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Published in:
Physiological Measurement

DOI:
10.1088/1361-6579/aaf978

2019

Document Version:
Peer reviewed version (aka post-print)

Monitoring Respiration using the Pressure Sensors in the Dialysis Machine

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December 2018

Abstract. *Objective:* Although respiratory problems are common among patients with end-stage renal disease, respiration is not continuously monitored during dialysis. The purpose of the present study is to investigate the feasibility of monitoring respiration using the pressure sensors of the dialysis machine. *Approach:* Respiration induces variations in the blood pressure that propagates to the extracorporeal circuit of the dialysis machine. However, the magnitude of these variations are very small compared to pressure variations induced by the dialysis machine. We propose a new method, which involves adaptive template subtraction and peak conditioned spectral averaging, to estimate respiration rate from the pressure sensor signals. Using this method, an estimate of the respiration rate is obtained every 5th second provided that the signal quality is sufficient. The method is evaluated for continuous monitoring of respiration rate in nine dialysis treatment sessions. *Main results:* The median absolute deviation between the estimated respiration rate from the pressure sensor signals and a reference capnography recording was 0.02 Hz (1.3 breaths per min). *Significance:* Our results suggest that continuous monitoring of respiration using the pressure sensors of the dialysis machine is feasible. The main advantage with such monitoring is that no additional sensors are required which may cause patient discomfort.

1. Introduction

3.3 million patients worldwide suffer from end-stage renal disease (ESRD) and rely on hemodialysis for their survival (Liyanage, Ninomiya, Jha, Neal, Patrice, Okpechi, Zhao, Lv, Garg, Knight, Rodgers, Gallagher, Kotwal, Cass & Perkovic 2015). Most of these patients spend three to four hours, three times a week, in dialysis treatment. Continuous monitoring during the treatment sessions can improve patient management and help to reduce the risk of adverse events. Recently proposed methods for improved patient monitoring during dialysis treatment includes those aiming at optimizing the dialysis dose (Fridolin, Karai, Kostin & Ubar 2013), predicting and preventing complications such as intradialytic hypotension (Sandberg, Bailón, Hernando, Laguna, Martínez, Solem & Sörnmo 2014), (Sörnmo, Sandberg, Gil & Solem 2012) and early detection of adverse events such as venous needle dislogement (Holmer 2017).

It is common that patients with chronic kidney disease also suffer from respiratory problems. Several complex mechanisms are involved in the cardio-pulmonary-renal interactions linking respiratory problems and ESRD; a recent review on this topic is given in (Husain-Syed, McCullough, Birk, Renker, Brocca, Seeger & Ronco 2015). Fluid overload can cause pulmonary edema, pleural effusions, and upper airway obstruction. Additionally, kidney disease is associated with chronic obstructive pulmonary disease and central sleep apnea. Sleep disturbances are extremely common in patients with ESRD, with sleep apnea occurring in 60% or more of such patients (Pierson 2006).

Monitoring of respiratory activity during hemodialysis can help to reduce the risk of hypoxia due to decreased alveolar ventilation. Respiration is regulated primarily by the respiratory center in the brain stem, that integrates neural, hormonal and chemical signaling and controls the respiratory movements. Dialysis treatment may cause alterations in pH and/or carbon dioxide levels in the blood that affects the signaling from the chemo receptors to the respiratory center and can induce hypoventilation and hypoxia. Hypoxia was a very common complication when hemodialysis was first introduced in the treatment of renal failure (Pierson 2006). Although hemodialysis treatment has improved significantly, and hypoxia is not as frequent, it still a complication that occurs during dialysis. In a retrospective cohort study conducted between 2012 and 2015, 10% of the 983 dialysis patients had prolonged intradialytic hypoxia. Prolonged intradialytic hypoxia was found to be associated with higher all-cause hospitalization and mortality (Meyring-Wösten, Zhang, Ye, Fuertinger, Chan, Kappel, Artemyev, Ginsberg, Wang, Thijssen & Kotanko 2016).

Continuous monitoring of respiratory rate can improve patient management and may help the nurses to prevent hypoxia by nasal oxygen administration. However, such monitoring is currently not part of the clinical routine, one reason being the discomfort caused by wearing respiratory sensors. Another reason is the additional work required by the clinical staff to attach the sensors. Hence, it is of vital clinical importance to develop a method for intradialytic monitoring of respiratory activity that does not cause discomfort or add to the workload of the staff. We have previously proposed a method for monitoring cardiac activity using the pressure sensors of the dialysis machine (Holmer, Sandberg, Solem, Grigonytė, Olde & Sörnmo 2015, Holmer, Sandberg, Solem, Olde & Sörnmo 2016). The objective of the present study is to investigate the feasibility of using a similar approach for continuous monitoring of respiratory activity during dialysis.

