Title:

Validation of a novel transabdominal fetal oximeter in a hypoxic fetal sheep model

Authors:

Daniel D. FONG, MS [a] ; Kaeli J. YAMASHIRO, DO [b] ; Michael Austin JOHNSON, MD, PhD [c, 1] ; Kourosh VALI, BS [a] ; Laura A. GALGANSKI, MD [b] ; Christopher D. PIVETTI, MS [b] ; Diana L. FARMER, MD [b] ; Herman L. HEDRIANA, MD [d] ; Soheil GHIASI, PhD [a]

University Affiliations:

[a] - Electrical and Computer Engineering, University of California Davis, Davis, CA, United States

[b] - Department of Surgery, University of California Davis Health, Sacramento, CA, United States

[c] - Department of Emergency Medicine, University of California Davis Health, Sacramento, CA, United States

[d] - Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, University of California Davis Health, Sacramento, CA, United States

Present Address for Michael Austin JOHNSON (below):

[1] - Division of Emergency Medicine, Department of Surgery, University of Utah, Salt Lake City, UT, United States

Conflict of Interest Statement: The authors report no conflict of interest.

Study conducted at: Davis, CA, United States

Study financially supported by: National Science Foundation, Grant No. IIS-1838939

Paper Presentation Info:

Will be presented at the Society for Maternal and Fetal Medicine's (SMFM) 40th Annual Pregnancy Meeting in Grapevine, Texas on February 3-8, 2020.

This paper is being submitted for **SMFM Fast-Track**.

SMFM Oral Presentation Number: **98**.

Corresponding Author:

Daniel D. Fong

One Shields Avenue, Davis, CA 95616

dfong@ucdavis.edu

Abstract word count: 341 words

Main text word count: 2065 words

ABSTRACT:

Objective: Current intrapartum fetal oxygen saturation (SaO2) monitoring methodologies are limited, mostly consisting of fetal heart rate monitoring which is a poor predictor of fetal hypoxia and associated with high false positive rates. With recent advances in technology, transabdominal fetal pulse oximetry may be able to determine fetal SaO2 non-invasively. This study is to validate a novel transabdominal fetal pulse oximeter (TFO) in determining fetal arterial oxygen saturation in a hypoxic fetal sheep model.

Study Design: Fetal hypoxia was induced in a pregnant ewe at term (136 days) by placing an aortic occlusion balloon infra-renally via the common femoral artery. A fetal carotid arterial line was placed for fetal arterial blood gases (ABGs) and continuous hemodynamic monitoring. The uterus was closed around the fetal neck and one ear of the lamb was sutured to the ewe's abdominal wall. The laparotomy was closed and the TFO was placed on the ewe's abdomen, leaving one fetal arm exposed for a conventional fetal pulse oximeter. The balloon catheter was inflated in a stepwise fashion to decrease the ewe's mean arterial pressure. The pressure was held at each step for 10 minutes, and fetal ABGs were recorded at 2.5-, 5-, and 10-minute intervals. The balloon catheter was deflated after two consecutive measurements of fetal SaO2 below 15% by ABG, and the fetus was recovered. This stepwise gradient was repeated two more times. The average fetal SaO2 from the TFO (SpO2) was derived at each hypoxic level and correlated with the average fetal SaO2 by ABGs.

Results: Fetal oxygen saturation from the ABGs ranged from 10.5% to 66%. The TFO SpO2 correlated with the ABG fetal SaO2 (coefficient of determination, r^2=0.856). The fetal SpO2 measurements from TFO were significantly different than the maternal ewe's SpO2 ($p<0.01$,

paired t-test), which suggests that the transcutaneous measurements are penetrating through the maternal abdomen sufficiently and are expressing the underlying fetal tissue physiology.

Conclusion: The recently developed transabdominal fetal oximeter non-invasively detected fetal SpO2, which correlated with fetal SaO2 on the ABGs and were significantly different than the ewe's SpO2.

KEYWORDS OR SHORT PHRASES:

aortic occlusion, fetal pulse oximetry, hypoxic fetal lambs, non-invasive, oxygen saturation, pregnant ewe, sheep, transcutaneous

MAIN TEXT

INTRODUCTION:

Currently, intrapartum assessment of fetal well-being is primarily accomplished through fetal heart rate monitoring, which performs real-time continuous assessment of the fetal heart rate (FHR) and displayed either on paper or digital imagery. It is thought that fetal bradycardia after a contraction is indicative of fetal asphyxia, and that surgical intervention may be needed.[1] Since the introduction of FHR monitoring as an intrapartum standard of care, the rates of cesarean deliveries (CDs) increased significantly, while the rates of adverse fetal outcomes associated with hypoxia remain unchanged.[2-4] The underlying problem is that many factors can cause a non-reassuring FHR tracing, some of which are normal physiological responses and may not necessitate intervention. For the detection of fetal hypoxia, fetal heart rate monitoring has high sensitivity, but low specificity. Clinically, this is manifested as a high rate of false positives, degrading patient outcomes and creating a malpractice nightmare.[4-7] Furthermore, the large variability of *inter*- and *intra*- observer interpretation of previously recorded indeterminate FHR traces clearly motivates the need for a more objective measure of fetal well-being.[8-11]

