Comparison of Intraoperative Heart Rate and Respiratory Rate Acquired Via ATLASense Raphael PolyMonitor and Standard Intraoperative Monitors

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1. STUDY AIM, BACKGROUND, AND DESIGN ABSTRACT

Vital signs are the objective foundation by which health care providers base clinical decisions. Thus, changes in vital signs serve as an important indicator of physiologic decline. To efficiently monitor for patient deterioration, we may benefit from technical innovation which improves upon traditional surveillance and reporting of these critical patient values. New remote monitoring technologies offer a method of obtaining continuous and comprehensive surveillance of patient vital signs, which can be transmitted to a remote working station for display and analysis [1]. Indeed, investigation into the accuracy of wireless monitoring devices in reporting key parameters such as heart rate (HR) and respiratory rate (RR) as compared to traditional monitoring have shown some promising results [1–3].

The ATLASense RAPHAEL PolyMonitor is an investigational wearable and wireless patient monitoring device. The monitor can be attached to a patient's chest, and collect continuous physiological signals including HR, RR, skin temperature, body movement, as well as non-invasive blood pressure (NIBP) and transmit this information remotely for display and analysis. Ultimately, this PolyMonitor may be able to process multiple physiologic signals simultaneously for early detection and predictive modeling of patient physiologic deterioration, change the way alerts are transmitted to clinicians, reduce infection risk of multiple monitors reused on patients, and extend perioperative physiologic monitoring beyond the operating room and recovery areas to a patients home. While this monitor has significant potential to improve the efficiency of patient monitoring, it has yet to undergo validation studies.

In this observational comparison study, we aim to compare the HR and respiratory RR of intraoperative surgical patients simultaneously recorded by standard intraoperative monitors and the ATLASense RAPHAEL PolyMonitor. We also aim to determine degree of data loss, data gap duration, and validate the PolyMonitor alert system for tachycardia and bradycardia. Additional parameters of non-invasive blood pressure (NIBP) and body temperature will also be compared between the PolyMonitor and standard intraoperative

monitors. Finally, this study will provide insight into the logistics of intraoperative use of the PolyMonitor.

The ATLASense Raphael PolyMonitor will be placed on the patient's left chest mid sternal line in the operating room. Traditional physiologic monitors described above will also be placed on the patient in the operating room. Data will be collected via the ATLASense system and through the traditional operating room monitors, and this data will be time matched through synchronization of the monitors post hoc. The time matched data pairs will undergo statistical analysis post hoc.

We anticipate that this study will validate the intraoperative HR and RR measured through the ATLASense Raphael PolyMonitor, providing adequate data points for statistical analysis with 95% limits of agreement, bias, and data loss/gaps. Success is also the logistical lessons learned for using this monitor in the intraoperative setting.

This study will provide a foundation for further investigation into the use of the ATLASense Raphael PolyMonitor as a tool for early detection and predictive modeling of patient physiological deterioration. With further study, this device has the potential to replace multiple traditional monitors, provide individualized data capture to build a predictive model for each patient and may extend perioperative physiologic monitoring beyond the operating room and recovery areas to a patient's home.

2. SUBJECT POPULATION AND ELIGIBILITY

Subject Population:

Adult patients who are scheduled to undergo general anesthesia during their elective surgery at Henry Ford Hospital - Main Campus between October 2021 and December 2021.

Inclusion criteria:

English speaking
Adult males or females (above the age of 18)
Scheduled to undergo general anesthesia during elective surgery

Exclusion criteria:

Pregnant adult female

Thoracic surgery
Left lateral decubitus positioning required during procedure
Surgery involving the left flank, or requiring surgical field involving the left flank
Surgery involving the left chest, or requiring surgical field involving the left chest
Allergy to adhesives
Open wound, rash, or sore involving the left chest
Presence of cardiac defibrillator, or pacemaker

Enrollment

The electronic medical record available of subjects scheduled for elective procedures at Henry Ford Hospital – Main Campus will be reviewed by the study team to screen subjects for eligibility. Minimal necessary variables that need to be obtained include: age, gender, pregnancy status, BMI, planned procedure, associated diagnosis, allergies, and co-morbidities (Hypertension, Congestive Heart Failure, Chronic Obstructive Pulmonary Disease, Diabetes Mellitus, ASA status). Subjects will be called via telephone at least one week prior to their procedure to briefly introduce the study to them. For in-patients, it is possible that a study team member will visit their location in the hospital to introduce the study and review the Informed Consent Form with them in the week prior to their surgery. If interested, they will be sent the Informed Consent Form via email or mail (whatever their preference) to ensure that they have adequate time to read the consent form and ask questions. Patients will be consented in person prior to their elective procedure and given a copy of the signed consent form.