It is well known that respiratory activity causes modulation of the blood pressure (BP). Three different types of respiratory induced variations are commonly seen in photoplethysmographic (PPG) signals: 1) baseline variation caused by thoracic pressure changes during the respiratory cycle; increased thoracic pressure during the inhalation phase causes a slight elevation of BP, and correspondingly the exhalation phase is associated with a slight reduction of BP, 2) cardiac pulse amplitude variation caused by variations in cardiac output due to the thoracic pressure variations and 3) heart rate variations caused by respiratory induced autonomic modulation (Charlton, Bonnici, Tarassenko, Alastruey, Clifton, Beale & Watkinson 2017). Our preliminary results shows

that respiration rate estimation based on variations in heart rate variations is unfeasible for dialysis patients due to impaired autonomic response (Sandberg, Holmer, Olde & Solem 2014). Hence, the focus of this study is on respiratory induced variations in BP magnitude.

This paper is organized as follows. The dataset obtained from patients with ESRD undergoing hemodialysis is described in Sec. 2.1. The method for extraction of respiratory information from the pressure sensors of the dialysis machine is described in Sec. 2.2, and a robust method for estimation of respiration rate from the extracted information is described in Sec. 2.3. The results comparing the estimated respiration rate to the respiration rate obtained from a reference capnographic signal are presented in Sec. 3, and discussed in Sec. 4.

2. Methods

2.1. Dataset

A clinical study was conducted at the Kidney and Transplantation Clinic at Skåne University Hospital in Malmö, Sweden 2012. Seven patients with ESRD (5 male and 2 female, age 72 ± 12 (mean$\pm$ std) years, dry-weight 88 ± 20 kg) on regular hemodialysis were included in the study. The study was approved by the local research ethics committee and all patients signed an informed consent. The patients were treated with Artis ^{TM} dialysis machines (Gambro). Pressure signals from the arterial and venous pressure sensor of the dialysis machine, sampled at 200 Hz were recorded throughout nine dialysis sessions, see Fig. 1. The pressure varies considerably over time, and respiratory induced pressure variations are concealed by much larger pressure pulses induced by the peristaltic blood pump of the dialysis machine, see Fig. 1 (c-d). The peristaltic pump is equipped with a Hall effect sensor which provides information about the angular position of the blood pump rotors; the resulting Hall sensor signal is sampled at 200 Hz. Reference respiratory capnography signals (Lifesense), sampled at 4 Hz, were also recorded throughout the dialysis sessions.

2.2. Extraction of Respiratory Information

Respiratory information is extracted from the arterial and venous pressure signals separately using a similar methodology for the respective signals, see Fig 2. First, as preprocessing, the DC level is removed from the pressure signals by subtracting the 5-min median value of the signal. The 5-min segments length is chosen to avoid removal of respiratory induced baseline variations and yet allow tracking of changes in the static pressure level. Outlier rejection is performed to remove samples in the original signals that are unreliable, and linear interpolation is performed to fill the gap; a sample is classified as an outlier if the difference between two consecutive samples is larger than 5mmHg. The preprocessed pressure signals from the venous and arterial pressure sensors are denoted $y_v(n)$ and $y_a(n)$, respectively.

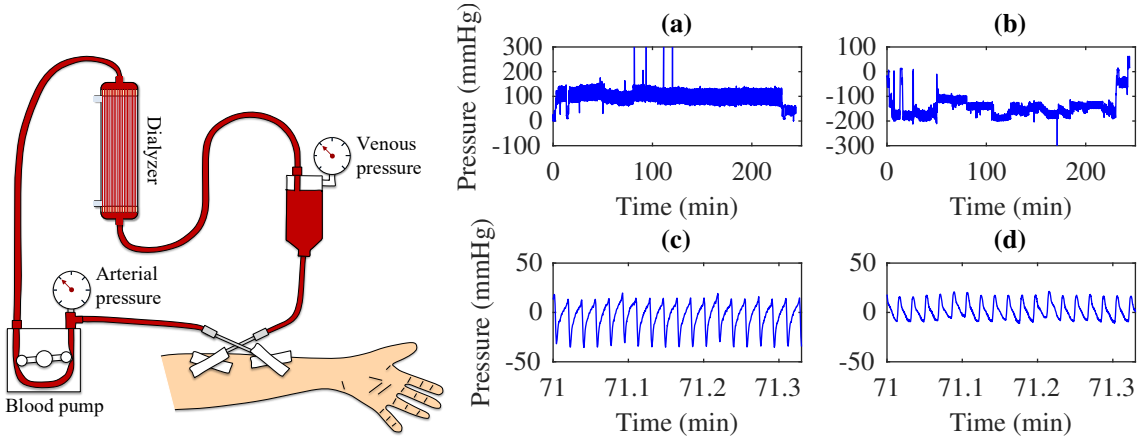

Figure 1. (left) The extracorporeal blood circuit of a hemodialysis machine with venous and arterial pressure sensors and a peristaltic blood pump. (right) Pressure signals from (a,c) the venous and (b,d) the arterial pressure sensor, respectively. Recordings from a whole dialysis session are displayed in (a,b), whereas (c,d) zoomed in on 20 seconds of the recording following preprocessing.

