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RESEARCH ARTICLE

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Respiratory rate monitoring in healthy volunteers by central photoplethysmography compared to capnography

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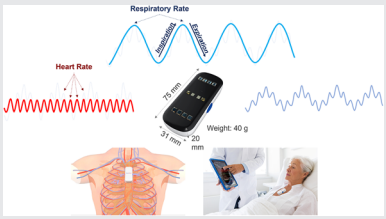
Abstract



Monitoring of respiration is a central task in clinical medicine, crucial to patient safety. Despite the uncontroversial role of altered respiratory frequency as an important sign of impending or manifest deterioration, reliable measurement methods are mostly lacking outside of intensive care units and operating theaters. Photoplethysmography targeting the central blood circulation in the sternum could offer accurate and inexpensive monitoring of respiration. Changes in blood flow related to the different parts of the respiratory cycle are used to identify the respiratory pattern. The aim of this observational study was to compare photoplethysmography at the sternum to standard capnography in healthy volunteers. Bland Altman analysis showed good agreement (bias −0.21, SD 1.6, 95% limits of agreement −3.4 to 2.9) in respiratory rate values. Photoplethysmography provided high-quality measurements of respiratory rate comparable to capnographic measurements. This suggests that photoplethysmography may become a precise, cost-effective alternative for respiratory monitoring.

KEYWORDS

capnography, emergency medicine, photoplethysmography, respiratory monitoring

1 | INTRODUCTION

Monitoring of respiration is a central task in clinical medicine and the capability to detect and interpret respiratory alterations is crucial to patient safety [1–4]. Traditionally, respiration has been monitored by manual counting of chest movements. This is labor intensive and associated with a high degree of error [5–8]. Although manual counting of chest movements remains the most common method to assess respiratory frequency, several other technical solutions are available [9–16]. For example, the use of changes in chest wall impedance over the respiratory cycle as detected by common ECG-leads, known as thoracic impedance pneumography, is a common feature in basic-level monitoring equipment [17, 18]. Impedance-based monitoring of respiration is, however, highly sensitive to disturbances due to body movement, and data are typically

Abbreviations: BPM, breaths per minute; ICU, intensive care unit; PPG, photoplethysmography; RH, RespiHeart.

presented as a moving mean value over a longer period of time, making the method prone to error and less suitable to detect rapid change [19]. The photoplethysmographic signal generated by peripheral pulse oximetry is also sometimes used for respiratory monitoring, but filtering of the respiratory signal is challenging making the method similarly prone to error [18]. However, provided a stable placement of the photoplethysmography probe, the technique per se is largely uninfluenced by movement, which makes it attractive for use in awake and mobile patients [20–23].

Measurements on the sternum are expected to be robust for acquiring photoplethysmographic signals, because of the central body location. Hence, we hypothesize that respiratory rate estimated from sternal photoplethysmography would more accurately reflect the respiratory rate estimated by capnography.

The current gold standard for noninvasive respiratory monitoring is capnography [24, 25], which uses the change in carbon dioxide concentration between inhaled and exhaled air, with the concentration being higher in exhaled air [26, 27]. This method requires the patient to be constantly connected to the capnograph via a special mask or nasal cannula. The equipment for capnography is comparatively expensive, limiting the access mostly to operating theaters and ICUs even in high-income countries [28]. Thus, there is a clear need for an accurate, less expensive and more mobile device for respiratory monitoring [13]. Some alternative solutions have been suggested, such as the use of radar detectors [29], advanced software processing of respiratory sounds [30] or camera-based solutions [31], but none of these are currently clinically available. We have previously suggested photoplethysmography, using a wearable device 75 × 31 mm in size, targeting the central blood circulation as a possible solution for accurate and inexpensive monitoring of respiration [23]. The device utilizes photoplethysmography in reflectance mode and consists of four photodetectors, two near-infrared light emitting diodes (810 nm) and two red light emitting diodes (660 nm) in a specific pattern and embedded in black colored polyurethane. The center-to-center distance between the light emitting diodes and the photodetectors of 20-22 mm facilitates monitoring of blood flow in deeper lying vessels in the sternum, which is supplied by the internal thoracic arteries and the anterior perforating branches of intercostal vessels. Changes in sternal blood volume in the due to local pressure variations during inhaling/exhaling are used to identify the respiratory pattern [20, 32]. At the sternum, respiration-related changes in blood flow are noticeably stronger than at more peripheral locations [20], thus making signal detection and filtering relatively uncomplicated. Previously, we have shown that this method seems to generate more reliable data on respiratory rate than impedance-based monitoring and, the method is well-tolerated by emergency patients in a clinical setting [23]. However, the specific performance of this method in relation to the gold standard for monitoring of respiratory frequency, that is, capnography, has not been tested. Thus, the aim of this study was to assess the feasibility and accuracy of monitoring the respiratory rate by comparing photoplethysmography at the sternum to standard capnography in healthy volunteers.

