Remote Closed-Loop Automatic Oxygen Control in Preterm Infants

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Abstract

Background Different automated systems have been developed to improve maintenance of target range of arterial oxygen saturation (SPO2) in premature infants with respiratory distress. This study aimed to develop a Remote Closed-Loop Automatic Oxygen Control (RCLAC) as an efficient monitoring device. Then the mean of fraction of inspired oxygen (FIO2) and SPO2 by routine manual control (RMC) and RCLAC were compared.

Methods A developmental-descriptive study was carried out in an Iranian hospital (Tehran-Iran; 2015-2017). Eighteen preterm infants with gestational age 24-28 weeks entered the study. A database was prepared based on pulse oximeter parameters. A Wi-Fi module was implemented to receive data from pulse oximeter and send inputs to user's mobile. Vibrate alarm was implemented for high or low FIO2. After receiving notifications associated with increase or decrease of FIO2 levels and user's confirmation; the alterations were applied on the ventilator.

Results The mean FIO2 in RMC system was significantly higher than RCLAC system (98.1± 2.67 vs. 79.5±16.03; p = 0.0001). According to the results, when the SPO2 reached close to target SPO2 range and consequently FIO2 changed (decreased or increased based on target SPO2), heart rate showed a regular beating with decrease in the numbers.

Conclusion Remote Closed-Loop Automatic Oxygen Control system as a simple device could prevent preterm neonates from sustained hypo-hyperoxemic and arrhythmia episodes. Moreover by using RCLAC, there was no need for continuous monitoring that may reduce workload of NICUs medical staff. Collecting reliable data and recording information in digital forms were also other benefits.

Introduction

Oxygen therapy for premature infants with respiratory distress is a critical subject. Hypoxemia can lead to permanent nervous system damage or organ failure resulting high morbidity and mortality rates. On the other hand, hyperoxemia in some cases may lead heart, lungs, brain, retina and hearing system damages. Maintenance of adequate blood oxygen concentration to minimize the risks of both hypoxemia and hyperoxemia are the main goal related mechanical ventilation in hospitalized premature infants (1–4).

Maintenance of oxygen saturation targets is monitored by pulse oximetry which detects arterial oxygen saturation (SPO_2) and fraction of inspired oxygen (FIO_2) indices. Adjustment of respiratory support within the clinically intended range of SPO_2 is affected by some factors like routine manual control (RMC) by clinical staff and their respond to SPO_2 frequent fluctuations. It is clear that a higher nurse-to-patient ratio can improve achievement of oxygenation targets by preventing neonate from spending long time above the clinically intended range of SPO_2 (1, 5).

Different automated systems have been developed to improve maintenance of target range of SPO_2 and decrease of limitations related routine manual control. Kwok et al. extracted basic rules to improve control respiratory devices by using adaptive neuro-fuzzy inference system (ANFIS) with multilayer perceptron (MLP) and the FAVeM algorithms. They could reduce the workload of physician resulting better decision making (6). Another control system was developed to automatically adjust the frequency of breaths and tidal volume of lungs. Proportional-integral-derivative (PID) control algorithm, feedback data from devices, and some physiological data were used to reduce fluctuations of arterial oxygen (7). An AUTOPILOT-BT control ventilator system was also designed based on a set of Fuzzy controllers combined with explicit physiological modeling and a neural network. This model could enhance mechanical ventilation therapy and decrease workload of intensivists (8). Another investigation demonstrated that a closed-loop automatic control (CLAC) could improve oxygen administration to preterm infants while reduced workload related to RMC (2).

Recently, several studies focused on mobile Health (m-Health) as a help in collecting more and easier information, constant monitoring, and reducing unnecessary medical interventions. Over 3.1 billion mobile around the world have the ability to connect wirelessly. This intended software algorithm with multi services providers may influence sooner clinical diagnosis and better medical management with lower costs and less time consuming (9–12).

