Estimation of Bilateral Asynchrony between Diaphragm Mechanomyographic Signals in Patients with Chronic Obstructive Pulmonary Disease

Luis Estrada, *IEEE Member*, Abel Torres, *IEEE Member*, Leonardo Sarlabous, José A. Fiz, Joaquim Gea, Juana Martínez-Llorens and Raimon Jané, *IEEE Member*

Abstract—**The aim of the present study was to measure bilateral asynchrony in patients suffering from Chronic Obstructive Pulmonary Disease (COPD) performing an incremental inspiratory load protocol. Bilateral asynchrony was estimated by the comparison of respiratory movements derived from diaphragm mechanomyographic (MMGdi) signals, acquired by means of capacitive accelerometers placed on left and right sides of the rib cage. Three methods were considered for asynchrony evaluation: Lissajous figure, Hilbert transform and Motto's algorithm. Bilateral asynchrony showed an increase at 20, 40 and 60% (values of normalized inspiratory pressure by their maximum value reached in the last inspiratory load) while the very severe group showed and increase at 20, 40, 80, and 100 % during the protocol.These increments in the phase's shift can be due to an increase of the inspiratory load along the protocol, and also as a consequence of distress and fatigue. In summary, this work evidenced the capability to estimate bilateral asynchrony in COPD patients. These preliminary results also showed that the use of capacitive accelerometers can be a suitable sensor for recording of respiratory movement and evaluation of asynchrony in COPD patients.**

I. INTRODUCTION

Respiration is an autonomous activity essential for life and responsible for regulating the gas exchange. The breathing process, made up by alternating inspiratory and expiratory activities, is oscillatory in nature and inside its mechanism underlies a respiratory rhythm generator. Synchronization, a complex phenomenon identified not only in living systems but also found in many other scientific scenarios, involves the adjustment of rhythmicity between oscillatory systems [1]. The breathing dynamics can present states of synchrony and non-synchrony during its time course. One of the most studied synchronization phenomena occurs between the excursion of thoracic (TH) and abdominal (AB) compartments, which exhibits a certain degree of shift in the course of breathing. The lack of coordination in the thoraco-abdominal (TA) motion can be a sign of respiratory diseases [2], sleep disorders [3], [4] and also be associated with patient-ventilator interactions [5], [6]. Moreover, a particular TA asynchrony condition, clinically known as paradoxical movement is referred when the TA motion is completely in opposite directions [7], [8]. Nowadays, one of the most widely accepted methods for evaluation of respiratory movement is the respiratory inductive plethysmography [9], but its effectiveness can be reduced when patient manipulation is a challenge (e.g. monitoring of neonates and small children) [10]. Additionally, several techniques based on conventional [11], [12] and also novel [13], [14] signal processing techniques have been suggested in order to obtain more accurate results when the respiratory signals are analyzed. In this context, several studies have employed accelerometer devices positioned at both sides of the body for the recording of the respiratory movement and extracting information about its mechanical activity [15], [16] [17]. Waisman et al. [15] observed that in animal model local chest wall displacement can be used as an index for early detection of deterioration of mechanical ventilation. On the other hand, Lapi et al. [16] analyzed the respiratory rate recorded in normal subjects and patients suffering from obesity and idiopathic scoliosis and it was concluded that the use of accelerometers can be a reliable alternative to actual technologies for monitoring of respiration-related chest wall movement. In a similar way, Sarlabous et al. [17] shown that in COPD patients can be possible monitoring respiratory activity through accelerometer devices. As it has been highlighted, the majority of the studies are focused on evaluating TA asynchrony. However, we consider that the assessment of respiratory discoordination is not only an exclusive task for the study between TH and AB compartments, but can also be essential for the evaluation of bilateral asynchrony (between left and right portions of the diaphragm). In fact, it has been reported symmetric patterns between left and right TA compartments in healthy male and female subjects from different age group [18]. Evidence related to the TA asynchrony have been found in patients suffering from Chronic Obstructive Pulmonary Disease (COPD), a condition that makes breathing difficult [7], [19]. However, to the best of our knowledge, bilateral asynchrony has not been explored in these patients. In this perspective, the aim of the present study was to examine the presence of bilateral asynchrony in COPD patients. To reach this objective, the low frequency component of diaphragm

The first author was supported by Instituto para la Formación y Aprovechamiento de Recursos Humanos and Secretaría Nacional de Ciencia, Tecnología e Innovación (IFARHU-SENACYT Program) from the Panama Government under grant 270-2012-273. This work was supported in part by Ministerio de Economía y Competitividad from the Spain Government under grant TEC2010-21703-C03- 01.