Previously, transvaginal fetal pulse oximetry was evaluated in a multicenter randomized control trial, which showed that providing fetal oxygen saturation can improve the confidence of intrapartum fetal well-being when a non-reassuring FHR trace is present.[12] This semi-invasive method was performed by inserting a reflectance-based pulse oximeter through the birth canal to contact the presenting fetal tissues, thus constraining the measurements to after the uterine

membrane is ruptured. The study showed that while there was a reduction in CD rates due to non-reassuring FHR traces, the overall CD rate remained the same due to an increase in CDs due to dystocia. As such, the American College of Obstetricians and Gynecologists published an opinion that additional studies were needed before the endorsing the utility of the device.[13] Although a follow-up study showed that low fetal SpO2 may be an indication for CD due to dystocia, the device was withdrawn from market, hampering the performance of any further investigation involving fetal oximetry.[14,15]

Fully non-invasive, transabdominal fetal pulse oximetry could potentially solve this problem by providing fetal oxygen saturation in a convenient manner, while also enabling the possibility for antepartum assessment. Using a reflectance-based optical patch, photons are sent through the maternal abdomen and fetus to non-invasively estimate fetal oxygen saturation.[16] Some of the photons that reach the fetus propagate back towards the skin-surface, where they are captured by a photodetector, and subsequently analyzed to extract fetal oxygen saturation. To investigate this approach, we recently designed and developed a novel transabdominal fetal pulse oximetry (TFO) system.[17]

The purpose of this study was to evaluate the feasibility of our transabdominal fetal pulse oximeter to capture relevant fetal oxygen saturation values in a hypoxic fetal sheep *in utero*.

MATERIALS AND METHODS:

We designed and built a transabdominal fetal pulse oximeter to provide a non-invasive measure of fetal oxygen saturation (SpO2) (Figure 1).[18-20] This system introduces photons into the tissue using near-infrared emitters, which allows for better optical penetration depth. After propagating through the tissue, some of the light is captured by photodetectors located on the optical probe (optode), where the radiant power from incident photons are transformed into electrical current through the photoelectric effect. This electrical current is then amplified and converted into a voltage signal, which is subsequently digitized and recorded through our embedded optode control system. The measurements are simultaneously streamed to a laptop running custom-written software, where they are visually presented for real-time feedback and recorded for further analysis.

At its core, oxygen saturation is derived from calibrated light intensity measurements, where conventional pulse oximetry calculations are used to analyze the changes in light intensity caused by cardiac-induced arterial pulsations.[21] Fundamentally, this is described through the modified Beer-Lambert Law (MBLL) which relates the temporal change in transcutaneous light intensity to changes in tissue composition.[22] Since oxy- and deoxy- hemoglobin have different absorption properties at red and near-infrared light, their relative contribution in arterial blood can be identified by analyzing the MBLL at each wavelength.[23] In TFO, only a portion of the photons captured by photodetectors at the mother's abdomen travel through fetal tissue. By analyzing the fetal contribution to the measured light intensity, the fetal SpO2 can be extracted from the transcutaneous measurements.[20]

To evaluate our TFO measurements on a known range of fetal oxygen saturation values, we employed an *in utero* hypoxic fetal sheep model. The study was approved by the UC Davis Institutional Animal Care and Use Committee (IACUC) and care was in compliance with the Guide for the Care and Use of Laboratory Animals. An aortic occlusion balloon catheter was inserted through the common femoral artery and positioned below the renal arteries of a pregnant ewe at term (136 days of gestation). The position of the balloon was confirmed via fluoroscopy. The fetal head was exposed, and a fetal carotid arterial line was placed for blood sampling and continuous hemodynamic monitoring. After replacing the lost amniotic fluid with warm saline, the uterus was closed around the fetal neck and one ear of the lamb was sutured to the ewe's abdominal wall to create a deterministic tissue geometry for transabdominal measurement. The laparotomy was then closed, leaving one fetal arm exposed for conventional fetal pulse oximetry monitoring. Another pulse oximeter was placed on the ewe at the laparotomy site to monitor the ewe's oxygen saturation at the abdomen. The TFO optical probe was then placed on the ewe's abdomen just above the underlying fetus, which captured continuous measurements throughout the experiments. A high-level illustration of the hypoxic fetal sheep model setup can be seen in Figure 2.

To induce varying levels of fetal hypoxia, the balloon catheter was inflated in a stepwise fashion to reduce the ewe's mean arterial pressure by 5-10 mmHg and decrease blood flow to the uterine artery. At each step, the pressure was held for 10 minutes, where fetal arterial blood gases (ABG) were recorded at 2.5-, 5-, and 10-minute intervals to derive fetal SaO2. ABG-derived fetal SaO2 values are considered to be the gold standard measurement modality. The

stepwise inflation continued until two consecutive measurements of fetal SaO2 fell below 15%, at which point the balloon catheter was deflated, allowing the fetus to recover. After recovery, this stepwise gradient was repeated two more times, for a total of three hypoxic rounds. The mean fetal oxygen saturation from the TFO (SpO2) was derived at each hypoxic level and compared against the mean ABG-derived fetal SaO2.

RESULTS:

Figure 3 shows a snippet of the light intensity signals captured by TFO in the time-domain (A) and their power spectrum in the frequency-domain (B). Strong peaks in the frequency spectra correspond to changes in the measured light intensity caused by the ewe and fetal lamb's physiology. Since these physiological signals are not pure sine waves, they cause harmonics to appear at integer multiples of the fundamental frequencies. These measurements were analyzed using the Modified Beer-Lambert Law at both wavelengths to derive the transabdominal, fetal oxygen saturation (TFO SpO2).