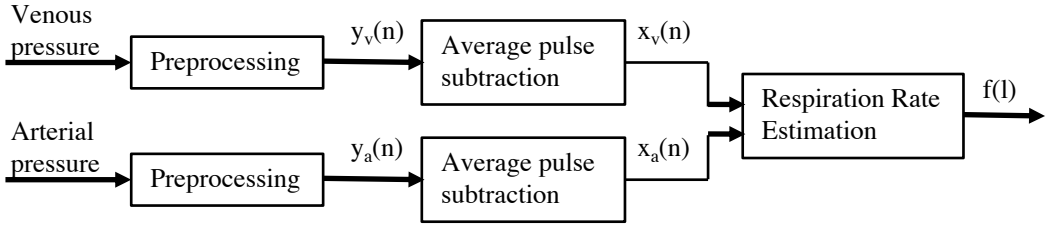

Figure 2. Overview of the method for estimating respiration rate from the arterial and venous pressure sensors in the dialysis machine.

Following preprocessing, a template pressure pulse is constructed. The preprocessed pressure signal $y(n) \in [y_v(n), y_a(n)]$ is resampled to obtain M synchronously sampled signal segments $\mathbf{y}_s(m)$ of length $N = 200$ containing pressure pulses corresponding to one revolution each.

$$\mathbf{y}_s(m) = \left[\begin{array}{cccc} y(t_s(mN)) & y(t_s(mN+1)) & \dots & y(t_s(mN+k)) \end{array} \right] \tag{1}$$

The sample times of the m:th pressure pulse are given by

$$t_s(mN+k) = t_p(m) + k\frac{t_p(m+1) - t_p(m)}{N}, \quad k = 0 \dots N-1 \tag{2}$$

where $t_p(m)$ denotes the onset time of the m:th pump revolution; the onset times are detected from a tachometer signal obtained using the Hall sensor on the peristaltic pump of the dialysis machine.

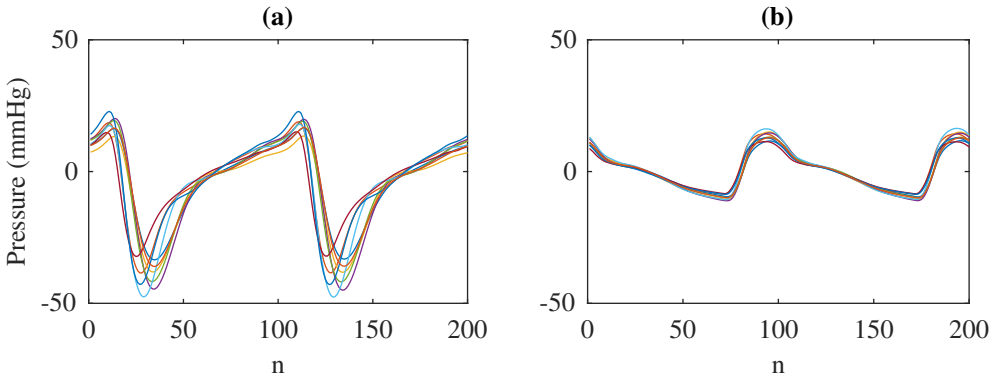

Figure 3. Template pressure pulses $\bar{\mathbf{p}}_\mathbf{s}$ obtained from (a) the venous pressure sensor signals and (b) the arterial pressure sensor signals in each of the 9 dialysis sessions.

Signal segments containing excessive noise or sudden changes are excluded from further analysis. Such segments are detected based on lack of similarity to a template pump pressure pulse. The template pressure pulse $\bar{\mathbf{p}}_\mathbf{s}$ is obtained using the global median of the synchronously sampled signal segments $\mathbf{y}_s(m)$, see Fig. 3 If $\mathbf{y}_s(m)$ deviates to much from the template pressure pulse $\bar{\mathbf{p}}_\mathbf{s}$, quantified by a correlation coefficient $r < 0.95$, the signal segment is removed from further analysis.

