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ORIGINAL RESEARCH

The evaluation of a non-invasive respiratory volume monitor in surgical patients undergoing elective surgery with general anesthesia

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Abstract Continuous respiratory assessment is especially important during post-operative care following extubation. Respiratory depression and subsequent adverse outcomes can arise due to opioid administration and/or residual anesthetics. A non-invasive respiratory volume monitor (RVM) has been developed that provides continuous, real-time, measurements of minute ventilation (MV), tidal volume (TV), and respiratory rate (RR) via a standardized set of thoracic electrodes. Previous work demonstrated accuracy of the RVM versus standard spirometry and its utility in demonstrating response to opioids in postoperative patients. This study evaluated the correlation between RVM measurements of MV, TV and RR to ventilator measurements during general anesthesia (GA). Continuous digital RVM and ventilator traces, as well as RVM measurements of MV, TV and RR, were analyzed from ten patients (mean 62.6 ± 7.4 years; body mass index 28.6 ± 5.2 kg/m^2) undergoing surgery with GA. RVM data were compared to ventilator data and bias, precision and accuracy were calculated. The average MV difference between the RVM and ventilator was −0.10 L/min (bias: −1.3 %, precision: 6.6 %, accuracy: 9.0 %. The average TV difference was 40 mL (bias: 0.4 %, precision: 7.3 %, accuracy: 9.1 %). The average RR difference was −0.22 breaths/minute (bias: −1.8 %, precision: 3.7 % accuracy: 4.1 %). Correlations between the RVM traces and the ventilator were compared at various points with correlations >0.90 throughout. Pairing the close correlation to ventilator measurements in intubated patients demonstrated by this study with previously described accuracy compared to spirometry in non-intubated patients, the RVM can be considered to have the capability to provide continuity of ventilation monitoring post-extubation This supports the use of real-time continuous

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RVM measurements to drive post-operative and post-extubation protocols, initiate therapeutic interventions and improve patient safety.

Keywords Non-invasive respiratory volume monitoring · Thoracic bio-impedance · General anesthesia · Ventilation monitoring in non-intubated patients

1 Introduction

Adequate ventilation monitoring in the post-operative period has long been regarded as critical to patient safety, particularly in the context of sedation or anesthesia. During general anesthesia, mechanical ventilation is used as an essential support therapy to maintain adequate gas exchange. Accurate assessment of respiratory status becomes especially important during post-operative care, after the patient has been extubated and is no longer supported by a ventilator. During this recovery phase, respiratory depression and subsequent adverse outcomes can arise due to residual operating room anesthetics and/or opioid administration for pain management [1].

There is a clear need to improve upon current practices in respiratory monitoring and respiratory care [2, 3]. Various organizations, including the American Society of Anesthesiology state that quantitative methods of respiratory monitoring are superior to qualitative methods with respect to patient safety and evolving practice standards increasingly require monitoring not only of oxygenation, but ventilation as well [4, 5]. Until recently, no technology has provided a comprehensive non-invasive solution for continuous ventilation monitoring in non-intubated patients.

A non-invasive respiratory volume monitor (RVM) has been developed to provide continuous, real-time, quantitative measurements of minute ventilation (MV), tidal volume (TV), and respiratory rate (RR). Parameter trends are also presented to demonstrate important changes in respiratory function in real time [6]. Previous work had demonstrated clinically relevant accuracy compared to turbine and closed cell spirometry (average errors in MV and TV less than 10 %) in a population of ambulatory subjects [6], however, the accuracy of RVM measurements had not been formally assessed in mechanically ventilated surgical patients. Other studies have used the RVM to demonstrate changes in ventilatory status in response to opioids in the post-anesthesia care unit (PACU) setting following elective orthopedic surgery [7]. This study aimed to assess the accuracy and relevance of the RVM in the clinical setting by evaluating the correlation of RVM to ventilator measurements in a surgical population. We hypothesize that relative bias, precision and accuracy of RVM measurements compared to a mechanical ventilator will be similar to previously published work against turbine and closed-cell spirometer.