At each hypoxic level, the fetal oxygen saturation was recorded from arterial blood gasses (ABG SaO2), conventional pulse oximetry at the exposed fetal arm (PO SpO2), and non-invasive TFO measurements (TFO SpO2). These fetal measurements are shown alongside the maternal ewe's oxygen saturation in Figure 4. Fetal oxygen saturation from ABGs ranged from 10.5% to 66%. The TFO SpO2 ranged from 12.2% to 74.4% and had a positive correlation with the ABG fetal SaO2 (coefficient of determination, r^2=0.856). The mean absolute error between the non-

invasive TFO SpO2 and the invasive, gold standard ABG measurements was 5.63% ± 3.10% (SD). In comparison, the conventional fetal pulse oximeter (placed on the exposed fetal arm) resulted with a mean absolute error of 15% ± 2.77% (SD).

Since tissue is an opaque and highly scattering optical medium, one concern is that the TFO measurements may not penetrate the superficial (maternal) tissues well enough to reach the deeper fetal tissues, thus causing the measurements to reflect maternal characteristics. Using a paired t-test, we determined that the TFO-derived fetal SpO2 measurements are significantly different than the maternal ewe's SpO2 ($p<0.01$), suggesting that the transcutaneous measurements are penetrating through the maternal abdomen sufficiently and is expressing the physiology seen in the underlying fetal tissues.

COMMENTS:

Principal Findings:

This study demonstrates the feasibility of our TFO system to non-invasively measure the fetal oxygen saturation on a hypoxic fetal sheep *in utero*. To investigate the ability of non-invasive TFO to identify critically hypoxic fetuses, we considered a wide range of relevant fetal oxygenation values (10.5% to 66%), resulting with a mean absolute error of 5.63%. These transabdominal measurements showed good correlation with invasive, gold standard SaO2 measurements from ABG, highlighting the TFO system’s ability to non-invasively measure fetal oxygen saturation.

Clinical implications:

An outcome from the high false positive rates of FHR monitoring is an increase in cesarean deliveries (CDs), while the rates of most adverse fetal health outcomes remain the same.[4] Currently one in three children are born via CD in the United States, which exceeds the recommended range suggested by the World Health Organization.[3,24] In addition to a mediocre *inter*- and *intra*- observer agreement of abnormal FHR traces, a significant proportion of CDs are performed partly in response to a non-reassuring FHR trace, highlighting that a more objective metric of fetal well-being is needed.[11,25] As shown through transvaginal fetal pulse oximetry, fetal SpO2 may provide a more objective metric of fetal well-being.[12] In one study, researchers showed that fetal SpO2 of less than 30% for at least 10 minutes has good predictive value for detecting fetal acidosis.[26] However, the transvaginal fetal pulse oximeter used in these studies is no longer commercially available, hampering further investigation of the clinical utility of fetal SpO2.[15]

Transabdominal fetal pulse oximetry may provide a solution to this issue. Given the non-invasive nature of these measurements, TFO could potentially provide fetal SpO2 during both intrapartum and antepartum periods. As an assessment tool, this new monitoring technology could enable future studies that evaluate the effect that fetal oxygenation may have on fetal outcomes during various periods of late pregnancy. As a step towards this goal, we designed and developed the TFO system used in this work to provide physicians with a non-invasive

measure of fetal SpO2.[18-20] This study provides initial results acquired on a relevant biological model, with varying levels of fetal hypoxia, using our TFO system.

Strengths and Limitations:

One of the strengths of the TFO system is that it is able to measure fetal oxygen saturation in a non-invasive manner, which is currently unavailable in obstetric practice. In comparison, transvaginal measures of fetal SpO2 required ruptured uterine membranes and a dilated cervix of at least 2 cm before application. Another benefit is that the study encompasses a wide range of fetal SpO2 values, improving our confidence in the device's ability to detect critically-hypoxic fetuses. Previous investigations involving non-invasive measures of fetal SpO2 used sophisticated optical instruments (photo-multiplier tubes), which can be difficult to translate towards widespread clinical-use due to their bulkiness, high voltage, over-sensitivity, and cost.[27,28] Alternatively, this system utilizes less-expensive, commodity optical components, which lend themselves well towards eventual clinical translation.[18-20]

A weakness of this preliminary study is its limited measurement size. While repeated measures were employed in this study, including more hypoxic fetal sheep can provide insight on the operating limits of the TFO system. In addition, to ensure that the proper placement of the optical probe was maintained throughout the experiments, a deterministic fetal geometry was created by suturing one ear of the fetal lamb to the underside of the ewe's abdomen. While others have also used this approach to acquire transabdominal measurements in sheep,[29] it is

264 less representative of a realistic antepartum scenario, where light has to travel further to reach
265 the fetus and the effects of spontaneous fetal movement are unknown.
266
267 **Research Implications:**
268 In this study, we induced varying levels of fetal hypoxia in an anesthetized pregnant ewe at
269 term to non-invasively measure fetal SpO2 using a TFO system. Prospective studies include
270 increasing the number of hypoxic fetal lambs investigated, as well as fully placing the fetal lamb
271 back into the uterus, to investigate the operating limits of the TFO system. Furthermore, the
272 increased blood-flow and change in fetal position during active labor may affect the system's
273 ability to measure fetal SpO2. Evaluating TFO during active labor, may provide additional insight
274 on the operating limits of the technology.
275

