Annals of Biomedical Engineering, Vol. 40, No. 10, October 2014 (© 2014) pp. 2072–2083
DOI: 10.1007/s10439-014-1073-x

Electrocardiogram Derived Respiratory Rate from QRS Slopes and R-Wave Angle

JESÚS LÁZARO,[1,2] ALEJANDRO ALCAINE,[1,2] DANIEL ROMERO,[2,3] EDUARDO GIL,[1,2] PABLO LAGUNA,[1,2] ESTHER PUEYO,[1,2] and RAQUEL BAILÓN[1,2]

[1]BSICoS group, Aragón Institute of Engineering Research (I3A), IIS Aragón, University of Zaragoza, Zaragoza, Spain; [2]Centro de Investigación Biomédica en Red en Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Madrid, Spain; and [3]Laboratoire Traitement du Signal et de l'Image, Université de Rennes I, Rennes, France

(Received 31 March 2014; accepted 16 July 2014; published online 14 August 2014)

Associate Editor Anastasios G. Bezerianos oversaw the review of this article.

Abstract—A method for estimating respiratory rate from electrocardiogram (ECG) signals is presented. It is based on QRS slopes and R-wave angle, which reflect respiration-induced beat morphology variations. The 12 standard leads, 3 leads from vectorcardiogram (VCG), and 2 additional non-standard leads derived from VCG loops were analyzed. The following series were studied as ECG derived respiration (EDR) signals: slope between the peak of Q and R waves, slope between the peak of R and S waves, and the R-wave angle. Information from several EDR signals was combined in order to increase the robustness of estimation. Evaluation is performed over two databases containing ECG and respiratory signals simultaneously recorded during two clinical tests with different characteristics: tilt test, representing abrupt cardiovascular changes, and stress test representing a highly non-stationary and noisy environment. A combination of QRS slopes and R-wave angle series derived from VCG leads obtained a respiratory rate estimation relative error of $0.50 \pm 4.11\%$ (measuring 99.84% of the time) for tilt test and $0.52 \pm 8.99\%$ (measuring 96.09% of the time) for stress test. These results outperform those obtained by other reported methods, both in tilt and stress testing.

Keywords—ECG-derived respiration (EDR), Exercise, Tilt test, Respiratory frequency, Robustness, QRS slopes, R-wave angle, Stress testing.

INTRODUCTION

Respiratory rate observation remains the first and often the most sensitive marker of acute respiratory dysfunction,[8] and it is a sensitive indicator of critical illness.[19] Respiration is also very relevant in sports training, since the anaerobic point (the point when the exercise shifts from aerobic to anaerobic) is determined from respiratory rate and other breathing-related parameters among others.[10] Respiration is usually recorded by techniques such as spirometry, pneumography or plethysmography. These techniques require cumbersome devices which may interfere with natural breathing and which are unmanageable in certain situations such as stress test or sleep studies.[2] Therefore, obtaining accurate respiratory information from non-invasive devices is very useful.

Several algorithms for deriving respiration from non-invasive devices such as pulse oximeters[5,13] or electrocardiographs[2,18] have been developed. Electrocardiogram (ECG)-based methods are so-called ECG derived respiration (EDR) methods. Known EDR methods can be divided by the information that they exploit. On one hand, it is well known that respiration modulates the heart rate making it higher during inspiration than during expiration.[9,28] On the other hand, respiration also affects beat morphology through impedance changes in the thorax and relative movements of the electrodes with respect to the heart. Many methods based on respiration-induced beat morphology variations have been developed. Some of them are based on R wave amplitudes either with respect to the baseline or to the S wave amplitude,[16] obtaining respiratory information from the ECG in a simple way. Other developed beat-morphology-based methods are more complex, such as those that exploit QRS area variations[21] or electrical axis rotation.[22] In Bailón *et al.*,[3] a method based on least squares estimation of the rotation angles of the heart electrical axis between successive VCG loops and a reference loop was evaluated in stress testing

Address correspondence to Jesús Lázaro, BSICoS group, Aragón Institute of Engineering Research (I3A), IIS Aragón, University of Zaragoza, Zaragoza, Spain. Electronic mail: jlazarop@unizar.es

0090-6964/14/1000-2072/0

recordings. Some EDR methods that exploit both beat occurrence and morphology have been also proposed.[14,27]

A new beat-morphology-based method is presented in this paper. It is based on QRS slopes and R-wave angle variations. QRS slopes have been previously studied as a marker of ischemia,[23,24] as well as R-wave angle.[25] A respiration-related modulation in QRS slopes was observed in Romero *et al.*,[24] but it was not studied. In this paper, the respiration-related modulation of QRS slopes and R-wave angle is studied and exploited to derive respiration from the ECG. The method based on electrical axis rotation angles presented in Bailón *et al.*[3] is chosen as reference for comparison method, because it is the EDR method that obtained the best results in Bailón *et al.*[3] and in Lázaro *et al.*[13]

Evaluation of the proposed methods is performed over two databases. One of them contains signals recorded during a tilt table test, representing an environment with abrupt cardiovascular changes. The other one is composed of signals recorded during stress test, representing a highly non-stationary and noisy environment.

Note that preliminary stages of the study described in this paper have been previously presented in two short conference papers.[11,12]

MATERIALS AND METHODS

Tilt Test Data

This database contains 17 (11 men) recordings from volunteers, aged 28.5 ± 2.5 years, during a tilt table test. The tilt table test is used for testing the sympathetic nervous system through the blood pressure response to postural changes.[7] In particular, the tilt table test was performed according to the following protocol: 4 min in early supine position, 5 min tilted head-up to an angle of 70°, and 4 min to later supine position. Transitions between stages last 18 s.

The standard 12-lead ECG were recorded by using Biopac ECG100C with a sampling rate of $F_s = 1000$ Hz, and the respiratory signal was recorded with a sampling rate of 125 Hz using Biopac RSP100C sensor and TSD201 transducer, representing a plethysmography-based technique. Further details of these data are given in Mincholé *et al.*[20]

Stress Test Data

This database contains recordings from 14 volunteers (10 males) aged 28 ± 4 years and 20 patients (16 males) aged 58 ± 14 years, referred to the Department of Clinical Physiology at the University Hospital of Lund, Sweden, for stress testing. The stress test was performed on a bicycle ergometer Siemens-Elema Ergoline 900C. The initial workload (50 W for males and 30 W for females) was increased at a rate of 15 W/min for males and 10 W/min for females, until a rate of perceived exertion (according to Borg scale) of 15 for volunteers and of 17 for patients was reached, unless other clinical stopping criteria (e.g., chest pain or tachycardia) occurred first.

As in Bailón *et al.*,[3] five subjects, all of them patients, were excluded from the study for different reasons including unattached electrodes, too low heart rate to assure aliasing-free estimation of the respiratory frequency, or the absence of a dominant peak at respiratory signal spectrum in at least 50% of the total duration of the exercise. Thus, a total of 14 volunteers and 15 patients were included.

The standard 12-lead ECG was recorded by using the Siemens-Elema Megacart front-end with a sampling rate of $F_s = 1000$ Hz. The respiratory signal was simultaneously recorded by an airflow thermistor (Sleepmate), amplified by Biopac DA100C, and digitalized by using Biopac MA100 with a sampling rate of 50 Hz. Further details of these data are given in Bailón *et al.*[3]

Preprocessing

Vectorcardiogram (VCG) was obtained by using the inverse Dower matrix.[6] QRS complexes in all ECG leads were automatically detected by using a wavelet-based detector,[15] and ectopic/misdetected beats were identified and removed using an algorithm described in Mateo *et al.*[17] Normal sinus beat locations are denoted $n_{N_{l,i}}$, where l represents ECG lead and i normal sinus beat order. Baseline was removed by a cubic-spline interpolation technique, which results in a linear filtering with a time-variable cut-off frequency, better tracking rapid baseline wander when compared to a fixed cut-off frequency approach while maintaining beat-to-beat variations.[26] Then, for each lead l and normal sinus beat i, wave delineation was performed by using a wavelet-based technique,[15] determining Q ($n_{Q_{l,i}}$), R ($n_{R_{l,i}}$), and S ($n_{S_{l,i}}$) peaks (or QRS end when no S wave is present), and QRS onset ($n_{ON_{l,i}}$).