L. Estrada, A. Torres, and R. Jané are with Universitat Politècnica de Catalunya (UPC), Institut de Bioenginyeria de Catalunya (IBEC) and Biomedical Research Networking Center in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), c/. Baldiri Reixac 4, 08028, Barcelona, Spain. (e-mail: lestrada@ibecbarcelona.eu,abel.torres@upc.edu, rjane@ibecbarcelona.eu).

L. Sarlabous is with CIBER-BBN (e-mail:lsarlabous@ibecbarcelona.eu).

J. A. Fiz is with Hospital Germans Trias i Pujol, Spain, IBEC and CIBER-BBN. (e-mail: jafiz@msn.com).

J. Gea and J.Martínez-Llorens are with Hospital del Mar, Barcelona, Spain (e-mail: jgea@imim.es, jmartinez@imas.imim.es).

mechanomyographyic (MMGdi) signals recorded on the left and right sides of the rib cage was studied.

II. Methods

A. Patient population

This study was carried out on a database previously recorded at Hospital del Mar in Barcelona, Spain. It consists of seven severe and four very severe male COPD patients. Table I reports the mean and standard deviation values of the clinical characteristics and the parameters of the pulmonary function tests the COPD patients.

TABLE I. DEMOGRAPHIC, ANTHROPOMETRIC AND SPIROMETRIC CHARACTERISTICS OF COPD PATIENTS

	Severe	Very severe
Age (yrs)	72.57 ± 3.78	63.00 ± 8.16
Height (m)	1.64 ± 0.07	1.69 ± 0.05
Mass (kg)	64.14 ± 12.25	61.75 ± 10.50
BMI (kg/m^2)	23.81± 3.73	21.69 ± 2.97
FEV_1 (%)	40.29± 6.02	20.50 ± 3.00
FVC (%)	60.43 ± 11.93	45.25 ± 3.30
FEV_1/FVC (%)	48.81± 2.79	33.11 ± 6.15

BMI = body mass index, FEV_1: Forced expiratory volume in one second, FVC: forced vital capacity, FEV_1/FVC: Proportion of the forced vital capacity exhaled in the first second.
%: percentage regarding the predicted value.
Data presented as mean ± standard deviation.

B. Signal acquisition

Inspiratory pressure (IP) was measured with a differential pressure transducer (TSD160, Biopac System, Santa Barbara, CA, USA). The MMGdi activity was recorded bilaterally (left: $MMGdi_L$, right: $MMGdi_R$) with two single-axial capacitive accelerometers (K-Beam 8305A, Kistler, Amherst, USA) located in the rib cage area at the level of the 7th and 8th intercostal spaces, along the midclavicular line. The recorded signals were amplified, analog filtered, digitized with an A/D system (MP100, Biopac Systems, Santa Barbara, CA, USA) with resolution of 12 bits and a sampling rate of 2 kHz. IP and MMGdi signals were decimated to a sampling rate of 200 Hz, to reduce the amount of data.

C. Respiratory protocol

All COPD patients were instructed to perform an incremental inspiratory load protocol. They were comfortably seated and breathed via a mouthpiece whilst wearing a disposable nose clip to prevent nasal breathing. IP was controlled by adding externals weights (50 g ~ 10 cmH_2O of IP) to a plunger, which occlude a patient respiratory circuit. Patients must perform an IP to open the circuit by lifting plunger and the added weights. Conversely, on exhalation, the breathing circuit allows patients to breathe out normally, without any obstruction. During the protocol, stepwise weights were added every two-minute intervals. Patients started to breathe spontaneously at tidal volume (without weights) and ended when they can no longer breathe (maximum weight reached and maximum IP). Additionally, medical staff encouraged patients to maintain the breathing patterns through the protocol.

D. Signal pre-processing

Smoothed low-frequency versions of $MMGdi_L$ and $MMGdi_R$ signals (LF_L and LF_R, respectively) were obtained by applying a procedure based on the empirical mode decomposition [20]. This procedure is described in detail in [21]. Fig. 1 shows an example of IP signal, and LF_L, LF_R components of two representative patients who performed the incremental inspiratory load protocol.