REFERENCES

1. Schifrin BS. Fetal Heart Rate Monitoring During Labor. *JAMA.* 1972;222(2):196-202. doi: 10.1001/jama.1972.03210020046012.
2. Nelson KB, Sartwelle TP, Rouse DJ. Electronic fetal monitoring, cerebral palsy, and caesarean section: asumptions versus evidence. *BMJ.* 2016;355:i6405.
3. Martin JA, Hamilton BE, Osterman JK, Driscoll AK, Drake P. Births: Final data for 2017. *National Vital Statistics Reports.* 2018;67(8)1:50.
4. Alfirevic Z, Devane D, Gyte GML, Cuthbert A. Continuous cardiotocography (CTG) as a form of electronic fetal monitoring (EFM) for fetal assessment during labour. *Cochrane Database Syst Rev.* 2017; Issue 2. doi:10.1002/14651858.CD006066.pub3.
5. Nelson KB, Dambrosia JM, Ting TY, Grether JK. Uncertain value of electronic fetal monitoring in predicting cerebral palsy. *New England Journal of Medicine*. 1996;334(10):613-19.
6. American College of Gynecologists, ACOG Practice Bulletin No. 106: Intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. *Obstet Gynecol*. 2009;114(1):192-202. doi:10.1097/AOG.0b013e3181aef106.
7. Garite TJ. The search for an adequate back-up test for intrapartum fetal heart rate monitoring. *Am J Obstet Gynecol.* 2013;208(3):163-4.
8. Nielsen PV, Stigsby B, Nickelsen C, Nim J. Intra- and inter- observer variability in the assessment of intrapartum cardiotocograms. *Acta Obstet Gynecol. Scand.* 1987;66(5):421-4.

9. Chauhan SP, Klauser CK, Woodring TC, Sanderson M, Magann EF, Morrison JC. Intrapartum nonreassuring fetal heart rate tracing and prediction of adverse outcomes: interobserver variability. *Am J Obstet Gynecol*. 2008;199(6):623.e1-5. doi:10.1016/j.ajog.2008.06.027.
10. Figueras F, Albela S, Bonino S, *et al.* Visual analysis of antepartum fetal heart rate tracings: inter- and intra-observer agreement and impact of knowledge of neonatal outcome. *J Perinat Med*. 2005;33(3):241-5. doi:10.1016/j.ajog.2008.06.027.
11. Sabiani L, Le Du R, Loundou A, *et al.* Intra- and interobserver agreement among obstetric experts in court regarding the review of abnormal fetal heart rate tracings and obstetrical management. *Am J Obstet Gynecol.* 2015;213(5):856e.1-8. doi:10.1016/j.ajog.2015.08.066.
12. Garite TJ, Dildy GA, McNamara H, *et al.* A multicenter controlled trial of fetal pulse oximetry in the intrapartum management of nonreassuring fetal heart rate patterns. *Am J Obstet Gynec.* 2000;183(5):1049-58. doi:10.1067/mob.2000.110632.
13. American College of Gynecologists, Committee on Obstetric Practice. ACOG Committee Opinion Number 258. *Obstet Gynecol.* 2001;98(3):523-4. doi:10.1016/s0029-7844(01)01557-5.
14. Porreco RP, Boehm FH, Dildy GA, *et al.* Dystocia in nulliparous patients monitored with fetal pulse oximetry. *Am J Obstet Gynecol.* 2004;190(1):113-7. doi: 10.1016/s0002-9378(03)00855-x.

15. East CE, Chan FY, Colditz PB, Begg LM. Fetal pulse oximetry for fetal assessment in labour. *Cochrane Database Syst Rev.* 2007;(2):CD004075. DOI:10.1002/14651858.CD004075.pub3.

16. Zourabian A, Siegel A, Chance B, Ramanujam N, Rode M, Boas DA. Trans-abdominal monitoring of fetal arterial blood oxygenation using pulse oximetry. *J Biomed Opt.* 2000;5(4):391-405.

17. Ghiasi S, Fong D, inventors; University of California, Davis, assignee. Robust, Clinical-grade Transabdominal Fetal Pulse Oximetry. US Patent Application 16/347,532 (pending). November 21, 2016.

18. Fong D, Knoesen A, Ghiasi S. Transabdominal fetal pulse oximetry: The case of fetal signal optimization. *Proceedings of the IEEE 19th International Conference on e-Health Networking, Applications and Services (Healthcom).* 2017;1–6. doi:10.1109/HealthCom.2017.8210799.

19. Fong DD, Knoesen A, Motamedi M, O'Neill T, Ghiasi S. Recovering the fetal signal in transabdominal fetal pulse oximetry. *Smart Health*. 2018;(9-10):23-36. doi:10.1016/j.smhl.2018.07.011.

20. Fong DD, Srinivasan VJ, Vali K, Ghiasi S. Optode Design Space Exploration for Clinically-robust Non-invasive Fetal Oximetry. *ACM Transactions on Embedded Computing Systems*. 2019;18(5s):63.1-22. doi:10.1145/3358207.

21. Chan ED, Chan MM, Chan MM. Pulse oximetry: understanding its basic principles facilitates appreciation of its limitations. *Respir Med.* 2013;107(6):789-99. doi:10.1016/j.rmed.2013.02.004.