Non-standard Leads

Two non-standard leads were derived: the loop derived lead (LDL) and the N-loops derived lead (NLDL). Both of them are based on VCG-QRS loops.

LDL was presented in Romero *et al.*[24] It tries to enhance the QRS magnitude by projecting VCG-QRS loop onto its dominant direction $\boldsymbol{u}_i$, obtained as:

$$\boldsymbol{u}_i = [u_{X_i}, u_{Y_i}, u_{Z_i}]^T = [l_X(n_{0_i}), l_Y(n_{0_i}), l_Z(n_{0_i})]^T \quad (1)$$

being $l_X(n)$, $l_Y(n)$, and $l_Z(n)$ the 3 VCG leads, and:

$$n_{0_i} = \arg\max_{n \in \Omega_{\mathrm{QRS}_i}} \left[l_X^2(n) + l_Y^2(n) + l_Z^2(n)\right] \tag{2}$$

where Ω_{QRS_i} is a 140 ms interval starting 10 ms before the earliest QRS onset in the 3 VCG leads, n_{ON_i}:

$$n_{\mathrm{ON}_i} = \min\{n_{\mathrm{ON}_{X,i}}, n_{\mathrm{ON}_{Y,i}}, n_{\mathrm{ON}_{Z,i}}\} \tag{3}$$

$$\Omega_{\mathrm{QRS}_i} = [n_{\mathrm{ON}_i} - 0.01F_s, \quad n_{\mathrm{ON}_i} + 0.13F_s]. \tag{4}$$

Then, the LDL $l_{\mathrm{LDL}}(n)$ is computed at each beat as:

$$l_{\mathrm{LDL}}(n) = \frac{[l_X(n), l_Y(n), l_Z(n)]\boldsymbol{u}_i}{||\boldsymbol{u}_i||}, \quad \forall n \in \Omega_{\mathrm{QRS}_i} \tag{5}$$

In this way, the beat-to-beat variations of the dominant direction of VCG-QRS loop are followed by $l_{\mathrm{LDL}}(n)$. Following these variations may be counterproductive in this application, since they are in part due to respiration.[3,21,22] For this reason, NLDL is proposed as a slight modification of LDL. The NLDL is similar to the LDL, but the dominant direction of VCG-QRS loops is estimated with the first N beats and it is not updated. In mathematical terms, the NLDL is defined as:

$$\bar{\boldsymbol{u}} = \sum_{i=1}^{N} \left\{ \frac{\boldsymbol{u}_i}{||\boldsymbol{u}_i||} \right\} \tag{6}$$

$$l_{\mathrm{NLDL}}(n) = \frac{[l_X(n), l_Y(n), l_Z(n)]\bar{\boldsymbol{u}}}{||\bar{\boldsymbol{u}}||} \tag{7}$$

being N set to 5 beats in this work. This value was chosen as the mininum value which attenuates the effect of noise or artifacts in the estimation of the dominant direction and reduces the respiratory influence (approximately above 0.2 Hz) on it.

QRS Slopes Measurement

QRS slopes were measured by using the algorithm presented in Pueyo *et al.*[23] For each beat, two slopes are measured: upward slope of the R wave ($\mathcal{I}_{\mathrm{US}_{l,i}}$) and downward slope of the R wave ($\mathcal{I}_{\mathrm{DS}_{l,i}}$).

First, time instants associated with the maximum variation points of the ECG signal between $n_{\mathrm{Q}_{l,i}}$ and $n_{\mathrm{R}_{l,i}}$, and between $n_{\mathrm{R}_{l,i}}$ and $n_{\mathrm{S}_{l,i}}$ are computed as:

$$n_{\mathrm{U}_{l,i}} = \max_{n \in \left[n_{\mathrm{Q}_{l,i}}, n_{\mathrm{R}_{l,i}}\right]} \{|l_l'(n)|\} \tag{8}$$

$$n_{\mathrm{D}_{l,i}} = \max_{n \in \left[n_{\mathrm{R}_{l,i}}, n_{\mathrm{S}_{l,i}}\right]} \{|l_l'(n)|\} \tag{9}$$

where $l_l'(n)$ is the first derivative of lead l:

$$l_l'(n) = l_l(n) - l_l(n-1). \tag{10}$$

Finally, a straight line is fitted to the ECG signal by least squares in two 8 ms-length intervals, one of them centred at $n_{\mathrm{U}_{l,i}}$ and the other one at $n_{\mathrm{D}_{l,i}}$. The slopes of these lines are denoted $\mathcal{I}_{\mathrm{US}_{l,i}}$ and $\mathcal{I}_{\mathrm{DS}_{l,i}}$, respectively. Figure 1 illustrates relevant points taking part in this measurement algorithm.

R-wave Angle Measurement

An R-wave angle is also used to derive respiratory rate in this work. This angle corresponds to the smallest one formed by the straight lines that define $\mathcal{I}_{\mathrm{US}_{l,i}}$ and $\mathcal{I}_{\mathrm{DS}_{l,i}}$, and it was measured as in Romero *et al.*[25] Assuming a two-dimensional euclidean space coordinate system, the general equation that defines this angle is:

$$\phi = \arctan\left(\left|\frac{\mathcal{I}_1 - \mathcal{I}_2}{1 + \mathcal{I}_1\mathcal{I}_2}\right|\right) \tag{11}$$

where $\mathcal{I}_1$ and $\mathcal{I}_2$ denote the slopes of the straight lines forming the angle.

The units of the horizontal axis (time) and vertical axis (voltage) were rescaled to match the particular case of conventional ECG tracings in clinical printouts, where a speed of 25 mm/s and a gain of 10 mm/mV are used as in Romero *et al.*[25]:

$$\phi_{\mathrm{R}_{l,i}} = \arctan\left(\left|\frac{\mathcal{I}_{\mathrm{US}_{l,i}} - \mathcal{I}_{\mathrm{DS}_{l,i}}}{0.4(6.25 + \mathcal{I}_{\mathrm{US}_{l,i}}\mathcal{I}_{\mathrm{DS}_{l,i}})}\right|\right). \tag{12}$$

Electrocardiogram Derived Respiration Signals

Based on QRS Slopes or R-Wave Angle

An EDR signal was generated for each one of the QRS slopes series by assigning to each beat occurrence $n_{\mathrm{N}_{l,i}}$, the value of its associated QRS slope:

$$d^u_{\{\mathrm{US,DS}\}_l}(n) = \sum_i \mathcal{I}_{\{\mathrm{US,DS}\}_{\mathrm{l,i}}}\delta(n - n_{\mathrm{N}_{l,i}}) \tag{13}$$

where the superindex "u" denotes the signal is unevenly sampled. An EDR signal was generated for each one of the R-wave angle series in a similar way:

$$d^u_{\mathrm{R}_l}(n) = \sum_i \phi_{\mathrm{R}_{l,i}}\delta(n - n_{\mathrm{N}_{l,i}}). \tag{14}$$

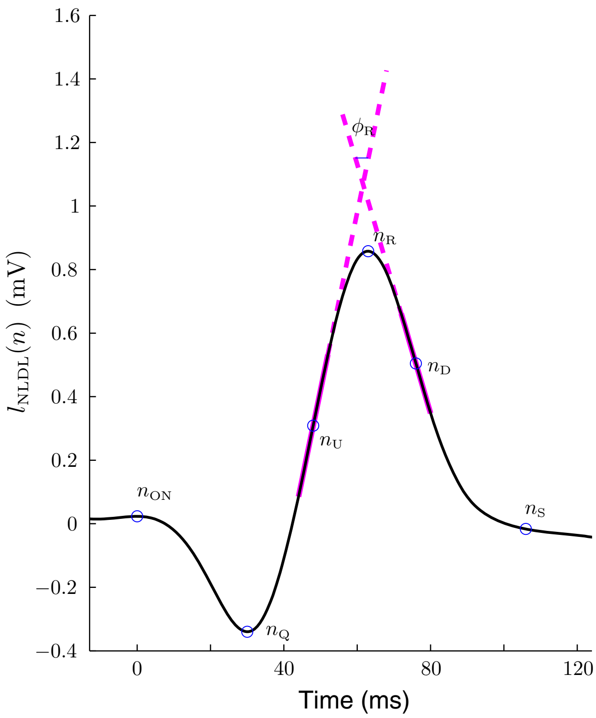

FIGURE 1. Relevant points over an example of QRS from $l_{\mathrm{NLDL}}(n)$. Thick magenta lines represent the two straight lines best suited to the QRS slopes by least square, and from which the slope series are obtained. R-wave angle series are obtained from the smallest angle formed by these two lines.

