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TITLE: Smart Oxygenation System (SOS) Provides Early Warning of Lung Injury

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RECIPIENT: The University of Texas Medical Branch at Galveston

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Background: Most pulmonary injuries are insidious and declare themselves over a period of hours or even days. Most recently, tactical military changes have resulted in increased time between casualty injury and definitive care e.g., prolonged field care, increased transport times and initial damage control surgery and resuscitation. The following types of injuries could increase due to longer time between injury and evacuation
1- smoke and chemical inhalation injury exposure
2- blast injuries resulting in concomitant pulmonary contusions [50% incidence of ARDS]
3- penetrating injuries to lung parenchyma
4- post resuscitation and acute lung injury
5-TBI induced lung dysfunction [neurogenic pulmonary edema]
6-atelectasis due to pain, over sedation and splinting after injury or initial surgery

15. SUBJECT TERMS
NONE LISTED

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
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1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

Background: Most pulmonary injuries are insidious and declare themselves over a period of hours or even days. Most recently, tactical military changes have resulted in increased time between casualty injury and definitive care e.g., prolonged field care, increased transport times and initial damage control surgery and resuscitation. Prompt recognition and treatment of pulmonary dysfunction will be need to be addressed. Towards this end, we have shown that closed loop control [CLC]-oxygen [FiO2] can better maintain target oxygen saturation [efficiency] while reducing oxygen utilization (improved efficiency with limited resources). Our group also demonstrated that CLC systems possess unique diagnostic utility. Specifically, activity of the CLC-FiO2 algorithm identifies pulmonary (dys)function, especially using the SpO2/CLC-FiO2 ratio. We have incorporated this index into a decision support smart oxygenation system (SOS), which alerts pulmonary distress hours earlier than standard monitoring. Further, our experimental data using this decision support SOS shows that it initiates life-saving interventions [LSI] e.g., rescue ventilation, earlier, which improves overall lung function e.g., reduces severity of acute respiratory distress syndrome [ARDS]. While this provides an excellent diagnostic frame in intubated patients, it has limits. We therefore identified a CLC system called FreeO2 [OxyNov] that works in spontaneously ventilated patients. Further, we identified a non-invasive monitor that measures tidal volume and minute ventilation called Exspiron [Respiratory Motion Inc.]

Objective and hypothesis: We hypothesize that seamless integration of CLC-FreeO_2 oxygen delivery system with Exspiron into our decision support SOS for at-risk casualties, will more rapidly assess and treat pulmonary injury. This approach will not only provide targeted therapeutic oxygen, but also, serve as a "watch dog" to rapidly and effectively assess and treat lung injuries in combat casualties. We will develop and perform proof of concept testing for the SOS prototype integrating FreeO2 system and Exspiron. We have three **Specific Aims:**

Aim 1: Develop robust SOS prototype for use in spontaneous ventilation

Aim 2: Measure oxygenation and ventilatory indices during progressive hypoxemia in volunteers (n=10) without (visit 1) and with (visit 2) an extra-thoracic restriction device to simulate ARDS

Aim 3: Pilot clinical testing and SOS algorithm tuning and software update

Study Design: We will first assemble hardware and software to link FreeO2 and Exspiron system into SOS. The hardware assembly, driver development, connectivity and system architecture and simulation testing will be performed before human testing. We will then test the predictability of the SOS in volunteers undergoing hypoxia or hypoxia plus extrathoracic restriction. On each study visit one and two, each volunteer will receive different levels of oxygen; either – room air (RA), O_2 via nasal cannula (NC: 2 L/min) or FreeO_2 after hypoxia. The difference for study visit two is that volunteers will undergo hypoxia plus extra-thoracic restriction. Outcomes will test timing when the $S/_{CLC}F$ ratio <250. Non-invasive ventilation indices from Exspiron will be also integrated into the SOS. Next, studies will be performed in selected patients undergoing extubation from the OR to post anesthesia recovery unit (PACU) [UTMB] and ICU [University of Cincinnati (UC)]. We envision PACU patients ASA I/II patients (n=40) and ASA III/IV patients (n=40) [n=80 total] will normalize (no LSI), a surrogate of reassuring pulmonary function. This will determine the impact of autonomous delivery of oxygen on timing of interventions (PACU efficiency. Other data will be integrated and analyzed similarly e.g., low minute ventilation by Exspiron, etc. Data generated from these studies will be incorporated into the decision support SOS prototype and used to develop future trials. Critical to this effort, additional software updating is needed to make the SOS more robust. This includes risk analysis as well as incorporating the SOS to provide predictive indices.

Relevance: Acute lung injury contributes to significant morbidity and mortality in military settings.

