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Conference Paper

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Publication date:
2016

Permanent link:
https://doi.org/10.3929/ethz-b-000122045

Originally published in:
https://doi.org/10.1109/EMBC.2016.7591663

X. -R. Ding, Y. -T. Zhang, H. K. Tsang and W. Karlen, "A pulse transit time based fusion method for the noninvasive and continuous monitoring of respiratory rate," 2016 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), 2016, pp. 4240-4243, doi: 10.1109/EMBC.2016.7591663.

A Pulse Transit Time Based Fusion Method for the Noninvasive and Continuous Monitoring of Respiratory Rate

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***Abstract* — The purpose of this study was to investigate whether pulse transit time (PTT) can be used for continuous monitoring of respiratory rate (RR). We derived PTT from the electrocardiogram and photoplethysmogram obtained from 42 recordings of CapnoBase, a publicly available benchmark data set for validating respiratory related measurements. The number of breaths in a minute ($RR_{\#}$) was estimated from the heart rate interval (HRI), pulse rate interval (PRI), and from PTT. In addition, to improve the estimation reliability, we investigated a fusion of the three HRI, PRI and PTT derived estimations. The root mean squared error (RSME) and a Bland-Altman plot were calculated using RR from capnography as reference. Finally, the proposed method was compared against the CapnoBase Smart Fusion RR benchmark estimation which estimates RR with three parameters extracted from the PPG signal alone. Thirty-seven recordings showed sufficient signal quality to estimate RR from PTT. The fused RR (RMSE 1.76 breaths/min) was more accurate than the estimations from PTT (RMSE 2.63 breaths/min), HRI (RMSE 1.96 breaths/min), and PRI (RMSE 2.73 breaths/min) alone. The proposed method also outperformed the CapnoBase benchmark (RMSE 3.08 breaths/min) algorithm. This study demonstrates that PTT is a valuable noninvasive parameter from which RR can be estimated.**

I. Introduction

Respiratory rate (RR) is an important vital sign and abnormal RR has been shown to be an early and sensitive indicator of diverse illnesses such as pulmonary embolus, pneumonia, congestive cardiac failure and metabolic emergencies [1]. The most common and basic methods for RR assessment are observing chest wall movements and auscultation with a stethoscope. These methods give only a snapshot of current situation rather than continuous measurement and have been shown to be inconsistent in clinical settings [2]. Instrumented RR measurement methods, such as detection of respiratory gas variations (i.e. through flow, temperature, humidity, O_2 or CO_2) or mechanical effort measured with strain gauges or impedance, provide continuous and more reliable RR measurements. However, these methods tend to be obtrusive and are cumbersome to apply, limiting their application [3]. Novel noninvasive, continuous and reliable RR estimation techniques are thus highly desirable.

Estimation of RR from noninvasively obtained physiological signals, such as electrocardiogram (ECG), photoplethysmogram (PPG), or arterial blood pressure (ABP) has been extensively studied [4, 5]. However, it is difficult to achieve accurate and robust RR by using ECG, PPG or ABP alone. To improve the reliability of the RR estimation, the fusion of multiple parameters was suggested, either from a single source [6] or multiples [7]. Pulse transit time (PTT) refers to the propagation time of a pulse wave between two places in the cardiovascular system. PTT is a marker for ABP [8] and features respiratory components [9]. Often, PTT is derived from ECG and PPG and also known as pulse arrival time [10]. This measurement method includes the pre-ejection time period and thus differs from the PTT that is calculated from two peripheral pulses. Several studies have previously addressed the potential of PTT calculated from ECG and PPG to evaluate respiratory effort associated with intrathoracic pressure changes [11, 12]. For example, Johansson et al. found correlations between PTT and RR under different ABP levels [13], but only the relative variation of PTT with respiration was reported and RR accuracy was not quantitatively estimated. It remains unclear whether PTT can accurately estimate RR in clinical situations and provide a continuous and reliable RR.

In this study, we compared estimations of RR from PTT with estimations obtained from heart rate interval (HRI) and pulse rate interval (PRI) extracted from ECG and PPG, respectively. Further, we investigated a known fusion method called Smart Fusion (SF) [6] to combine all three estimations with the aim to improve the estimation reliability.