To extract the cardio-resipratory component of the pressure signal, an adaptively updated template pump pressure pulse $\mathbf{p}_s(m)$ is subtracted from each of the remaining synchronously sampled signal segment $\mathbf{y}_s(m)$.

$$\mathbf{x}_s(m) = \mathbf{y}_s(m) - \mathbf{p}_s(m), \quad m = 0 \dots M-1. \tag{3}$$

where

$$\mathbf{p}_s(m) = \gamma \mathbf{p}_s(m-1) + (1-\gamma)\mathbf{y}_s(m-1), \quad m = 0 \dots M-1. \tag{4}$$

and the forgetting factor $\gamma = 0.95$. The initial template pump pressure pulse $\mathbf{p}_s(0)$ is set to $\bar{\mathbf{p}}_\mathbf{s}$.

The signal segments $\mathbf{x}_s(1), \mathbf{x}_s(2), \dots, \mathbf{x}_s(M)$ are concatenated to construct the length MN signal $x_s(l)$. The synchronously sampled signal $x_s(l)$ is then uniformly resampled at the original sampling rate $F_s = 200$ Hz to obtain the signal $x(n) \in [x_v(n), x_a(n)]$. The process of obtaining $x(n)$ from $y(n)$ is summarized in Fig. 4, and a signal example is given in Fig. 5.

2.3. Estimation of Respiratory Rate

A robust estimate of the respiration rate is obtained by combining information from the venous and arterial pressure signals, $x_v(n)$ and $x_a(n)$, respectively, using a method inspired by the work of (Lázaro, Alcaine, Romero, Gil, Laguna, Pueyo & Bailón 2014). In this method, referred to as peak conditioned spectral averaging, the frequency spectra of sufficient quality are averaged to produce a spectrum from which the respiration rate

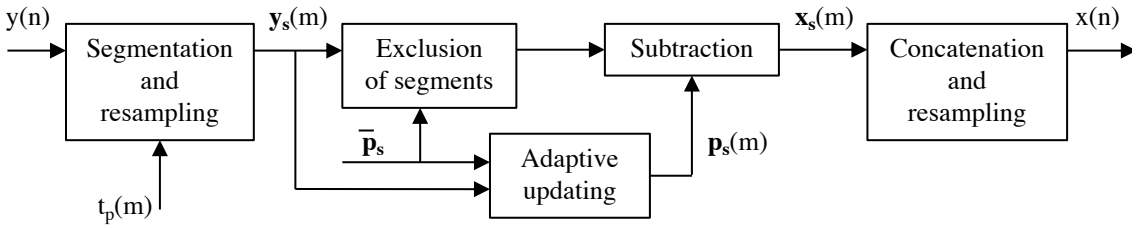

Figure 4. Overview of the process of average pulse subtraction for obtaining $x(n)$ from $y(n)$.

