Monitoring the respiratory rate of preterm infants using an ultrathin film sensor embedded in the bedding

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Monitoring the respiratory rate of preterm infants using an ultrathin film sensor embedded in the bedding: a comparative feasibility study

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Introduction

Respiratory instability is common in preterm infants owing to surfactant deficiency, poor respiratory drive and increased compliance of the chest wall (Di Fiore et al. 2016, Bancalari and Claure 2018). In neonatal intensive care units (NICU), monitoring the respiratory rate (RR) is, therefore, an important part of routine patient monitoring. While multiple techniques for monitoring respiration are available, the modality of choice is largely determined by the reliability of monitoring, ease of use and whether it is deemed comfortable for infants over longitudinal measurements that may last several weeks (Al-Khalidi et al. 2011, Di Fiore 2004).

The most accurate measures of RR are obtained via airflow sensors, but these are poorly tolerated in spontaneously breathing infants, especially over long periods (Di Fiore 2004). Another method for monitoring respiration is based on inductance plethysmography, although in infants it is not used beyond research settings and sleep laboratories. Its use in NICUs over long periods is uncommon owing to friction and the increased physical effort required to breathe against the resistance of the inductance bands that need to be secured around the abdomen and the thorax (Pesin et al. 2014). De facto, across NICUs worldwide, the most common modality for monitoring respiration is based on the chest impedance (CI) signal acquired through the ECG electrodes (Di Fiore 2004). While CI measurements are commonplace, long-term use of ECG electrodes causes discomfort, skin irritation, and potential scarring, especially in extremely preterm infants where skin integrity is poor, and skin breakdown can easily occur (Sardesai et al. 2011). Moreover, the RR acquired via CI (RR-CI) is often unreliable as exemplified by a study where the 95% limits of agreement of RR-CI compared to visual counts was 20 breaths per minute (bpm) (Kohn et al. 2016).

Alternative modalities for monitoring respiration such as those based on acquiring the RR through diaphragmatic electromyography (dEMG), motion sensors (accelerometers) and laser Doppler vibrometry (LDV) have...
also been tested in clinical studies (Scalise et al 2011, Marchionni et al 2013, Kraaijenga et al 2015, Kohn et al 2016). These studies used dEMG, motion sensors, and LDV in supine infants and had 95% limits of agreement of approximately 15 brpm compared to CI, visual count and ventilator-based measurements respectively. Like the CI, the dEMG and motion-sensors are obtrusive since they require the attachment of sensors to the skin. While the LDV-based approach offers the opportunity for truly unobtrusive monitoring, it remains unclear whether using LDV for monitoring the RR will be motion-robust (Werth et al 2017). Furthermore, since the LDV-device is placed outside the incubator, it may be impractical for use in incubators that are covered, or with infants supported through positioning materials and covered with blankets.

An alternative approach for non-obtrusively monitoring respiration is using pressure sensors, in the form of films and mats that can be placed underneath the mattress or the bedding. Nizami et al have demonstrated the feasibility of reliably acquiring the RR using a pressure sensitive mat, even in light-weight infants, by using a neonatal simulator weighing 900 g (Nizami et al 2018). In this paper, we describe a comparative clinical study in preterm infants and demonstrate the possibility of non-obtrusively monitoring respiration using an ultrathin and flexible film-like pressure sensor. This study extends our previous work where we used the same sensor for accurately monitoring infant motion with implications for use in monitoring sepsis, sleep-wake cycles, apneas, and seizures (Joshi et al 2018).

Materials and methods

This study was conducted in the level III NICU of Máxima Medical Center, Veldhoven, the Netherlands between May–June 2017. Based on a safety evaluation, and in accordance with the Dutch law on medical research with humans, the medical ethical committee provided a waiver (registered as N16.068) for this observational study. Clinically stable preterm infants of varying body weight were enrolled after written informed consent was obtained from the parents. Exclusion criteria were congenital abnormalities and the use of invasive mechanical ventilation. The study was of an observational nature, and routine nursing care including the repositioning of infants took place as usual. All infants were recorded for 6–8 h following which two sessions of one hour or longer, generally a few hours apart, were selected for analysis. When possible, these sessions were selected with infants lying in different positions to determine whether the system under consideration was sensitive to positioning.

