Detecting low respiratory rates using myriad, low-cost sensors

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Abstract: The underlying problem for two of the three most common patterns of unexpected hospital deaths (PUHD) is hypoventilation[1]. Current methods of post-operative respiratory monitoring give delayed signals and have a high false positive rate leading nurses to ignore alarms. We hypothesize there exists a combination of low cost sensors which are capable of providing real time feedback and alarms regarding obstructive sleep apnea and ventilatory depression. Such a monitor would be useful during space travel when monitoring personnel are limited following an injury or if astronauts were to be sedated during extended travel. Methods: Twenty-six subjects were recruited to participate in a study of the effects of Propofol and Remifentanil. Throughout the day, these patients were exposed to varying levels of both drugs simultaneously via target controlled infusions. These patients were attached to breathing and oxygen monitors including chest bands, pulse oximeters, nasal pressure sensors, CO_2 capnography, breathing microphones, and thermistors. The patients were then observed for types of apnea or ventilatory depression. Results: The study is currently ongoing however preliminary analyses of the data indicate multiple low cost sensors are capable of detecting respiratory rate as well as obstructive events and apnea. Conclusion: Using only a combination of low cost sensors, we can provide real time respiratory event data to nurses and practitioners.

INTRODUCTION & BACKGROUND

The underlying problem for two of the three most common patterns of unexpected hospital deaths (PUHD) is hypoventilation[1]. Type II PUHD (CO_2 narcosis) involves a reduction in respiratory rate and/or tidal volume, and if supplemental oxygen is being provided, a pulse oximeter will not detect the problem until the hypercarbia is significantly advanced and the patient is near respiratory arrest. Type III PUHD is induced by obstructive sleep apnea in the presence of arousal failure, and is recognized as a repetitive sequence of cyclic apneas and self-arousals which precede the final apnea. A pulse oximeter alarms with each apneic period and will likely be interpreted as generating many false positive alarms.[1] The risk of opioid-induced respiratory depression in postoperative patients is greatest in the first 24 hours after initiation of opioids[2], and opioids are the most commonly used drug for treating pain in the postoperative period.[3]

These problems would be especially apparent in space travel where monitoring personnel are limited due to either sedation of crew members or an injury rendering the crew short-handed.

Respiratory depression is caused by drug-induced inhibition of the breathing control center of the brain stem. Partial to full airway obstruction is an anatomic problem involving the soft palate, tongue base, and/or epiglottis, caused by drug-induced decreases in airway patency and muscle

tone. Sedatives and opioids depress the response to elevated CO_2 (reduced drive to breathe), worsen arousal, cause airway obstruction, and change sleep patterns[4-8]

In the postoperative period, most adverse respiratory events occur during the first 24 hours of opioid administration.[2] During this period, pulse oximeter monitoring, supplemental oxygen, incentive spirometry, and intermittent nursing observation are the primary interventions used to fend off adverse respiratory events. For inpatient monitoring, pulse oximetry is often inadequate. On a busy hospital floor, it is difficult to respond to multiple remote advisory pulse oximetry alarms. Pulse oximeter alarms are ignored because they have a high false-positive alarm rate due to movement artifact and displacement.[9,10] Pulse oximetry primarily monitors oxygenation instead of ventilation; the SpO_2 signal is a delayed indicator for apnea or hypopnea, particularly when supplemental oxygen is given. By the time the pulse oximeter alarms, an apneic patient is already in danger of hypoxia, brain injury and death.

Existing technologies may improve monitoring of adverse respiratory events in this setting, but are either costly or difficult to implement. For example, monitoring ventilation with capnography is expensive and it can be problematic to sample the exhaled gas with a face mask or nasal cannula in non-intubated patients.[11] Acoustic respiratory rate monitoring may be able to detect airway obstruction, but it is costly and may not have sufficient sensitivity to reliably detect apnea events.[12] Additionally, most modern devices have been verified for the clinical setting where patients are intubated and may not function adequately in the non-intubated setting. We

suggest that there is an urgent need for a low cost, reliable respiratory depression monitoring technique that can be integrated with the signals from the pulse oximeter to give additional physiologic information about a patient's sufficiency of both ventilation and oxygenation in the non-intubated setting.