Keeping arterial oxygen saturation (SPO2) in a standard range for premature infants is of importance. On the other hand, continuous monitoring constrains extra workload for NICUs medical staff especially in crowded wards with undeveloped medical infrastructures. It is supposed that a Closed-Loop Automatic Oxygen Control system conducting a remote monitoring device may facilitate managing target SPO_2 with features such as acoustic, exhibition and vibrating alert. Moreover, collection of reliable data in digital form may reduce staff's workload. This study aimed to develop a Remote Closed-Loop Automatic Oxygen Control (RCLAC) as a quick and efficient monitoring device. Then the mean of FIO_2 and SPO_2 by RMC and RCLAC were compared.

Materials And Methods

Study design:

A developmental-descriptive study carried out in the NICU of Yas Women Hospital affiliated to Tehran University of Medical Sciences in collaboration with School of Allied Medical Science and Saadat CO. (Tehran-Iran) from October 2015 to July 2017.Twenty preterm infants with gestational age 24-28 weeks entered the study. Congenital diaphragmatic hernia, cyanotic heart disease, severe apnea, perfusion index (PI) < 0.4 and any medical conditions with deviation from the usual SPO_2 target range was considered as exclusion criteria.

Firstly, a checklist was prepared according to literature review to define some important demographic and physiologic parameters related maintaining of PaO_2 in a target range (gestational age, sex, temperature, heart rate, results of arterial blood gas test, FIO_2, SPO_2, PI, PH, pCO_2, pO_2, Hct,…). In the next step, eight expert neonatologists and pediatric intensivists were asked to prioritizethese parametersby score 1 to 10.

Of 19 variables, 4criteria had the greatest scores. The efficiency index(from 1 to 5) was calculated for each important criterion(Table 1).Hence, alterations of these important variables should be constantly considered and all decisions should be made based on them. After determining the significant variables associated arterial oxygen status, physicians were asked to design a medical algorithm (Figure 1).

Development and implementation of devices

After algorithm design, database software was prepared based on pulse oximeter parameters. A Wi-Fi module (designed by Saadat CO.) was implemented to receive data from pulse oximeter and send inputs to user'smobile. Moreover, a mobile application was also developedwitha particular service for reading input data from the module. Differentmobile alerting approachesincluding text message, sound alarm and vibrating alarm detected different variables; vibrate alarm was implemented for high or low FIO_2 and sound-vibrate alarm was designed for demonstrating heart rate, temperature, PI, sudden fluctuations or device disconnection from patient. It should be noted that all of these alarms type were optional for staff to set for each patient's events based on the importance of the events.

Mobile phone was connected through Wi-Fi network. User (neonatologist or NICU nurse) could receive information related patient's situation to perform or order the necessary cares. Using this new algorithm could provide a controlling system to change FIO_2 under the direct supervision of medical specialist. After receiving notifications associated increase or decrease of FIO_2 levels and user's confirmation; the alterations were applied on the ventilator. If this alarm was not confirmed by user, the alterations were notapplied, as well (Figure 2, 3).

Sample size

First, a pilot experimental study was carried out on 10 participants to compare FIO_2 between RMC and RCLAC groups. A significant difference was observed between groups regarding to FIO_2 (in RMC group= 97.4 ±3.2 vs. in RCLAC group= 74.1±19; p= 0.0001). Then, based on using Compare Means formula; with the proposed sample size of 8, the study had a power of 90% and an alpha error of 0.05. Finally, according an investigation by Hallenberger et al. (2), 18 subjects entered the study for better data analysis with appropriate power.

Protocol

In the present study, two approaches (RMC and RCLAC) in twenty-four–hour periods were compared. Nurses were asked to pay special attention to signs and warnings. With software alerts, the nurse should increase or decrease the amount of FIO2. After nurse confirmation, the alerts were applied on ventilator. If the alarm was not confirmed by nurse, alerts would not be applied on ventilator. Similarly, the software did not change the amount of FIO2. The nurse-patient ratio at NICU was 1:2 to 1:3.

Primary/ Secondary outcomes:

The FIO_2 algorithm was tested and compared among premature neonates with RMC and RCLAC to keep SPO_2 in the target range as the primary outcomes. Heart rate alterations following decrease or increase of SPO2 and FIO2 were also sassed as our secondary outcomes.