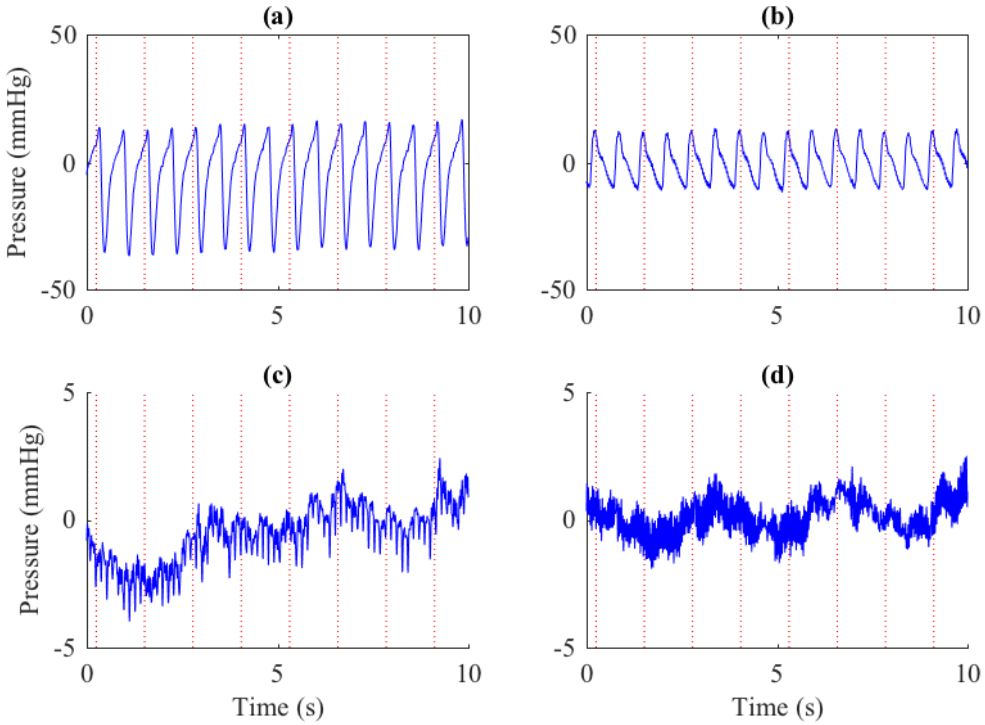

Figure 5. (a) Pressure signal from the venous pressure sensor $y_v(n)$ and (c) corresponding $x_v(n)$ and (b) pressure signal from the arterial pressure sensor $y_a(n)$ and (d) corresponding $x_a(n)$. Red dotted lines denotes the pump pressure pules onset times t_m detected using the Hall sensor signal.

is estimated; the peakedness of the spectrum of each signal segment is used to decide if the signal quality is sufficient.

First, $x_v(n)$ and $x_a(n)$ are lowpass filtered, using a 6:th order Butterworth filter with cutoff frequency of 2 Hz, and resampled to 4 Hz to obtain the signals $\tilde{x}_v(n)$ and $\tilde{x}_a(n)$ containing respiratory induced pressure variations. Sequential Welsh periodograms are estimated from sliding 40-s segments of $\tilde{x}_v(n)$ and $\tilde{x}_a(n)$, respectively. New periodograms $S_k^v(f)$ and $S_k^a(f)$ are obtained every 5:th second by averaging power spectra of 50% overlapping 12-s subintervals after power normalization in the $0-1$ Hz interval; k is a running index.

Sequential periodograms $S_k^v(f)$ and $S_k^a(f)$ of sufficient quality are averaged to produce power spectra from which the respiration rate can be estimated more robustly. A periodogram is considered of sufficient quality if 1) it has a sufficiently large spectral peak in an interval around a reference respiration rate f_R and 2) the energy in the spectral peak interval is sufficiently large. The interval around the reference respiration rate is set to $[f_R - 0.125\text{Hz}, f_R + 0.25\text{Hz}]$, where the lower bound is constrained to be above 0.15 Hz and the upper bound is constrained to be below 0.5 Hz. The spectral peak is considered sufficiently large if its magnitude is more than 85% of the magnitude of the largest peak in the spectra; the frequency of the spectral peak closest to f_R that fullfils these criteria is denoted $f_p(k)$. The spectral peak interval is set to $[f_p(k) - 0.048\text{Hz}, f_p(k) + 0.048\text{Hz}]$ and the energy in this interval is considered sufficient if it contains $> 30\%$ of the total energy in the spectra. If the energy in the peak interval differs more than 5% between $S_k^v(f)$ and $S_k^a(f)$, only the spectrum with the most energy in the peak interval is used for averaging.

Averaged spectra $S_l(f)$ are produced by averaging consecutive spectra $S_k^v(f)$ and $S_k^a(f)$ of sufficient quality for $k = l - 4 \ldots l$. The respiration rate is estimated by tracking $f_p(l)$ in the averaged spectra, i.e., the position of the spectral peak that is closest to the reference respiration rate f_R. The respiration rate $f_r(l)$ of the l:th segment is given by $f_r(l) = 0.7 f_p(l) + 0.3 f_r(l-1)$. The reference respiration rate is initially set to $f_R(0) = 0.275\ Hz$, and is adaptively updated using $f_p(l)$ so that $f_R(l) = 0.8 f_R(l-1) + 0.2 f_p(l)$. If the averaged spectra $S_l(f)$ has insufficient quality or is lacking due to insufficient quality of $S_k^v(f)$ and $S_k^a(f)$, no estimate of the respiration rate $f_r(l)$ is produced and the reference respiration rate is not updated, i.e., $f_R(l+1) = f_R(l)$.

2.4. Evaluation

The accuracy of the respiration rate estimates obtained from the pressure sensors of the dialysis machine is evaluated by comparing to respiration rates obtained from simultaneously recorded capnography signals $x_{\text{capno}}(n)$. The respiration rate is estimated from $x_{\text{capno}}(n)$ using peak conditioned spectral averaging as described in Sec 2.3; sequential Welsh periodograms of sufficient quality obtained from $x_{\text{capno}}(n)$ are used to produce the averaged spectra $S_l^c(f)$ from which the reference respiration rate $f_r^c(l)$ is estimated.