2. KEYWORDS: Provide a brief list of keywords (limit to 20 words).

Acute lung injury, closed loop oxygenation for therapy and diagnosis, smart oxygenation system (SOS), human testing, oxygen “watch dog”

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

What were the major goals of the project?

List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Objective 1: Develop a robust SOS for spontaneous ventilation	**Timeline (Months) estimate**	**QTR Period**	**Date/ Month actual**
Major Task 1: SOS hardware assembly			Complete yr1
Major Task 2: Driver development, connectivity & architecture for SOS.			Complete yr1
Major Task 3: Simulation testing and study support			Complete yr1
Objective 2: Implementing oxygenation and ventilatory indices after hypoxia ± CWR	**Timeline (Months)**	**QTR period**	**Date/month actual**
Major Task 1: Obtain Regulatory Approvals			
Subtask 1: Submit human use protocol for local IRB review	pre-award	-	0
Subtask 2: Submit human use protocol HRPO review	pre-award	-	0
Milestone: final Local IRB approval	3	1	2
Milestone(s): final HRPO approval	3	1	2
Major Task 2: Study enrollment - Hypoxia alone with and without chest wall restriction (CWR)	Timeline	Site 1 UTMB	Site 2 UC
Subtask 1: Enroll subjects; collect oxygenation and ventilation data before /after hypoxia ± CWR	13-22	Kinsky	2 subjects enrolled – COVID19 issues

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

Our accomplishments are structured based on fulfilling the primary objectives. Since we have just completed year one of the project, the bulk of the reporting will focus on Objective 1.

Objective 1: months 0-12. The PI and team will work with Arcos Inc., to develop connectivity and interoperability of two primary systems (OxyNov's FreeO2 system and Respiratory Motion's Exspiron system). Engineers from Arcos will provide hardware and software (table computer system with Java based communication drivers) that incorporates oxygenation/ventilation indices from these two systems to develop a graphical user Decision Support interface called Smart Oxygenation System (SOS). Towards this end, a user manual, risk analysis, driver connectivity and start-up instructions, simulation testing and implementation will be key milestones for year 1.

Objective 2: months 13-24. The SOS will be utilized in healthy volunteers. Specifically, oxygenation and ventilatory indices will be captured during progressive hypoxemia in volunteers (n=10) without (visit 1) and with (visit 2) an extra-thoracic restriction device to simulate ARDS. Tasks and key milestones in this objective will test the predictability and timing of the SOS to identify pulmonary distress in volunteers undergoing hypoxia or hypoxia plus extrathoracic restriction (when the SpO2/CLC-FiO2 ratio <250). A manuscript will be prepared and submitted.

Objective 3 [option]: months 25-36. Pilot clinical testing and SOS algorithm tuning will be performed in selected patients undergoing extubation from the OR to post anesthesia recovery unit (PACU) [UTMB] and ICU [University of Cincinnati (UC)]. Tasks in this objective will determine the impact of autonomous delivery of oxygen on timing of interventions (PACU efficiency vs ICU rescue ventilation). Other data will be integrated and analyzed similarly e.g., low minute ventilation by Exspiron, etc. Data generated from these studies will be incorporated into a manuscript(s) and the decision support SOS prototype for developing future trials.

Objective 1:

- **Complete [figure 1 shows SOS device complete]**

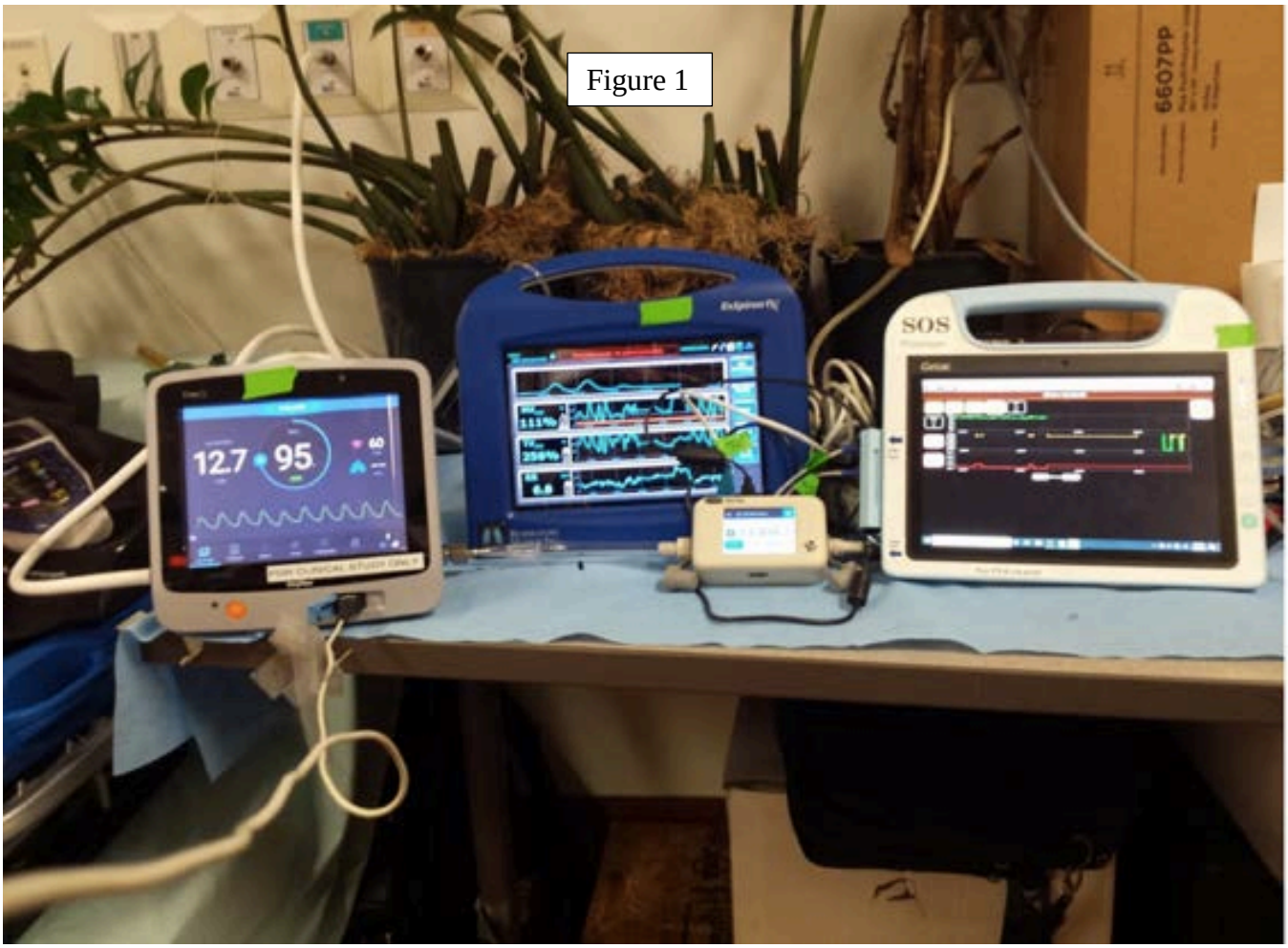
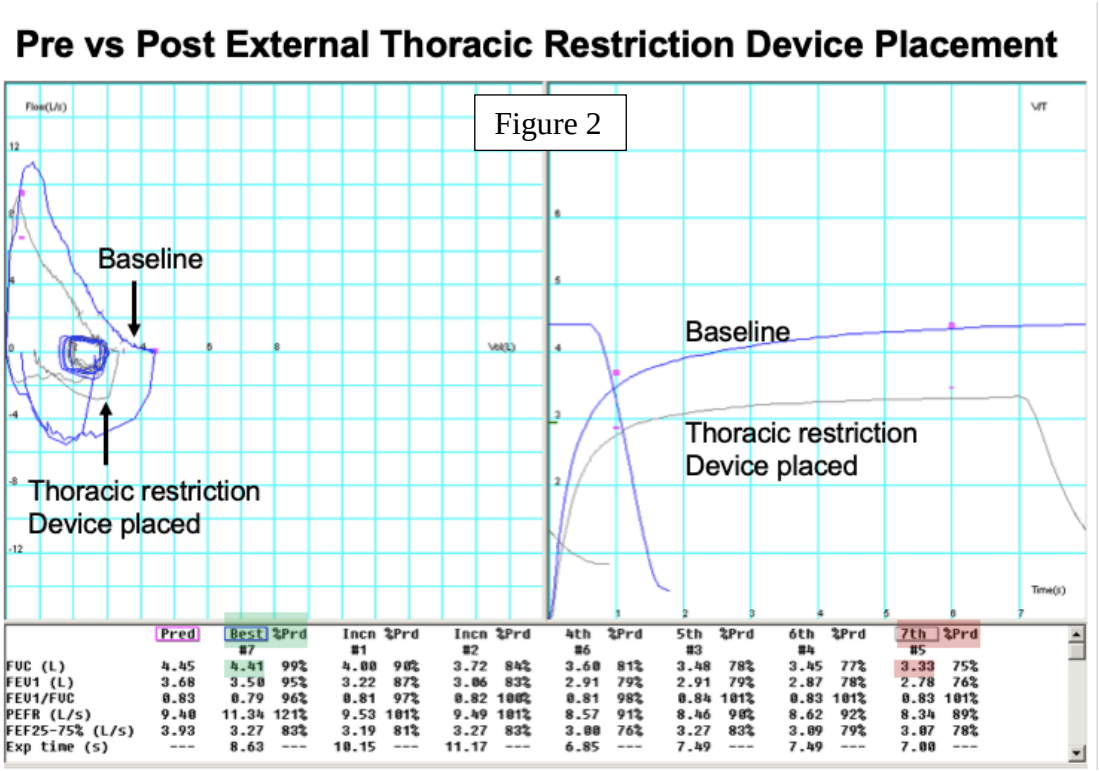