3. STUDY PROCEDURES

Study Design and Outcomes

This will be a prospective observational study comparing HR and RR of intraoperative surgical patients simultaneously recorded by standard intraoperative monitors and the ATLASense RAPHAEL PolyMonitor. Funding for this study will be provided internally. This study will fall under regulatory oversight by the FDA.

This study will consist of an initial chart review of patients scheduled to undergo elective procedures at Henry Ford Hospital – Main Campus from October 2021, to December 2021. The study team will review their medical record in EPIC prior to their scheduled procedure and screen them to ensure that they meet all eligibility requirements. Patients will be contacted at least one week prior to their scheduled

procedure to provide them with a brief introduction to the study. If they are interested, they will be sent an Informed Consent Form via mail or email (whichever is their preference). This will ensure that the patients have adequate time to review the consent form and ask questions prior to their procedure. They will then be consented in person prior to their procedure and given a copy of the signed consent form.

Our **primary study aim** is to determine if the ATLASense RAPHAEL PolyMonitor can reliably measure intraoperative HR and RR as compared to traditional intraoperative monitors. In order to evaluate this aim, our primary outcome will be bias and precision (95% limits of agreement) of HR and RR of the PolyMonitor compared with the traditional monitors. It is hypothesized that the ATLASense RAPHAEL PolyMonitor will provide HR and RR measurements within ± 10% of the reference monitor or ± 3 breaths/min or ± 5 beats/min [4].

A secondary outcome that will examined include technical reliability in terms of data loss occurrences, and data gap duration. Additional secondary outcomes include reliability in detecting bradycardia and tachycardia, as well as bias and precision (95% limits of agreement) of skin temperature and NIBP of the PolyMonitor compared with traditional monitors.

Further lessons include the logistics of employing this PolyMonitor in intraoperative setting including device placement, surgical practices that may impede data collection (body placement, etc), device placement, patient feedback on wearable, and patient positioning considerations.

Data Collection

The information that will be pulled from patient charts in EPIC is as follows:

Age
Gender
Race
Height
Weight
Pregnancy status
BMI
Planned surgery and associated diagnosis
Allergies

Co-morbidities
ASA status

On the day of surgery, the ATLASense RAPHAEL PolyMonitor will be placed on the patient's left chest mid sternal line in the operating room by the anesthesia provider. Traditional physiologic monitors including the GE E-PSMP-00 Monitor/Datex Ohmeda Aisys CS2: EKG HR, Ventilator RR, End Tidal CO2 RR, blood pressure cuff, *** core temperature probe will also be placed on the patient in the operating room.

Data acquisition will include: HR, RR, NIBP, core body temperature, data loss events (instances when data was not recorded/saved for any reason by the polymonitor or other monitors) and duration of data gaps, bradycardic events, and tachycardic events. Acquisition of data from the ATLASense PolyMonitor will be confirmed after the device is applied. Data will initially by tracked via medical record number (MRN). Following data acquisition, subjects will be deidentified using a random number generator to assign data sets for further data tracking.

Data will be collected via the ATLASense system and through the traditional operating room monitors, and this data will be time matched through synchronization of the monitors post hoc. Data collection intervals will be every 1 minute starting prior to induction of anesthesia and ending at the time of intraoperative monitor removal in the operating room. The ATLASense PolyMonitor will be removed at the same time as traditional physiologic monitors.

ATLASense RAPHAEL PolyMonitor

The ATLASense RAPHAEL PolyMonitor is a small, non-intrusive, wireless, wearable multi-sensor device, attached to the patient's torso either with adhesive disposable patch or as a smart shirt. It continuously collects multiple physiological signals, analyzes them and transmits them to the ATLASense server. The PolyMonitor is composed of a rechargeable lithium polymer battery (3.6 Volts, 370 milliamp hour), an independent charger (5 volt input via mini USB/USB cable) which employs a universal 90-240 VAC 50/60 Hz to 5VDC converter and four FDA-approved hydrogel electrodes. The device has safe fault limit on electrical current which exceeds regulatory requirements.