Currently, we are exploring the value of integrating the information from a set of low-cost physiologic monitors that can be adapted to monitoring patients in a hospital floor setting. In addition to the red and infrared component signals that comprise the pulse oximeter plethysmography waveform, we intend to integrate information from respiratory inductance plethysmography sensors on the body, temperature, pressure and carbon dioxide sensors embedded in a nasal cannula and acoustic respiratory rate via a microphone on the throat. We will determine from the tested set the fewest number and least costly types of sensors that can be used to accurately identify and quantify ventilatory depression and airway obstruction, provide reliable measures of oxygenation AND ventilation, provide specific alarms, and avoid artifact. We will evaluate this multi-sensor set for volunteers who receive medications to produce ventilatory depression and/or partial to complete airway obstruction.

Our team previously characterized various effects of sedatives combined with opioids using drug interaction models. Specifically, we characterized the interaction of Propofol and Remifentanil on metrics of airway obstruction and intolerable ventilatory depression in volunteers.[8] We defined intolerable ventilatory depression as a respiratory rate less than 6 breaths per minute and airway compromise as either partial (tidal volume less than 3 mL/kg in the

presence of a respiratory effort) or complete obstruction. Respiratory compromise was defined as either intolerable ventilatory depression or airway obstruction or both.

Using this model, predictions of respiratory compromise (0 to 100%) can be made for various dosing schemes of Propofol and remifentanil.[8] (Figure 1). In general, dosing schemes that led to high concentration of Propofol were more likely to produce airway obstruction and higher doses of Remifentanil were more likely to produce intolerable ventilatory depression.
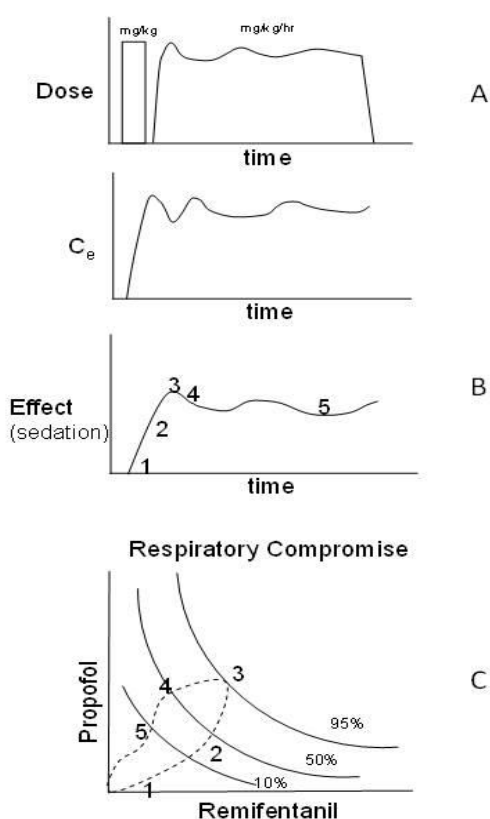

Figure 1: A: Dose of a drug over time. B: effect site concentration (Ce) Corresponding to the given dose and C: Observed effect (sedation) for a single administered drug. Time points 1-5 correspond to a different effects on respiration

METHODS

A 20 gauge venous catheter was placed in an antecubital vein under local anesthesia (0.2 mL of 0.5% lidocaine) for the purpose of hydration and drug administration. The IV site was similar in all subjects. A maintenance infusion of 0.9% sodium chloride was administered at 1 ml/kg/hour throughout the study. Continuous infusions of Remifentanil and Propofol was infused into this peripheral IV.