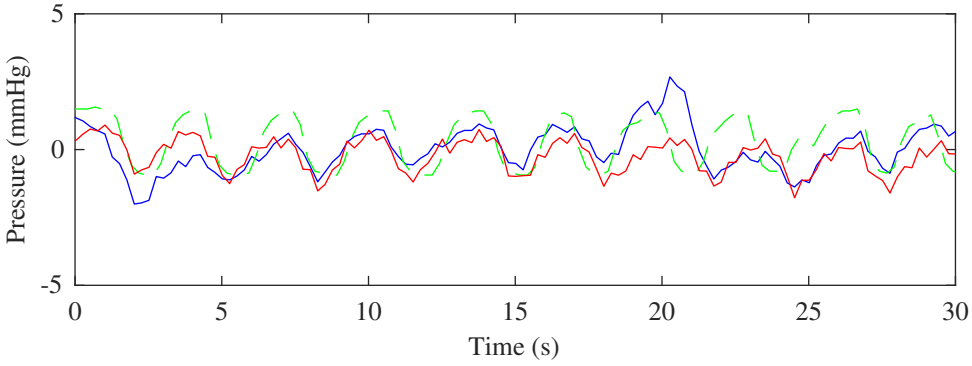

Figure 6. Extracted respiratory signal from (solid blue line) the venous pressure sensor $\tilde{x}_v(n)$ and (solid red line) the arterial pressure sensor $\tilde{x}_a(n)$ and (dashed green line) corresponding reference corresponding reference capnography signal $x_{\text{capno}}(n)$.

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3. Results

An example of extracted respiratory signals $\tilde{x}_v(n)$ and $\tilde{x}_a(n)$ and corresponding reference capnograhpy signal $x_{\text{capno}}(n)$ are displayed in Fig. 6. On average $\tilde{x}_v(n)$ can be extracted from 70% of the venous pressure sensor signals (range 57% to 79%) and $\tilde{x}_a(n)$ can be extracted from 51% arterial pressure sensor signals (range 5% to 81%).

Sequential periodograms $S_k^v(f)$ and $S_k^a(f)$ and corresponding averaged spectra $S_l(f)$ and estimated respiration rate $f_r(l)$ from one treatment session are displayed in Fig 7. In this recording $f_r(l)$ could be obtained in 47% of the analyzed segments. On average $f_r(l)$ was obtained in 43% of the segments in a recording (range 5% to 74%).

The estimated respiratory rate from the pressure sensors $f_r(l)$ and the corresponding $f_r^c(l)$ from one treatment session are displayed in Fig. 8. The respiration rate changes considerably during the treatment session, $f_r^c(l)$ ranges from 0.21 Hz to 0.48 Hz (12.7 to 29.1 breaths per min) and $f_r(l)$ varies correspondingly. In this session, the median absolute difference between $f_r(l)$ and $f_r^c(l)$ was 0.02 Hz (1.2 breaths per min), and $f_r(l)$ was obtained in 63% of the recording. The median absolute difference between $f_r(l)$ and $f_r^c(l)$ in the treatments sessions ranged from 0.017 Hz to 0.21 Hz (median 0.022 Hz, IQR 0.008 Hz); the difference was below 0.03 Hz (1.8 breaths per min) in all recordings except one.

A Bland-Altman plot comparing $f_r(l)$ and $f_r^c(l)$ in all analyzed segments is presented in Fig. 9 (a), and a histogram showing the distribution of the differences between $f_r(l)$ and $f_r^c(l)$ is displayed in Fig 9 (b). The median absolute differences between $f_r(l)$ and $f_r^c(l)$ is 0.022 Hz (1.3 breaths per min); in 79% of the analyzed segments the difference between $f_r(l)$ and $f_r^c(l)$ was smaller than 0.05 Hz (3 breaths per min).