II. Methods

A. Pulse Transit Time Measurement and Preprocessing

We calculated PTT as the time difference between the R wave peak of the ECG signal and the peak of the first derivative of the PPG signal (dPPG). HRI and PRI were measured from peak to peak of ECG and peak to peak of dPPG, respectively (Fig. 1).

PTT, HRI and PRI obtained from each cardiac cycle were intermittent variables and therefore interpolated using a spline function to 300 Hz. Low frequency noise and other components lower than normal respiratory frequencies, were removed with a 'db3' wavelet transform at level 16.

This work was supported in part by the Guangdong Innovation Research Team Fund for Low-cost Healthcare Technologies in China, the External Cooperation Program of the Chinese Academy of Sciences (Grant GJHZ1212). Asterisk indicates corresponding author.

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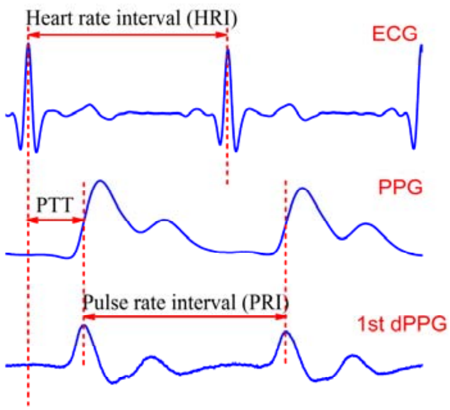

Figure 1. Calculation of pulse transit time (PTT), heart rate interval (HRI) and pulse rate interval (PRI) from synchronized recordings of ECG and PPG.

B. *Respiratory Rate Measurement with Pulse Transit Time and Smart Fusion*

The interpolated PTT, HRI and PRI signals were segmented into 60 s windows with a sliding window of three seconds. For each window we derived the number of breaths in one minute ($RR_{\#}$), the instantaneous RR (RR_{inst}) and RR_{PSD} derived from the maximum peak of the power spectral density (PSD). $RR_{\#}$ was calculated by counting the number of peaks in a window. RR_{inst} was measured as the average instantaneous rate for each window, where the instantaneous rate was calculated as the time interval between two peaks divided by 60. The PSD was calculated using Welch's method. The previously developed SF method in Karlen et al. [6] was adapted to use $RR_{\#}$, RR_{inst} and RR_{PSD} as inputs. For each window, the three components were fused by calculating their average and standard deviation. Windows with standard deviations larger than four breaths per minute (breaths/min) were considered untrustworthy, subsequently eliminated, and no estimation was provided for analysis.

C. *Validation*

The performance of the proposed RR estimation method was evaluated on the CapnoBase Respiratory Rate Benchmark data set [14]. In this set, continuous ECG, PPG and capnogram sampled at 300 Hz were collected during elective surgery and routine anesthesia from 42 subjects (aged 20.9 ± 19.5 years) under spontaneous or controlled ventilation for 8 minutes.

The root mean square error (RMSE) was calculated for each estimation type against the validated CapnoBase reference RR obtained from capnography. The significance level was tested with the Kruskal-Wallis ANOVA test. P values less than 0.05 were considered as statistically significant. The agreements between the estimations and the reference RR were depicted with scatter and Bland-Altman plots and by calculating the Pearson correlation coefficient as well as the bias and confidence intervals.

In addition to the reference comparison, we compared the fusion of RR estimations against a benchmark algorithm. We selected the original SF algorithm that operates with three respiratory estimations from the PPG signal (PPG SF method) and that was previously tested against the CapnoBase benchmark data set [6].

III. Results

Five of the 42 CapnoBase benchmark cases (0031, 0115, 0128, 0147, and 0331) had too poor signal quality for calculating PTT, HRI and PRI and were excluded for further analysis.

A. *Respiratory Rate Estimation with Pulse Transit Time*

PTT varied during each breath cycle and the dominant frequency spectrum corresponded to that of the reference respiratory signal (Fig. 2). Furthermore, the $RR_{\#}$, RR_{inst} and RR_{PSD} estimated from PTT followed well the dynamic changes of the reference RR, however with unequal delays (Fig. 3).