Then, a median absolute deviation (MAD)-based outlier rejection rule was applied as in Bailón *et al.*[3], and subsequently, a 4 Hz evenly sampled version of each EDR signal was obtained by cubic-splines interpolation. Finally, a band-pass filter (0.075–1) Hz was applied. These filtered signals are denoted with the same nomenclature than the unevenly sampled versions, but without the superindex "u", e.g., $d_{\mathrm{US}_{\mathrm{NLDL}}}(n)$ is the 4-Hz, outlier-rejected, evenly sampled, band-pass filtered version of $d^{u}_{\mathrm{US}_{\mathrm{NLDL}}}(n)$.

Figure 2 shows an example of some EDR signals and the reference respiratory signal $r(n)$ from stress test dataset during resting, stress peak and recovery phases. It can be observed that EDR signals and $r(n)$ are oscillating at very similar rates, which notably differ at each phase of the protocol.

A total of 51 EDR signals were studied corresponding to the 2 QRS slopes and 1 angle series ($\mathcal{I}_{\mathrm{US}_{l,i}}$, $\mathcal{I}_{\mathrm{DS}_{l,i}}$ and $\phi_{\mathrm{R}_{l,i}}$) in the 17 studied leads.

Based on Electrical Axis Rotation Angles

Three additional EDR signals were also studied for comparison purposes. These EDR signals were presented in Bailón *et al.*[3] and they are based on heart-electrical-axis-rotation angle variations induced by respiration. They were processed in the same way than QRS slopes EDR signals obtaining three EDR signals denoted $d_{\Phi_X}(n)$, $d_{\Phi_Y}(n)$ and $d_{\Phi_Z}(n)$ in this paper.

Respiratory Rate Estimation Algorithm

Respiratory rate estimation is based on the algorithm presented in Lázaro *et al.*[13] It allows to combine information from several EDR signals increasing the robustness of the estimation. Let M be the number of EDR signals used for estimating respiratory rate. The algorithm can be divided into 3 phases: the power spectrum (PS) estimation, the peak-conditioned average, and the respiratory rate estimation.

The PS estimation is performed by using the Welch periodogram. For the jth EDR signal and kth running interval of T_{s}-s length, the PS $S_{j,k}(f)$ is generated by an average of PS obtained from subintervals of T_{m}-s length ($T_{\mathrm{m}} < T_{\mathrm{s}}$) using an overlap of $T_{\mathrm{m}}/2$ s, after a power normalization in [0, 1] Hz band. A spectrum is generated every t_{s} s.

The second phase is a peak-conditioned average. First, for each $S_{j,k}(f)$, the location of largest peak $f^{\mathrm{I}}_{\mathrm{P}}(j,k)$ is detected. Subsequently, a reference interval $\Omega_{\mathrm{R}}(k)$ where respiratory rate is estimated to be, is defined as:

$$\Omega_{\mathrm{R}}(k) = [f_{\mathrm{R}}(k-1) - \delta, \quad f_{\mathrm{R}}(k-1) + \delta] \tag{15}$$

where $f_{\mathrm{R}}(k-1)$ is a respiratory frequency reference obtained from previous $(k-1)$ steps.

Then, $f^{\mathrm{II}}_{p}(j,k)$ is chosen as the nearest peak to $f_{\mathrm{R}}(k-1)$, among all peaks larger than 85% of $f^{\mathrm{I}}_{p}(j,k)$ inside $\Omega_{\mathrm{R}}(k)$. Note that $f^{\mathrm{II}}_{p}(j,k)$ can be the same $f^{\mathrm{I}}_{p}(j,k)$ if the largest peak is inside $\Omega_{\mathrm{R}}(k)$ and it is also the nearest to $f_{\mathrm{R}}(k-1)$. An example of selection of $f^{\mathrm{I}}_{p}(j,k)$ and $f^{\mathrm{II}}_{p}(j,k)$ is shown in Fig. 3.

Afterwards, L_{s} spectra $S_{j,k}(f)$ are "peak-conditioned" averaged; only those $S_{j,k}(f)$ which are sufficiently peaked take part in the averaging. In this paper, "peaked" denotes that $f^{\mathrm{II}}_{p}(j,k)$ exists and a certain percentage ξ of the spectral power must be contained in an interval centred around it. In mathematical terms, this averaging is defined as:

$$\bar{S}_{k}(f) = \sum_{l=0}^{L_s-1} \sum_{j} \chi^{\mathrm{A}}_{j,k-l} \chi^{\mathrm{B}}_{j,k-l} S_{j,k-l}(f) \tag{16}$$

where $\chi^{\mathrm{A}}_{j,k-l}$ and $\chi^{\mathrm{B}}_{j,k-l}$ represent two criteria aimed at deciding whether power spectrum $S_{j,k-l}(f)$ is peaked enough or not, preventing those not peaked enough spectra from taking part in the average. On one hand, χ^{A} lets those spectra whose peakness is greater than a fixed value take part in the average, as shown in Eq. (17), and on the other hand, χ^{B} compares the spectra of