Ethical considerations:

The present study was taken from a medical student thesis with ID; IR290-441. Ethics approval was obtained from the institutional review board of Tehran University of Medical Sciences according to Helsinki declaration (IR.TUMS.SPH.REC.1395.1537). All participants' parents gave written consent before enrollment. All gathered data were considered confidential and no extra cost was imposed on our participants.

Data Acquisition and Analysis

RCLAC software had the ability to record and save data correlated demographic characteristics, respiratory or heart co-morbidities, FIO2, SPO_2, PI, temperature, and ABG results on the mobile phone. Moreover, this database had the potential to be connected to central database. Local database from the mobile phone were transferred to a PC-Computer. Then information was extracted from database with SQL query. All data were classified by patients file numbers. Recorded data were analyzed to compare the FIO2 between RMC and RCLAC groups. All statistical analyses were conducted using SPSS 19. Data were presented as mean±standard deviation for continuous variables and n (%) for categorical variables. Kolmogorov-Smirnov Test and T-Test were used for analyzing the relationships between variables.

Results

After storing information in the database, reliable and classified data had been available. Table 2 presents the summary of patient’s demographic characteristics. Twenty two preterm infants with gestational age 24-28 weeks entered the study. Of all, 4 neonates with severe apnea or PI < 0.4 were excluded. Eighteen neonates (10 males and 8 females) with the mean birth weight865±241 gr were included. The Kolmogorov-Smirnov Test showed normal distributions in all variables including birth weight (p=0.991), gestational age (p=0.991, age (p=0.957), RMC FIO_2 (p=0.084), RCLACFiO_2 (p=0.123) and PI (p=0.389).

T-Test analysis showed that the mean FIO2 in RMC system was significantly higher than RCLAC system (98.1±2.67 vs. 79.5±16.03; p = 0.0001).

Comparing FIO_2 and target SPO_2 in RCLAC and RMC systems, a box and whisker plot demonstrates (Figure 4) a fall in FIO_2 level based on target SPO_2 by applying RCLAC. The mean of FIO_2 value decreased from 97 to 79%.Moreover, regarding to SPO_2 setting by physician’s recommendations, the mean of SPO_2 level dropped from >98% to approximately 88%.

According to the results, when the SPO_2reached close to target SPO_2range and consequentlyFIO_2 changed (decreased or increased based on target SPO_2), heart rate showed a regular beating with decrease in the numbers. As detailed data are shown in Figure 5; after setting the target SPO_2on 93%, FIO_2dropped from 100 to 82% at 1:52 PM and heart rate decreased undergoing to90 bpm.

Figure 6indicateswhen the target $SPO_2$was set on 90% (after 1:49 PM), the FIO_2 decreased to below 60%, and the SPO_2 value reached close to 90%. After reaching to desirable SPO_2 level, the chart showed a decrease in heart rate fluctuation with regular rhythms. At that time the heart rate was shown close to 140 bpm.

Figure 7 shows that the lungs were able to supply oxygen and the patient did not need any supplementary oxygen. Decreasing FIO_2 from 100to below 80% caused no SPO_2alterations. Slight fluctuations in heart rate and SPO_2 were observed with reducing $FIO_2$to about 50%.This trend continued until the natural environment (21% oxygen) was achieved. However, after 1:04PM, the heart rate was regular and its rate reduced to below 140 bpm.

Discussion

In the present study we designed a Remote Closed-Loop Automatic Oxygen Control system as a simple device to keep arterial oxygen saturation (SPO2) in a standard range for premature infants. Moreover by using RCLAC besides managing target SPO_2, there was no need for continuous monitoring that may reduce workload of NICUs medical staff. Collecting reliable data and recording information in digital forms were also other benefits. The strength of our study was consideration of neonate's heart rate during FIO_2-SPO_2controlling.