Data acquisition

Based on routine patient monitoring, the CI waveform (62.5 Hz), oxygen saturation (SpO₂, 1 Hz) and the heart rate (HR, 1 Hz) were acquired from patient monitors (Philips IntelliVue MX 800, Boeblingen, Germany) via a data warehouse (DWH, IIC IX, Data Warehouse Connect, Philips Medical Systems, Andover, MA).

An electromechanical film sensor (L-series EMFi, Emfit, Kuopio, Finland) of dimensions 580 mm × 300 mm × 0.4 mm served as the pressure sensor in this study. This EMFi sensor is shown in appendix A. The soft and flexible nature of the sensor, as well as the fact that it is electrically passive, makes it well suited for use in the NICU where safety concerns are paramount. The sensor was placed between the mattress and the bedding while infants lay on the bed, often supported by positioning material (SnuggleUp, Philips, Amsterdam, The Netherlands) and possibly covered by a blanket. Additional technical specifications and further details of the sensor are provided in a previous publication (Joshi et al 2018). Briefly, the sensor is sensitive to mechanical movement in the direction vertical to its surface and thereby to the body movement and respiratory motion of the infant. A custom-made signal acquisition system was used to acquire the ballistographic (BSG) signal from this sensor at a sampling frequency of 250 Hz. This BSG signal is reflective of all infant motion including respiratory movement (RR-BSG) which in turn can be separated from body movement since the latter typically occurs at frequencies lower than that of respiration (Joshi et al 2018).

Signal processing

The BSG waveform and the data from the patient monitor were obtained in a synchronized manner as the internal clock of the custom-made signal acquisition device was synchronized to the time on the patient monitors, before each recording.

Based on findings in previous research, both the BSG and CI signals were band-pass filtered (0.45–1.45 Hz) to preferentially capture the respiratory waveforms (11). Next, the peaks and troughs of the filtered CI and BSG waveforms, corresponding to inhalation and exhalation, were algorithmically detected to calculate the breathing rate.

Statistical analysis

The average RR was calculated over one-minute epochs at 30 s intervals for both the CI and BSG waveforms. Measures of RR for all the one-minute epochs served as independent observations. Comparative analysis of the acquired RR was performed by estimating Pearson’s correlation coefficient (r) while the Bland–Altman plot was used to assess the mean difference (MD) and the limits of agreement (LOA; MD ± 1.96 SD) between the RR-BSG and the RR-CI. Throughout the analysis, we used the RR-CI as the clinical reference standard. We also
calculated the percentage of total time when the RR-BSG was within 10% of the RR-CI. Since large errors in the MD of RR are particularly undesirable, a metric that accentuates large errors in the RR should also be used for comparing the RR-BSG with the RR-CI. Therefore, we also calculated the root mean square error (RMSE) for different respiratory frequencies to identify whether the error rate is dependent on the RR.

Results

Ten infants characterized by gestational age of 28.1 ± 2.7 weeks were included in the study from whom nearly 27 h of data were acquired. The postmenstrual age and weight of infants on the day of the measurements were 31.4 ± 2.3 weeks and 1422 ± 402 g respectively (table 1). About respiratory support, six infants were on CPAP, two were on high flow oxygen delivered through a nasal cannula, and two were spontaneously breathing room air. The mean duration of each recording was 81 (±4) min. Of the 20 recorded sessions, 15 recordings were acquired while infants were in the lateral position (seven left lateral + eight right lateral) whereas three and two recordings respectively were acquired from infants in the prone and supine positions. For 18 of the 20 sessions, infants were supported by positioning materials. Also, for 17 sessions infants were at least partially covered with a blanket.

The entire dataset, consisting of 3182 epochs of one-minute duration was used for analysis. RR-BSG was significantly correlated to RR-CI (r = 0.74, p = 0) while the Bland–Altman plot showed a mean difference in RR of −0.3 brpm with 95% LOA between −10 and 9.8 brpm (figure 1). Table 1 shows the MD and the 95% LOA for each of the 20 recordings. In summary, irrespective of the nature of the respiratory support or the position of the infant, respiratory waveforms could be acquired from the prone and supine positions. For 18 of the 20 sessions, infants were within 10% of the time, the RR-BSG was within 10% of the RR-CI.