Subjects were instrumented with a noninvasive blood pressure cuff, ECG leads, pulse oximeter(s), motion sensors, respiratory inductance plethysmography "chest bands", capnography nasal cannula, nasal gas pressure sensor, nasal thermistor and an acoustic respiratory rate sensor. These or similar monitors were placed to measure respiratory rate, tidal volume, end-tidal CO_2, SpO_2, blood pressure, body motion and heart rate. Chest and abdominal wall excursion were measured with the attached motion sensors and the respiratory inductance plethysmography bands. Changes in respiration pattern were displayed as real-time changes in CO_2 waveforms. A processed EEG monitor and/or a cerebral oximeter were optionally placed to record data for later analysis. A motion sensor was also placed on the bed. These devices were operational during the entire study day. Data from devices was electronically captured and recorded for later analysis. Continuous variables such as motion waveforms, pulse oximetry waveform, capnogram, and nasal airway pressure were digitized during data collection periods at 50-1000Hz during data collection periods at each target effect site concentration pair. Discrete variables were recorded every 5 seconds or as soon as data were available during data collection

periods. Examples of discrete variables include heart rate, SpO_2, $PetCO_2$, systolic blood pressure, diastolic blood pressure and respiratory rate. The tidal volume was occasionally measured with a differential pressure flow sensor attached to an anesthesia mask or mouthpiece in order to calibrate the respiratory inductance plethysmography bands.

Each subject received Propofol and Remifentanil. Similar to previously collected data from our volunteer laboratory (Kern et al, 2004), each drug was administered using a computer controlled (Stanpump[14]) continuous infusion pump (Pump 22; Harvard Apparatus, Limited, Holliston, MA) to achieve selected target effect site concentrations. The effect site concentration refers to the drug concentration at the pharmacologic site of action. Pharmacokinetic parameters published by Minto *et al.*[15] and Schnider et al.[16] was used for Remifentanil and Propofol respectively.

We administered Propofol and Remifentanil pairs in a dose escalation scheme with small steps in order to creep up to the desired target effects of respiratory depression, airway obstruction and both effects while avoiding overshoot. To accomplish this, the Propofol was dosed in a range of 0.75 - 4 mcg/mL in dose escalation steps of approximately 0.5 mcg/mL. Remifentanil was dosed in a range of 0.75 to 4.0 ng/mL in escalation steps of approximately 0.25-0.5 ng/mL. If overshoot was observed for a given target effect site concentration pair, the target effect site concentrations were lowered so assessments could be made during the target effects of respiratory depression or airway obstruction or both. Once the drug concentration pair was identified which

resulted in the target effects for a given subject, the steady state drug dose was maintained for a period of data collection.

In previous NASA space grant publications, a preliminary analysis was performed on these sensors which analyzed them for their ability to detect obstructive and central apneas denoted by a lack of signal. The current aim of the project is to detect specific breaths in each sensor and use these breath marks to analyze periods of low respiratory rates.

A custom breath detection algorithm was developed which detects breaths in a signal based on peaks which are above or below a moving threshold. This algorithm works functionally the same for each signal and adapts based on specific thresholds which were manually identified for each sensor.

Data were isolated from periods during which the patient was unperturbed, not talking, and breathing normally (no obstruction present). This data was segmented into individual minute-by-minute segments. Segments which had more than 10 breaths in them (as counted by the respiratory inductance plethysmography bands) were excluded from the analysis.

Bland-Altman and linear regression analysis were performed on the data in order to analyze the confidence intervals for breath rates. A sample Bland-Altman plot for the capnogram is shown in figure 2.

The next analysis involved restricting the data set even further to get an estimation of how often the alarm would falsely report on the patient condition at a clinically relvant respiratory rate of 5 or fewer breaths—commonly diagnosed as 'ventilatory depression'.

Each signal was analyzed so that at each respiratry rate less than or equal to 10, the signal was compared against the reference signal (RIP bands) and the number of times that the signal was incorrectly diagnosing 'ventilatory depression' was counted.

An additional endeavor of this data set analysis was extracting respiratory rate from the photoplethysmography (PPG) signal (pulse oximetry). An envelope filter was used to obtain the baseline signal (related to respiration) from the PPG. The RIP band (as the reference respiratory rate signal) and the PPG signal were analyzed in order to explore the potential for using PPG to monitor respiratory rate below 10 breaths per minute (BPM). Examples of the filtered signal are shown in figures 4, 5, and 6.

RESULTS

Figure 2 shows a sample of a Bland-Altman analysis performed on the capnogram with the RIP bands as the reference signal. The signal shows no change in relative bias and consistent deviation at all respiratory rates. The x-axis represents the mean of respiratory rates reported by the capnogram and the RIP bands. The y-axis represents the difference in the reported respiratory rates.

