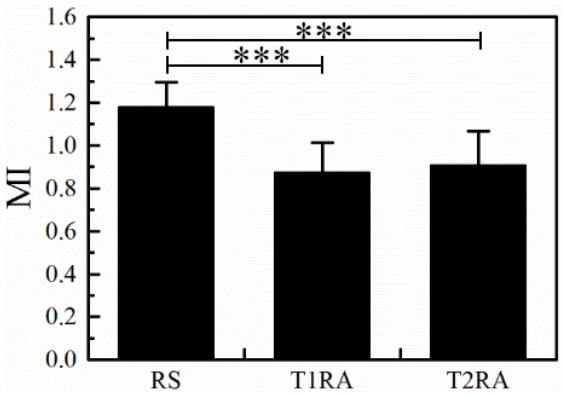

FIGURE 5. Mean mutual information between left and right lung bio-impedance signals for respiration movement symmetry (RS), respiration movement asymmetry type I (T1RA), and respiration movement asymmetry type II (T2RA). The three types of respiration movement signal are illustrated in Fig. 3. MI: mutual information; *** indicates a statistically extremely significant difference ($p < 0.001$).

the correlation between two lung bio-impedance signals was usually greater than 0.9. As illustrated in the lower panel of Fig. 3, the left lung bio-impedance signal had a lower amplitude than the right lung bio-impedance signal in the left lateral position. And the correlation between two lung bio-impedance signals was usually greater than 0.9.

Based on the waveform morphology, three types of respiration movement are defined by combination of the differences of correlation and amplitude between the two lung bio-impedance signals. **Respiration movement symmetry (RS), respiration movement asymmetry type I (T1RA),** and **respiration movement asymmetry type II (T2RA)** were defined as corresponding to breathing in the supine position, the right lateral position, and the left lateral position.

B. SIMILARITIES BETWEEN LEFT AND RIGHT LUNG RESPIRATION MOVEMENT

Correlation coefficients were calculated to assess similarities between left and right lung respiration movement. Fig. 4 shows the mean of CC between the left and right lung respiration signals in RS, T1RA, and T2RA during spontaneous breathing. The value of CC decreased from RS to T1RA and a further reduction was seen in T2RA.

Post hoc analysis indicated that the CC between left and right lung respiration movement was significantly larger in RS compared to T1RA and T2RA ($p < 0.001$ and $p < 0.001$, respectively). There was no significant difference in mean of CC between T1RA and T2RA. The results showed that left and right lung respiration movement was symmetric in RS but not in T1RA and T2RA. The similarities between left and right lung respiration movement were much greater in RS compared to T1RA and T2RA.

C. COUPLING BETWEEN LEFT AND RIGHT LUNG RESPIRATION MOVEMENT

Mutual information was calculated to quantify the coupling strength (shared information) between left and right lung respiration movement. Fig. 5 showed the mean of MI between the left and right lung respiration bio-impedance signals in RS, T1RA, and T2RA during spontaneous breathing. The mean of MI decreased from RS to T1RA, and slightly increased from T1RA to T2RA. Post hoc analysis indicated that the MI between left and right lung respiration movement was significantly larger in RS compared to T1RA and T2RA ($p < 0.001$ and $p < 0.001$, respectively). There was no significant difference in MI between T1RA and T2RA. The results revealed that the coupling strength between left and right lung respiration movement was greater in RS compared to T1RA and T2RA. The coupling strength between left and right lung respiration movement in T1RA was similar to T2RA.

D. INTERACTION BETWEEN LEFT AND RIGHT LUNG RESPIRATION MOVEMENT

Transfer entropy was used to characterize the transfer of information in both directions, i.e., from the left to the right lung and vice versa. Fig.6 showed the results of the transfer of information from the left to the right lung respiration movement (TE(L→R)) and the transfer of information from the right to left lung respiration movement (TE(R→L)) in RS, T1RA and T2RA. For the results of TE(L→R), Post hoc analysis indicated that the mean of TE(L→R) was significantly larger in T1RA ($p < 0.001$) and lower in T2RA ($p < 0.001$) compared to RS. The mean of TE(L→R) was significantly larger in T1RA ($p < 0.001$) compared to T2RA. For the results of TE(R→L), the mean of TE(R→L) increased from RS to T1RA, and a further increment was seen in T2RA. Post hoc analysis indicated that the TE(R→L) was significantly lower in RS compared to T1RA ($p < 0.001$), and T2RA ($p < 0.001$). TE(R→L) also was significantly lower in T1RA compared to T2RA ($p < 0.001$). These results indicated that there was a significantly effect of left and right lung respiration movement asymmetry on the amount of information transferred between left and right lung.