Figure 2 shows that across different frequency bands, the RMSE of the RR estimated from the BSG waveform was within seven brpm of RR-CI. Figure 3 depicts the respiratory waveforms acquired from the BSG and CI when both provided a comparable RR—both waveforms resemble one another. Figure 4 depicts exemplary BSG and CI waveforms for periods with discrepancies in the RR acquired from these modalities. While figure 4(A) depicts an epoch where RR-BSG is higher than RR-CI, figure 4(B) indicates an epoch where RR-BSG is lower than RR-CI.

Based on a previously developed algorithm for quantifying movement using the BSG signal, we identified the 25% most and the 25% least movement-affected epochs from all 20 recorded sessions (Joshi et al 2018). This stratification of epochs was used to generate the Bland–Altman plots, which are depicted in appendix B. The results indicate that the MD (−1.3 versus 0.06 breaths min$^{-1}$) and 95% LOA (−12 to 9.3 versus −10 to 10 breaths per min) for RR are comparable in both cases.

Discussion

This paper describes the first clinical study showcasing that a pressure sensor placed underneath the bedding of preterm infants can yield reliable respiratory waveforms in the NICU environment. Specifically, the RR-BSG compares favorably with the RR derived from CI—the current clinical standard. The BSG-based approach appears to be a promising solution for monitoring the RR for infants across a range of bodyweight and irrespective of body position, for both, infants breathing without respiratory support as well as for those receiving non-invasive respiratory support. Further, the RMSE is both small and comparable across different frequency ranges, indicating the absence of bias in estimating the RR for the typical breathing frequencies of preterm infants. Reassuringly, upon evaluating the RR-BSG for epochs most and least affected by infant motion, the 95% LOA were found to be comparable, indicating that the BSG-based modality for monitoring respiration is not unduly affected by infant-motion.

This BSG-based approach for monitoring respiration is an attractive alternative to the use of wired adhesive electrodes needed in the case of CI, dEMG, and accelerometer-based modalities. This approach entirely avoids the discomfort, skin irritation and potential scarring due to long-term use of adhesive electrodes on the fragile skin of preterm infants (Sardesai et al 2011). In conjunction with pulse oximetry, which also provides HR, the use of BSG opens up the possibility of avoiding ECG electrodes for routine cardiorespiratory monitoring, at least in those infants where the ECG waveform does not add direct clinical value. Additionally, in many units, owing to the fragility of the epidermis, especially in infants less than 26 weeks PMA, ECG electrodes are not used, and thus RR is not monitored. The use of BSG can enable the monitoring of RR in this very vulnerable patient population. Further, unlike modalities where the adhesion of electrodes is required, sensor disconnections cannot occur while using the modality described in this work, thereby increasing monitoring coverage and reducing technical alarms, an important issue in the NICU (Joshi et al 2016, 2017).

Another advantage of using BSG as opposed to CI for monitoring respiration is that CI may experience interference from the phasic flow of blood through the heart, especially during low HR, while the BSG-based approach described herein does not (Lee et al 2012). By virtue of the mechanical design, the BSG-based modality is largely free from cardiac interference since forces generated by the heart are mainly along the longitudinal direction while the BSG sensor is sensitive to forces only in the vertical direction. Further, based on observations we noted that the respiration waveform acquired from the BSG signal was more stable and less prone to sudden increases and
decreases—likely because, unlike BSG, the CI waveform is affected by the quality of electrode contact. In particular, distortion of the BSG-waveform due to amplitude saturation (clipping) did not occur—a problem that is unfortunately common with the CI-waveform. In general, superior signal characteristics, especially concerning the stationarity of the signal augers well for any subsequent signal processing algorithms that may use the respiratory waveform.

Further, as can be noted from figure 3, the amplitude of the BSG signal is time-varying. The amplitude variation is potentially a reflection of the respiratory effort and work of breathing which, if ascertained, is of clinical interest for titrating the level of respiratory support, including weaning of ventilation. Thus, the BSG signal may possibly offer clinically relevant information beyond the respiratory rate although this would require further investigation.