2 | EXPERIMENTAL SECTION

2.1 | Material and method

The study was approved by the Regional Ethical Review Board in Linköping (permit number 2016-15-31 and amendment 2020-00337).

The study was designed as an observational study to assess feasibility and noninferiority of a dual wavelength photoplethysmographic module (RespiHeart AB, Linköping, Sweden) with a standard monitoring device (Philips IntelliVue MX450 and capnograph Philips M3015B Microstream CO_2 Module) measuring respiratory rates on healthy subjects at an emergency department (Linköping University Hospital, Sweden) in 2020 (August to October).

The primary outcome measure was agreement, as determined by Bland Altman analysis, between the photoplethysmographic module, and Philips IntelliVue MX450 equipped with capnograph Philips M3015B for respiratory rate values.

A sample of 30 healthy volunteers (10 males, 20 females, mean age 43 ± 12 years) was recruited to monitor respiratory patterns at various respiratory rates, and a standard informed consent procedure was followed.

Inclusion criteria were:

•Generally healthy

•Voluntary and informed participation

Exclusion criteria were:

•Unwillingness to participate or inability to provide informed consent

•Known allergy to adhesive materials (for instance acrylates or methacrylates; adhesives were used to attach the device to the sternum).

All statistical analysis was performed using GraphPad Prism version 9.1.2 for Windows, GraphPad Software, San Diego, California USA, www.graphpad.com at an alpha level of 0.05.

2.2 | Experimental setup

Subjects were placed in a bed at a semi upright position and connected to the capnograph via an oral/nasal sample line

(Smart CapnoLine™ Plus O2, Microstream® EtCO2, Philips Medical Systems). The photoplethysmographic module was attached to the skin of the sternum, just below the manubrium, by double adhesive tape (Stokvis Tapes Sverige AB, Norrköping, Sweden). Any body hair was removed by gentle shaving of the skin before attachment. Subjects were asked to breathe normally for 2 minutes and then momentarily increase their respiration rate for 2 minutes before returning to the original rate for another 2 minutes. This breathing routine was repeated, the second time aiming at an even higher respiratory rate compared to the first cycle of increased respiration. Finally, subjects were asked to decrease the respiratory rate below their normal breathing rate for 2 minutes, followed by 1 minute of resting/normal breathing rate.

2.3 | Data acquisition

Measurement data from the photoplethysmographic module were transferred via Bluetooth to a PC with a sampling rate of 100 Hz. The capnograph signal from the MX450 and M3015B was transferred via Ethernet LAN at 62.5 Hz to the same PC. A specially implemented software program received and stored the two data streams (Copyright 2017-19 John George K., xeonfusion@users.sourceforge.net). Signals were stored in comma-separated values files (Figure 1).

2.4 | Analysis

The signal generated by the photoplethysmographic module was analyzed in a specially designed MATLAB program (MATLAB, R1017a, Mathworks, Massachusetts, USA) to determine the respiratory rate. For the photoplethysmographic module, the respiratory related signal from the near-infrared channel (810 nm) were first separated from the pulse related signal by applying electronic filtering (Butterworth, 9th order low pass at 0.5 or 1.2 Hz). The local maxima and time for each identified peak were determined by setting two parameters called Window and Limit. The Window-value was based on an estimated or actual peak frequency and was used for calculating local maxima and time point for each identified peak (numbered blue dots in Figure 2). The Limit value restrained the amplitude of each peak and was by default set to 20 but could be adjusted if necessary. Once the Window and Limit values were set, inspiration-related photoplethysmographic signal peaks were tracked and the time in seconds between two consecutive inspiratory signal peaks was determined. This information was used to determine the respiratory rate in breaths per minute for each breath and for all 15 breathing intervals in each subject.