Table 1 shows the relevant statistics from the Bland-Altman analysis not only from the capnogram but also from the thermistor and impedance signals.

Figure 3 illustrates an analysis in which sections of data were organized by breath rate, and the observed percentage of misdiagnosis (regarding a RR greater than, or less than 5 BPM) was graphed. The capnogram illustrated the lowest range of misdiagnosis. The error of the impedance monitor varied wildly with respiratory rate.
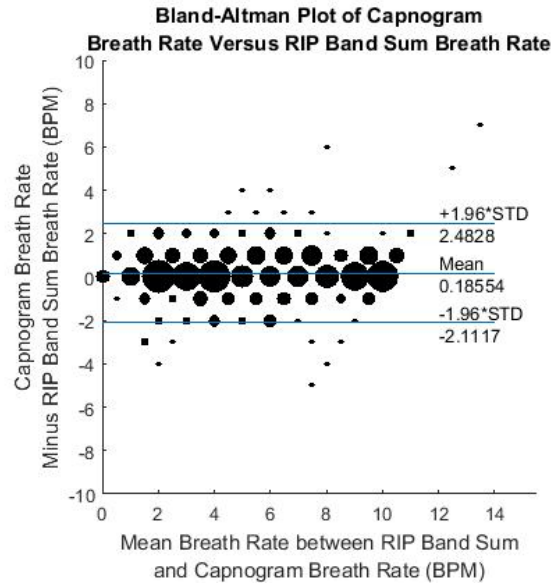

Figure 2: Bland-Altman plot of capnogram reported breath rate versus RIP band breath rate. X-axis is the mean of the reported breath rates and y-axis is the difference (capnogram-RIP bands) in reported breath rates. Bias and confidence intervals are depicted by the indicated lines.

Table 2: Bland-Altman statistics from the impedance, thermistor, and capnogram monitors. Upper and lower confidence intervals are reported as Bias±1.96*STD

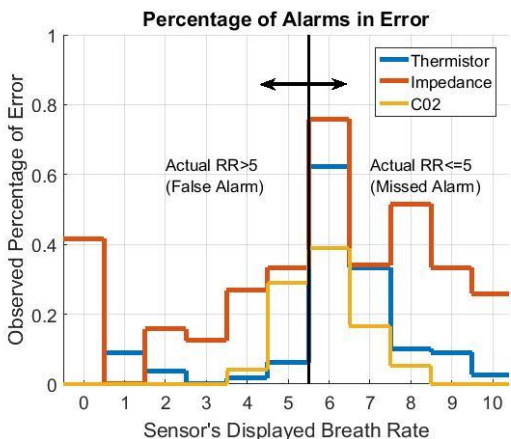|	Capno-graphy	Impedance	Thermistor
Bias (BPM)	0.18	0.64	0.51
Std (BPM)	1.18	3.96	2.09
Upper 95% Confidence Interval (BPM)	2.5	8.39	4.61
Lower 95% Confidence Interval (BPM)	-2.13	-7.12	-3.58

Figure 3: The observed percentage that the respiratory rate displayed by a given sensor was in error about a low RR (BPM<=5) diagnosis. The right side of the black vertical line is the observed percentage that a sensor displayed a RR>5 when the actual respiratory rate was <=5 (Missed alarm). The opposite case (test RR<=5, actual RR>5) (False alarm) is shown on the left side of the black vertical line.

The error of the thermistor was high around 5-6 breaths per minute but relatively low elsewhere.

Figure 4 shows an example of an optimal case for using the PPG signal to measure respiratory rate. In this sample, the breath rate is roughly 20 and the filtered PPG signal almost exactly mirrors the RIP band signal.