22. Delpy DT, Cope M, van der Zee P, Arridge S, Wray S, Wyatt J. Estimation of optical pathlength through tissue from direct time of flight measurement. *Phys Med Biol.* 1988;33(12):1433-42.

23. Webster JG. *Design of Pulse Oximeters.* Boca Raton, FL: CRC Press; 1997.

24. Appropriate Technology for birth - World Health Organization. *The Lancet*. 1985;2(8452):436-7.

25. Barber EL, Lundsberg LS, Belanger K, Pettker CM, Funai EF, Illuzzi JL. Indications contributing to the increasing cesarean delivery rate. *Obstet Gynecol.* 118(1):29-38. doi:10.1097/AOG.0b013e31821e5f65.

26. Kühnert M, Seelbach-Göebel B, Butterwegge M. Predictive agreement between the fetal arterial oxygen saturation and fetal scalp pH: results of the German multicenter study. 1998;178(2):330-5.

27. Vintzileos AM, Nioka S, Lake M, Li P, Luo Q, Chance B. Transabdominal fetal pulse oximetry with near-infrared spectroscopy. *Am J Obstet Gynecol.* 2005;192(1)129-33. doi:10.1016/j.ajog.2004.07.022.

28. Nioka S, Izzetoglu M, Mawn T, Nijland MJ, Boas D, Chance B. Fetal transabdominal pulse oximeter studies using a hypoxic sheep model. *J Matern Fetal Neonatal Med.* 2005;17(6):393-9.

29. Choe R, Durduran T, Guoqiang Y, *et al.* Transabdominal near infrared oximetry of hypoxic stress in fetal sheep brain in utero. *PNAS*. 2003;100(22):12950-4.

FIGURE LEGENDS

Figure 1. Transabdominal fetal oximetry (TFO) system on the pregnant ewe during experiment. The TFO system is comprised of an optical probe (optode), embedded optode control system, and custom software running on a laptop.

Figure 2. Hypoxic fetal lamb animal setup. Various levels of fetal hypoxia were induced through stepwise inflation of an aortic occlusion balloon catheter.

Figure 3. Time-series measurements and Power-spectra of the transcutaneous light intensity signal. **(A)** Light intensity signal captured by our system in the time-domain and **(B)** corresponding power spectra in the frequency-domain at emitters 1 (*blue*) and 2 (*orange*) during the first hypoxic round (R1.3). Strong peaks in the power spectra correspond to annotated physiological expressions (respiratory and heart rate or RR and HR) seen in the light intensity at corresponding fundamental frequencies (*solid arrow*) and their harmonics (*dotted arrow*).

Figure 4. Arterial oxygen saturation during fetal lamb hypoxia. **(A)** Mean oxygen saturation at each hypoxic level measured through fetal arterial blood gasses (ABG) (*square-filled, black*), transabdominal fetal oximetry (TFO) (*circle-filled, red*), and conventional pulse oximetry on the fetal lamb (*up-triangle-open, blue*) and ewe (*down-triangle-open, green*) and **(B)** regression curve (*dotted*) of the fetal oxygen saturation derived from TFO and ABG. *Note that TFO measurements at R2.0 were not captured due to a technical error during the experiment.