2 Methods

2.1 Subjects

In a blinded, observational study, data from 37 patients undergoing elective lower extremity joint replacement surgery under general anesthesia were collected. For this manuscript a subset of patients were selected for analysis Patients with right lateral positioning, ongoing excessive manipulation of the leg or excessive electromagnetic interference from electrocautery during surgery were excluded. While some segments of data from all 37 patients studied were usable for analysis, the described exclusion criteria, known to cause distortion of the RVM signal intra-operatively for substantive portions of the procedure, rendered the data in 27 of the patients unsuitable for continuous analysis. The ten remaining patients were analyzed further for this study (six females, age 61.6 ± 7.4, body mass index (BMI) 28.6 ± 5.2; Table 1). They underwent the following procedures: six right hip arthroplasties, one right knee arthroplasty, two left knee arthroplasties and one left knee arthroplasty revision. In this cohort the procedure times varied between 65 and 420 min. Opioids and other anesthetic and analgesic agents were administered intermittently throughout the procedure. This study was approved by the Partners Institutional review Board (IRB) and written informed consent was obtained prior to enrollment.

2.2 Instrumentation

All patients were intubated and received general anesthesia with mechanical ventilation. Intra-operatively, digital respiratory traces were collected continuously from a bio-

Table 1 Cohort demographics

Gender	
Male	4 (40 %)
Female	6 (60 %)
Age (mean ± SD)	61.6 ± 7.4 years
Height (mean ± SD)	65.7 ± 3.7 in
Weight (mean ± SD)	175.5 ± 32.8 lbs
BMI (mean ± SD)	28.6 ± 5.2 kg/m^2
Procedure	
Knee	4
Hip	6
Procedure time (min)	65–420
Cardio-pulmonary diseases	0/10

SD standard deviation, *BMI* body mass index

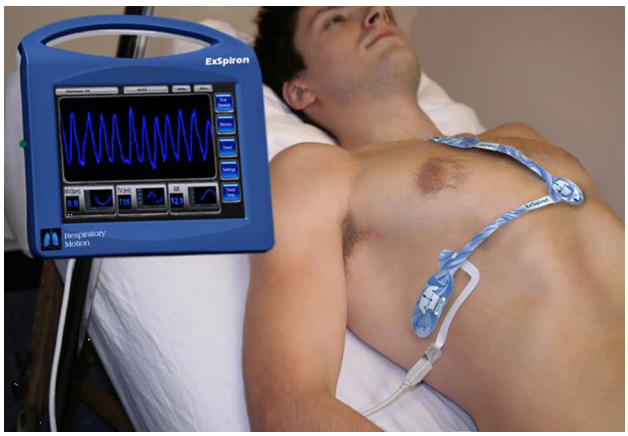

Fig. 1 Standard PadSet Placement. A non-invasive Respiratory Volume Monitor (RVM, ExSpiron, Respiratory Motion, Inc.) that provides continuous, real-time, non-invasive measurements of MV, TV and RR. Figure shows standard electrode placement. One electrode is placed at the sternal notch, another is placed on the xiphoid and the third is placed in the right mid-axillary line at the level of the xiphoid

impedance based RVM (ExSpiron, Respiratory Motion, Inc., Waltham, MA, USA) as well as from the patient ventilator (Draeger Apollo, Andover, MA, USA). The anesthesia providers managing the patient were blinded to the RVM measurements. Standard placement of the RVM electrode PadSet placed on the thorax was used, with electrodes positioned at the sternal notch, xiphoid and in the right mid-axillary line at the level of the xiphoid (Fig. 1). The RVM provided a continuous respiratory volume trace from which MV, TV, and RR measurements were calculated. The ventilator provided simultaneous continuous pressure, flow, and volume curves from which the corresponding MV, TV, and RR values were calculated.

2.3 Data collection

For each patient, a 30-s period near the beginning of surgery, within 5 min following intubation and the initiation of mechanical ventilation was identified. This "quiet period" was selected when the surgical team was neither using electrocautery nor performing excessive manipulations of the patient. This period was used as a proxy for the "start of surgery". For each 5-min period during the procedure, a 30-s segment that free from electrocautery artifact and major manipulation was selected. A similar "quiet period" was defined prior to extubation, after the cessation of mechanical ventilation and transition to spontaneous breathing, as the "end of surgery".