Figure 1. Shows the connection hardware for the SOS, which includes Exspiron and the FreeO2 system in closed loop oxygen control mode along with a pulse oximeter. Integrated from the FreeO2 oxygen output, a flow sensor is connected to the SOS, which allows for second to second display of O2 via nasal cannula [L/min], SpO2 and the CLC SpO2/FiO2 ratio [based on L/min conversion]. The SOS allows for ventilatory parameters primarily from Exspiron and oxygenation parameters from the FreeO2 pulse oximeter + flow sensor. Detailed warning alerts and alarms are displayed via built in software.

Objective 2: [Year 2]

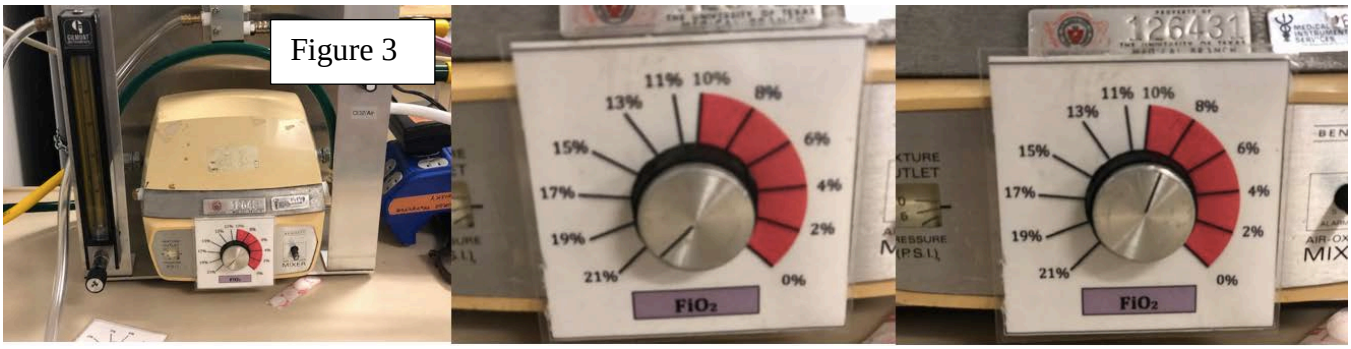
- All IRB and HRPO documentation to test the SOS prototype for YR 2 studies were completed in QTR 1.
- **Pre-testing for thoracic restriction and simulation testing:**
    - The PI/team developed a thoracic restriction device that can reduce vital capacity by 1 L. This was performed by measuring pre-and post-forced vital capacity (FVC) before and after placing bound elastic banding.
    - Repeat testing on different subject – shown below – demonstrates consistency



	Pred	Best	%Prd	Incn #1	%Prd	Incn #2	%Prd	4th #6	%Prd	5th #3	%Prd	6th #4	%Prd	7th #5	%Prd
FVC (L)	4.45	4.41	99%	4.00	90%	3.72	84%	3.60	81%	3.48	78%	3.45	77%	3.33	75%
FEV1 (L)	3.68	3.50	95%	3.22	87%	3.06	83%	2.91	79%	2.91	79%	2.87	78%	2.78	76%
FEV1/FVC	0.83	0.79	96%	0.81	97%	0.82	100%	0.81	98%	0.84	101%	0.83	101%	0.83	101%
PEFR (L/s)	9.40	11.34	121%	9.53	101%	9.49	101%	8.57	91%	8.46	90%	8.62	92%	8.34	89%
FEF25-75% (L/s)	3.93	3.27	83%	3.19	81%	3.27	83%	3.00	76%	3.27	83%	3.09	79%	3.07	78%
Exp time (s)	---	8.63	---	10.15	---	11.17	---	6.85	---	7.49	---	7.49	---	7.00	---