Figure 1

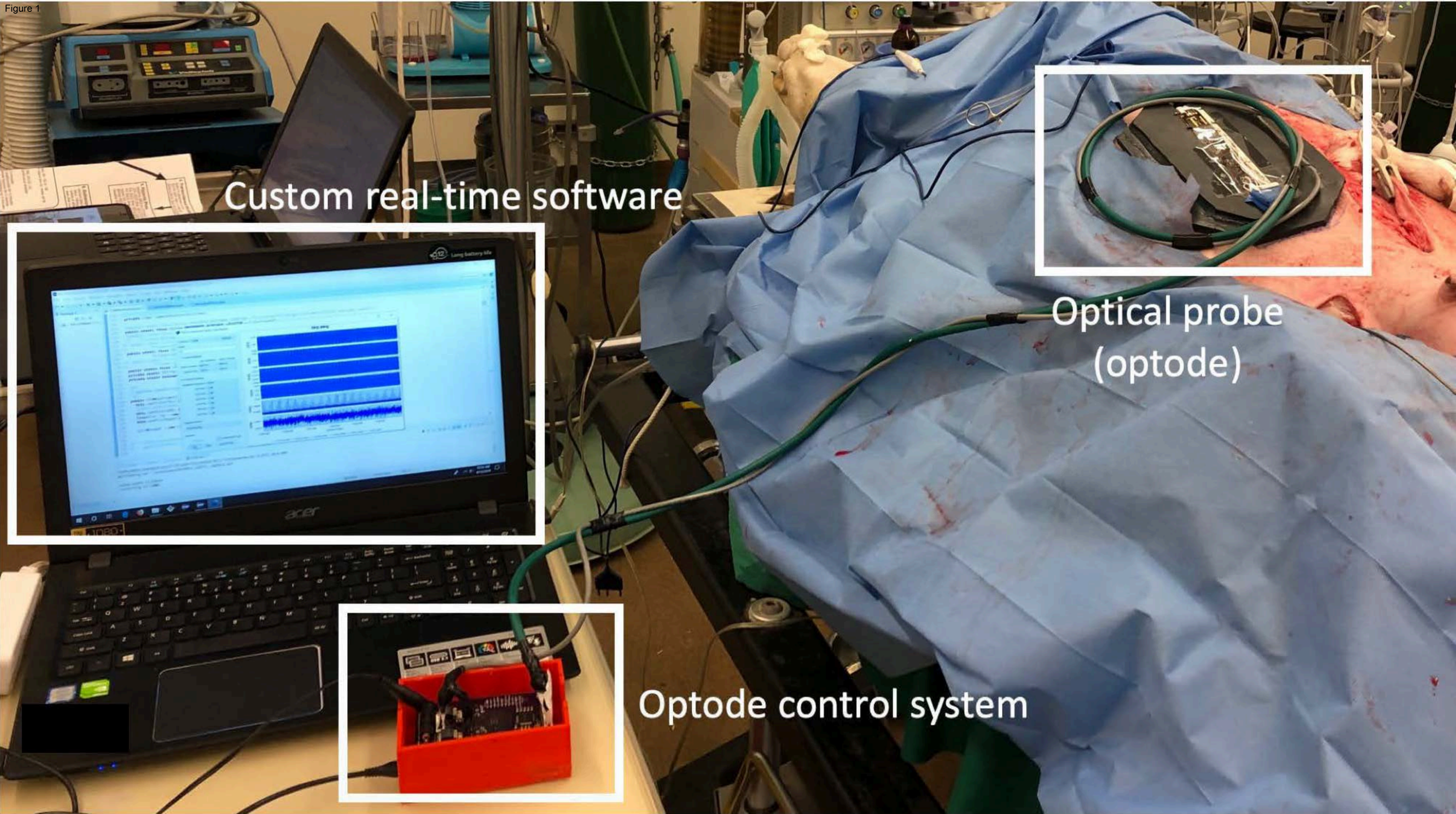

Custom real-time software
Optical probe
(optode)