The photoplethysmographic signal was resampled from 100 to 62.5 Hz to allow direct comparison. The signal from the capnograph was naturally inverted to the plethysmographic signal, with the capnograph showing peak signal intensity at expiration as compared to inspiration for the plethysmographic signal. Thus, the capnograph signal was inverted before the MATLAB program described above was used to track the peaks (numbered blue dots in Figure 2B). To determine a full breath, a limit was set where peaks were disregarded if the CO_2 concentration was less than half of the subjects maximal CO_2 concentration.

Both the photoplethysmographic and capnograph signals were manually checked for number of peaks per minute to verify that the software had made correct calculations. The automatic peak detection failed on several occasions during periods of increased respiratory rate to correctly detect all peaks in the photoplethysmographic signal. The low pass filter value was then changed from 0.5 to 1.2 Hz and a new calculation of local maxima and time between peaks was performed.

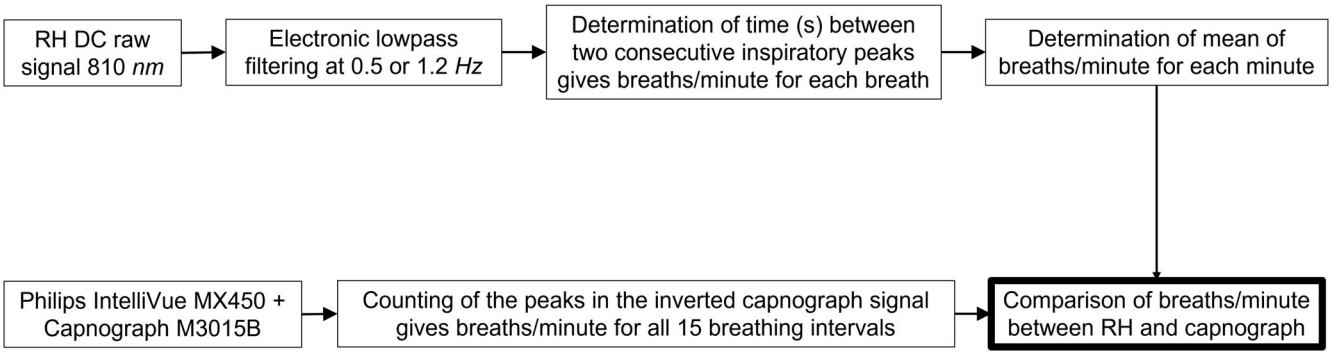


FIGURE 1 Flow chart describing the analysis process of the photoplethysmographic (RH) and Philips M3015B capnograph signals