According to the results, by implementing RCLAC system, the mean FIO_2 (considering target SPO_2) was kept in a lower range compared with RMC system. Using such an adaptive model could responsible for setting the minimum FIO_2 for the target SPO_2keeping preterm neonates from high O_2 exposure, sustained hyperoxemic episodes or fluctuations in SPO_2 levels resulting enhanced outcomes. Compatible to our finding, Hallenberger et al. designed a Closed-Loop Automatic Oxygen Control system (CLAC) using a laptop computer executing the FIO2 software connected to pulse oximeter and ventilator. They demonstrated that by implementation of system, oxygen administration to preterm infants was improved and optimized. The percentage of time spent within the SPO_2 target range (Target %) in CLAC group was significantly higher in comparison with RMC group. They concluded that by using such systems, unnecessarily high or low O_2 exposure could be prevented (2).

Another point associated RCLAC system in comparison with RMC systemwas maximum and minimum feedback times for inhaling oxygen. The results of present study have shown that the maximum time to reduce FIO2 was 3 minutes and the mean of 20 seconds was needed to increase FIO2 levels. Morozoff et al. have illustrated that by using adaptive control modes, within two or five minute periods, the controller could adjust the FiO2-SPO2 relationship resulting normoxemia (14). Tehrani et al. demonstrated that the time less than 20 seconds was required for returning the arterial oxygen saturation to the normal safe range by implementation of their proposed closed-loop automatic control system (15).

Based on the results, after adjusting desirable FIO2-SPO_2 levels by our proposed controller system, a decrease and regularity in heart rate chart were notable. Decrease of heart rate fluctuation with regular rhythms not only protect neonate from arrhythmia and its related adverse outcome but also can decrease NICU staff's stress. Moreover, this benefit could prevent patient from more medical interventions that may affect respiratory function. Up to our knowledge, our study was the only investigation that evaluated participants' heart rates during maintenance of FiO_2-SPO_2 in the normal ranges.

Former studies have confirmed that manually administering oxygen therapy is difficult and time consuming (1–3, 14,15). Results of present study demonstrated that by using RCLAC system, the workloads of the staff related to full FIO_2 control were reduced. Furthermore, with the systematization of daily reports related with RCLAC system, clinical staff did not waste lots of time for completing patient's medical records. RCLAC software had the ability to record and save all demographic characteristics data. This database had the potential to be connected to central database that facilitated availability of data for medical staff. By adjusting FIO_2, the patient and NICU's stresses could be alleviated that may influence the prognosis of disease and personnel efficiency. Finally, RCLAC system as an easy applicable and not-complex system was designed to warn NICU nurse based on patients’ condition. Staff by alarms related to the patients' status was being promptly informed.

Our study had some limitations. We did not design the sensors controlling PEEP and PIP under Wi-Fi network. Therefore, the data associated sensors detecting increase or decrease of FIO2 was not considered. Use of PEEP and PIP control sensors was strongly suggested in

Strengths Of Study

The previous studies have shown some risks related to development of mechanized control systems in oxygen therapy for respiratory complicated patients (1, 3, 5). Therefore, a system was designed and implemented that could easily and promptly warn nurses based on patients’ condition. Besides that, this system would be helpful for staff; they were informed by alarms related to the patients' status instead of full control monitoring.

Conclusion

Remote Closed-Loop Automatic Oxygen Control system as a simple device could keep preterm neonates from sustained hypo-hyperoxemic and arrhythmia episodes. Moreover by using RCLAC, there was no need for continuous monitoring that may reduce workload of NICUs medical staff. Collecting reliable data and recording information in digital forms were also other benefits.

Abbreviations

Arterial oxygen saturation; SPO_2

Remote Closed-Loop Automatic Oxygen Control; RCLAC

Fraction of inspired oxygen; FIO_2

Routine manual control; RMC

Neonatal intensive care unit; NICU

Declarations

Ethics approval and consent to participate

The present study was taken from a medical student thesis with ID; IR290-441. Ethics approval was obtained from the institutional review board of Tehran University of Medical Sciences according to Helsinki declaration (IR.TUMS.SPH.REC.1395.1537). All participants' parents gave written consent before enrollment.

Consent for publication

The present manuscript contains no individual person's data.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that there is no conflict of interests.