Optode control system

Figure 2

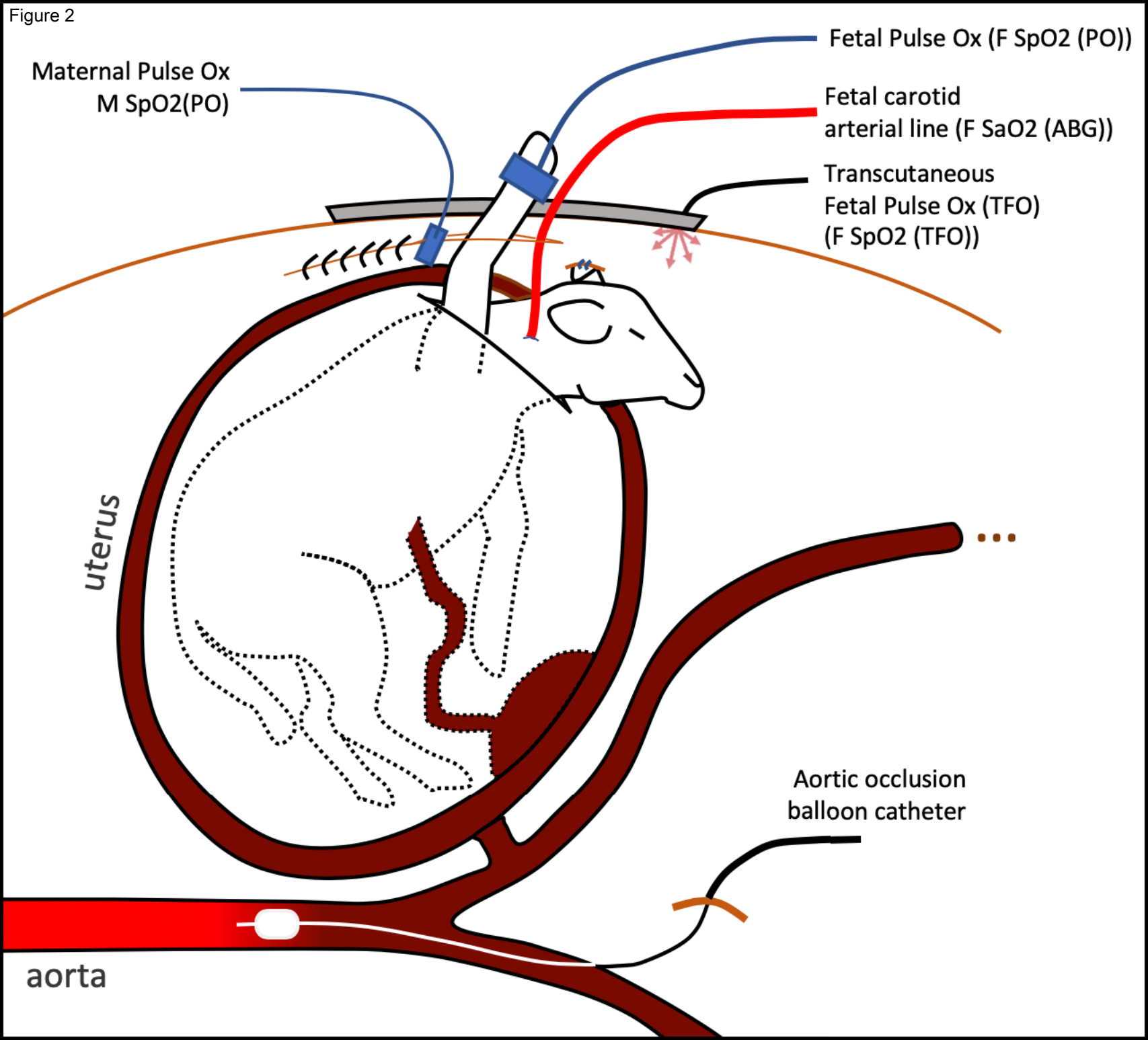
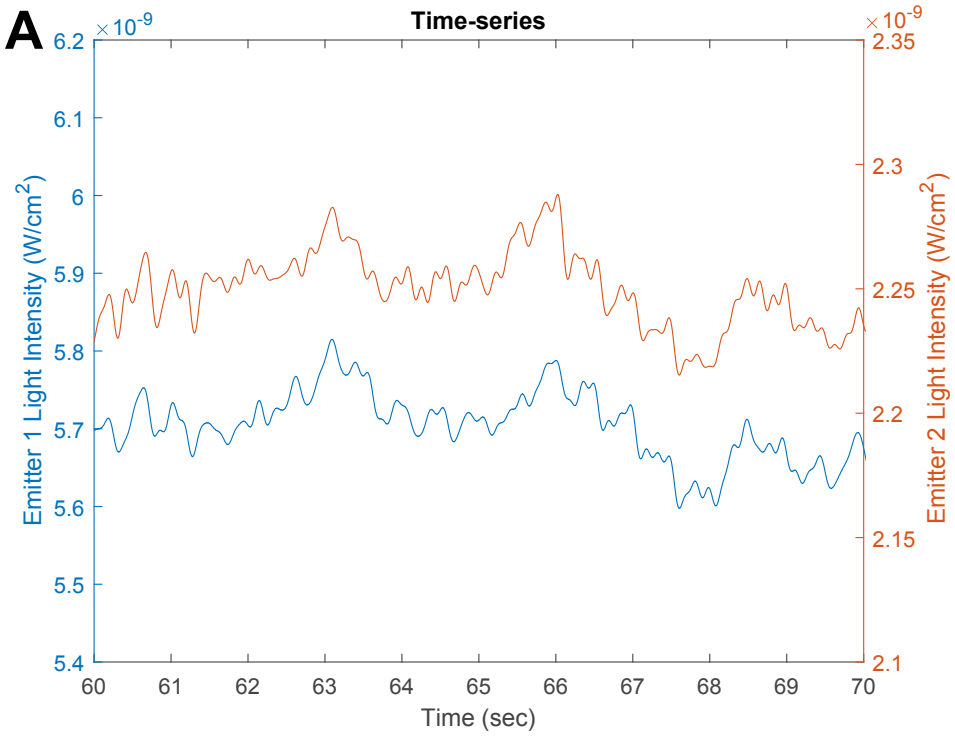