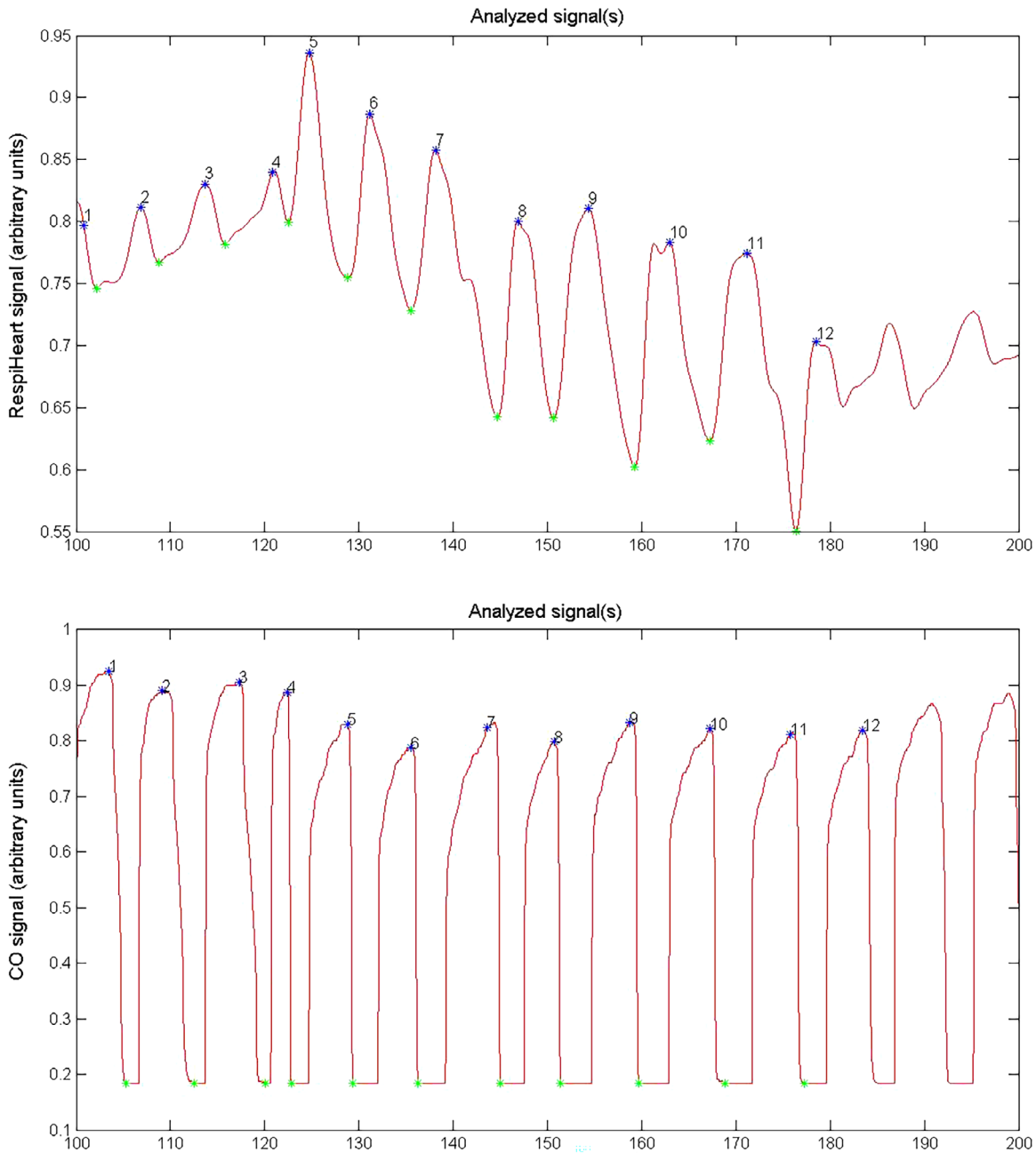


FIGURE 2 (A) The respiratory peaks (numbered dots) in the photoplethysmographic signal are detected by a program in MATLAB. (B) After inversion of the capnograph signal variations in carbon dioxide concentration are determined in a similar way. Both figures show respiratory patterns from the same subject during increased inspiratory and expiratory effort

3 | RESULTS AND DISCUSSION

3.1 | Results

Of the originally 30 subjects, data from 4 subjects were excluded from the final analysis due to data loss caused by technical problems, and in 9 of the remaining subjects, parts of the data were lost or excluded from analysis. For further details on data loss, see Table 1.

As determined by Bland Altman analysis (Figure 3), there was good agreement (bias −0.21, SD 1.6, 95% limits of agreement −3.4 to 2.9) in respiratory rate values derived from the photoplethysmographic module and from capnography by Philips M3015B.

An initial graph of the average number of respiratory rates over 60 seconds at all 15 breathing intervals and in all subjects, indicated a strong agreement between the two methods (Figure 4) The correlation and linear regression analysis of the data showed a r^2 value of 0.96, 95% CI = 0.93-0.97. The *P*-value for the overall slope being zero (no relationship) was below 0.0001 (Figure 5). The regression equation was expressed as: $y = 0.95 \times X + 0.48$.