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Authors' contributions

Dr. Zarkesh and Kalhori carried out the design and coordinated the study, participated in most of the experiments. Dr Saeedi and Mr. Habibelahi coordinated and carried out all the experiments, Analysis of data and participated in manuscript preparation. Dr Panahi and Mr. Moradi designed the device and provided assistance for all experiments and prepared the manuscript. All authors have read and approved the content of the manuscript.

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Tables

Table 1: Scoring of important variables by physicians

Variables	Physicians scores; n=8								Mean *scores*	Efficiency index
FIO2	10	9	9	9	10	9	9	9	9.2	4.6
SPO2	9	9	8	10	10	8	9	10	9.1	4.8
Temperature	8	6	9	7	9	9	7	8	7.8	2.6
Perfusion Index	7	8	6	9	9	6	7	8	7.5	4.7
Heart rate	4	3	2	3	3	4	5	7	3.8	3.6

Table 2: Demographic and clinical characteristics of 18 participants

Variables	Total number=18
Gender (n %)	
Male	10 (55.6)
Female	8 (44.4)
Mean birth weight (Grams)	865±125
Mean gestational age (Weeks)	27.3±2.4
FIO2 at study entry [Median% (min-max)]	98(80-100)
FIO_2 in RMC group (Mean)	98.11±2.67
FIO2 in RCLAC group (Mean)	79.50±16.03
Ventilation mode (n %)	
Mechanical ventilation	12(66.66)
CPAP*	6 (33.33)
Surfactant treatment (n %)	7 (38.8)
No	11 (61.2)
yes	
History of multiple gestations (n %)	14 (77.77)
No	4 (22.22)
yes	
PI** [Median (min-max)]	0.78 (0.3-1.9)
Age [Days; median (min-max)]	27 (1-51)