Figures 5 and 6 both illustrate some of the issues that arise when trying to use the same signal to detect low respiratory rates. In both cases, the respiratory rate is 6 or less. In figure 5, there is an additional peak present between breaths identified by the RIP bands. In figure 6, the filtered PPG signal demonstrates much more noise than the 'optimal' case and shows a situation in which the PPG signal creates a double-peak during a single breath identified by the RIP bands.
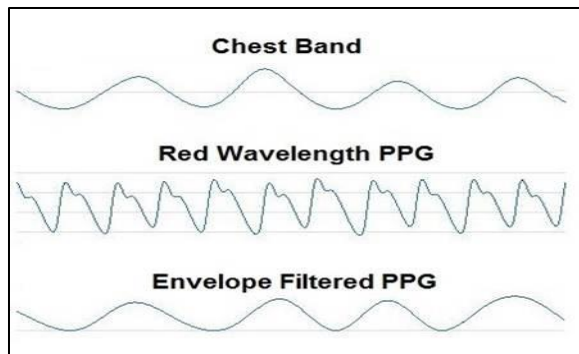

Figure 4: A 20-second window of RIP bands, PPG waveform, and an envelope filtered PPG waveform are displayed at a RR of 20 BPM. The filtered PPG signal modulates in time with inspiration and expiration as confirmed by the RIP waveform.
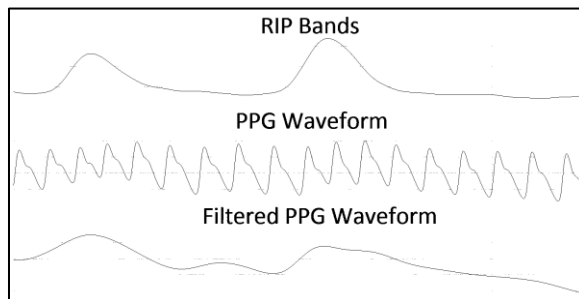

Figure 5: A 20-second window of RIP bands, PPG waveform, and an envelope filtered PPG waveform are displayed at a RR of <5 BPM. The filtered PPG waveform changes during the same time period as the RIP waveform, but with multiple peaks.
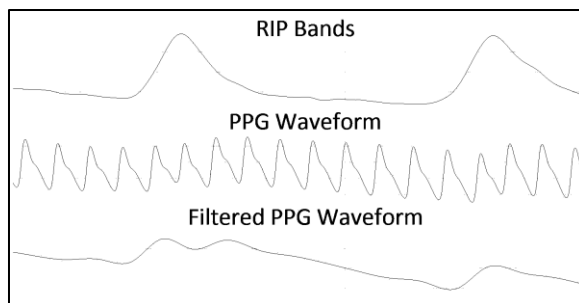

Figure 6: A 20-second window of RIP bands, PPG waveform, and an envelope filtered PPG waveform are displayed at a RR of <5 BPM. The filtered PPG signal has deflections between breaths indicated by the RIP bands.

CONCLUSION

A low cost, accurate, and minimally sized respiratory monitor would be useful during space travel when personnel are limited following an injury/emergency procedure or if astronauts were to be sedated during extended voyages.

The primary goal of this analysis was to identify the best way to analyze a signal for its clinical utility and to test this analysis on some sample signals.

Figure 3 showed a new method of analyzing signals which relies on analyzing the number of 'false alarms' that a sensor might display when monitoring a patient. These false alarms were specifically related to clinically relevant low respiratory rates. The logic behind this is that most monitors will perform adequately in the range of 'normal breathing' but may not perform adequately when it comes to raising alarms. The capnogram demonstrated that it has the ability to distinguish between different respiratory rates remarkably well at low respiratory rates. The impedance monitor, on the other hand, was subject to much lower signal-to-noise ratio at these respiratory rates and performed poorly with respect to properly raising alarms.

This facet of signals performing differently at different respiratory rates is highlighted by the case of the PPG signal. At a respiratory rate of 20 depicted in figure 4, the PPG signal almost perfectly mimics the RIP bands (which are used as the reference in this study for their relatively high accuracy). However when the respiratory rate becomes low (less than 6 breaths per minute), the signal becomes erratic and much more susceptible to noise. A number of physiological effects of respiration on the bloodstream could be the reasoning behind this. One of which is the sympathetically mediated vasoconstriction which occurs at high tidal volumes. These tidal volumes may be more likely when the patient is breathing intermittently and the vasoconstriction effect may be more pronounced when there is less of a respiration signal to mask it.

We intend to continue this analysis on a number of different signals and analyze how each signal performs specifically at the clinically relevant respiratory rates we are hoping to detect. Preliminary analysis indicate that multiple sensors may be of use in detecting these conditions.

ACKNOWLEDGEMENTS

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