2.4 Analyses

Temporally aligned segments from the RVM's respiratory trace and the ventilator's volume trace were compared using linear regression analysis. RVM and ventilator measurements of MV, TV, and RR were compared with Pearson correlation analysis and using Bland–Altman analysis methodology [8]. Repeated measures single factor analysis of variance (ANOVA) was used to assess the effect of "time from calibration" on the difference between the RVM and ventilator measurements. Additionally, single-factor ANOVA was used to evaluate differences in measurement variability between the two devices. All analyses were performed in Matlab R2012b (Mathworks, Natick, MA, USA).

Continuous digital respiratory traces from both the RVM and ventilator were analyzed simultaneously. Temporally aligned (between the two devices) 30-s segments were used to calculate each pair of MV, TV and RR measurements. The error between each pair of measurements was defined as follows:

$$\text{error} = \frac{\text{RVM measurement} - \text{ventilator measurement}}{\frac{1}{2}(\text{RVM measurement} + \text{ventilator measurement})}$$

For each individual subject we calculated measurement "bias", "un-signed bias", "precision" and "accuracy" in the following manner:

- "bias" is a mean value of all errors
- "un-signed bias" is the mean of the absolute value of all errors
- "precision" is the standard deviation of all errors
- "accuracy" is the square-root of the mean-squared-error.

When estimating the population averages and confidence intervals we calculated the average and SD of these metrics and reported the data as the average ± 2 SD.

3 Results

Careful review of the continuous data streams revealed marked similarity between RVM and ventilator respiratory traces during surgery. Figure 2 shows example respiratory trace segments from a representative subject recorded by both the RVM and the ventilator. During continuous mechanical ventilation the correlation coefficients between the traces from both devices were in the range of 0.94 and 0.99. The correlation coefficient was slightly lower during the transition period from pure mechanical ventilation to spontaneous breathing, possibly due to the RVM being more sensitive to spontaneous variations in the respiratory pattern than the ventilator, as evidenced by the small pattern variations present on the RVM trace but completely missing from the ventilator trace (Fig. 2e).

A systematic analysis of the MV, TV and RR measurements sampled in 5 min intervals from the ventilator