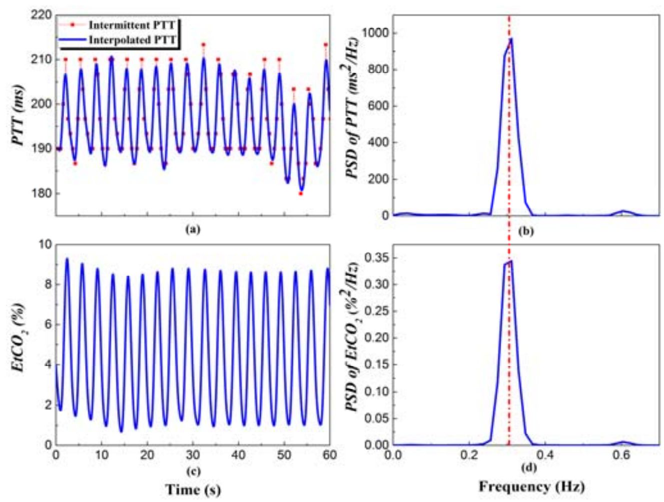

Figure 2. Time series and PSD of PTT (a, b) and end tidal CO_2 ($EtCO_2$) (c, d) for one representative sample.

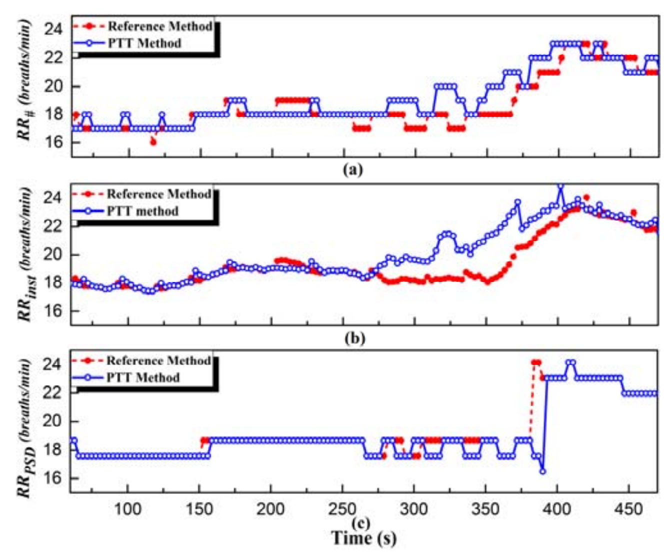

Figure 3. The estimated respiratory rate (RR) (unfilled circle continuous line) compared with that of the reference (filled circle dashed line) for one representative example for (a) number of breaths ($RR_{\#}$), (b) instantaneous RR (RR_{inst}) and (c) RR obtained from PSD (RR_{PSD}).

B. Respiratory Rate Estimation Using Smart Fusion Method

The RMSE of the PTT-HRI-PRI SF estimation method was significantly lower than any of the estimates from PTT, HRI or PRI alone and the fusion of the estimate from both HRI and PRI, independent of the RR calculation method (Fig. 4). The biggest effect was seen for the RR_{PSD} where the RMSE was reduced by more than 2.7 breaths/min compared to the individual estimations.

The fusion of PTT, HRI, and PRI estimations correlated with the reference for $RR_{\#}$ (r=0.97), RR_{inst} (r=0.95) and RR_{PSD} (r=0.96) (Fig. 5 a, c, e). The limits of agreements were -2.61 to 3.85 breaths/min ($RR_{\#}$), -2.51 to 5.77 breaths/min (RR_{inst}) and -3.80 to 3.50 breaths/min (RR_{PSD}) and the bias at 0.62, 1.63 and -0.15 breaths/min, respectively (Fig. 5 b, d, f). The SF method eliminated untrustworthy estimations in 22.4% of windows for the RR_{PSD} estimation, while there were only 1.8% and 3.9% windows eliminated for $RR_{\#}$ and RR_{inst}, respectively.

The PTT-HRI-PRI SF was comparable to the benchmark PPG SF algorithm (Fig. 6a) with a narrower limit of agreement (PPG SF -5.17 to 6.59 breaths/min, Fig. 6b).