E. Asynchrony estimation

Bilateral asynchrony was estimated between LF_L and LF_R signals by the following techniques:

1) *Lissajous figure:* also known as Kono-Mead plot, is a parametric representation (Cartesian plane) of the motion between two compartments [8], [11], [12]. The phase angle is calculates by

$$\theta = \sin^{-1}\left(\frac{m}{s}\right) \quad (1)$$

Where θ is the phase angle, m is the width of Lissajous figure in the middle of the ordinate excursion and s is the width of the Lissajous figure at its largest abscissa excursion.

2) *Motto's algorithm*: given two signals $x_1(t)$ and $x_2(t)$, they are converted into binary numbers, and then are inputs to a logic or exclusive (XOR) gate. The phase difference φ is given by [13]

$$\varphi = \frac{\tau}{T} \quad (2)$$

where τ is the total time where signals are different over a period of time T.

3) *Hilbert transform:* give the instantaneous amplitude and phase for a signal $x(t)$ via construction of the analytical signal $\zeta(t)$, which is a complex function of time defined as [1]

$$\zeta(t) = x(t) + ix_H(t) = A(t)e^{i\phi(t)} \quad (3)$$

where $x_H(t)$ is the Hilbert transform of $x(t)$.

The instantaneous amplitude $A(t)$ and phase $\phi(t)$ are defined as

$$A(t) = \sqrt{x^2(t) + x_H^2(t)} \quad (4)$$

$$\phi(t) = \tan^{-1}\left(\frac{x_H(t)}{x(t)}\right) \quad (5)$$

Given two signals $x_1(t)$ and $x_2(t)$, where $\phi_1(t)$ and $\phi_2(t)$ are its respective instantaneous phases, the instantaneous phase difference $\phi_1(t) - \phi_2(t)$ can be obtained by

$$\Delta\phi(t) = \tan^{-1}\left(\frac{x_{H1}(t)x_2(t) - x_1(t)x_{H2}(t)}{x_1(t)x_2(t) + x_{H1}(t)x_{H2}(t)}\right) \quad (6)$$

F. Data analysis

Respiratory cycles were identified by detecting the start of inspiratory cycle in IP signal. An estimation of asynchrony was obtained by averaging five consecutive values of asynchrony for each 2-min interval stepwise weights if, through visual inspection, they were not corrupted by movement, cough or other artifacts. The asynchrony was set to [0º, 180º] interval. With the aim of comparing data, the IP signal was normalized by their maximum value reached in the last inspiratory load. Six normalized increasing inspiratory loads (5, 20, 40, 60, 80 and 100 %) were analyzed. The signal analysis was performed in MATLAB (v. R2011, Natick, Massachusetts).

III. RESULTS

A phase shift between LF_R and LF_L components have been observed in patients suffering from COPD during the incremental inspiratory load protocol. Fig.1 illustrates two COPD patients during (a) a stepped increase of 10 cmH_2O in the IP signal, the right (b) and left (c) low frequency of both hemidiaphragms and the (d) asynchrony estimation using Motto's algorithm for each breathe. Patient 1 (left panel) showed lower asynchrony in comparison to patient 2 (right panel).

For a better visual inspection of bilateral asynchrony, two segments, before and after the increase of IP, were highlighted for patient 1 (226.0-244.0 s and 260.7-280.5) and for patient 2 (337.7-345.3 and 367.1-374.3). Moreover, Fig. 2 reflects the progression of bilateral asynchrony in the severe two COPD patients during the incremental inspiratory load protocol evaluated by the Lissajous figure, Hilbert transform and Motto's algorithm. Results are presented by using a moving average with a window size of 5 and a step size of 1. Patient 2 (Fig. 2b) showed a predominant asynchrony along the protocol in comparison to patient 1 (Fig. 2a). The three techniques showed a similar performance for the phase shift evaluation. Fig 3 illustrates the effect of the gradually increasing inspiratory load (normalized to the maximum IP reached) over bilateral asynchrony evaluated by Motto's algorithm in severe and very severe COPD patients.

For the case of severe group, it was observed an increase in the bilateral asynchrony at 20, 40 and 60% values of normalized IP whilst the very severe group showed an increase at 20, 40, 80, and 100 %. Both COPD groups have shown phases shift values ranging from few degrees to 160 degrees with high variability during the protocol (Fig.3).