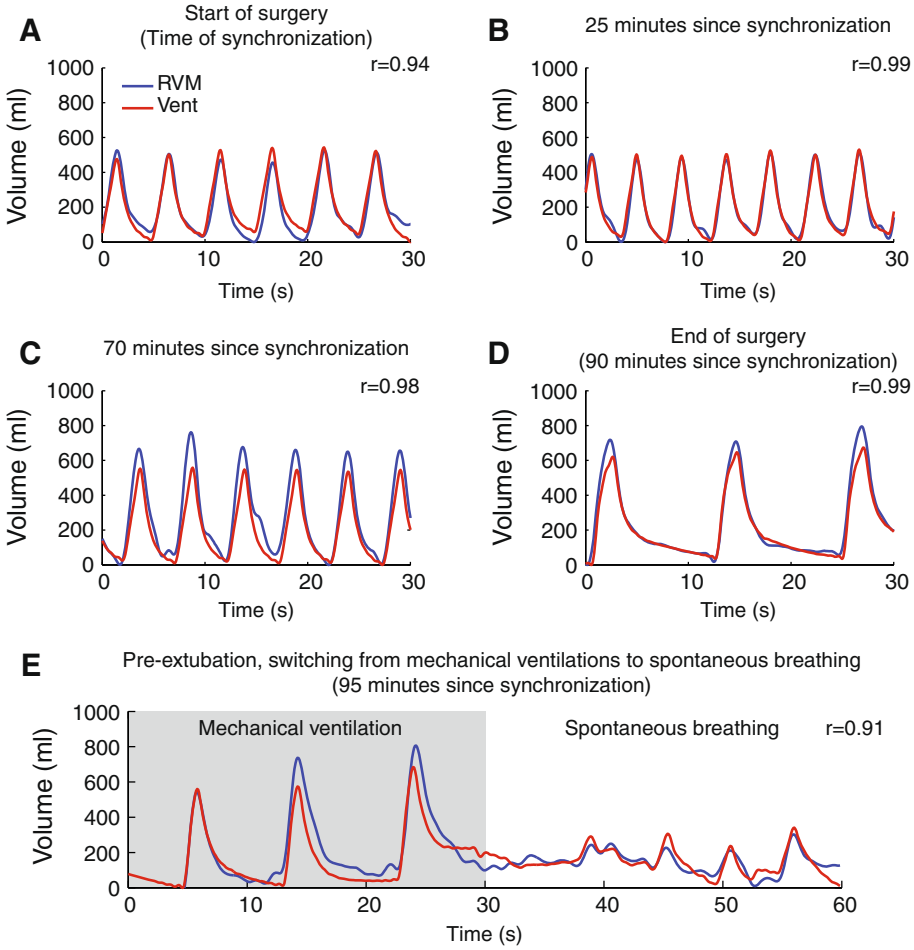

Fig. 2 Example pairs of RVM (*blue*) and ventilator (*red*) respiratory traces throughout the course of surgery. **a** At the start of surgery (synchronization period) the respiratory traces were similar with a correlation coefficient of 0.94. **b–d** At various time-points during surgery (25, 70 and 90 min after the start) the similarity between the respiratory traces remained and the correlation coefficients were all above 0.97 (0.99, 0.98 and 0.99, respectively). **e** At the end of surgery when the patient was switched from mechanical ventilation to spontaneous breathing the higher fidelity of the RVM signal easily captures spontaneous breathing attempts which are omitted by the ventilator, yet the correlation coefficient between the corresponding respiratory traces remained greater than 0.90

and RVM revealed that the errors between devices are temporally independent. Figure 3a–c shows the errors in all three measurements between the two devices as a function of time. Repeated measures ANOVA found no effect of time on the absolute differences between MV, TV, and RR measurements between the two devices ($p > 0.2$ for all three measures). Removing the temporal component of the data and plotting individual measurements from the ventilator and RVM revealed that 100 % of the MV (Fig. 3d), 99.4 % of the TV (Fig. 3e), and 100 % of the RR (Fig. 3f) RVM measurements are within 20 % of the corresponding ventilator measurements.

In order to account for the trial-to-trial variability in the data (given that the relative device error is likely temporally invariant) we computed the average measurement errors per subject. Across all 10 subjects the, the average un-signed bias was 5.5 % for MV, 5.8 % for TV and 1.7 % for RR and the maximum un-signed bias was 11.8, 12.7, and 4.4 %, respectively. These values are comparable to what has been previously reported when comparing RVM measurements against spirometry [6].

Next we computed the individual measurement differences in MV, TV, and RR between the ventilator and the RVM (Fig. 4, y-axes) and plotted them as a function of the best estimate of the actual MV, TV, and RR measurement (Fig. 4, x-axes). The resulting Bland–Altman plots show the distribution of measurement differences as a function of the measurement values. The average measurement difference in MV was −0.10 L/min with a corresponding 95 % CI (±2 SD) from −0.99 to 0.80 L/min. The average measurement difference in TV was 0.4 mL with a 95 % CI from −70.1 to 70.2 mL. The average measurement difference in RR was −0.22 breaths/min with a 95 % CI from −0.55 to 0.11 breaths/min. Table 2 summarizes the statistics of these measurement differences, calculated as a percentage of the measurement values. The average MV difference between the RVM and ventilator had a measurement bias of −1.3 %, precision of 6.6 %, and accuracy of 9.0 %. The average TV difference had bias of 0.4 %, precision of 7.3 %, and accuracy of 9.1 %. The average RR difference had a bias of −1.8 %, precision of 3.7 % and accuracy of 4.1 % (Table 2).