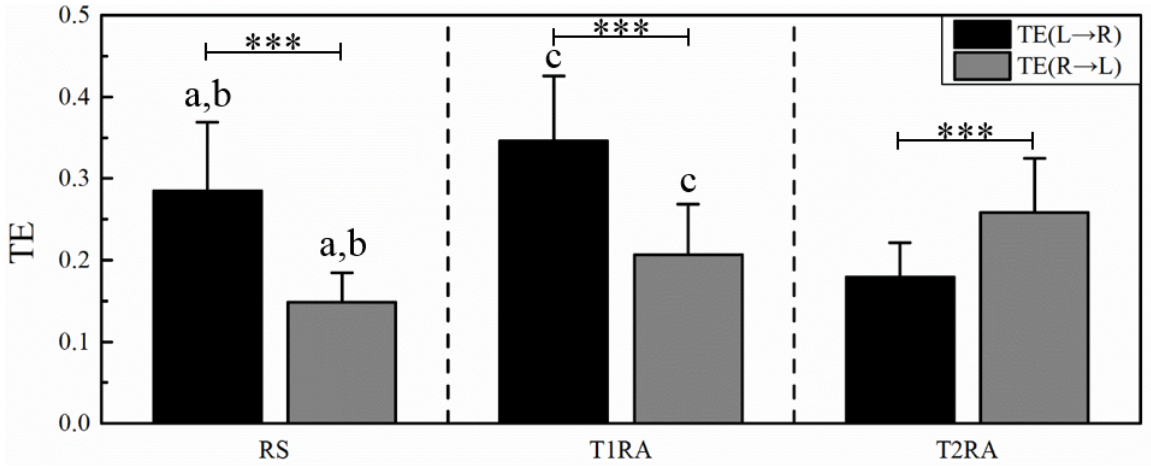

FIGURE 6. Transfer entropy in both directions (from left lung to right lung and vice versa) for respiration movement symmetry (RS), respiration movement asymmetry type I (T1RA), and respiration movement asymmetry type II (T2RA). The three types of respiration movement signal are illustrated in Fig. 3. *** indicates a statistically extremely significant difference ($p < 0.001$). a indicates $p<0.001$ when RS versus T1RA; b indicates $p<0.001$ when RS versus T2RA; c indicates $p<0.001$ when T1RA versus T2RA.

In addition, Fig. 6 illustrated the differences of the amount of information transferred between two directions, i.e. from the left to the right lung and vice versa. There was significantly difference between the TE(L→R) and TE(R→L) in RS, T1RA and T2RA, respectively. The ANOVA results showed that the mean of TE(L→R) was significant larger than the mean of TE(R→L) in RS ($p < 0.001$). The mean of TE(L→R) also was significant larger than the mean of TE(R→L) in T1RA ($p < 0.001$). However, the mean of TE(L→R) was significant lower than the mean of TE(R→L) in T2RA ($p < 0.001$). These results revealed that the main direction of information transfer was influenced by the type of respiration movement asymmetry.

V. DISCUSSION

The main aim of this study was to investigate the respiratory movement asymmetry of two lungs. Based on bio-impedance technique, we proposed two potential indices, including MI and TE, to assess the asymmetry of two lungs from the aspect of interaction. The major findings of this study are as follows. First, we tested three types of respiration movement asymmetry (RS, T1RA and T2RA) with three body positions. Second, the MI between left and right lung were greater for RS compared to T1RA and T2RA. This was evidence that MI is a potential tool to detect symmetry and asymmetry of two lungs. Third, the characteristics of interaction between two lungs for three types of respiration movement asymmetry were evaluated by TE. This supported the fact that TE is a potential tool to detect two types of asymmetry of two lungs.