Occasionally, as shown in figure 4(A), the RR-BSG was higher than the RR-CI. This may be, for instance, due to infant motion leading to variations in the quality of electrode contact, thereby affecting the input impedance and the resulting CI waveform. Similarly, as shown in figure 4(B), sometimes the RR-BSG is lower than

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### Table 1.

Patient characteristics on the day of measurement as well as the agreement between RR-BSG and RR-CI for different sessions, as obtained from individual Bland–Altman plots with RR-CI serving as the reference.

<table>
<thead>
<tr>
<th>Infant</th>
<th>PMA (weeks + days)</th>
<th>Weight (gram)</th>
<th>Session</th>
<th>Position</th>
<th>Respiratory support</th>
<th>No. of one-min epochs</th>
<th>MD (min⁻¹)</th>
<th>95% LOA (min⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant 1</td>
<td>30 + 3</td>
<td>1350</td>
<td>Session 1</td>
<td>Left lateral</td>
<td>CPAP</td>
<td>152</td>
<td>2.80</td>
<td>6.72</td>
</tr>
<tr>
<td>Infant 2</td>
<td>35 + 5</td>
<td>2250</td>
<td>Session 2</td>
<td>Right lateral</td>
<td>CPAP</td>
<td>160</td>
<td>0.22</td>
<td>5.92</td>
</tr>
<tr>
<td>Infant 3</td>
<td>29 + 1</td>
<td>1165</td>
<td>Session 1</td>
<td>Right lateral</td>
<td>CPAP</td>
<td>155</td>
<td>2.57</td>
<td>8.42</td>
</tr>
<tr>
<td>Infant 4</td>
<td>33</td>
<td>1570</td>
<td>Session 2</td>
<td>Prone</td>
<td>CPAP</td>
<td>166</td>
<td>–1.49</td>
<td>8.88</td>
</tr>
<tr>
<td>Infant 5</td>
<td>29 + 3</td>
<td>1140</td>
<td>Session 1</td>
<td>Right lateral</td>
<td>CPAP</td>
<td>158</td>
<td>–4.4</td>
<td>13.04</td>
</tr>
<tr>
<td>Infant 6</td>
<td>27 + 5</td>
<td>700</td>
<td>Session 2</td>
<td>Right lateral</td>
<td>CPAP</td>
<td>158</td>
<td>–7.48</td>
<td>14.63</td>
</tr>
<tr>
<td>Infant 7</td>
<td>33 + 3</td>
<td>1400</td>
<td>Session 1</td>
<td>Right lateral</td>
<td>High flow</td>
<td>158</td>
<td>–0.6</td>
<td>5.81</td>
</tr>
<tr>
<td>Infant 8</td>
<td>32 + 1</td>
<td>1675</td>
<td>Session 2</td>
<td>Left lateral</td>
<td>High flow</td>
<td>158</td>
<td>1.8</td>
<td>7.76</td>
</tr>
<tr>
<td>Infant 9</td>
<td>31 + 4</td>
<td>1450</td>
<td>Session 1</td>
<td>Left lateral</td>
<td>None</td>
<td>158</td>
<td>–1.93</td>
<td>8.74</td>
</tr>
<tr>
<td>Infant 10</td>
<td>31 + 3</td>
<td>1520</td>
<td>Session 2</td>
<td>Right lateral</td>
<td>High flow</td>
<td>158</td>
<td>0.18</td>
<td>6.43</td>
</tr>
</tbody>
</table>

Abbreviations: PMA-postmenstrual age; CPAP-continuous positive airway pressure; MD-mean difference; LOA-limits of agreement.