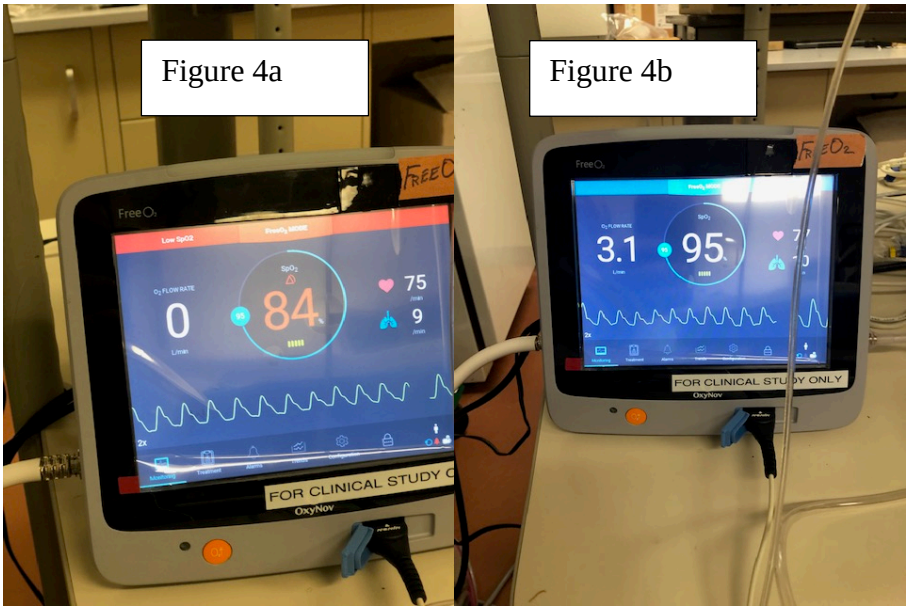
Figure 2. Pulmonary function data show a marked reduction in forced vital capacity pre intervention [(baseline) 4.41 L] to 3.33L post implementation of external thoracic restriction. The subject noted some discomfort in breathing, specifically on exhalation. Minimal change in respiratory dynamics and tidal volume at rest [data not shown but minute ventilation via Exspiron unchanged].

Hypoxia studies. The PI was able to determine the parameters to induce hypoxia in volunteers via collaboration with OxyNov. Their group provided a table of air + nitrogen flow rates to induce varying levels of hypoxia [21% to 5%]. The air and nitrogen are essentially altered based on flow to designate a specific FiO2. Essentially, air and nitrogen sources are regulated with flow meters. Two “tubes” are connected in a Y shaped pattern and then connected to a facemask (used for patients requiring oxygen) with a small reservoir bag. For example, if 10 L of Air, which contains a FiO2 of 0.21 (since the constituents of atmospheric gases is 79% nitrogen and 21% oxygen) is mixed with 10 L of nitrogen the resulting FiO2 would be about 0.105 (or 11%). While, we initially thought that this approach could be used for hypoxia studies, the facemask connection could not provide an adequate seal. Towards this end, we constructed an alternative approach that incorporates a direct contact mask airway (used in anesthesiology and resuscitation). This provides a complete seal between the subject and mask allowing for inhalation and exhalation of respiratory gases. We believe that this design is more robust scientifically, as it allows us to determine how external oxygen via nasal cannula can be integrated and contained. Further, the direct mask seal allows for direct measures, via standard of care Datex monitor, of end-tidal carbon dioxide and other gases [inhaled and exhaled FiO2] as well as tidal volume and respiratory rate. This provides a check on the Exspiron and our current equipment set up for adjusting FiO2 based on admixing nitrogen and air [see below - figure 3, which shows the ability to directly adjust the FiO2 to induce hypoxia].



Working with our team, we were able to construct a more effective gas delivery system. In brief, the gas admixture allows for oxygen, nitrogen and air [as well as carbon dioxide if needed] to be regulated. For this system, air is mixed with nitrogen and adjusted using the dial based on total flow out. The total flow output, which connects to the subject via a modified Jackson-Reese system can be adjusted to ensure adequate minute ventilation with no rebreathing of external gas input. Most importantly, the FiO2 can be specifically tailored. The FiO2 will be mainly adjusted using this system and checked using our Datex gas analyzer. The advantage of this system versus a bifurcated dial-in system is that allows for direct oxygenation and ventilatory components.

Induction of hypoxia and hardware system check for CLC FiO2 and O2.
We conducted preliminary data [subject] in which we induced hypoxia for short duration of time. In brief, the mask was sealed [small straps] to ensure no leakage of gases. We conducted two experimental phases. In Phase 1, hypoxia was induced by setting the FiO2 to 8% by mixing nitrogen in air at a flow rate of 10 L/min [above minute ventilation] (see figure 4a). A nasal cannula was inserted between the mask and subject, however, the oxygen source was not connected and therefore the flow was zero. A fairly rapid reduction in FiO2 occurred [approximately 1 min] and oxygen saturation (SpO2) decreased to 84%. For Phase 2, hypoxia was induced as before [set to 8%], however, the oxygen source via nasal cannula was connected and patent (figure 4b). While the FiO2 decreased to 8%, SpO2 was maintained above 94% [set point just for this prelim study]. Oxygen flow increased to 3.1 L/min. This allowed rapid and correct titration of O2 and indicated the oxygen needs in face of hypoxia.