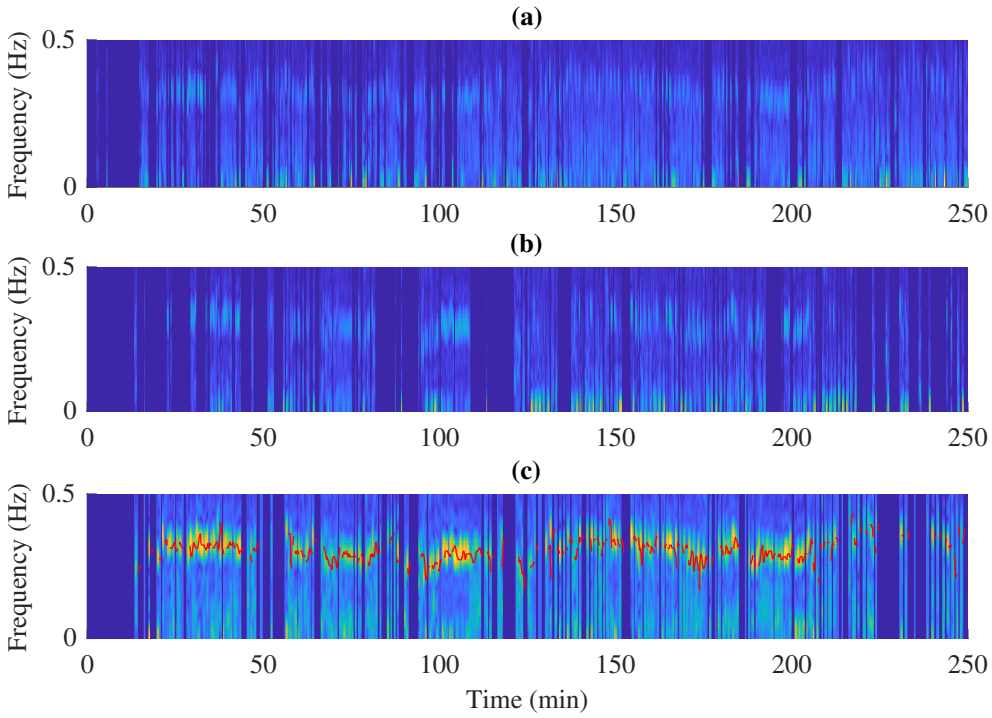

Figure 7. Concatenated sequential peroiodograms (a) $S_k^v(f)$ and (b) $S_k^a(f)$ and (c) corresponding concatenated averaged spectra $S_l(f)$ and (red solid line) estimated respiration rate $f_r(l)$ from the pressure sensor signals during one dialysis session.

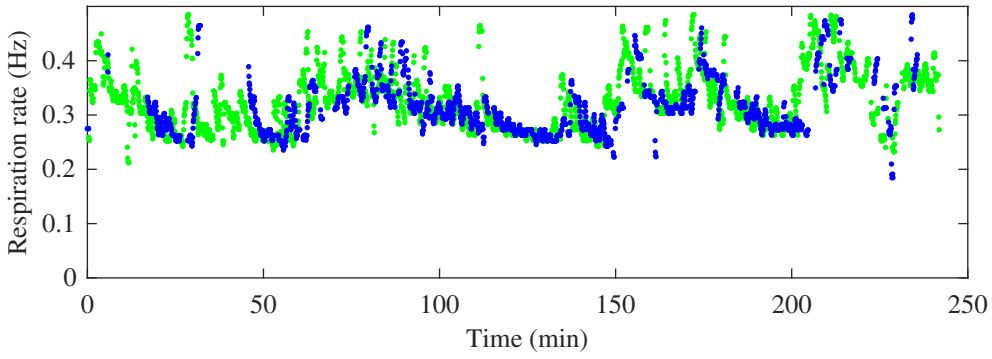

Figure 8. Respiration rate estimated from (blue) the pressure sensor signals $f_r(l)$ and (green) the corresponding reference capnograpy signal $f_r^c(l)$.

4. Discussion

Our results show that respiration rate can be accurately estimated using the pressure sensors of the dialysis machine. The proposed method allows continuous monitoring and detection of sudden changes in respiration rate. In a preliminary study, we used linear filtering of the pressure sensor signals in the 0.15–0.4 Hz band to obtain respiratory information in selected 20-min segments (Sandberg, Holmer, Olde & Solem 2014). Although the results of that study were comparable to the results of the present study,

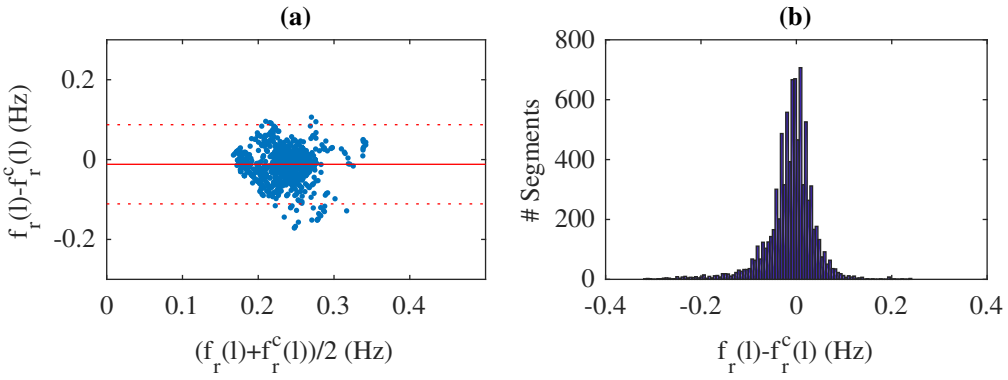

Figure 9. (a) Bland-Altman plot comparing $f_r(l)$ and $f_r^c(l)$. (solid line) Mean $f_r(l) - f_r^c(l)$ and (dashed lines) mean±1.96 std. (b) Histogram of $f_r(l) - f_r^c(l)$ in all analyzed segments.

such approach is unfeasible for continuous monitoring of respiration, partly due to lack of signal quality control. Quality control is crucial for the performance of the proposed method and is done in two steps. The first step is to exclude signal segments with sudden changes or excessive noise from analysis. The second step is to only include frequency spectra of sufficient quality when estimating respiration rate.