A. THE RELATIONSHIP OF IMPEDANCE CHANGES WITH THE ASYMMETRY OF TWO LUNGS

The bio-impedance technique is well suited to studying variations in the air content and fluids induced conductive changes of lung tissue. It is well known that the impedance changes correlate well with actual lung volume changes [29]. The magnitude of impedance change was smaller in dependent lung than nondependent lung as shown in Fig.3. It was interesting to observe that there was a reversal results between T1RA and T2RA.

The reduction of magnitude of impedance change in dependent lung can probably be attributed to two reasons. One is that the inspired air decreased in dependent lung, because of the compression of dependent lung resulted from the weight of heart [30] and prevention of unilateral chest wall expandability [31]. Several observers have noted that the functional residual capacity of dependent lung was smaller than that of the nondependent lung in lateral positions [30] and the endexpiratory lung volume was significantly increased in the non-dependent lung regions of lateral positions [32]. Another one is the gravitational effect that may impact the distribution of blood and fluid in the lung [3], [33]. It was documented that the lung impedance values of CHF were lower on account of larger fluid volumes in their lungs [34]. The reduction of impedance change is probably explained by better blood and fluid in dependent lung.

Based on bio-impedance technique monitoring left and right lung respiration movement, we verified three types of respiration movement asymmetry (RS, T1RA and T2RA). Since unilateral lung disease patients (e.g., unilateral pulmonary edema, lobar pneumonia, or pneumothorax) presents worsening ventilation/perfusion mismatch and decreasing oxygenation with lung injure [2]. Thus, it is likely that three types of respiration movement asymmetry in unilateral lung disease patients are more serious.

B. MI AS A TOOL TO DETECT RESPIRATION SYMMETRY AND ASYMMETRY

The correlation coefficient is traditionally used to assess the similarity of waveforms and determine the approximately linear relationship between respiratory movement

signals [35], [36]. In this study, we confirmed the characteristics of three types of respiration using correlation coefficients. The results indicated that CC was greater than 0.95 for respiration symmetry, whereas CC was lower than 0.91 for both types of respiration asymmetry (T1RA and T2RA). These results suggest that respiration asymmetry could lead to decreasing similarity between left and right lung respiration movement for T1RA and T2RA. This finding is consistent with a previous study in which respiratory coordination between the left and right lungs was found to be best in dorsal decubitus, as indicated by the correlation coefficient for dorsal decubitus being significantly greater than for lateral positions [12].

MI has the potential to detect respiration movement symmetry and asymmetry. Respiration asymmetry leaded to a decrease in coupling strength between the two lungs. The results of MI between two lungs were similar to the results of CC, but there were some interesting differences in the findings that shed light on lung respiratory physiology. A comparison of respiration symmetry with respiration asymmetry (T1RA or T2RA) shows that the coupling strength between the two lungs is approximately reduced by 20%, which is significantly larger than the difference in the CC, by approximately 10%. This finding suggests that MI is a better tool than the CC for detecting respiration movement symmetry and asymmetry. The reason for this could be that CC only detects linear relationships between respiratory signals, whereas MI quantifies the coupling, which reflects the internal dynamics between respiratory signals. Because lungs respiratory activity depends on coordinated activity of respiratory muscles [37], the coupling strength could be utilized to reveal the common control input of bilateral respiratory muscles to lungs. When unilateral chest wall expandability is pressed in T1RA or T2RA, the reduce of coordinated activity of respiratory muscles leads to the decline of coupling strength between the two lungs.

C. TE AS A TOOL TO DETECT RESPIRATION ASYMMETRY (T1RA AND T2RA)

MI quantifies the non-directional nature of coupling between two lungs, but it has the disadvantage of being unable to discriminate the two types of respiration movement asymmetry. TE not only quantifies coupling strength, but also depicts directional information of interaction [38]. As Fig.6 showed, the amount of information transferred from left to right lung (TE(L→R)) was larger in T1RA compared to T2RA. Moreover, the amount of information transferred from right to left lung (TE(R→L)) was lower in T1RA compared to T2RA. Thus, the results of Fig.6 revealed that TE has the potential to detect respiration movement asymmetry (T1RA and T2RA).