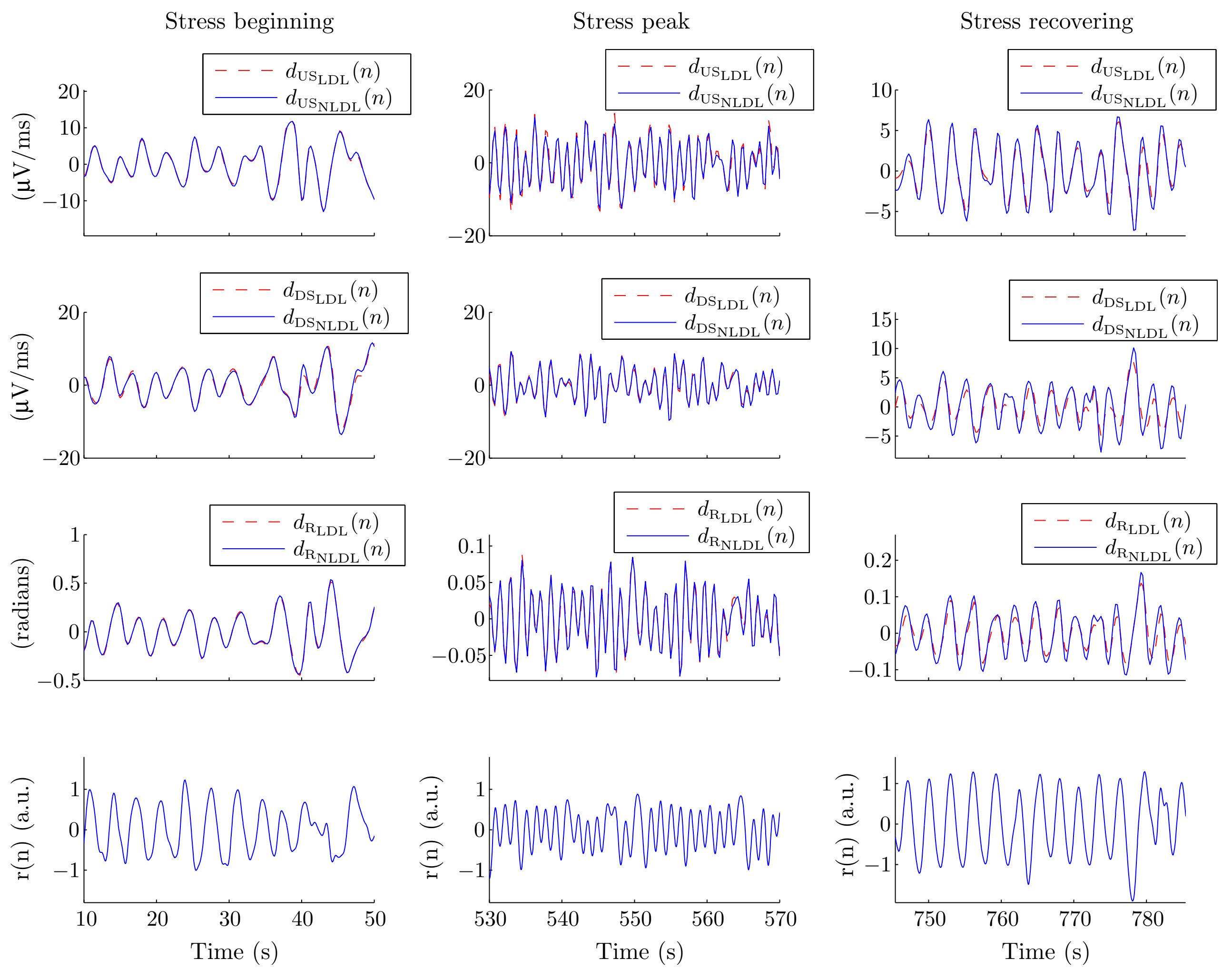

FIGURE 2. Example of some EDR signals and the reference respiratory signal *r*(*n*) from stress test dataset during different phases of the protocol: stress beginning (≈0.3 Hz), peak (≈0.7 Hz) and recovery (≈0.35 Hz). It can be observed that EDR signals and *r*(*n*) are oscillating at very similar rates, which notably differ at each phase of the protocol.

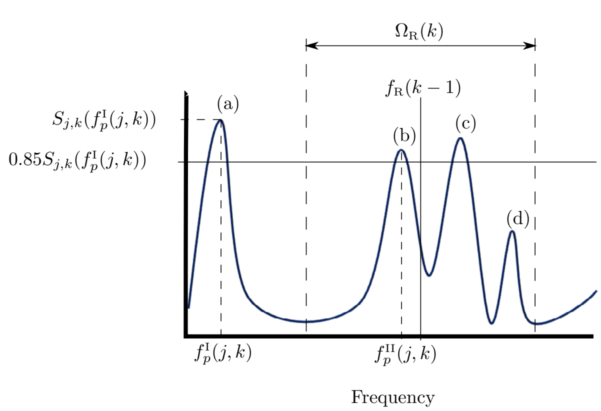

FIGURE 3. Example of selection of $f_p^{\mathrm{I}}(j,k)$ and $f_p^{\mathrm{II}}(j,k)$ for an hypothetical $S_{j,k}(f)$ and for a given $f_{\mathrm{R}}(k-1)$. Peak (a) is selected as $f_p^{\mathrm{I}}(j,k)$ because it is the highest peak. Then, peaks higher than 85% of the amplitude of peak (a) within $\Omega_{\mathrm{R}}(k)$ are detected, finding peaks (b) and (c), and discarding peak (d). Peak (b) is selected as $f_p^{\mathrm{II}}(j,k)$ because it is the nearest to $f_{\mathrm{R}}(k-1)$.

different EDR signals, letting those spectra more peaked in each time instant take part in the average, although all them had passed the χ^{A} criterion, as shown in Eq. (18). Note that χ^{B} has no effect if the estimation is being accomplished from only one EDR signal ($M = 1$).

$$\chi_{j,k}^{\mathrm{A}} = \begin{cases} 1, & P_{j,k} \geq \xi \\ 0, & \text{otherwise} \end{cases} \tag{17}$$

$$\chi_{j,k}^{\mathrm{B}} = \begin{cases} 1, & P_{j,k} \geq \max_{j}\left\{P_{j,k}\right\} - \lambda \\ 0, & \text{otherwise} \end{cases} \tag{18}$$

where $P_{j,k}$ is defined by the percentage of power around $f_p^{\mathrm{II}}(j,k)$ with respect to the total power in $\Omega_{\mathrm{R}}(k)$:

$$P_{j,k} = \frac{\int_{\max\left\{f_p^{\mathrm{II}}(j,k)-0.4\delta,\, f_{\mathrm{R}}(k-1)-\delta\right\}}^{\min\left\{f_p^{\mathrm{II}}(j,k)+0.4\delta,\, f_{\mathrm{R}}(k-1)+\delta\right\}} S_{j,k}(f)\mathrm{d}f}{\int_{f_{\mathrm{R}}(k-1)-\delta}^{f_{\mathrm{R}}(k-1)+\delta} S_{j,k}(f)\mathrm{d}f}. \quad (19)$$

Then, the algorithm searches the largest peak $f_p^{\mathrm{I}_a}(k)$ in $\bar{S}_k(f)$, and subsequently $f_p^{\mathrm{II}_a}(k)$ defined as the nearest to $f_{\mathrm{R}}(k-1)$ inside $\Omega_{\mathrm{R}}(k)$ which is at least larger than 85% of $f_p^{\mathrm{I}_a}(k)$. At this time the reference frequency $f_{\mathrm{R}}(k)$ is updated as:

$$f_{\mathrm{R}}(k) = \beta f_{\mathrm{R}}(k-1) + (1-\beta) f_p(k) \quad (20)$$

where β denotes the forgetting factor and $f_p(k)$ is defined by

$$f_p(k) = \begin{cases} f_p^{\mathrm{II}_a}(k), & \exists f_p^{\mathrm{II}_a}(k) \\ f_p^{\mathrm{I}_a}(k), & \text{otherwise} \end{cases}. \quad (21)$$

Finally, estimated respiration rate $\hat{f}(k)$ is defined as:

$$\hat{f}(k) = \alpha \hat{f}(k-1) + (1-\alpha) f_p(k) \quad (22)$$

$$\alpha = \begin{cases} \alpha_2, & \exists f_p^{\mathrm{II}_a}(k) \\ \alpha_1, & \text{otherwise} \end{cases} \quad (23)$$

where $\alpha_2 \leq \alpha_1$, providing more memory when $f_p^{\mathrm{II}_a}(k)$ could not be set.

Note that $\bar{S}_k(f)$ is the result of an average from zero up to $M \times L_{\mathrm{s}}$ power spectra. If no spectrum takes part in the average, the algorithm increases the reference interval by doubling the δ value and repeat the process from the search of $f_p^{\mathrm{II}}(j,k)$ in individual power spectra. In the case that no spectrum is peaked enough after this second iteration, respiratory rate is not estimated at that time instant.

At initialization time, in order to reduce the risk of spurious frequency selection, δ is set to 0.125 Hz and $f_{\mathrm{R}}(0)$ is set to 0.275 Hz, allowing the algorithm to pick peaks inside the normal range of spontaneous respiratory rate ([0.15, 0.4] Hz). Occasionally, respiratory rate can be outside this band so algorithm could not be initialized as proposed. To deal with that issue, if $f_{\mathrm{R}}(k)$ is not set after 5 averages $\bar{S}_k(f)$, then δ is increased allowing algorithm to pick peaks in full [0, 1] Hz studied band.

Concatenation of all $\bar{S}_k(f)$ results in a time-frequency map $\bar{S}(k,f)$ as shown in Fig. 4. The parameter values for the Welch periodograms used in Lázaro *et al.*[13] are also used here: $L_{\mathrm{s}} = 5$, $T_{\mathrm{s}} = 42$ s, $T_{\mathrm{m}} = 12$ s and $t_{\mathrm{s}} = 5$ s. Parameter β, which controls the change of location of $\Omega_{\mathrm{R}}(k)$, was set to 0.7 as in Bailón *et al.*[2]; δ was set to 0.1 which is slightly higher than 0.08 used in Lázaro *et al.*[13] in order to allow faster changes in respiratory rate, more adequate for stress test recordings; α_1 and α_2 were set to 0.7 and 0.3 respectively as in Lázaro *et al.*,[13] fixing the maximum allowed changes in respiratory frequency inside (α_2) and outside (α_1) $\Omega_{\mathrm{R}}(k)$. λ was set to 0.05 as in Lázaro *et al.*[13] because that value was observed to achieve a good compromise for peak spectrum acceptance/rejection. The minimum peakness to fulfill the χ^{A} criterion, ξ, was set to 0.65 based on a study with a different dataset containing 3-leads ECG recordings during stress testing,[4] thus avoiding overfitting.