*Continuous positive airway pressure **perfusion index

Figures

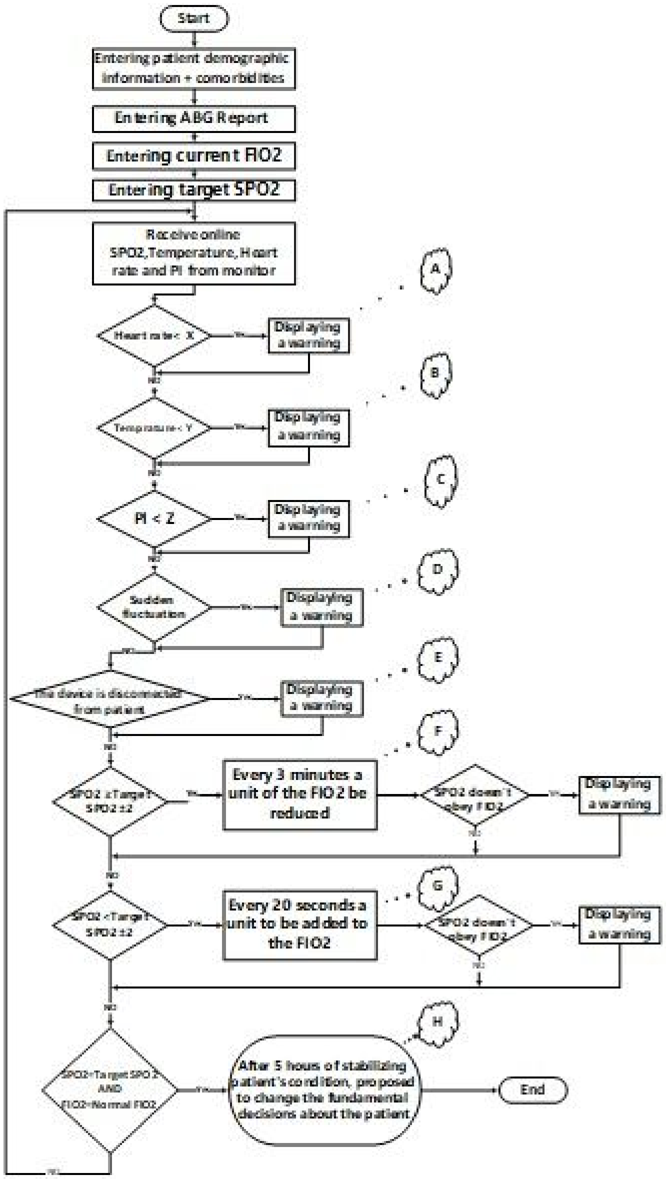

Figure 1

Flow chart of clinical approach to the treatment A: Heart rate drops in deep sleep. So, heart rate 80 bpm was considered as the default. B & C: In cases of body temperature (arms or legs) < 36°C or PI <2, a mistake might be happened in pulse oximetry measures (13). So, the accuracy of pulse oximetry signals should be considered in doubt. C: In PI values lower than 2, we could not count on SPO2 signals from pulse oximetry. In practice, this value for infants was 0.7, so PI< 0.4 was not considered. However, system user could define minimum heart rate, minimum temperature and minimum PI depending on patient's condition. D: Preventing neonate from sudden fluctuations in oxygen status, 10 units were considered for checking FIO2 alterations and SPO2 feedbacks. Increase of FIO2 after a block in airway or FIO2 decreasing without any changes in SPO2 value could indicate a trap in the system. In such situations, an alarm should be sent to the user. There were also other options; first, neonatologist could change FIO2 based on patient's condition. Second, system warned following sudden rise or drop (± 10%) of SPO2 values in less than 40 seconds. E: Separating probe from patient's body, monitor sent values regarding to SPO2 and heart rate while system displayed an alarm to warn neonatologist. F & G: Considering feedback of FIO2 from pulse oximetr, different opinions from 20 seconds to 5 minutes have been reported (2, 7, 14). So, the minimum time was considered to add one unit per 20 seconds. Moreover, a time near median (between 2 to 5 minutes) was considered to reduce one unit per 3 minutes. Regarding to part F, there were 3 reasons to reduce FIO2. First, neonate should be able to breathe normally (21% oxygen). Second, hyperoxia should be prevented because of its side effects. Third, according to Oxyhemoglobin dissociation curve, there is a nonlinear association between SPO2 and PaO2 in PaO2 levels more than 98%, the accurate SPO2 values could not be calculated in these ranges. H: Five hours after stabilizing patient's condition, final decision was made by neonatologist to change approach to the treatment.