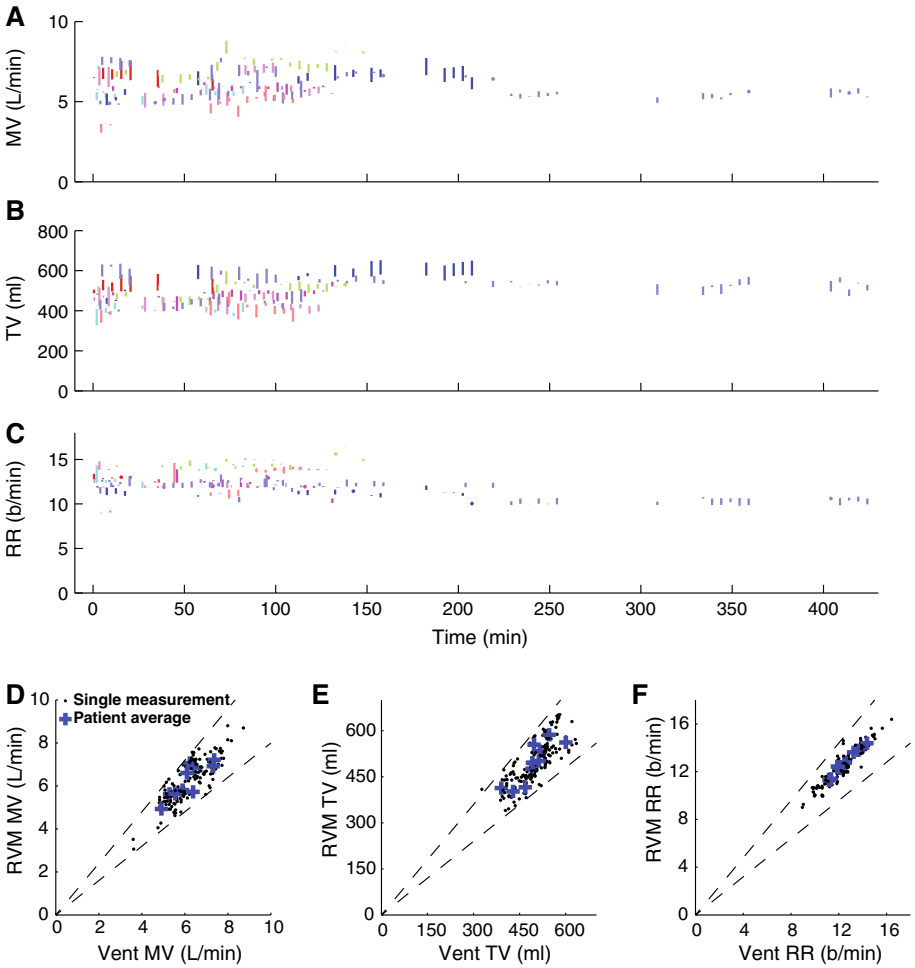

Fig. 3 Measurement differences between RVM and the ventilator. **a–c** Differences in the absolute measurements as a function of time in surgery on the ventilator. All traces are aligned to the beginning of the case (time 0) and each color represents a single patient. The height of each *vertical bar* corresponds to the difference between a particular pair of RVM and ventilator measurements, whereas the x-position of each bar corresponds to the specific time at which these measurements were recorded. **d–f** Plots of the relative relationship of between the RVM and the Draeger Apollo ventilator. **d** Minute ventilation **e** tidal volume and **f** respiratory rate. The *black dots* depict the individual measurement pairs and the *blue* 'plus' signs depict the patient average measurements. The *black dashed lines* depict the region of space where measurements are within 20 % relative error between the two devices. Note that nearly all measurements are within the 20 % error margins

4 Discussion

Based on continuous traces from both the RVM and ventilator, we observed close correlation (>94 %) between calculated RVM MV, TV and RR and ventilator measurements collected from intubated patients undergoing elective orthopedic surgery. Data presented here supplement previous data demonstrating >90 % measurement accuracy when the RVM was compared to turbine spirometry (Wright Respirometer, nSpire Health, Inc. Longmont, CA, USA) and closed-cell (SpiroAir-LT, Morgan Scientific, Haverhill, MA, USA) spirometry measurements [6]. This study demonstrates similar accuracy of the RVM when compared with the ventilator in intubated patients in the hospital setting and validates its use in this patient population. Previous pilot data comparing RVM data collected in intubated patients in the cardiac ICU following median sternotomy demonstrated strong correlation between RVM TV's and ventilator measurement ($r = 0.97$) [9], but analysis was compromised by the fact that the Puritan Bennett ventilator does not present or store digital data, but only intermittent numerical data points. This prompted the current study utilizing a ventilator from which streaming digital data could be extracted for comparison with the RVM data.

This study addresses potential concerns that previous comparisons between RVM and spirometry were based on an ambulatory volunteer population. The data presented here, collected in the perioperative setting validates the accuracy of RVM in this surgical cohort. It further supports previous work which has described changes in RVM volume measurements associated with opioid administration in the PACU.

Respiratory complications and deaths continue to occur despite increased awareness [10, 11]. The importance of providing a real-time, continuous, quantitative assessment of ventilation in non-intubated patients has long been understood. Unfortunately, previous monitoring technologies have been unable to provide continuous, non-invasive, real-time measurements of ventilation. Pulse oximetry continues to be the primary technology used to assess respiratory status in non-intubated [12], but adequate oxygenation is not well correlated with adequate ventilation [13].