As indicated below, COVID19 created substantial setbacks in conducting these studies. We now have clearance to conduct these studies in a laboratory that contains necessary respiratory gases and safety equipment. The time delay did allow for further alterations in our overall study design, which we believe will be more scientifically robust. We have recruited and screened volunteers and will start ASAP.

Objective 3:
The PI has been working with the Program Officer for option year funding [which was received]. Specifically, and in line with the statement of work, human testing on a smaller scale is performed [originally ICU patients were proposed for objective 3, however, that would require FDA clearance or IND. A smaller scale study with direct clinician engagement is likely feasible with using the SOS connected to FreeO2 system in "black box" mode – but in the post anesthesia recovery room]. Additionally, there is a strong need of further software work e.g., risk analysis and programming to make the SOS more robust and to further increase its readiness level.

Overall goal of this project is to improve the Smart Oxygenation System (SOS) prototype from previous work in 2019. Dr. Kinsky intends to use the SOS with recently extubated patients in the PACU under an IRB-approved protocol. The SOS will be used only to record data in the PACU at UTMB. Other devices, such as the Free O2 system, might be used for therapy under the protocol.

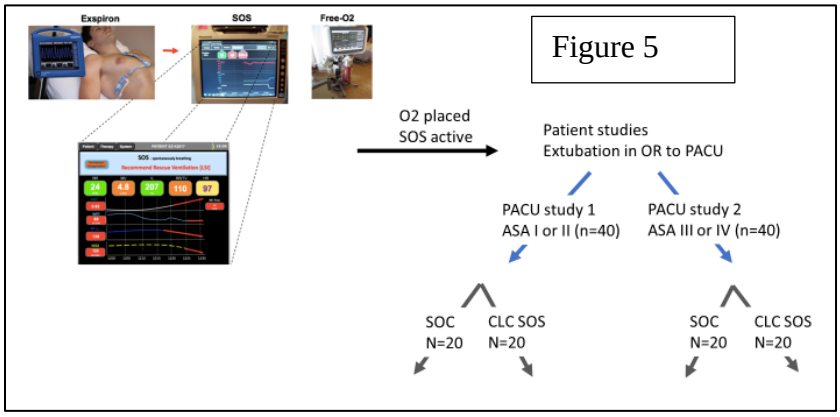


Figure 5 - Overview of the study

Studies will be performed in selected patients undergoing extubation from the OR to post anesthesia recovery unit (PACU) [UTMB] and ICU [University of Cincinnati (UC)]. We envision PACU patients ASA I/II patients (n=40) and ASA III/IV patients (n=40) [n=80 total] will normalize (no LSI), a surrogate of reassuring pulmonary function. This will determine the impact of autonomous delivery of oxygen on timing of interventions (PACU efficiency. Other data will be integrated and analyzed similarly e.g., low minute ventilation by Exspiron, etc. Data generated from these studies will be incorporated into the decision support SOS prototype and used to develop future trials. Critical to this effort, additional software updating is needed to make the SOS more robust. This includes risk analysis as well as incorporating the SOS to provide predictive indices.

Software update & Arcos' Statement of Work

Under Dr. PI's direction, Arcos will complete the following technical objectives:

1. SOS Prototype Improvements

1. Automate SOS start-up and set-up
2. User interface improvements
3. Refine data logger and update manager as needed
4. Update decision support recommendations as needed
5. Regulatory Plan and Draft Documents for 510(k) or IDE
    1. Address TSI flowmeter in clinical use
    2. User's Manual, Risk Management, etc.

2. Assemble an SOS prototype
    1. Procure hardware (Nonin + Expiron + SOS tablet + TSI flowmeter) and assemble
    2. Software safety and reliability testing, provide a test report
3. Support UTMB's bench testing and clinical study use
4. Analyze UTMB provided respiratory data and develop a predictive algorithm with machine learning

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Nothing to report

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of

these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to report

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

- Begin to recruit for healthy volunteer studies [all ready]
- Complete Volunteer studies
- Have Pre-FDA meeting with Arcos/FDA regarding SOS
- Obtain IRB approval for PACU study and start studies