Four different combinations were studied: the QRS slopes and R-wave angle from the standard 12 leads (12ECG), from VCG, from LDL, and from NLDL. In order to study whether respiratory information in QRS slopes and R-wave angle is complementary or redundant, respiratory rate was also estimated from combinations of only QRS slopes ($12\mathrm{ECG_S}$, $\mathrm{VCG_S}$, $\mathrm{LDL_S}$, $\mathrm{NLDL_S}$) and only R-wave angles ($12\mathrm{ECG_R}$, $\mathrm{VCG_R}$, $\mathrm{LDL_R}$, $\mathrm{NLDL_R}$). For comparison purposes, a combination composed of the three rotation angle series[3] (Φ) was also studied.

Figure 5 illustrates a block diagram of this algorithm.

Performance Measurements

In order to evaluate the proposed methods, two performance measures were used: the relative and absolute error of the respiratory rate estimations defined as:

$$e_{\mathrm{A}}(k) = \hat{f}(k) - f_{\mathrm{RES}}(k) \quad (24)$$

$$e_{\mathrm{R}}(k) = \frac{e_{\mathrm{A}}(k)}{f_{\mathrm{RES}}(k)} \quad (25)$$

where $f_{\mathrm{RES}}(k)$ is the respiratory rate estimated from the reference respiratory signal. Note that the same absolute differences can correspond to very different relative error due to the $f_{\mathrm{RES}}(k)$ normalization.

RESULTS

The mean and standard deviation (SD) of absolute and relative error signals were computed for each subject. Then, the intersubject mean of those means and SDs were also computed. Obtained results from the studied combinations of EDR signals are shown in Table 1 for the tilt test dataset, and in Table 2 for the stress test dataset. For each studied combination, the EDR signals that obtained the best and worst results in terms of root mean square of e_{R} (k) (less is better) are also shown.

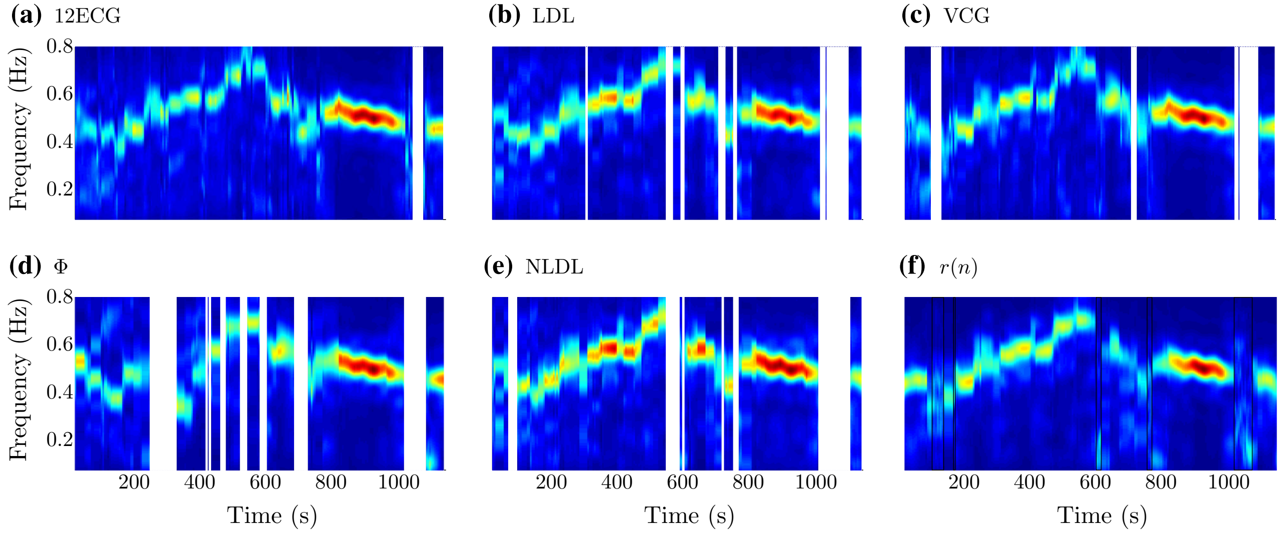

FIGURE 4. Example of peak-conditioned averaged running spectra obtained from the studied combinations: (a) 12ECG, (b) LDL, (c) VCG, (d) Φ, (e) NLDL, and (f) reference respiratory signal. Note that a time instant at which spectrum is not drown (white) means that no spectrum was peaked enough at that time instant. In case of reference respiratory signal, the time instants where no spectrum was peaked enough are represented by black rectangles at where a concatenation of Welch periodograms ($S_{r,k}(f)$) is shown for visual purposes.

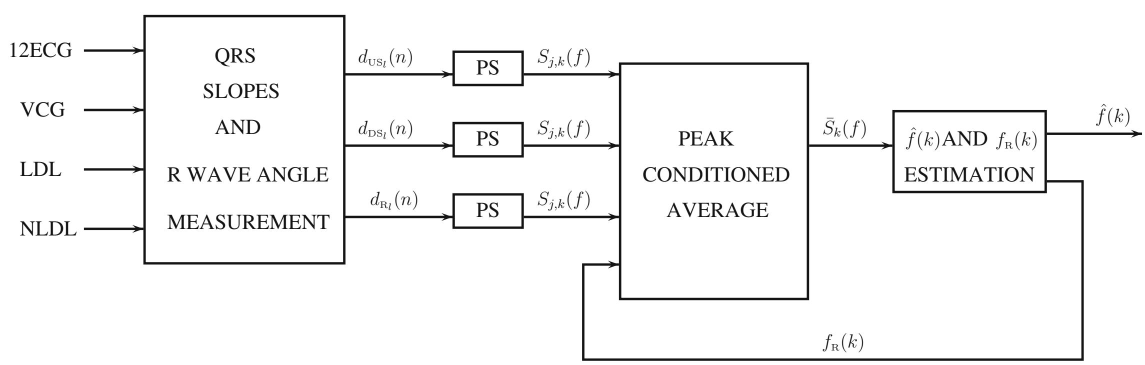

FIGURE 5. Block diagram of respiratory rate estimation algorithm.

Results obtained for combinations of only slopes and only R-wave angles are shown in Table 3.

In order to study the performance of the methods at different respiratory rates, they were evaluated separately as a function of the rate of reference respiratory signal. Furthermore, recordings from patients of stress test dataset were observed to have more irregular breathing patterns when compared with healthy volunteers (see Fig. 6). This makes the task of deriving respiratory rate more challenging with patients than with volunteers. Table 4 shows results for different ranges of respiratory rate, and for patients and volunteers separately.

DISCUSSION

In this paper a new beat-morphology-based method for deriving respiration rate from the ECG is presented. First, EDR signals are estimated based on the beat-to-beat variations of QRS slopes and R-wave angle, which have been obtained from different leads. Then, respiratory rate is estimated using an algorithm which includes peak-conditioned averaging to selectively combine information from different EDR signals, and restricted interval peak search. The method has been evaluated in two different challenging scenarios: tilt table test and stress test.