The system enables monitoring a multiple array of physiological, postural and emotional parameters. For this study, the Heart rate (HR) and Respiration rate (RR) derived parameters will be calculated and updated every second, stored in internal

memory, and transmitted. Measurements and alerts are transmitted via a low-power radio protocol (BT 4.2 Low Energy) to hotspots ("gateways" connected to the hospital communication network). The data is sent to ATLASense central server and to the healthcare service provider's server connected with the electronic medical record.

ATLASense RAPHAEL PolyMonitor – HR Detection

The electrocardiogram is recorded and processed to calculate the average HR by analyzing a single-lead electrocardiogram, which is preprocessed first to filter the raw electrocardiogram signal in order to minimize noise due to motion and muscle artifacts. Heart rate is measured using an algorithm developed by ATLASense.

The algorithm checks electrodes' contact to assure credibility, detects the R wave, computes several valid interbeat intervals, and computes the running HR with low latency. HR is calculated by computing inter-beat intervals (IBI), limiting IBI to one in every 300 mSec before the next beat (refractory period). The average HR is acquired by calculating the reciprocal of the average of 4 IBIs. Accuracy of resting HR is reported to be +/-1% or +/- 2 BPM, whichever is greater, and range of detection is reported to be from 30-240 BPM.

ATLASense RAPHAEL PolyMonitor – RR Detection

The PolyMonitor incorporates three independent respiration measures for increased reliability: Piezoelectric respiration sensor with two, additionally derived respiration measures from two biopotential electrodes concurrently monitoring the torso ECG and EMG. The algorithm excludes from the calculation segments that are corrupted by motion artifacts or other irregular patterns. Accuracy of resting RR is reported to be +/- 5% or +/- 1 Breaths/Min, whichever is greater. A default RR alert is generated for no single breath in a 10 second period.

ATLASense RAPHAEL PolyMonitor – NIBP detection

The ATLASense RAPHAEL PolyMonitor detects NIBP at up to 1 minute intervals, and can derive the NIBP as an average over multiple measurements, or as a single NIBP measurement. The latency period between measuring these intervals and calculating an average for data recording and display is ~ 1 second when employing a local server.

ATLASense RAPHAEL PolyMonitor – Temperature detection

The ATLASense RAPHAEL PolyMonitor detects skin temperature at up to 1 minute intervals, and derives measurements as an average based on multiple interval measurements. The latency period between measuring these intervals and calculating an average for data recording and display is ~ 1 second when employing a local server.

CARESCAPE™ Monitor B850 - HR Detection

This multiparameter high acuity patient monitor is intended for use in multiple areas within a health care facility. Within the perioperative setting it is indicated for monitoring of multiple different hemodynamic parameters. However, for our study we will be acquiring data from its ECG monitoring function, and calculated HR. The heart rate will be measured at 1 minute intervals and then compared with time-matched HR acquired through the ATLASense PolyMonitor.

GE Aisys CS2™ - RR Detection

The Aisys CS2 is functionally integrated ventilation, respiratory monitoring, and breathing system. Module bays allow for the physical integration of legacy Datex-Ohmeda patient monitors and supports mounting of other GE Healthcare monitors, including the CARESCAPE™ Monitor B850. The Aisys CS2 Anesthesia System is intended to provide general inhalation anesthesia and ventilatory support to a wide range of patients. Respiratory rate is calculated with this system from the frequency of peak (end tidal) CO2 measurements per minute. A breath is defined as a change in the CO2 signal that exceeds 1% (8 mmHg). All concentrations are measured and displayed breath by breath.

CARESCAPE™ Monitor B850 – Non-Invasive Blood Pressure Measurement

The CARESCAPE Monitor B850 employs the oscillometric technique for blood pressure measurement. In brief, this technique involves inflation of the cuff to a preset pressure. The pressure is then gradually reduced. With every arterial pulse wave there is a small rise and fall in volume within the vessel. This creates an increase and subsequent decrease in the pressure within the encircling blood pressure cuff, which can be detected using a solid-state transducer [5]. Various proprietary algorithms then calculate the mean arterial pressure (MAP), diastolic, and systolic blood pressures. The CARESCAPE™ Monitor B85 employs the use of the DINAMAPTM SuperSTAT advanced NIBP algorithm from GE Healthcare.