TABLE 1 Data not included in the final analysis

Excluded data	
Subject	**Cause**
4	No data due to data recording software error
5	No data due to data recording software error
13	Large variations in CO_2, talking
15	No capnograph data due to technical problems

Partially excluded data		
Subject	**Timepoint (s)**	**Cause**
1	450-570	Hyperventilation
3	840-900	No CO_2 readings
11	600-840	Large variations in capnograph RR
18	120-180, 720-840	Large variations in capnograph RR
20	0-60	Delayed CO_2 response
27	0-60	Missing RH data
28	0-60	Missing capnograph data
29	0-60, 480-540	Missing capnograph data, Hyperventilation
30	780-900	Large variation in capnograph RR

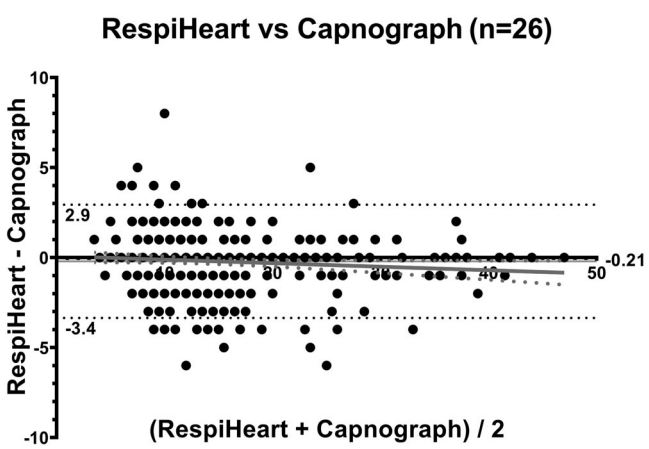


FIGURE 3 Bland Altman plot showing the respiratory rate measured by the photoplethysmographic module and Philips M3015B capnograph vs. the mean of the two measurements. The bias of −0.21 units (SD 1.6) is represented by the gap between the *X* axis, corresponding to a zero difference, and the parallel gray line to the *X* axis. Solid gray line represents the regression line and dotted gray lines represent CI limits. Black dotted lines represent limits of agreement from −1.96 to +1.96 s (−3.4 to 2.9)

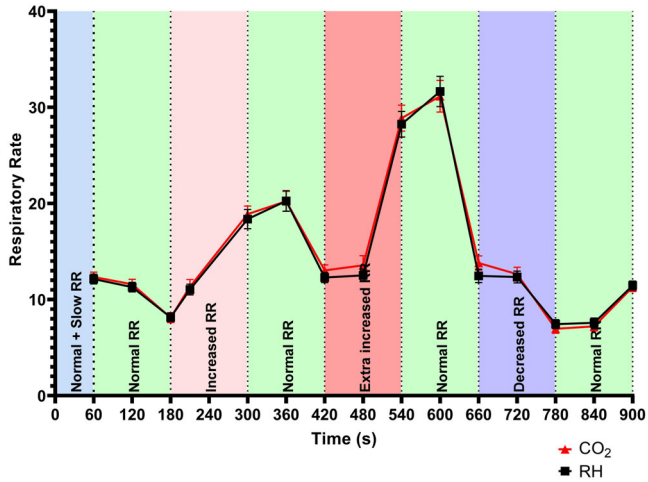


FIGURE 4 Mean respiratory rate (RR), over 60 seconds, as measured by the photoplethysmographic module (black) and Philips M3015B capnograph (red) in 26 healthy volunteers. Error bars represent standard error of the mean (SEM)

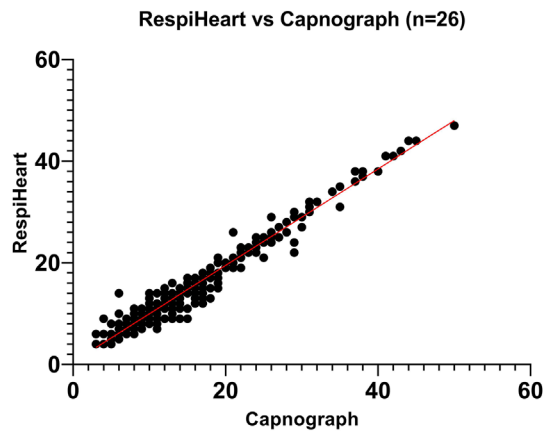


FIGURE 5 The regression line for photoplethysmographic and capnograph measurements of respiratory rate. Regression equation is expressed as: $y = 0.95 \times X + 0.48$. Regression line has a slope of 0.95 (0.93 to 0.97) and an intercept of 0.48 (0.15 to 0.81). Correlation coefficient between the two methods is $r = 0.96$, 95% CI = 0.93-0.96, nonsignificantly nonzero slope $P < .0001$

3.2 | Discussion

In this paper, we showed good agreement between photoplethysmography on the sternum and standard capnography in determining respiratory frequency, indicating that photoplethysmography may play a role as an inexpensive alternative to standard capnography, especially in settings where capnography is not currently readily available.