The performance of the methods is assessed in terms of the respiration rate estimation error, as well as of the percentage of the record duration where an estimate is given (measuring time). In the tilt table test scenario, combining information from different EDR signals results in a reduction of estimation error and an increase of the measuring time for all sets of analyzed leads. In the stress test scenario, characterized by noisier and more non stationary signals, combining information from different EDR signals always results

TABLE 1. Inter-subject mean of means and SDs of e_A (k) and e_R (k) obtained for the tilt test dataset.

	e_R (k) (%)		e_A (k) (mHz)		Time measuring (%)
	Mean	SD	Mean	SD	Mean
12ECG					
Combination	0.46	5.69	–0.05	10.50	100
Best ($d_{R_{V6}}(n)$)	–1.68	5.63	–5.18	13.94	89.42
Worst ($d_{US_{aVR}}(n)$)	16.23	23.80	18.16	44.06	38.81
VCG					
Combination	0.50	4.11	0.20	7.56	99.84
Best ($d_{R_X}(n)$)	–0.49	7.27	–2.83	14.68	92.30
Worst ($d_{DS_Y}(n)$)	0.35	12.03	–5.72	24.48	77.68
LDL					
Combination	0.66	4.80	0.48	8.54	96.36
Best ($d_{US_{LDL}}(n)$)	0.02	5.47	–0.72	10.30	94.19
Worst ($d_{DS_{LDL}}(n)$)	1.10	7.36	0.43	13.89	85.21
NLDL					
Combination	0.71	4.61	0.52	8.58	95.37
Best ($d_{US_{NLDL}}(n)$)	–0.20	6.34	–3.14	13.26	73.62
Worst ($d_{R_{NLDL}}(n)$)	3.05	8.24	5.04	14.64	87.33
Φ					
Combination	0.48	6.19	–0.81	12.18	96.26
Best ($d_{\Phi_X}(n)$)	1.29	6.84	0.49	12.26	91.32
Worst ($d_{\Phi_Y}(n)$)	16.04	22.02	17.11	30.81	63.59

TABLE 2. Inter-subject mean of means and SDs of e_A (k) and e_R (k) obtained for the stress test dataset.

	e_R (k) (%)		e_A (k) (mHz)		Time measuring (%)
	Mean	SD	Mean	SD	Mean
12ECG					
Combination	1.95	9.26	4.76	28.63	99.81
Best ($d_{R_{V4}}(n)$)	–0.63	7.38	–3.46	26.18	62.55
Worst ($d_{R_I}(n)$)	1.32	14.36	–19.66	53.65	38.96
VCG					
Combination	0.52	8.99	0.46	30.36	96.09
Best ($d_{US_Z}(n)$)	–1.14	8.03	–11.05	29.75	73.05
Worst ($d_{R_Y}(n)$)	–5.32	13.17	–34.51	47.98	49.32
LDL					
Combination	0.04	8.30	–2.10	28.15	85.17
Best ($d_{DS_{LDL}}(n)$)	–0.65	8.48	–4.34	28.90	67.39
Worst ($d_{R_{LDL}}(n)$)	–2.40	10.95	–12.61	38.53	66.66
NLDL					
Combination	0.76	7.30	1.43	22.53	85.07
Best ($d_{R_{NLDL}}(n)$)	–0.03	7.76	3.27	27.30	68.21
Worst ($d_{US_{NLDL}}(n)$)	–1.47	9.80	–14.66	30.76	67.18
Φ					
Combination	–1.62	9.65	–14.80	39.72	91.07
Best ($d_{\Phi_Z}(n)$)	–1.99	10.74	–17.45	38.50	70.38
Worst ($d_{\Phi_Y}(n)$)	3.38	16.39	4.64	52.45	72.93

in an increase of the measuring time but, sometimes, at the expense of a slight increase of the estimation error. However, even in those cases (12ECG), the combination is advantageous since the slight increase in estimation error ($1.95 \pm 9.26\%$ [4.76 ± 28.63 mHz] vs. $-0.63 \pm 7.38\%$ [-3.46 ± 26.18 mHz]) is more affordable than the decrease in measuring time (37.26%).

Best performance as a compromise between estimation error and measuring time is achieved by VCG combination in both scenarios (estimation error of $0.50 \pm 4.11\%$, measuring time of 99.84% in tilt table test, estimation error of $0.52 \pm 8.99\%$, measuring time of 96.09% in stress test). VCG combination outperforms 12ECG combination in estimation error terms ($0.50 \pm 4.11\%$ vs. $0.46 \pm 5.69\%$ in tilt test, and $0.52 \pm 8.99\%$ vs. $1.95 \pm 9.26\%$ in stress test), suggesting that inverse Dower transformation enhances beat morphological variations induced by respiration.

TABLE 3. Inter-subject mean of means and SDs of e_A (k) and e_R (k), obtained for combinations of only QRS slopes and only R-wave angles.

	Tilt test dataset					Stress test dataset				
	e_R (k) (%)		e_A (k) (mHz)		Time measuring (%)	e_R (k) (%)		e_A (k) (mHz)		Time measuring (%)
	Mean	SD	Mean	SD	Mean	Mean	SD	Mean	SD	Mean
$12ECG_S$	0.55	6.89	−0.84	14.40	100.00	2.11	9.50	5.74	29.02	98.65
$12ECG_R$	−0.07	6.44	−1.90	12.82	100.00	−0.23	10.11	−2.82	36.74	96.44
VCG_S	0.80	5.06	0.46	8.93	99.42	1.95	9.11	4.89	26.63	93.85
VCG_R	0.31	4.61	−0.41	9.29	96.87	0.56	9.51	−0.35	26.18	87.17
LDL_S	1.20	6.24	1.06	10.76	93.75	−0.60	7.53	−5.07	26.09	77.32
LDL_R	0.53	6.33	−0.52	13.42	85.70	−2.40	10.95	−12.61	38.53	66.66
$NLDL_S$	0.51	6.43	−0.52	11.75	88.39	0.47	7.19	−0.11	21.85	78.94
$NLDL_R$	3.05	8.28	5.04	14.64	87.33	−0.03	7.76	−3.27	27.30	68.21

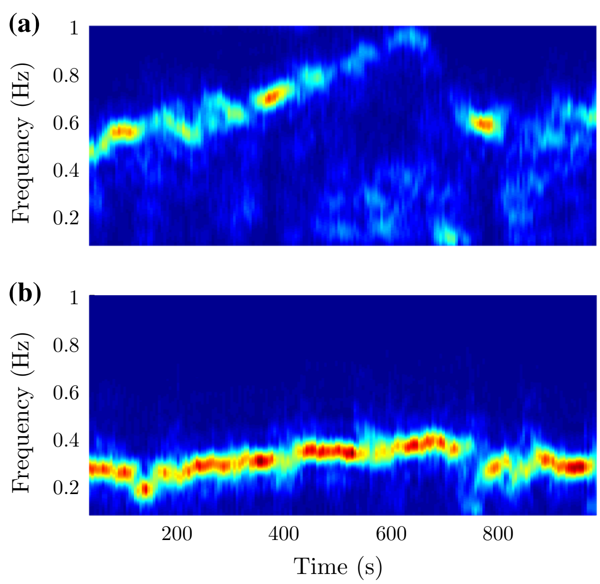

FIGURE 6. Example of Welch periodograms obtained from reference respiratory signal of a patient (a), and a volunteer (b). Volunteer is breathing more regularly, so respiratory rate is more marked in the associated spectrum.

Although there is a clear advantage in combining information from different EDR signals, it is preferable to use less EDR signals with higher signal to noise ratio (SNR) than more EDR signals with lower SNR. Leads LDL and NLDL also combine information from VCG leads. However, in tilt table test EDR signals derived from LDL and NLDL do not achieve better performance results than VCG combination. On the contrary, in the stress test scenario, NLDL combination obtains less estimation error, at the expense of reducing measuring time (from 96.09 to 85.07%). There is a reduction in estimation error from 0.52 ± 8.99% (0.46 ± 30.36 mHz) to 0.76 ± 7.30% (1.43 ± 22.53 mHz), which may be justified in applications where an accurate estimation of respiratory frequency is needed.[1] In applications where the interest is in the evolution of respiratory frequency during stress test, it may be more practical to have slightly less accurate estimates but during more time. In the stress test scenario, EDR signals derived from NLDL slightly outperforms those from LDL in estimation error terms. Moreover, NLDL does not require the update of the dominant direction beat-to-beat, representing a computational advantage.