CARESCAPE™ Monitor B850 – Arterial Line Blood Pressure Measurement

In patients with an arterial line placed during surgery, the CARESCAPE™ Monitor B850 will be used to monitor blood pressure. The CARESCAPE™ Monitor B850 employs an invasive blood pressure module which is able to transmit data obtained from the Arrow® arterial catheterization device. the Arrow® ASK-4500-HFH3 arterial catheterization device permits access to peripheral arterial circulation, and allows for

hydraulic coupling between the arterial circulation and a Wheatstone bridge piezoresistive transducer. This transducer converts the change of pressure transmitted within the arterial catheter with each heart contraction into a change of current which can then be displayed on the CARESCAPE™ monitor. The monitor filters the raw signal from the transducer and converts it into a visual waveform. Various proprietary algorithms then calculate the mean arterial pressure (MAP), diastolic, and systolic blood pressures.

CARESCAPE™ Monitor B850 – Temperature Measurement

The Vyaire M1024215VY temperature sensor is a disposable device which can be inserted into a patient's esophagus and transmit core body temperature measurements at 1-minute intervals. The Vyaire M1024215VY has a direct input in order to display temperature information on the CARESCAPE™ Monitor B850.

Project Timeline

The primary end-point of the study is the collection of 14,303 time-matched HR and RR data pairs to power the study for 95% level of agreement (N = 14,303). This would require approximately 238 hours of intraoperative data collection if 1-minute intervals are used for time-matched data pairs. We estimate that 60-70 patients will need to be recruited based on surgical procedures with anticipated durations of 2-5 hours. Data collection is estimated to take approximately 3 months. Data analysis, and manuscript preparation is estimated to take an additional 6 months.

Protection of Privacy

Subject name and MRN will be recorded out of necessity during subject screening, recruitment and data acquisition so that data can be appropriately tracked. However, the PI and Co-investigators will take appropriate steps to minimize risk to the subject and ensure protected health information is secured. The information will be de-identified by a broker from HFHS Data Analytics prior to being given to the study team for analysis. The identifiable information will be stored in a secure REDCap database and will be destroyed as soon as possible after the record maintenance period. All study data will remain on secure HFHS password-protected computers and stored on secure HFHS servers.

Statistical Analysis

The data pairs of HR and RR measurements obtained in 1-minute intervals derived from the wireless sensors and the traditional physiologic monitors will be analyzed using the Bland and Altman method for repeated measurements [6]. The Bland and Altman method will also be used to account for within-subject variation by correcting for the differences across patients and the variance of differences between the average differences. The bias (mean difference) between the ATLASense RAPHAEL PolyMonitor sensors and reference monitor and the 95% limits of agreement (± 1.96 SD) will be determined for both HR and RR data.

PolyMonitor bradycardia and tachycardia alert notifications will be time matched with the HR measurements from the traditional monitor. Reliability in determining tachycardic and bradycardic events will be assessed by calculating sensitivity, specificity, positive predictive value and negative predictive value from paired data. True positive tachycardia will be defined as HR > 100 BPM via the traditional monitor. True positive bradycardia will be defined as HR < 60 BPM via the traditional monitor. Based on the data points from our primary aim (N=14303), we have 99% power to detect a change in sensitivity from 0.5 to 0.8 using a two-sided binomial test and 99% power to detect a change in specificity from 0.5 to 0.8 using a two-sided binomial test. The target significance level is 0.05. The prevalence of tachycardia and bradycardia is assumed to be 0.01 to 0.02[2,7].

Data pairs for skin temperature and NIBP obtained in 1 to 5 minute intervals derived from the wireless sensors and the traditional physiologic monitors will be analyzed using the Bland and Altman method for repeated measurements [6]. The Bland and Altman method will also be used to account for within-subject variation by correcting for the differences across patients and the variance of differences between the average differences. The bias (mean difference) between the ATLASense RAPHAEL PolyMonitor sensors and reference monitor and the 95% limits of agreement (± 1.96 SD) will be determined for both HR and RR data. Sample size calculation was estimated based on the primary study aim.

Technical performance will be analyzed by the duration of data loss and the total amount of data loss. Reliability will be defined as the time until the first occurrence of data loss (defined as duration of a gap within the data of 2 min, 15 min, 1 hour or 4 hours) and the overall amount of data loss. The time to first occurrence of data loss will be analyzed with Kaplan-Meier survival plots. Data analysis will be performed by a statistician from the

HFHS Public Health Sciences.