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

The proposed will test a clinical prototype that is suitable for military and civilian clinical testing, in patients and volunteers in different patho-physiologic states. Our initial vision would be to incorporate other non-invasive ventilation indices e.g., Exspiron [non-invasive minute ventilation (MV)] into the SOS, which would increase diagnostic capabilities. Our long-term vision is to incorporate $S/_{CLC}F$ ratio, cardiopulmonary indices (MV and perfusion – production of carbon dioxide, or VCO2) into a SOS monitoring algorithm such as automated decision-support those evolve for use in military and civilian trauma patients. We anticipate that the SOS algorithms will use threshold values or targets e.g., to define specific interventions such as need for rescue ventilation or other airway interventions. An advantage of this SOS is that it is non-invasive, seamless (coupled to supportive systems), easy to interpret by any skill level (as SpO2 and oxygen are known entities) and usable at any echelon. While we have outlined how this proposal fits into current capability gaps, it closely aligns with combat casualty care research program, research and development of technologies to diagnose and reduce acute secondary organ damage and health technology.

If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

The technology and studies outlined in this proposal are highly relevant to hospital and ICU medicine, perioperative care and especially home health, pre-hospital and triage care.

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Not at this time

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

The impact here is potential change in behavior and decision making.

5. **CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

COVID-19 has led to significant problems with conducting our clinical studies. We initially began recruiting subjects in January/February 2020 and had a few subjects slated to be screened. Due to supply chain ordering, we anticipated conducting studies in March. Then, COVID19 "hit". Like many programs, all clinical research was suspended that was not related to COVID19. In May/June 2020, we began re-engagement for the ability to do non-COVID19 research. However, Texas [Houston-Galveston area] underwent a significant wave of hospitalizations. This resulted in our center in another suspension. Specifically, we planned on using the perioperative post-anesthesia care unit [PACU] to conduct our hypoxia studies. The rationale for the PACU site was it provided oxygen and air directly from the hospital unit. Unfortunately, UTMB COVID19 case load underwent exponential expansion [from one hospital unit to more than 4 units]. The PACU was now designated as an overflow space and thus prevented us from this space utilization. Several amendments were submitted to the IRB to produce an alternate site. We recognized that our main animal lab [Building 21] housed fresh gases for oxygen and air. To ensure site safety, we ordered mitigating equipment and monitoring for a lab in Building 21. Safety equipment included gas monitoring, defibrillator, transducer monitoring etc. We received IRB approval and performed equipment testing. Recruitment flyers were sent out in August. Two subjects were screened and approved in September and slated for testing in the next few weeks. Dry runs have been performed and initial "wet-runs" [inducing hypoxia and recording responses] are shown in data [figure 3 and 4].

Additionally, in July 2020, we have had significant personnel changes (main research assistant Mr Salter, who has worked with the PI for 14 years, officially retired). The PI hired a new highly experienced research assistant (Ms Weihua Cui).

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

As described above, the biggest challenge has been COVID19 and its fall-out. Like many institutions, UTMB was hit hard physically and financially. We have had significant personnel changes (main research assistant Mr Salter officially retired). The PI hired a new research assistant (Ms Weihua Cui) has been trained and has taken over Mr Salter's responsibilities.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

As above – COVID 19 and loss of personnel

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

None to report

Significant changes in use or care of vertebrate animals.

Not applicable

Significant changes in use of biohazards and/or select agents

None to report

6. PRODUCTS: List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report

  Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: Author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report

Other publications, conference papers, and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to report

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

Nothing to report

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

We have a patent for the SOS

- **Other Products**
  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment, and/or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:
  - *data or databases;*
  - *biospecimen collections;*
  - *audio or video products;*
  - *software;*
  - *models;*
  - *educational aids or curricula;*
  - *instruments or equipment;*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
  - *clinical interventions;*
  - *new business creation; and*
  - *other.*

Software and other analysis have been submitted in previous quarterly reports

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."

Name: *Michael Kinsky, MD*
Project Role: *PI*
Researcher Identifier (e.g. ORCID ID): 0000-0002-2103-546X
Nearest person month worked: *1 mo/QTR*
Contribution to Project: *The PI has directed the efforts for acquiring requisite components, working with Dr. Kramer and Mr. Branson and Ms. Khan to develop the technical requirements for all of Arcos work this quarter*

Name: *George Kramer, PhD*
Project Role: *CO-I*
Researcher Identifier (e.g. ORCID ID): 0000-0003-0894-6768
Nearest person month worked: *<1 mo/QTR*
Contribution to Project: *The Co-I has dedicated his efforts for coordinating the technical requirements for all of Arcos work this quarter*

Name: *Rich Branson, MS RRT*
Project Role: *CO-I*
Researcher Identifier (e.g. ORCID ID): 0000-0002-0912-3360
Nearest person month worked: *<1 mo/QTR*
Contribution to Project: *The Co-I has dedicated his efforts for coordinating the technical requirements for all of Arcos work this quarter*