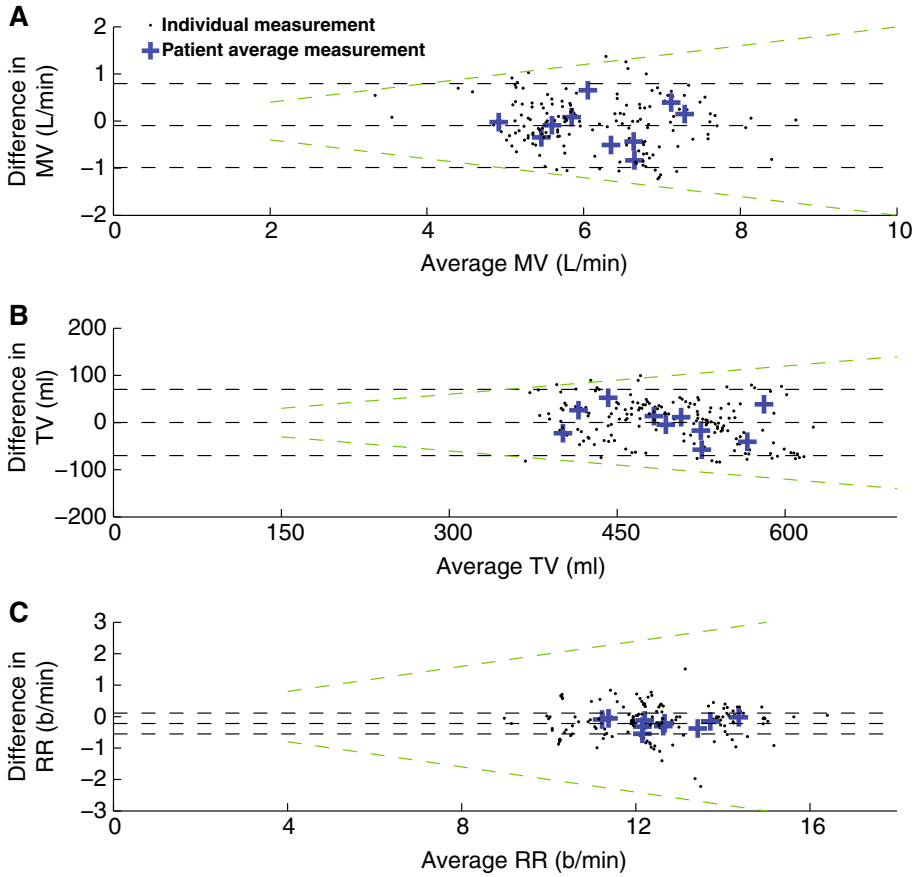

Fig. 4 Measurement error analysis of the cohort data. Bland–Altman plots of minute ventilation (MV), tidal volume (TV), and respiratory rate (RR). *Black data points* represent individual measurements, *blue* "plus" signs are computed as the average for a single subject. In each of the three plots, the abscissa is computed as the average between the RVM and the ventilator and the y-axis is the difference between the two. **a** Differences in MV measurements. The *middle black dashed line* shows the average difference (−0.10 L/min) and the *upper and lower dashed lines* depict the 95 % CI (±2 SD, −0.99 to 0.80 L/min). **b** Differences in TV measurements. The average TV difference was 0.4 mL (95 % CI −70.1 to 70.2 mL). **c** Differences in RR measurements. Average RR difference is −0.22 breaths/min (95 % CI −0.55 to 0.11 breaths/min). Note that the *green dashed lines* in all plots contain the region of space where relative error is below 20 %

Table 2 Absolute differences, measurement bias, precision, and accuracy across the patient cohort

Parameter	All statistics are reported as average ± SD across patients		
	MV	TV	RR
Absolute difference	−0.10 ± 0.45 (L/min)	0.04 ± 35.1 (mL)	−0.22 ± 0.16 (b/min)
Bias (%)	−1.3 ± 7.0	0.4 ± 7.0	−1.8 ± 1.3
Precision (%)	6.6 ± 1.8	7.3 ± 1.5	3.7 ± 1.5
Accuracy (%)	9.0 ± 3.0	9.1 ± 2.6	4.1 ± 1.5