Maternal Pulse Ox
M SpO2(PO)
Fetal Pulse Ox (F SpO2 (PO))
Fetal carotid
arterial line (F SaO2 (ABG))
Transcutaneous
Fetal Pulse Ox (TFO)
(F SpO2 (TFO))
uterus
Aortic occlusion
balloon catheter
aorta

Figure 3


A
Time-series
×10^-9
6.2
6.1
6
5.9
5.8
5.7
5.6
5.5
5.4
Emitter 1 Light Intensity (W/cm^2)
×10^-9
2.35
2.3
2.25
2.2
2.15
2.1
Emitter 2 Light Intensity (W/cm^2)
60
61
62
63
64
65
66
67
68
69
70
Time (sec)

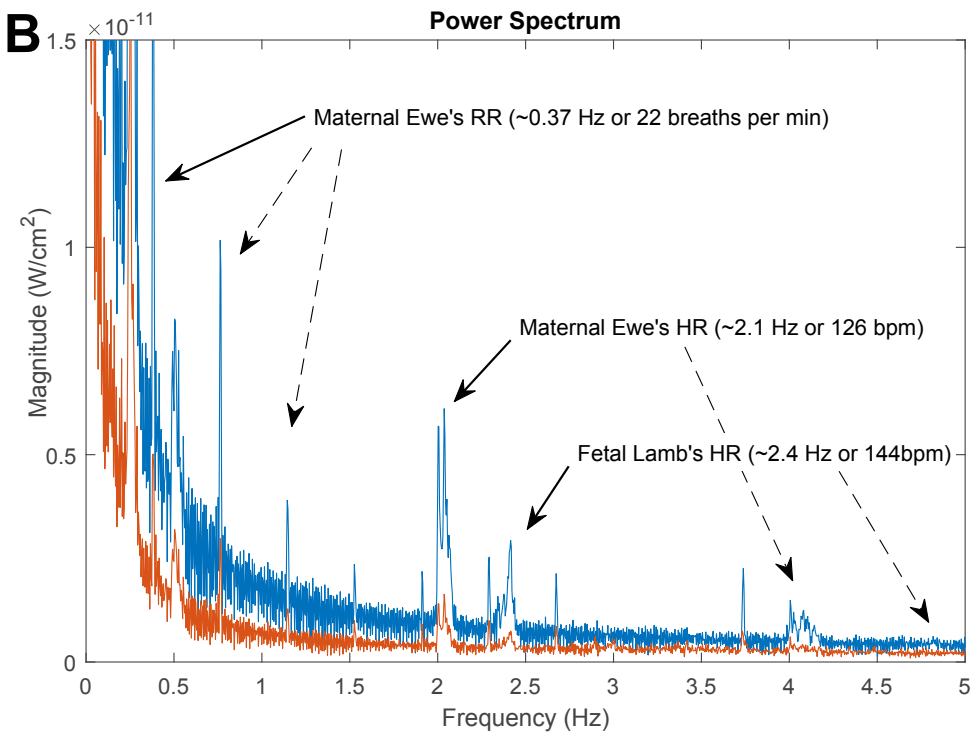
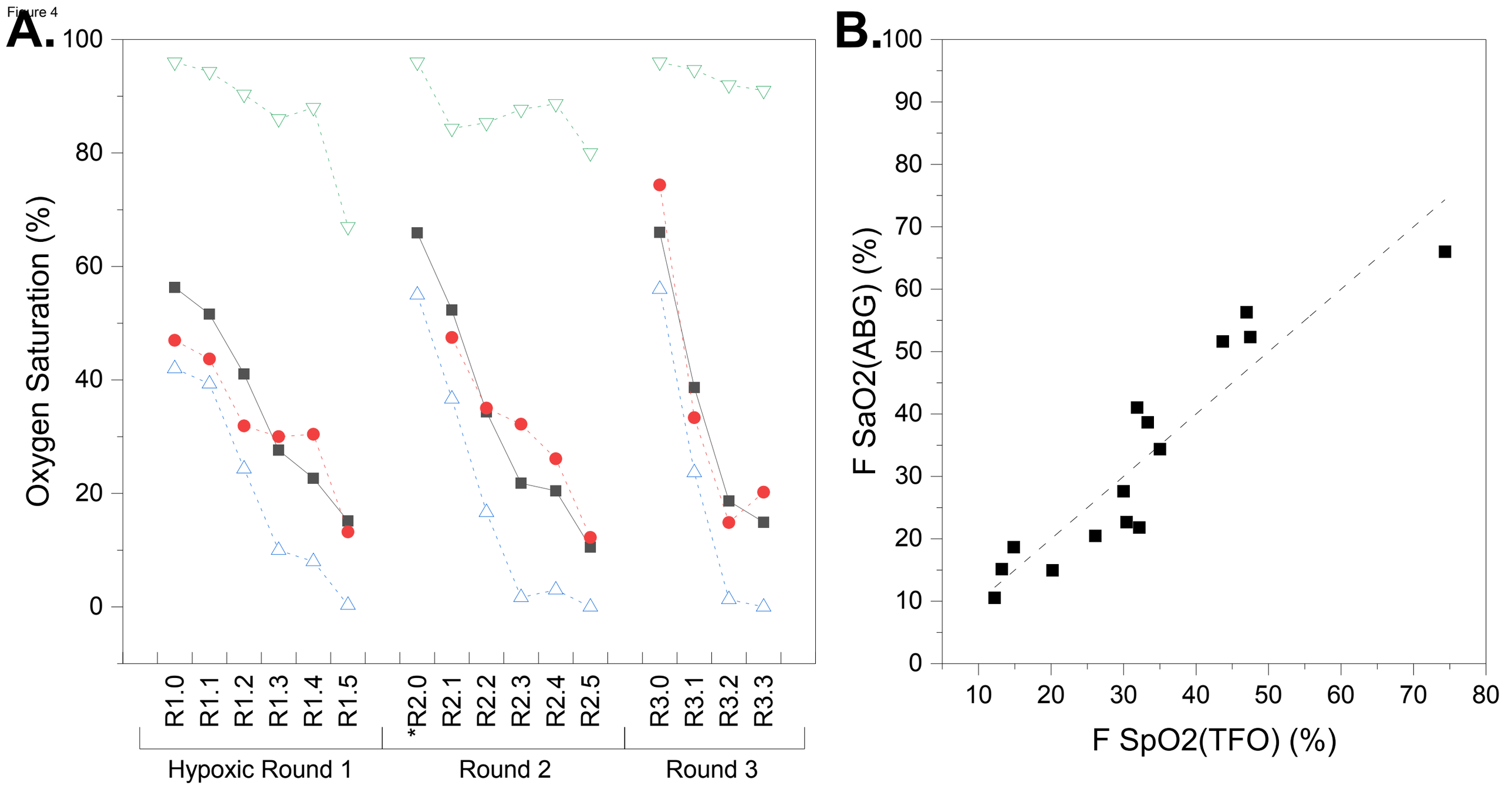

B
Power Spectrum
×10^-11
1.5
1
0.5
0
Magnitude (W/cm^2)
Maternal Ewe's RR (~0.37 Hz or 22 breaths per min)
Maternal Ewe's HR (~2.1 Hz or 126 bpm)
Fetal Lamb's HR (~2.4 Hz or 144bpm)
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
Frequency (Hz)

Figure 4


A.
Oxygen Saturation (%)
100
80
60
40
20
0
R1.0
R1.1
R1.2
R1.3
R1.4
R1.5
*R2.0
R2.1
R2.2
R2.3
R2.4
R2.5
R3.0
R3.1
R3.2
R3.3
Hypoxic Round 1
Round 2
Round 3
B.
F SaO2(ABG) (%)
F SpO2(TFO) (%)
100
90
80
70
60
50
40
30
20
10
0
10
20
30
40
50
60
70
80