For comparison purposes, a combination composed of the three electrical axis rotation angle series has been included, which yields an estimation error of 0.48 ± 6.19% with measuring time of 96.26% in tilt table test, and an estimation error of –1.62 ± 9.65% with measuring time 91.07% in stress test. These results indicate that the proposed methodology outperforms electrical axis rotation angles in terms of estimation error and measuring time.

A possible explanation for the improvement of results for VCG combination with respect to Φ may be that, although both methods use the same ECG signals ($l_X(n)$, $l_Y(n)$ and $l_Z(n)$), QRS slopes and R-wave angles are more robust in those situations when there is so much noise in one of the leads. Each one of the EDR signals combined in Φ (rotation angle series) uses the three VCG leads. Thus, if one lead is affected by noise or artifacts, the three EDR signals are affected. In opposite, each one of EDR signals used in VCG combination (QRS slopes and R-wave angle from each one of the VCG leads) are based on only one lead, so only those EDR signals based on that lead are affected and their contribution to the respiratory rate estimate can be attenuated by the peaked-conditioned PS average.

In general, methods obtained similar results in absolute error terms for rates below 0.7 Hz. Worse performance is observed for respiratory rates above 0.7 Hz, either in absolute error terms or in percentage of time measuring. This may be due to the fact that respiratory rate is above 0.7 Hz only in 5 recordings

TABLE 4. Inter-subject mean of means and SDs of e_A (*k*) and e_R (*k*) obtained for the stress test dataset for different respiratory rate ranges for the stress test dataset, and from patients and volunteers separately.

	e_R (*k*) (%)		e_A (*k*) (mHz)		Time measuring (%)
	Mean	SD	Mean	SD	Mean
12ECG					
$f_{RES}<0.3$	1.61	8.68	4.34	23.11	98.05
$f_{RES} \in [0.3, 0.5)$	0.28	8.63	–3.23	33.14	94.01
$f_{RES} \in [0.5, 0.7)$	–1.92	5.73	–10.78	32.07	96.58
$f_{RES} \geq 0.7$	–5.00	1.76	–35.92	12.99	100
Patients	1.86	8.88	5.90	32.45	99.63
Volunteers	2.04	9.68	3.55	24.95	100
VCG					
$f_{RES}<0.3$	1.74	8.46	4.80	21.62	90.13
$f_{RES} \in [0.3, 0.5)$	0.55	5.53	2.18	21.25	90.80
$f_{RES} \in [0.5, 0.7)$	0.39	3.48	2.60	19.16	96.05
$f_{RES} \geq 0.7$	1.01	1.86	7.29	13.42	81.43
Patients	0.98	7.23	4.29	29.41	95.66
Volunteers	0.03	10.87	–3.65	31.38	96.55
LDL					
$f_{RES}<0.3$	3.19	7.06	8.64	18.23	76.50
$f_{RES} \in [0.3, 0.5)$	–0.30	5.40	–1.05	21.30	76.66
$f_{RES} \in [0.5, 0.7)$	–2.87	4.61	–16.26	26.90	73.56
$f_{RES} \geq 0.7$	–5.57	4.19	–44.92	32.29	48.18
Patients	–0.56	7.82	–4.56	34.11	81.54
Volunteers	0.68	8.81	0.53	21.76	89.03
NLDL					
$f_{RES}<0.3$	1.74	8.46	4.80	21.62	72.96
$f_{RES} \in [0.3, 0.5)$	–0.45	4.37	–2.61	16.70	79.78
$f_{RES} \in [0.5, 0.7)$	–2.66	3.16	–14.43	18.04	77.78
$f_{RES} \geq 0.7$	–1.25	2.01	–9.04	14.39	42.11
Patients	1.34	6.75	3.46	24.19	80.35
Volunteers	0.15	7.90	–0.74	20.75	90.14

belonging to patients, who present more irregular breathing patterns (see Fig. 6).

Regarding the separation of patients and healthy volunteers, a slight decrease in performance can be observed in patients with respect to volunteers in absolute error terms while relative error is slightly lower for patients, due to the fact that respiratory rate is higher for patients than for volunteers. The percentage of time offering estimates was also lower for patients than for volunteers.

All proposed combinations use in some way the 12-lead ECG, but having that number of leads is unmanageable in some situations, such as ambulatory scenarios based on Holter devices. All the 220 possible combinations of 3 leads from the 12-lead ECG were studied. The best results in relative error terms were obtained by the combination of V2, V5 and I leads (–1.05 ± 8.61% during 95.52% of the time), and the worst results were obtained by the combination of V4, V5 and V6 (10.05 ± 15.85% during 89.90% of the time). This suggests it is better to place electrodes in a spatially-dispersed way than placing them proximately to each other, and also that the area covered by the posterior leads is the one less suited for EDR since respiration induced changes at those ECG leads results in the lower EDR performance.

Furthermore, to assess the incremental value of QRS slopes and R-wave angle in estimating respiratory rate, they have been evaluated separately. Combination of QRS slopes and R-wave angles reduces estimation error and increases measuring time with respect to QRS slopes or R-wave angles alone. Although R-wave angles are computed from QRS slopes, their relation is non-linear, which may exploit complementary respiratory information to that obtain by the linear combination of QRS slopes.

The algorithm for respiratory rate estimation is slightly different from that presented in Lázaro *et al.*,[13] which has to be modified to adapt to the highly non-stationary and noisy environment of stress test. The main modifications include: (i) the reference interval for estimating respiratory frequency is symmetric with respect to the reference frequency $f_R(k-1)$, since EDR signals in this study are not contaminated with sympathetic-related low frequency components; (ii) respiratory rate is not estimated when no spectrum is peaked enough according to χ^A and χ^B, which prevents from spurious estimates in very noisy signal segments.

TABLE 5. Inter-subject mean of means and SDs of $e_A(k)$ and $e_R(k)$ obtained with the method presented in Lázaro et al.[13]

	$e_R(k)$ (%)		$e_A(k)$ (mHz)	
	Mean	SD	Mean	SD
Tilt test dataset				
12ECG	0.17	5.32	–0.51	10.57
VCG	–0.10	5.37	–1.33	9.94
LDL	0.69	4.75	0.44	8.54
NLDL	0.82	4.76	0.59	9.14
Stress test dataset				
12ECG	3.08	10.05	5.37	28.68
VCG	1.25	11.32	–4.25	45.54
LDL	0.85	12.44	–5.37	43.19
NLDL	1.70	10.34	–0.16	35.20

Note that those periods of time when respiratory rate is not estimated are not necessarily associated with artifacts in the ECG signal. The exclusion criteria discards spectra where the respiration is not clearly marked in a specific EDR signal at a specific time instant, either because QRS slopes or R-wave angles are not oscillating at respiratory frequency or because other sources are also modulating them (such as movement oscillations) and the respiration peak cannot be identified. For comparison purposes, Table 5 displays estimation errors achieved by the studied EDR signals using the respiratory rate estimation algorithm in Lázaro *et al.*[13] Note that with this algorithm an estimate is always given, so measuring time is 100%. As expected, results are similar to the ones presented in this manuscript in tilt table test, but worse in stress test scenario.

The two databases contains registers obtained during specific clinical tests involving different cardiovascular changes, so a measure of accuracy of the proposed methods in normal rest conditions has not been given. As a reference for this, respiratory rate estimation during only the first part of tilt test protocol (4 minutes in supine position) was evaluated for the four proposed combinations. The obtained results in $e_R(k)$ terms were 0.31 ± 4.22% (mean ± SD) during 100% of time for 12ECG, 0.88 ± 3.03% during 100% of time for VCG, 0.87 ± 3.41% during 99.39% of time for LDL, and 1.10 ± 2.92% during 100% of time for NLDL. For the four combinations, obtained results are better than those obtained when evaluating during the complete three parts of tilt test. This was expected since the first part of tilt test (rest) has no significant cardiovascular changes, nor usually significant respiratory rate changes.