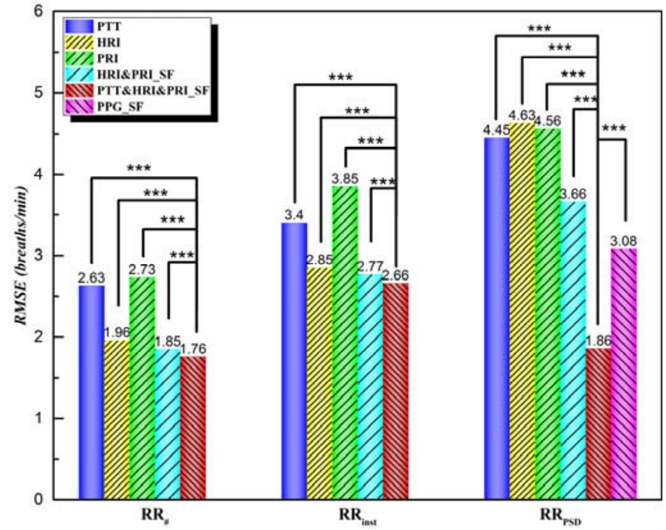

Figure 4. RMSE for PTT (yellow), HRI (cyan), PRI (magenta), the PTT-HRI-PRI smart fusion (PTT SF) method (blue), and the benchmark PPG SF method (red) for number of breaths ($RR_{\#}$), instantaneous RR (RR_{inst}) and RR from PSD (RR_{PSD}). *** indicates significance level < 0.001.

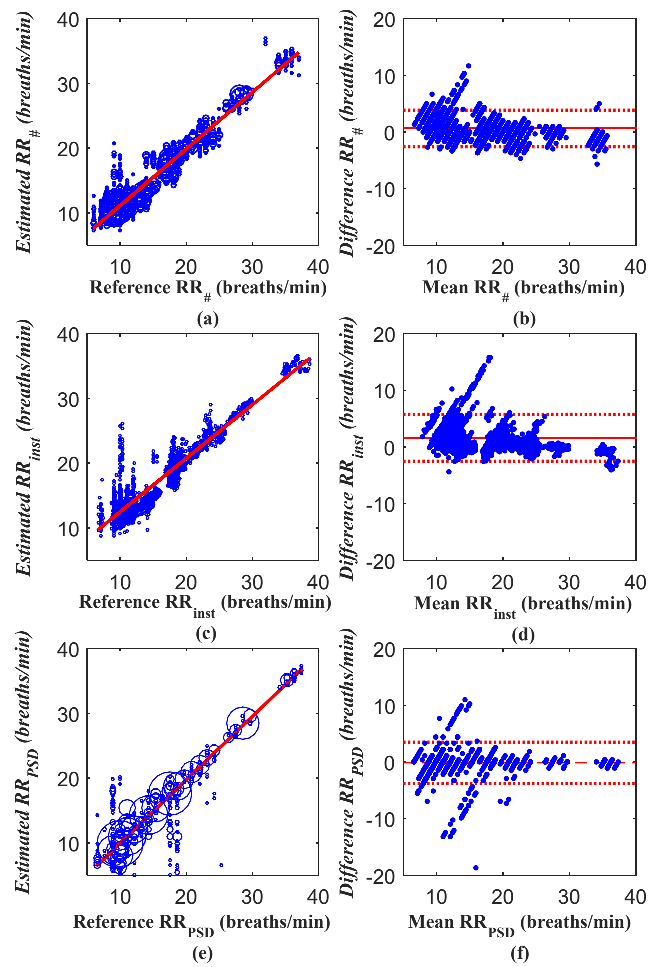

Figure 5. Scatterplot and Bland-Altman plot of the RR estimation of the *PTT-HRI-PRI smart fusion* method against the reference RR for number of breath ($RR_{\#}$) (a, b), instantaneous RR (RR_{inst}) (c, d) and RR detected by PSD (RR_{PSD}) (e, f).

IV. Discussion

We have shown that RR can be estimated from the PTT using existing and simple signal processing methods with RMSE as low as 2.6 breaths/min. The fusion of HRI, PRI, and PTT estimations and the eliminations of unreliable estimations lead to a significant reduction of RMSE to as low as 1.8 breaths/min.

Prior work has shown that respiratory events and respiratory variation are present in the PTT. Research by Foo et al. involved the detection of central respiratory events in infants using PTT and indicated that PTT changes with in respiratory efforts [15]. Drinnan et al. investigated the relationship between changes in heart rate and PTT during paced respiration [9]. Both findings demonstrated that PTT varied with respiration. We have confirmed these observations and quantitatively assessed the accuracy of RR estimation using PTT. The low error of the proposed method suggested that PTT has potential for noninvasive and continuous estimation of RR that has also clinical relevance.