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**Figure 1.** (A) The correlation between the RR-BSG and the RR-CI. The black line shows the best line of fit ($r = 0.74$) while the dotted lines show the 95% LOA. RMSE and $n$ refer to the root mean square error and the total number of observations. (B) Bland–Altman plots comparing the difference in RR between BSG and CI with RR-CI. The black line indicates the mean difference while the dotted lines indicate the 95% LOA. The solid square, circle, and the pentagram are representative of epochs where the RR-BSG was equal to, higher than, and lower than RR-CI respectively.
RR-CI—this is because the respiration peak detection algorithm did not detect the small fluctuations in the BSG waveform as separate breaths. However, upon visual inspection, it was not possible to discern whether the small fluctuations in the respiratory waveform constitute separate breaths or not. For instance, these smaller fluctuations might be cardiac artefacts or respiration interrupted by suck-swallow events (Tarrant et al 1997). A superior reference standard such as nasal flowmeters will be needed to identify the cause behind these variations.

The strengths of this study are that repeated and continuous measurements were acquired from infants of varying body weight in different positions—an important element of the experimental design since the weight and position of the infant can affect the mechanical forces of respiration and thus the quality of the BSG signal. The results of the study indicate that BSG signals of reliable quality can be acquired in different body positions and even from light-weight infants. Owing to the observational nature of the current study, the use of positioning materials and blankets, which can dampen the BSG signal, was allowed. Finally, we did not exclude periods of nurse intervention or periods when infants were crying or fidgeting, excluding which would likely improve performance. Retaining these periods ensured that the two RR-monitoring modalities were compared in the most naturalistic and real-world scenario possible.

The BSG-based modality for monitoring the RR attained a 95% LOA of 10 brpm compared to RR-CI based on continuous measurements acquired from infants in varying body positions during which time nursing procedures were not restricted. In contrast, a study using dEMG for monitoring RR in supine infants, in the absence
of nursing procedures, achieved a 95% LOA of approximately ±15 brpm which improved to ±10 brpm when considering only stable epochs (Kraaijenga et al 2015).

This study is limited by the fact that only a modest number of non-invasively ventilated infants were included. Also, similar to other studies, the RR-BSG was compared to RR-CI which, while the clinical standard, is often inaccurate (Kraaijenga et al 2015). However, the results of the current study indicate the non-inferiority of the BSG-based approach for monitoring respiration compared to CI and provide sufficient data to motivate future studies with nasal pneumotachometers and chest inductance plethysmography as reference standards. Based on

Figure 4. (A) The BSG-based RR (70 brpm) is higher than RR-CI (58 brpm) possibly because of an unstable CI waveform (circle, figure 1). (B) The BSG-based RR (42 brpm) is lower than RR-CI (70 brpm) because the algorithm does not detect small fluctuations in the BSG waveform as separate breaths (pentagram, figure 1).
the data from this study, future studies with adequate sample size and power calculation can also look into the
effects of body weight and body position on the MD and LOA between RR-BSG and the RR acquired from a gold
reference standard. Finally, in the current study, we did not evaluate the ability of the BSG-based modality for
identifying apnea, an important issue that can be explored in the future.

In conclusion, this study shows that non-obtrusively acquiring the respiratory rate of preterm infants using
film-like pressure sensors placed underneath the bedding is feasible and that the RR acquired using BSG is similar
to that obtained from CI. In the NICU setting, using the BSG-based approach can reduce chronic stress in infants
owing to the long-term use of adhesive electrodes. The non-obtrusive nature of BSG modality also lends itself to
use in lower acuity and home-monitoring settings.

Acknowledgments

This research was performed within the framework of e/MTIC.

Conflict of interest

No financial assistance was received in support of this study. Rohan Joshi is employed by Philips Research. The
other authors report no conflicts of interest.

Appendix A

The EMFi electromechanical film sensor used in the study. The dimensions of the sensor were
580 mm × 290 mm × 0.4 mm. The sensor was placed underneath the bedding of the infant, and a custom-made
signal acquisition device was used to acquire the resulting BSG signal. This BSG signal was processed to obtain
the respiratory waveform from which the RR was derived.

Appendix B

Figure A1. An illustration of the film sensor used in the study.

Figure B1. Bland–Altman plots evaluating agreement in monitoring respiration among epochs most and least affected by infant
motion.
Bland–Altman plots corresponding to 789 and 803 epochs of one-min duration that were most (A) and least (B) affected by infant movement. The 95% LOA of the RR remain comparable, indicating that the BSG-based modality for monitoring respiration is not unduly affected by motion artefacts.

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