This is important because an abnormal respiratory rate is known to be an early and sensitive predictor of clinical deterioration and adverse events such as cardiac

arrest and admission to an ICU [1, 2, 4, 5, 33, 34]. Despite the uncontroversial role of altered respiratory frequency as an important sign of impending or manifest deterioration, reliable measurement methods are mostly lacking outside of ICUs and operating theaters, where capnography is typically available. Development of accurate and inexpensive respiratory monitoring, which can be widely implemented, is therefore important to improve basic quality of care [20]. By implication, more widespread access to high-quality respiratory monitoring will also be important to further improve prognostic models building on vital sign analysis.

Since capnography is currently a limited asset even in well-funded healthcare systems, the proposed method potentially expands the scope for reliable respiratory monitoring also to low- and middle-income settings, as well as to arenas where this type of high-fidelity monitoring has not previously been in use. Thus, it will be relatively uncomplicated to implement a photoplethysmographic method in devices with different form factors and physical properties, such as wireless or cable-based signal transfer, battery or wire-based power supply, as well as in the form of a disposable patch. The reason for this adaptability is the large variations in sternal blood flow caused by the intrathoracic pressure changes over the respiratory cycle, which facilitates the acquisition of a strong signal and makes the signal processing comparatively uncomplicated. Furthermore, the pressure changes are relatively unaffected by body position, movement and other typical sources of error which are known to negatively affect the precision of other methods such as impedance pneumography [19]. Interestingly, this limitation is also present in many other alternative methods for respiratory monitoring which have been recently proposed. Thus, both radar- and camera-based methods are dependent on a relatively constant body-position of the subject in relation to the detector, which means they will mainly work in a prone patient who is either sleeping or sedated. An incidental finding, which highlights the fact that even capnography has some limitations even under normal circumstances was that the capnograph, in some instances, could not distinguish between CO_2 alterations resulting from normal speech and respiration, which was the reason for the exclusion of one subject (see Table 1). This is not widely known as a limitation of capnography, presumably since it is mainly used in anesthesia and critical care, where patients are often sedated. However, normal speech does not seem to be as challenging to photoplethysmography, since the intra-thoracic pressure changes due to normal vocalization will mostly be more limited than for a full breath. Although this was not the specific purpose of the present study, this finding should warrant further investigation of the limitations of capnography.

In summary, the proposed method could potentially reduce or eliminate several well-known problems associated with current methods for respiratory monitoring while retaining the precision gained by measuring the direct physical effects of the respiratory work [21, 23, 35]. Since the proposed method allows the attachment of both signal emitters and photodetectors directly to the patient, photoplethysmography on the sternum should be especially well suited to measure respiratory frequency in ambulatory conditions and freely moving patients, which will most likely be the main arena of future expansion for respiratory monitoring.

3.3 | Limitations

Healthy subjects were used for all measurements, which precludes generalization to patients in a clinical setting. Based on our previous study in emergency patients, however, we know that the method per se is applicable in a normal clinical setting.

As the study was done using healthy volunteers, we have no data on the accuracy of the method in unconscious subjects. Furthermore, all measurements were done with the subjects at rest and more work is needed to determine the feasibility and clinical significance of respiratory rate measurements during movement. Further clinical trials are needed to quantify the number of patients where clinical decisions could be usefully supported by data that a RespiHeart type sensor is able to provide.

4 | CONCLUSION

In summary, the present results show that photoplethysmography on the sternum provides measurements of respiratory rate comparable to capnography. This suggests that photoplethysmography on the sternum may become a precise, cost-effective alternative to capnography expanding the scope of respiratory monitoring to new arenas.

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CONFLICT OF INTEREST

The authors declare no financial or commercial conflict of interest.

AUTHOR CONTRIBUTIONS

Joakim Henricson was involved in, investigation, writing—original draft, project management. Joakim Glasin and Sandra Rindebratt were involved in review and editing. Daniel Wilhelms was involved in funding, conceptualization, writing—original draft.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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