From a physiological mechanism standpoint, the TE can reveal pulmonary ventilation redistribution. A general conclusion from Fig.6 is that TE(non-dependent lung → dependent lung) is larger than TE(dependent lung → non-dependent lung). In T1RA, TE(L→R) was significantly larger than TE(R→L) whereas TE(L→R) was significantly lower than TE(R→L) in T2RA. It demonstrated that the non-dependent lung has predominance on improving pulmonary ventilation. It can be speculated that the increase of pulmonary ventilation in nondependent lung is caused by the increase of lung compliance. It has documented that both static and dynamic lung compliance were increased from supine posture to lateral postures [39].

TABLE 1. The results of time-lagged correlation and zero-lag correlation.

Type	CC(n.u.)	Left_CC(n.u.)	Right_CC(n.u.)
RS	**0.974±0.030**	0.971±0.031	0.942±0.031
T1RA	0.909±0.063	**0.925±0.060**	0.859±0.071
T2RA	0.869±0.133	0.837±0.137	**0.871±0.126**

The data were expressed in terms of mean ± SD. CC: $CC(Z_x(i) * Z_y(i))$, Correlation coefficient; Left_CC: $CC(Z_x(i-1) * Z_y(i))$, one point time lag in left respiration impedance signal . Right_CC : $CC(Z_x(i) * Z_y(i-1))$, one point time lag in right respiration impedance signal. CC is zero-lag correlation. Left_CC and Right_CC are time-lagged correlation.

Other findings of our study also deserve to be discussed. As Fig.6 showed, TE(L→R) was significantly larger than TE(R→L) in RS, which was consistent with the result of T1RA. It can be speculated that the disturbance of cardiac motion may contribute to the difference in RS. The human heart is situated in the middle mediastinum, but approximately two thirds of it on the left side of the middle mediastinum [40]. Therefore, the interference effect of cardiac impulse on the respiration motion of the left lung is more serious, which probably leads to the larger value of TE(L→R) in RS.

From another point of view, the causality relation between two lungs is also verifiable by using the time-lagged correlations. As shown in Table 1, the value of Left_CC is larger than CC in T1RA and the value of Right_CC is larger than CC in T2RA. These results suggested that there was a time lag between two lungs in information interaction. Moreover, these results indicated that it is feasible for TE to evaluate the causality relation between two lungs.

D. LIMITATIONS

In this study, we found that MI and TE are powerful indices to evaluating the asymmetry between two lungs. In order to validate the practicality of new features, linear discriminant analysis was used to determine RS, T1RA, and T2RA. RS were separated from other two types of respiratory asymmetry with a classification accuracy rate of 78.1%. T1RA were separated from T2RA with an accuracy rate of 80.9%. It is noteworthy that the classification performances of detecting ULD would be better after modifying proposed method by reference to doctor's expertise and patient involvement.

At present, our study is preliminary finding which suggest that MI and TE has potential to detect differences between heathy subject and ULD patients. In the future, we will refer to doctor's expertise and combine clinical indicators and new features to improve accuracy of detecting ULD patients. In addition, using proposed method, we can develop a wearable medical device based on body sensors network proposed in previous study [41], [42]. Another limitation of this study is that we did not perform the experiment under well-controlled conditions that would have considered several related factors, such as gender and body fat percentage. In future research, it will be necessary to control these factors well to verify the effect of each factor on complex physiological interactions between two lungs.

VI. CONCLUSION

To investigate the asymmetry between left and right lung, we exploited the bio-impedance approach to characterize respiratory movement signals in the left and right lung. Then, we evaluated the complex physiological interactions between the two lungs, using MI and TE to characterize lung respiration movement asymmetry. We can draw the following conclusions from this study:

1) MI assessed the coupling strength between the two lungs and was able to detect respiration movement symmetry and asymmetry between the two lungs. Comparing respiration symmetry to respiration movement asymmetry, an approximately 20% gap in MI was found.

2) TE assessed the amount of information transferred in both direction and was able to detect the two types of respiration movement asymmetry (T1RA and T2RA). TE(R→L) was found to increase progressively when shifting RS to T1RA and then to T2RA.

3) MI and TE are useful tools to characterize respiration movement in the complex physiological interactions between the two lungs. These indices probably have important clinical implications in evaluating and determining the asymmetry in ULD.

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