Another reason to why the 0.15–0.4 Hz bandpass filtering approach is unfeasible for continuous monitoring is that subtile changes in the pump induced pressure variations may overshadow respiratory induced variations in this frequency band. Since pump induced pressure variations are of much larger magnitude than the respiratory induced pressure variations, meticulous removal of pump pressure pulses is crucial for the performance of the method. Accurate determination of pump pressure pulse onset times was achieved using information about the angular position of the blood pump rotor obtained from a Hall sensor in the Artis dialysis machine. To account for variations in pump rate and pump pressure pulse morphology, synchronous resampling and adaptive updating of the template pressure pulse was employed. In our previous work (Holmer et al. 2015, Holmer et al. 2016, Holmer, Martínez, Gil, Sandberg, Olde & Sörnmo 2018) a more computationally demanding method, where an iteratively refined pump model signal was subtracted from the pressure signals, was used since the AK200 dialysis machine used in those studies did not provide information on the angular position of the blood pump rotor.

Other techniques for non-contact monitoring of cardiac and respiratory activity during dialysis treatment includes camera-based PPG (Tarassenko, Villarroel, Guazzi, Jorge, Clifton & Pugh 2014). Although this technique seems promising, it is still sensitive to movements and variations in ambient light. Further, issues relating to integrity using video monitoring remains to be solved. Continuous monitoring of arterial oxygen saturation during dialysis can be achieved with the CritLine monitor which measures light absorption at different wavelengths in the blood of the extracorporeal circuit (Campos, Chan, Zhang, Deziel, Vaughn, Meyring-Wösten & Kotanko 2016).

However, monitoring of oxygen saturation cannot replace monitoring of respiration rate since these measurements provide complementary information. The correlation between respiration rate and oxygen saturation is generally poor (Mower, Sachs, Nicklin, Safa & Baraff 1996)

The estimated respiration rate was accurate in all treatment sessions except one. In that treatment session, the pressure recordings contained very prominent oscillations in the 0-0.15 Hz band that precluded accurate detection of a respiratory peak in the spectra. Such low-frequency (LF) blood pressure oscillations has been studied during hemodialysis, suggesting that dialysis induced changes in LF blood pressure oscillations may be a marker of peripheral vascular disease (Titapiccolo, Cerutti, Garzotto, Cruz, Moissl, Tetta, Signorini, Ronco & Ferrario 2012). However, the feasibility of monitoring such LF blood pressure oscillations using the pressure sensors of the dialysis machine remains to be established and is outside the scope of the present study.

In the present study, capnography, which is based on measurements of carbon dioxide levels in expired gas, was used as reference. It should be noted that the respiratory information obtained from the pressure sensors of the dialysis machine has more in common with the measurements of respiratory effort that can be obtained using a chest belt. However, the evaluation is based on respiration rate which can be accurately estimated from both measurements.

In the present study signal analysis was performed off-line, however, the method can easily be modified for on-line analysis. The template pressure pulses obtained using the global mean of each recording were very similar, cf. Fig. 3, and could be replaced by a generic template pressure pulse. A generic template pressure pulse could serve to initialize the adaptively updated pressure pulse to be subtracted from the pressure signals and a slowly adapted generic template pressure pulse could replace the global median pressure pulse for detection and exclusion of signal segments with excessive noise.

The main limitation with the present study is the small dataset, the reason being the discomfort for the patients caused by wearing a reference capnography sensor throughout the dialysis session. A followup study including a larger study population and several dialysis clinics is required to validate the findings of this study.

5. Conclusion

We have proposed a new approach to monitor respiration during hemodialysis using information extracted from the pressure sensors of the dialysis machine. The proposed method, which involves adaptive template subtraction and peak conditioned spectral averaging, is robust to artefacts and does not require additional sensors. Our results show that the estimated respiration rate is in agreement with respiration rate estimated from reference capnography recordings. A followup study including a larger study population at several dialysis clinics is required to validate the findings.

6. Acknowledgment

This work was partially funded by the Swedish innovation agency VINNOVA 2015-06530.

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