IV. DISCUSSION

In the current work, bilateral asynchrony was evaluated in severe and very severe patients suffering from COPD who performed an incremental inspiratory load protocol. With this intention, Lissajous figure, Hilbert transform and Motto's algorithm were used to measure the phase shift between the LF_R and LF_L components of MMGdi signals collected from both sides of thoracic cage. The use of the three techniques showed comparable results. Asynchrony analysis can be influenced due to noisy signals [11],[14], and also be affected by the different waveforms found in the respiratory movement [12]. We reported a wide range of phase shifts, from a few degrees to values close to 160 degrees in the protocol for the COPD patients. The severe COPD group showed an increase at 20, 40 and 60% of the normalized inspiratory load and the very severe COPD group at 20, 40, 80 and 100%, reflecting the latter higher variability.

It can be argued that when patients breathe against an inspiratory load, they can present greater bilateral asynchrony. Moreover, because of the fact that sustain a medical protocol is a challenge for COPD patients, the phase shifts can be attributed to simple distress or fatigue, factors which are present in TA studies [8]. However, as it has been reported, the variability of asynchrony does not necessary reflect a fatigue condition, and hence it cannot be a reliable predictor of respiratory muscle fatigue [8]. Classically, TA asynchrony can be evaluated by means of RIP; but, this technique cannot allow the study of bilateral asynchrony by itself. On the other hand, Ragnarsdóttir and Kristinsdóttir [18] have reported symmetrical breathing movements between TA compartments in healthy male and female subjects from age groups. The preliminary findings of this study have confirmed the presence of bilateral asynchrony through evaluation of mechanical signals acquired from capacitive accelerometers. This study is, to knowledge of the authors, the first attempt to examine bilateral asynchrony in COPD patients who accomplished an incremental

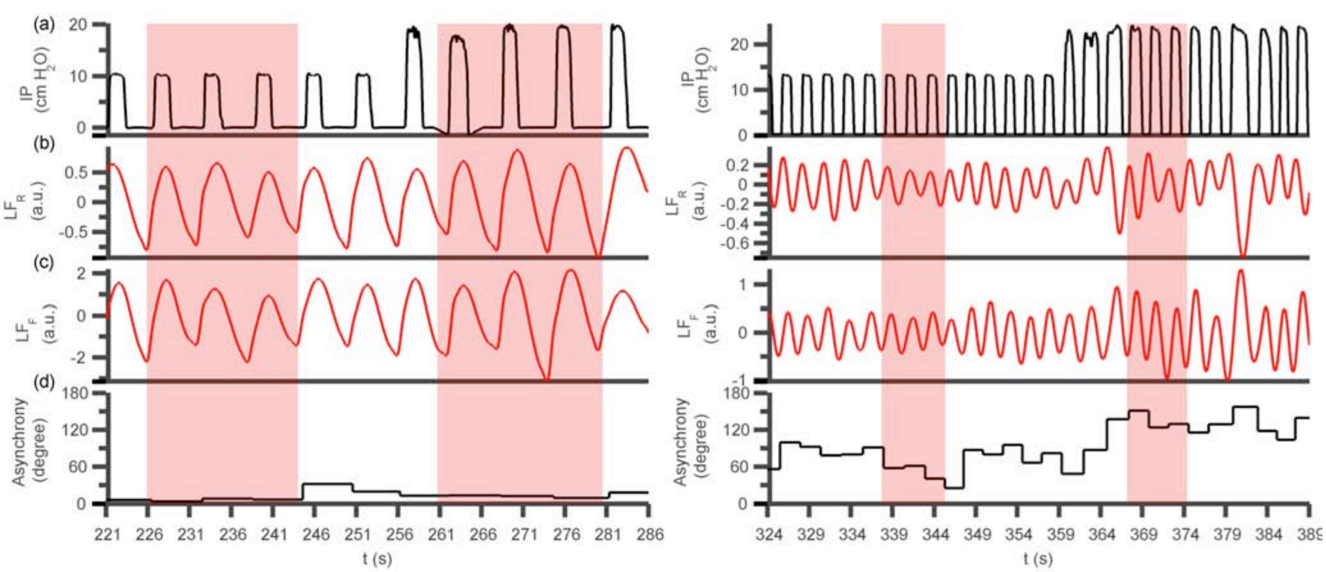

Figure 1. Two severe COPD patients performing the incremental inspiratory load protocol with (a) an increase of IP in ~ 10 cmH_2O and evolution of (b) LF_R and (c) LF_F components and (d) bilateral asynchrony. First patient (left panel) does not present a visible asynchrony as it is shown in the intervals (226.0 – 244.0 s) and (260.7 – 280.5 s). Second patient (right panel) showed a mild relative asynchrony (337.7 – 345.3 s) and a high asynchrony (367.1 – 374.3 s). Intervals are highlighted by vertical light red bars. Asynchrony values presented from Motto's algorithm results.