Name: *Muzna Khan, MS RRT*
Project Role: *CO-I*
Researcher Identifier (e.g. ORCID ID): 0000-0002-8096-981X
Nearest person month worked: *<1 mo/QTR*
Contribution to Project: *The Co-I has dedicated her efforts for coordinating the technical requirements for all of Arcos work this quarter.*

Name: *Michael Salter, MS*
Project Role: *Research technician*
Researcher Identifier (e.g. ORCID ID): https://orcid.org/0000-0002-8096-981X
Nearest person month worked: *<1 mo/QTR*
Contribution to Project: The research associated has worked with the PI to assist in technical work, ordering parts, maintaining documentation and working with Arcos for initial instrument testing.

Name: *Roger Seeton, RN*
Project Role: *Research Nurse*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *1 mo/QTR*
Contribution to Project: The research nurse has worked with the PI to help with all documentation for IRB/HRPP and human subject material. As well as recruitment material. He has also helped with Arcos to ensure human safety.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

no

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.
Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

University of Cincinnati

Arcos Inc.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating PI and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to **https://ers.amedd.army.mil** for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.

SMART OXYGENATION SYSTEM (SOS) PROVIDES EARLY WARNING OF LUNG INJURY
0011121518-0001/ USAMRAA
W81XWH18C0156

PI: Michael Kinsky, MD Org: University of Texas Medical Branch at Galveston Award Amount: $718,879 [option not included]

Study/Product Aim(s)

Hypothesis: At-risk casualties, suffering from lung injury, can more rapidly be assessed and treated using a smart oxygenation system (SOS) that connects to a stand-alone closed loop control (CLC) oxygen system and a non-invasive ventilation monitor

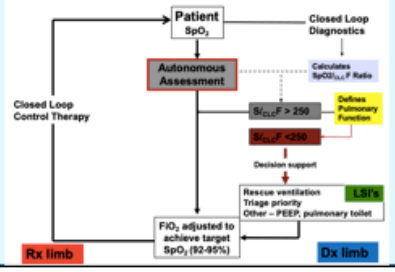
Specific Aims

Aim 1: Develop robust SOS prototype for use in spontaneous ventilation
Aim 2: Measure oxygenation and ventilatory indices during progressive hypoxemia in volunteers (n=10) without (visit 1) and with (visit 2) an extra-thoracic restriction device to simulate ARDS – months 13-24
Aim 3: Pilot clinical testing and SOS algorithm tuning– months 25-36 [OPTION]

Approach

We will develop a user manual, connectivity to OxyNov's (closed loop control oxygen for spontaneous (sp.) ventilation) and Respiratory Motion's (non-invasive minute ventilation and tidal volume and respiratory rate) communication protocol to extract data packets e.g., SpO_2,, estimated FiO_2 and $S/_{CLC}F$ ratio, minute ventilation and respiratory rate, which will then be graphically displayed in real time. SOS Prototype will be tested in human volunteers first [hypoxia ± chest wall restriction (CWR)] and then patients [option] to determine pulmonary dysfunction.

Smart Oxygenation System (SOS): Strategy



Accomplishments: Exspiron driver complete. Sub-contract w/ Arcos finalized. FreeO2 system received [communication protocol pending]. Aim 2 continued review approved

Timeline and Cost

Activities CY	18	19	20	21
Develop robust SOS for sp. ventilation				
Implementing oxygenation and ventilatory indices after hypoxia ± CWR				
Pilot clinical testing [option]				
Estimated Budget ($K)	**$360K**	**$360K**	**($option 400K)**	

Updated: (September 30 2019)

Goals/Milestones (Example)

CY18 Goal – SOS hardware assembly, driver development and support
☑✔SOS hardware requirements and user need
☑✔- Driver development, connectivity and architecture for SOS
☑☐ Simulation testing and study support [Risks/ prototype demo]
CY19/20 Goals – Obtain regulatory approval, study enrollment
☐✔ Regulatory approval
☐Complete prototype and experimental testing
CY21 Goal – Option [Pilot testing]
☐Regulatory approval
☐Data collection in PACU patients [SOS vs standard of care (SOC)]
☐Data collection in ICU patients [SOS vs SOC)]

Comments/Challenges/Issues/Concerns

- Decided to use OxyNov with adapter flowmeter and pulse ox. This allows for CLC O2 Rx [Oxynov] and independent Dx intel

Budget Expenditure to Date

Projected Expenditure: 360K
Actual Expenditure: 290K pre-encumbered + subcontract

9. **APPENDICES:** Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.