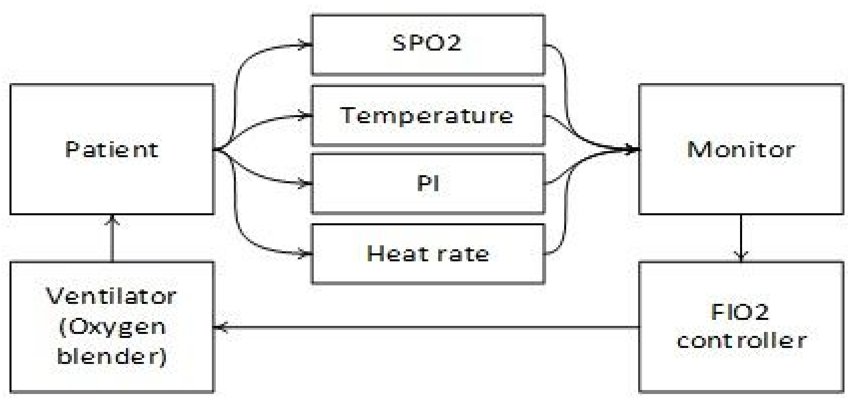

Figure 2

General algorithm

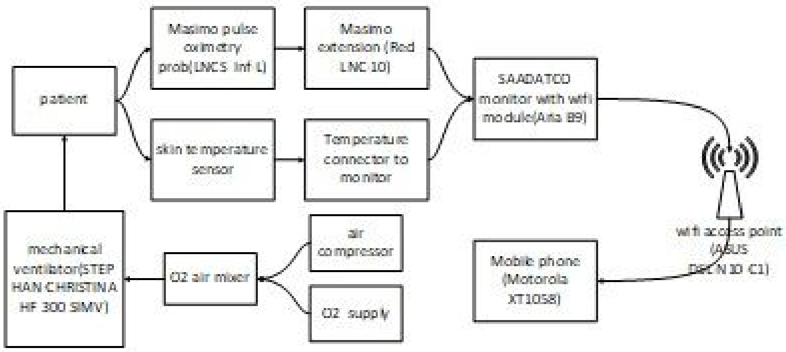

Figure 3

Equipment setup

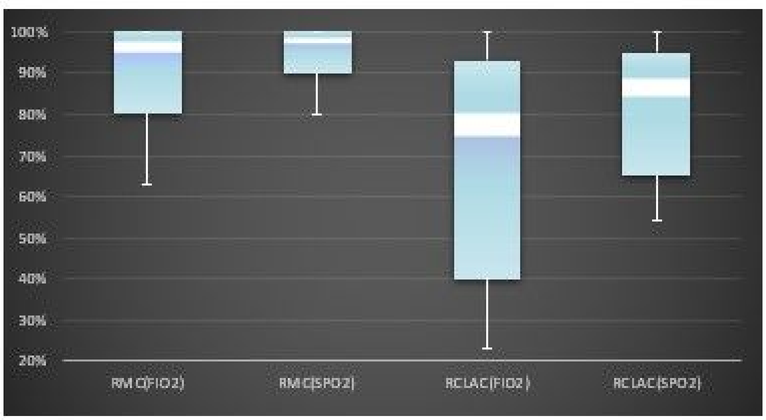

Figure 4

Box and whisker plot comparing FIO2 and target SPO2 in RCLAC and RMC systems

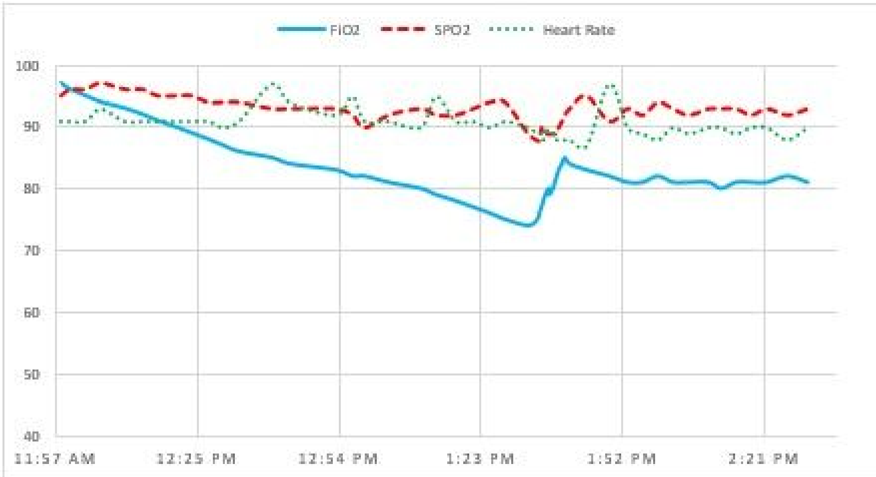

Figure 5

Example of RCLAC control of process-target SPO2 (93%)

Figure 6

Example of RCLAC treatment process-target SPO2 (90%)

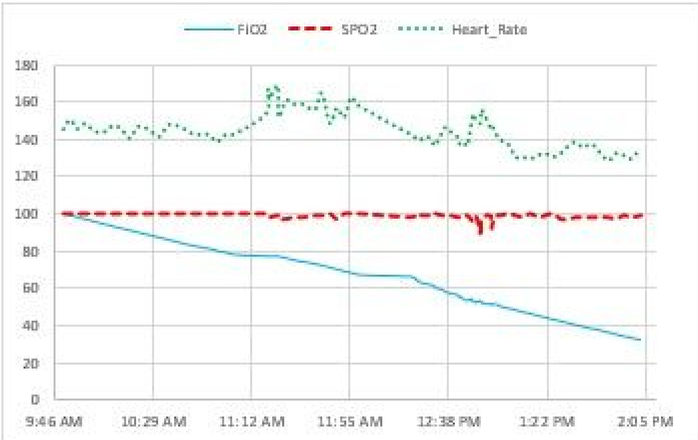

Figure 7

Example of RCLAC treatment process-target SPO2 (95%)