Results suggest that the proposed methods based on QRS slopes and R-wave angle series are the most suitable for respiratory rate estimation from ECG signals in tilt and stress test. In the stress test database, combination of EDR signals from NLDL lead achieved the lowest estimation error (0.76 ± 7.30%) while 12ECG combination obtained the largest measuring time (99.81%). Combination of EDR signals from VCG leads displayed the best trade-off between accuracy and measuring time (estimation error of 0.52 ± 8.99%, measuring time of 96.09%), outperforming existing methods in literature.

ACKNOWLEDGMENTS

Thanks to Dr. A. Mincholé, Dr. L. Sörnmo, Dr. G. Blain and Dr. S. Bermon for providing the authors with datasets. This work is supported by Universidad de Zaragoza under fellowship PIFUZ-2011-TEC-A-003, by Ministerio de Economía y Competitividad (MINECO), FEDER; under projects TEC2010-21703-C03-02, TEC2010-19410, TEC2013-42140-R, TIN2013-41998-R and FIS-PI12/00514, by CIBER de Bioingeniería, Biomateriales y Nanomedicina through Instituto de Salud Carlos III, and by Grupo Consolidado BSICoS from DGA (Aragón) and European Social Fund (EU). Esther Pueyo acknowledges the financial support of Ramón y Cajal program from MINECO.

REFERENCES

[1] Bailón, R., L. Mainardi, M. Orini, L. Sörnmo, and P. Laguna. Analysis of heart rate variability during exercise stress testing using respiratory information. *Biomed. Signal Process.* 5:299–310, 2010.

[2] Bailón, R., L. Sörnmo, and P. Laguna. ECG-derived respiratory frequency estimation. In: Advanced Methods and Tools for ECG Data Analysis, edited by G. Clifford, F. Azuaje, and P. McSharry. Norwood: Artech House Inc., 2006, pp. 215–244.

[3]Bailón, R., L. Sörnmo, P. Laguna. A robust method for ECG-based estimation of the respiratory frequency during stress testing. *IEEE Trans. Biomed. Eng*. 53(7):1273–1285, 2006.
[4]Blain, G., O. Meste, A. Blain, and S. Bermon. Time-frequency analysis of heart rate variability reveals cardiolocomotor coupling during dynamic cycling exercise in humans. *Am. J. Physiol. Heart Circ. Physiol*. 296:H1651–H1659, 2009.
[5]Chon, K. H., S. Dash, and K. Ju. Estimation of respiratory rate from photoplethysmogram data using time-frequency spectral estimation. *IEEE Trans. Biomed. Eng*. 56(8):2054–2063, 2009.
[6]Edenbrandt, L., and O. Pahlm. Vectorcardiogram synthesized from a 12-lead ECG: superiority of the inverse dower matrix. *J. Electrocardiol*. 21(4):361–367, 2008.
[7]Freeman, R. Assessment of cardiovascular autonomic function. *Clin. Neurophysiol*. 117(4):716–730, 2006.
[8]Gravelyn, T. R., and J. G. Weg. Respiratory rate as an indicator of acute respiratory dysfunction. *J. Am. Med. Assoc*. 244(10):1123–1125, 1980.
[9]Grossman P., and K. Wientjes. Respiratory sinus arrhythmia and parasympathetic cardiac control: some basic issues concerning quantification, applications and implications. In: Cardiorespiratory and Cardiosomatic Psycophysiology, edited by P. Grossman, K. Jansenn, and D. Waitl. New York: Plenum Press, 1986, pp. 117–138.
[10]James, N. W., G. M. Adams, and A. F. Wilson. Determination of anaerobic threshold by ventilatory frequency. *Int. J. Sports Med*. 10(3):192–196, 1989.
[11]Lázaro, J., A. Alcaine, E. Gil, P. Laguna, and R. Bailón. Electrocardiogram derived respiration from QRS slopes. Engineering in Medicine and Biology Society (EMBC), 2012 Annual International Conference of the IEEE, 2013, pp. 3913–3916.
[12]Lázaro J., A. Alcaine, D. Romero, E. Gil, P. Laguna, L. Sörnmo, and R. Bailón. Electrocardiogram derived respiration from QRS slopes: evaluation over stress testing recordings. In: Computing in Cardiology, 2013, pp. 655–658.
[13]Lázaro, J., E. Gil, R. Bailón, A. Mincholé, and P. Laguna. Deriving respiration from photoplethysmographic pulse width. *Med. Biol. Eng. Comput*. 51(1–2):233–242, 2013.
[14]Leanderson, S., P. Laguna, and L. Sörnmo. Estimation of the respiratory frequency using spatial information in the VCG. *Med. Eng. Phys*. 25(6):501–507, 2003.
[15]Martínez, J. P., R. Almeida, S. Olmos, A. P. Rocha, and P. Laguna. A wavelet-based ECG delineator: Evaluation on standard databases. *IEEE Trans. Biomed. Eng*. 51(4):570–581, 2004.
[16]Mason, C. L., and L. Tarassenko. Quantitative assessment of respiratory derivation algorithms. In: Engineering in Medicine and Biology Society, 2001. Proceedings of the 23rd Annual International Conference of the IEEE, Vol. 2, 2001, pp. 1998–2001.
[17]Mateo, J., and P. Laguna. Analysis of heart rate variability in presence of ectopic beats using the heart timing signal. *IEEE. Trans. Biomed. Eng*. 50(3):334–343, 2003.
[18]Mazzanti, B., C. Lamberti, and J. de Bie. Validation of an ECG-derived respiration monitoring method. In: Computers in Cardiology, 2003, pp. 613–616 (2003).
[19]Meredith, D. J., D. Clifton, P. Charlton, J. Brooks, C. W. Pugh, and L. Tarassenko. Photoplethysmographic derivation of respiratory rate: a review of relevant physiology. *J. Med. Eng. Technol*. 36(1):1–7, 2012.
[20]Mincholé, A., E. Pueyo, J. F. Rodríguez, E. Zacur, M. Doblaré, and P. Laguna. Quantification of restitution dispersion from the dynamic changes of the T wave peak to end, measured at the surface ECG. *IEEE Trans. Biomed. Eng*. 58(5):1172–1182, 2011.
[21]Moody, G. B., R. G. Mark, A. Zoccola, and S. Mantero. Derivation of respiratory signals from multi-lead ECGs. In: Computers in Cardiology, 1985, pp. 383–386.
[22]Pinciroli F., R. Rossi, and L. Vergani. Detection of electrical axis variation for the extraction of respiratory information. In: Computers in Cardiology, 1986, pp. 499–502.
[23]Pueyo, E., L. Sörnmo, and P. Laguna. QRS slopes for detection and characterization of myocardial ischemia. *IEEE Trans. Biomed. Eng*. 55(2):468–477, 2008.
[24]Romero, D., M. Ringborn, P. Laguna, and E. Pueyo. Depolarization changes during acute myocardial ischemia by evaluation of QRS slopes: standard lead and vectorial approach. *IEEE Trans. Biomed. Eng*. 58(1):110–120, 2011.
[25]Romero, D., M. Ringborn, P. Laguna, and E. Pueyo. Detection and quantification of acute myocardial ischemia by morphologic evaluation of QRS changes by an angle-based method. *J. Electrocardiol*. 46:204–214, 2013.
[26]Sörnmo, L., and P. Laguna. ECG signal processing. In: Bioelectrical Signal Processing in Cardiac and Neurological Applications, edited by L. Sörnmo and P. Laguna New York: Elsevier, 2005, pp. 453–566.
[27]Varanini, M., M. Emdin, F. Allegri, M. Raciti, F. Conforti, A. Macerata, A. Taddei, R. Francesconi, G. Kraft, A. L. Abbate, and C. Marchesi. Adaptive filtering of ECG signal for deriving respiratory activity. In: Proceedings of the Computers in Cardiology, 1990, pp. 621–624.
[28]Zhang, P. Z., W. N. Tapp, S. S. Reisman, and B. H. Natelson. Respiration response curve analysis of heart rate variability. *IEEE Trans. Biomed. Eng*. 44(4):321–325, 1997.