Historically, there have been many challenges to providing effective, accurate monitoring of respiratory status in spontaneously breathing patients. To supplement pulse oximetry, end-tidal carbon dioxide ($EtCO_2$) monitoring assesses respiration non-invasively through the measurement of carbon dioxide tension of expired gas [14, 15]. $EtCO_2$ measurement technologies, generally considered to accurately reflect $PaCO_2$ for intubated patients, have not met their promise of clinical utility for non-intubated patients [14]. Issues with adequate sampling and patient compliance have limited implementation in the post-operative period [15]. Changes in breathing patterns affect the $EtCO_2$ waveform making it less useful in patients with erratic breathing patterns, a common occurrence in the post-operative setting [16, 17]. Additionally, supplemental oxygen administration can dilute $EtCO_2$, making changes in respiratory status difficult to assess [18]. Even in the face of optimal respiratory rate measurements, ventilation status cannot be adequately assessed without knowledge of adequacy of air exchange reflected in tidal volume measurements.

Lynn and Curry highlighted the fact that minute volume is the earliest indicator in the spiral leading to respiratory

failure [13]. RVM has now been demonstrated to provide MV, TV and RR measurements, which accurately reflect ventilation status in both intubated and non-intubated patients. The Center for Medicare and Medicaid Services (CMS) Center for Clinical Standards and Quality Survey and Certification Group has recently issued a document defining "Requirements for Hospital Medication Administration, Particularly Intravenous (IV) Medications and Post-Operative Care of Patients Receiving IV Opioids." This document requires that continuous monitoring of respiratory status in all post-operative patients receiving opioids be instituted as part of routine care [19]. In this context, RVM can provide continuity of monitoring across the continuum of care, not only during the critical time immediately post-extubation. Extension of RVM monitoring into the post-operative period provides the opportunity to continuously observe apneic and hypopneic episodes and monitor patient response to opioids. With the continuity with ventilator volume measurements provided by the RVM, it now becomes possible to not only monitor ventilation but also to assist in the detections and prevention of respiratory failure, with protocols that address OSA with CPAP and opioid induced ventilatory insufficiency (OIVI) with modification of pain management regimens.

A limitation of this study is that the RVM device was not designed for use during electrocautery or with variable pressure placed on the electrode PadSet. For this reason, patients where data was grossly distorted by electrical interference or aggressive patient manipulation were excluded from the study. This enabled analysis of multiple consecutive time points necessary for robust analysis. While this study demonstrates that the RVM's MV, TV, and RR measurements are comparable to a mechanical ventilator widely used in clinical practice, it should be noted that the prime utility of the RVM is in the post-operative, post-extubation period. Under normal conditions of patient motion and standard care protocols, the RVM has been shown to accurately track respiratory parameters [7]. During surgery, however, the RVM measurements are susceptible to distortion due to major changes in patient's posture, gross manipulations of patient's lower extremities which may lead to deformation of the chest cavity and/or compression of the diaphragm, and the use of external electrical devices (like electrocautery) which deliver high levels of current into the patient. While clinicians are aware that such external sources of noise and measurement variability have similar effects on other electrically-based physiological measurements (e.g. ECG, EMG, and EEG), it is important to understand that like these other monitors, the RVM will not track well during certain portions of a surgical procedure. The RVM measurements analyzed here were collected during "quiet periods" between episodes of substantial external perturbations. Due to the homogeneity of the patient population, the effects of patient BMI on the accuracy of the RVM measurements could not be assessed; however, based on previous work [7] any BMI-related effects are likely to be minimal.

5 Conclusion

These results demonstrate the accuracy of the RVM when compared to the ventilator, supplementing previous studies which demonstrated the accuracy of the RVM when compared to the spirometry measurements [7] and supporting the capability of the RVM to provide continuity in the assessment of respiratory status perioperatively. The capability of the RVM to non-invasively report MV, TV and RR, gives healthcare providers accurate, quantitative, clinically relevant measurements of respiratory status. Further work is needed to develop an understanding of the RVM's direct impact on decreasing post-operative respiratory complications and healthcare costs and on improving patient safety.