The RR estimation accuracy was dependent on the calculation method. The estimations of $RR_{\#}$ and RR_{inst} were more reliable than RR_{PSD}. This was observed on the one hand by the higher RMSE in individual estimations of RR_{PSD} of more than 4.40 breaths/min compared to less than 3.85 breaths/min in the other calculations. On the other hand, the introduction of the SF eliminated the highest number of estimation windows (22.4%) and also reduced the RMSE by more than 2.5 breaths/min, a much higher difference than in the other calculations. One possible explanation for this could be the limited frequency resolution when calculating PSD. This implies that the time-domain RR calculations $RR_{\#}$ and RR_{inst} might be better parameters for RR monitoring.

Fusion multiple data sources for estimating RR is not new. In the study by Karlen et al., we have fused the frequency, intensity and amplitude of PPG signal [6]. In the present work we directly compared the results for RR_{PSD}. The obtained RMSE of 3.0 breaths/min for the PPG approach was

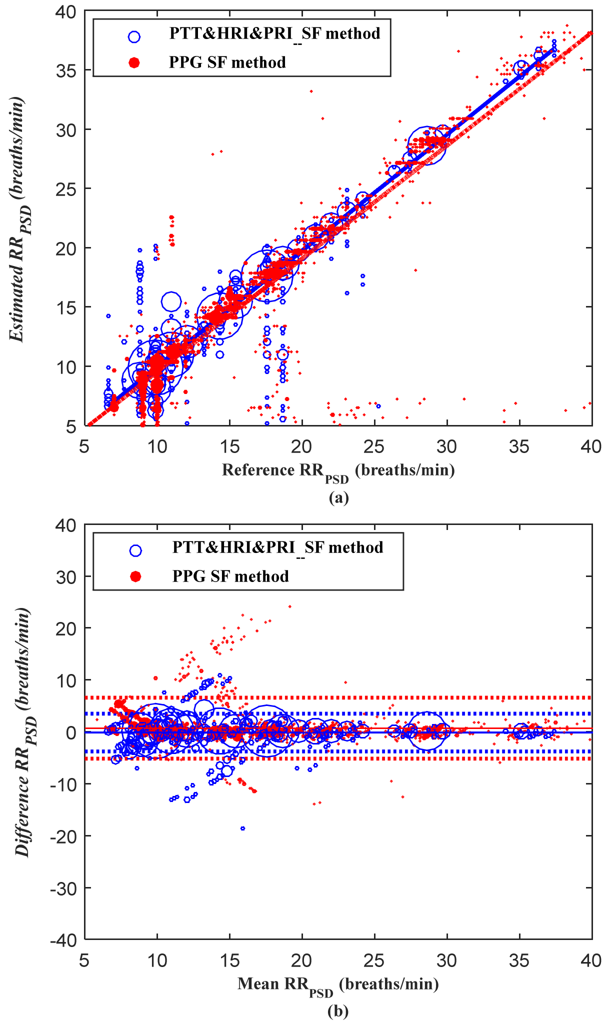

Figure 6. Scatter plot (a) and Bland-Altman plot (b) of RR_{PSD} from PTT-HRI-PRI smart fusion (PTT SF) method (blue circle) and PPG smart fusion (PPG SF) benchmark method (red filled circle).

significantly higher than the 1.86 breaths/min of the fusion of HRI, PRI and PTT, suggesting a benefit of using multiple physiological signals in the fusion. Orphanidou et al. fused the ECG derived respiratory sinus arrhythmia and R-peak amplitude with an autoregressive method [16], resulting in a mean absolute error of 0.80 breaths/min for 40 healthy subjects.

The PTT calculation was inherently limited to be more sensitive to noise compared to ECG and PPG signals, since it was derived from both signals for each cardiac cycle. In this study five cases needed to be excluded from the benchmark data set because of too high noise levels. An alternative estimation method is needed for such situations. Furthermore, the data set used in this study was limited to a small number of ventilated subjects. To derive a more generalized finding about robustness and accuracy of the proposed methods, experiments should be repeated with more diverse recordings that include spontaneously breathing subjects over longer periods of time.

V. Conclusion

We have adopted PTT for continuously estimating RR and proposed to integrate RR estimations from PTT, HRI and PRI with the SF method to enhance the estimation reliability. The obtained accuracy is clinically relevant and compares favorably to performance of other previously published methods. This study demonstrated that PTT is an additional noninvasive parameter from which RR can be extracted.

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