4. ANTICIPATED RISKS

This study involves minimal risk for participants. The placement of the investigational device will not require deviation from standard practices. The risk to the participant includes breach of confidentiality in terms of inadvertent or unanticipated release of identifying information during the data acquisition process. The identifiable information will be stored in a secure REDCap database and will be destroyed as soon as possible after the record maintenance period. This risk will be mitigated by limiting data access to the principle investigator and co-investigators. Identifying information will be removed as soon as possible by a third party after the data acquisition process. All study data will remain on secure HFHS password-protected computers and stored on secure HFHS servers.

There is minimal to no risk with regards to placement of the study device. Risk may include allergic reaction upon placement of the device electrodes. This risk will be mitigated by excluding subjects with a known allergy to skin adhesive, and by monitoring the patient's skin following device placement and removal. In the event of an allergic reaction to the skin adhesive, the device will be removed, data collection will stop, and the patient will be treated as appropriate for an allergic reaction. The incidence will be documented in the study REDCap database. A member of the study team will follow up with the patient in recovery.

5. ANTICIPATED BENEFITS

There are no anticipated direct benefits to the patient. The research will allow for validation of the device in obtaining intraoperative heart rate and respiratory rate. The data will lay the foundation for further study of this device which may improve upon the standard intraoperative monitor and improve perioperative patient monitoring.

6. RENUMERATION/COMPENSATION

No compensation or renumeration will be offered.

7. COSTS

There is no additional cost for participants associated with participation in this study.

8. ALTERNATIVES

The alternative is that subjects do not have to participate in the research.

9. CONSENT PROCESS AND DOCUMENTATION

This study consists of an initial chart review of information that is routinely collected as standard of care for all patients undergoing elective surgical procedures. Subjects deemed eligible for the study based on inclusion and exclusion criteria will be contacted and provided information about the study per a pre-determined telephone script. Subjects who are interested in participating will be sent the informed consent documents via mail or e-mail (per their preference) at least one week prior to their scheduled procedure. Patients will be provided the opportunity to privately ask questions by contacting research personnel prior to their scheduled procedure (via contact information provided on the informed consent form), as well as on the day of their procedure prior to placement of the device in the operating room.

Patients will be consented prior to their enrollment in the study by research personnel when they arrive to the hospital on the day of their procedure and provided with a copy of the signed consent. Physical copies will also be retained and held securely in a locked file within the department of anesthesiology office. After data collection is complete, records will be retained for the required record maintenance period before being destroyed.

10. WITHDRAWAL OF SUBJECTS

The subjects will be withdrawn from the research if the procedure cannot be completed for any reason. Subjects will also be withdrawn from the research if they indicate a desire to withdraw. If data acquisition has already begun or has been completed, data obtained will be destroyed along with any possible identifiers.

11. PRIVACY AND CONFIDENTIALITY

We will be screening patient charts to verify that they meet eligibility requirements for the study. During the data collection period, recorded patient information will be entered in a secure REDCap study database containing patient names and medical record numbers. Data will be de-identified by a broker from HFHS Data Analytics and assigned a numerical code before it will be given to the study team for analysis. Following data collection, this information will be destroyed as soon as possible following the record maintenance period and the REDCap database will be deleted. HIPAA Authorization will be obtained prior to the patient's procedure, at the time of obtaining documented consent.

12. DATA AND SAFETY MONITORING PLAN

Data will be maintained in a secure REDCap database, and only research staff will have access to the data. The PI will check the data for integrity every month. If there are discrepancies, this will be discussed with the study team and rectified. Data will be monitored on a monthly basis. If there is an issue, Cory McCurry DO MSc will contact IRB via email within one week, depending on the nature of the issue.

13. QUALIFICATIONS OF THE INVESTIGATOR(S)

Trevor Szymanski M.D. M.B.A completed his undergraduate degree at the University of Michigan, then completed his M.D at Tufts University School of Medicine. He completed his anesthesiology residency at Brigham and Women's Hospital – Harvard Medical School, and completed a fellowship in cardiothoracic anesthesiology at Massachusetts General Hospital – Harvard Medical School. He completed his Masters of Business Administration at the University of Michigan – Stephen M. Ross School of Business.

He has been involved with numerous previous studies[8–11], including most recently a comparison study examining outcomes of transfemoral transcatheter aortic valve replacement using pre-sedation radial versus post-sedation femoral arterial sites for blood pressure monitoring[12].

14. REFERENCES

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