Acknowledgments C. Marshall MacNabb, Dr. Brayanov Dr. Freeman and Dr. Ladd are employed by Respiratory Motion, Inc. Drs. Voscopoulos, Qin, Mullen and George have no financial relationship with Respiratory Motion, Inc.

Conflict of interest C. Marshall MacNabb, Dr. Brayanov Dr. Freeman and Dr. Ladd are employed by Respiratory Motion, Inc. Drs. Voscopoulos, Qin, Mullen and George declare that they have no conflict of interest.

References

1. George JA, Lin EE, Hanna MN, Murphy JD, Kumar K, Ko PS, Wu CL. The effect of intravenous opioid patient-controlled analgesia with and without background infusion on respiratory depression: a meta-analysis. J Opioid Manag. 2010;6(1):47–54.
2. Jones DA, DeVita MA, Bellomo R. Rapid-response teams. N Engl J Med. 2011;365:139–46.
3. Ramsay MA, Usman M, Lagow E, Mendoza M, Untalan E, De Vol E. The accuracy, precision and reliability of measuring ventilatory rate and detecting ventilatory pause by rainbow acoustic monitoring and capnometry. Anesth Analg. 2013; 117(1):69–75.
4. American Society of Anesthesiologists: Committee for Standards and Practice Parameters: Standards for basic anesthetic monitoring. October 10, 2010; effective data July 1, 2011.
5. Futier E, Pereira B, Jaber S. Protective lung ventilation in operating room: systematic review. Minerva Anestesiol. 2014;80: 726–35.
6. Voscopoulos C, Brayanov J, Ladd D, Lalli M, Panasyuk A, Freeman J. Special article: evaluation of a novel noninvasive respiration monitor providing continuous measurement of minute ventilation in ambulatory subjects in a variety of clinical scenarios. Anesth Analg. 2013;117(1):91–100.
7. Voscopoulos CJ, Ladd D, Brayanov J, George E. Non-invasive respiratory volume monitoring to develop a risk algorithm for the safe use of opioids. Crit Care Med. 2013;41:A16.

8. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307–10.
9. Marengi N, Brayanov J, England M, MacNabb CM, Campana L, Pham DT, Ianchulev, S. Use of a continuous non-invasive respiratory volume monitor in postoperative cardiac surgery patients before and after endotracheal extubation. Anesth Analg. 2013;116:S-289.
10. Pesaro C. Opioid-induced sedation and respiratory depression: evidence-based monitoring guidelines. J Perianesth Nurs. 2012;27:208–11.
11. Willens JS, Junquist CR, Cohen A, Polomano R. ASPM survey-nurses' practice patterns related to monitoring and preventing respiratory depression. Pain Manag Nurs. 2013;14:60–5.
12. Fouzas S, Politis P, Skylogianni E, Syriopouloe T, Priftis N, Chatzmichael A, Anthracopoulos MB. Knowledge on pulse oximetry among pediatric health care professionals: a multicenter survey. Pediatrics. 2010;126:e657–63.
13. Lynn LA, Curry JP. Patterns of unexpected in-hospital deaths: a root cause analysis. Patient Safety in Surgery 2011. BioMed Central, Ltd. www.pssjournal.com/content/5/1/3.
14. Liu SY, Lee TS, Bongard F. Accuracy of capnography in non-intubated surgical patients. Chest. 1992;102:1512–5.
15. Cheifetz IM, MacIntyre NR. Respiratory controversies in the critical care setting. Respir Care. 2007;52:636–44.
16. Good ML. Capnography: uses, interpretation, and pitfalls. JB Lippincott Co., editor. Philadelphia, PA: Amer Soc Anesthesiologists, 1990. p. 1–23. Print.
17. Kaneko Y. Clinical perspectives on capnography during sedation and general anesthesia in dentistry. Anesth Prog. 1995;42:126–30.
18. Fu ES, Downs JB, Schweiger JW, Miguel RV, Smith RA. Supplemental oxygen impairs detection of hypoventilation by pulse oximetry. Chest. 2004;126:1552–8.
19. United States Department of Health and Human Services: Centers for Medicare and Medicaid Services. Requirements for Hospital Medication Administration, Particularly Intravenous (IV) Medications and Post-Operative Care of Patients Receiving IV Opioids. 2014. http://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/SurveyCertificationGenInfo/Downloads/Survey-and-Cert-Letter-14-15.pdf.