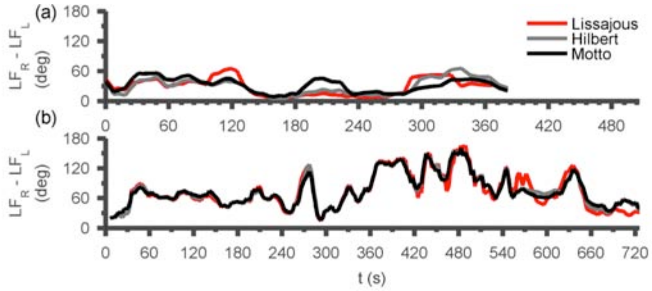

Figure 2. Time evolution of bilateral asynchrony from the (a) first and (b) second COPD patients using the Lissajous, Hilbert and Motto's technique. Data was smoothed using a moving average (window size: 100 and step size: 1).

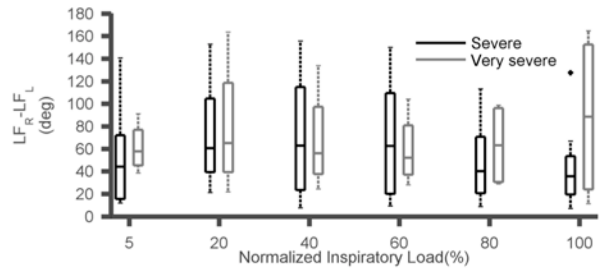

Figure 3. Effect of gradually increasing inspiratory load in (a) severe and (b) very severe COPD patients during the incremental inspiratory load protocol. Asynchrony values presented from Motto's algorithm results. The IP signal was normalized by their maximum value reached in the last inspiratory load.

inspiratory load protocol. Recently, Lapi et al. [16] assessed respiratory rate in signals recorded by accelerometers positioned on opposite sides of the chest wall. They briefly reported a minimal phase shift between accelerometric and respiratory signal. Nonetheless, the trigger of bilateral asynchrony phenomenon has to be investigated.

V. Conclusions

This work has shown evidence of how to estimate bilateral asynchrony in COPD patients through the use of accelerometers. Due to its flexibility to be positioned at different parts of the body these devices are gaining widely acceptation to measure mechanical respiratory patterns. These preliminary findings should be confirmed in a large patient population and also be compared with healthy subjects. Further studies would require confirming asynchrony in COPD patients and its relationship with severity and inspiratory loads. In a future, accelerometers can be a complementary tool for asynchrony evaluation not only bilateral but also between TH and AB compartments.

References

[1] A. Pikovsky, M. Rosemblum, and J. Kurths, *Synchronization: A Universal Concept in Nonlinear Sciences. Vol. 12*. New York: Cambridge University Press, 2001.

[2] G. M. Davis, D. M. Cooper, and I. Mitchell, "The measurement of thoraco-abdominal asynchrony in infants with severe laryngotracheobronchitis," *Chest*, vol. 103, no. 6, pp. 1842–1848, Jun. 1993.

[3] S. A. Immanuel, M. Kohler, Y. Pamula, M. M. Kabir, D. A. Saint, and M. Baumert, "Increased variability in respiratory parameters heralds obstructive events in children with sleep disordered breathing," in *Proc 35th Annu Int Conf IEEE EMBS*, 2013, pp. 2024–2027.

[4] A. De Groote, J. Groswasser, H. Bersini, P. Mathys, and A. Kahn, "Detection of obstructive apnea events in sleeping infants from thoracoabdominal movements," *J Sleep Res*, vol. 11, no. 2, pp. 161–8, Jun. 2002.

[5] C. Sinderby, S. Liu, D. Colombo, G. Camarotta, A. S. Slutsky, P. Navalesi, and J. Beck, "An automated and standardized neural index to quantify patient-ventilator interaction," *Crit Care*, vol. 17, no. 5, p. R239, Oct. 2013.

[6] C. S. Sassoon and G. T. Foster, "Patient-ventilator asynchrony," *Curr Opin Crit Care*, vol. 7, no. 1, pp. 28–33, Feb. 2001.

[7] A. Aliverti, M. Quaranta, B. Chakrabarti, A. L. Albuquerque, and P. M. A. Calverley, "Paradoxical movement of the lower ribcage at rest and during exercise in COPD patients," *Eur Respir J*, vol. 33, no. 1, pp. 49–60, Jan. 2009.

[8] J. Hammer and C. J. L. Newth, "Assessment of thoraco-abdominal asynchrony," *Paediatr Respir Rev*, vol. 10, no. 2, pp. 75–80, Jun. 2009.

[9] A. Eberhard, P.-Y. Carry, P. Baconnier, P. Cotte, and G. Benchetrit, "Evaluation of respiratory inductive plethysmography: accuracy for analysis of respiratory waveforms," *Chest*, vol. 111, no. 4, pp. 910–915, 1997.

[10] L. J. Goldman, "Nasal airflow and thoracoabdominal motion in children using infrared thermographic video processing," *Pediatr Pulmonol*, vol. 47, no. 5, pp. 476–486, May 2012.

[11] S. Golemati, I. Moupagiatzis, D. Athanasopoulos, M. Vasilopoulou, C. Roussos, and I. Vogiatzis, "Comparative analysis of phase difference estimation methods quantifying asynchronies between compartmental chest wall volume signals," in *Proc 31th Annu Int Conf IEEE EMBS*, 2009, pp. 2871–2874.

[12] G. K. Prisk, J. Hammer, and C. J. L. Newth, "Techniques for measurement of thoracoabdominal asynchrony," *Pediatr Pulmonol*, vol. 34, no. 6, pp. 462–472, Dec. 2002.

[13] A. L. Motto, H. L. Galiana, K. a Brown, and R. E. Kearney, "Automated estimation of the phase between thoracic and abdominal movement signals," *IEEE Trans Biomed Eng*, vol. 52, no. 4, pp. 614–621, Apr. 2005.

[14] S. Immanuel, M. Kohler, Y. Pamula, M. M. Kabir, D. a Saint, and M. Baumert, "Thoraco-abdominal asynchrony in children during quiet sleep using Hilbert transform," *Proc 34th Annu Int Conf IEEE EMBS*, vol. 2012, pp. 3448–51, Jan. 2012.

[15] D. Waisman, A. Faingersh, C. Levy, E. Konyukhov, F. I. C. Klotzman, A. Rotschild, and A. Landesberg, "Early detection of deteriorating ventilation by monitoring bilateral chest wall dynamics in the rabbit.," *Intensive Care Med*, vol. 38, no. 1, pp. 120–127, Jan. 2012.

[16] S. Lapi, F. Lavorini, G. Borgioli, M. Calzolai, L. Masotti, M. Pistolesi, and G. a Fontana, "Respiratory rate assessments using a dual-accelerometer device," *Respir Physiol Neurobiol*, vol. 191, pp. 60–66, Jan. 2014.

[17] L. Sarlabous, A. Torres, J. a Fiz, J. Gea, J. M. Martinez-Llorens, and R. Jane, "Evaluation of the respiratory muscular function by means of diaphragmatic mechanomyographic signals in COPD patients," in *Proc 33st Annu Int Conf IEEE EMBS*, 2009, pp. 3925–3928.

[18] M. Ragnarsdóttir and E. K. Kristinsdóttir, "Breathing movements and breathing patterns among healthy men and women 20-69 years of age. Reference values," *Respiration*, vol. 73, no. 1, pp. 48–54, Jan. 2006.

[19] R. Priori, A. Aliverti, A. L. Albuquerque, M. Quaranta, P. Albert, and P. M. A. Calverley, "The effect of posture on asynchronous chest wall movement in COPD," *J Appl Physiol*, vol. 114, no. 8, pp. 1066–1075, Apr. 2013.

[20] N. E. Huang, Z. Shen, S. R. Long, M. C. Wu, H. H. Shih, Q. Zheng, N.-C. Yen, C. C. Tung, and H. H. Liu, "The empirical mode decomposition and the Hilbert spectrum for nonlinear and non-stationary time series analysis," *Proc R Soc A Math Phys Eng Sci*, vol. 454, no. 1971, pp. 903–995, Mar. 1998.

[21] L. Estrada, A. Torres, L. Sarlabous, J. A. Fiz, and R. Jané, "Respiratory Rate Detection by Empirical Mode Decomposition Method Applied to Diaphragm Mechanomyographic Signals," in *Proc 36th Annu Int Conf IEEE EMBS*, 2014 (in press).