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TITLE: Supplemental Perioperative Oxygen to Reduce Surgical Site Infection After High Energy Fracture Surgery

PRINCIPAL INVESTIGATOR: Robert V. O'Toole, MD

CONTRACTING ORGANIZATION: University of Maryland, Baltimore
Baltimore, MD 21201

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14. ABSTRACT Our study is a multi-center prospective randomized treatment trial investigating if supplemental perioperative oxygen use will reduce surgical site infection after surgery on fractures with a high risk of infection. The study utilizes the DOD-funded Major Extremity Research Consortium (METRC). The study population is calcaneus, pilon, and tibial plateau fractures. During the first year we created a protocol committee, designed and approved the protocol and CRFs, obtained IRB approval. We have enrolled 624 patients to date at 20 centers. Follow up rate has been strong with 88% at 12 months. The study will likely receive a major enrollment boost when the competing METRC VANCO study finishes enrollment this year and high volume sites switch to OXYGEN thus allowing completion of the OXYGEN study in a reasonable time.					
15. SUBJECT TERMS Supplemental perioperative oxygen, surgical site infection, fracture fixation complications					
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1. INTRODUCTION:

The overall scope of this project is to address the treatment of high-energy military fractures, which has historically been shown to have poor outcomes and continues to be associated with high rates of infection. Perioperative oxygen has been studied in several thousand general surgery patients and shows promise to reduce surgical site infection in these patients. This technique might have tremendous public health consequences as it is already available in all operating rooms throughout the world and has almost no cost or risks. Outside of a pilot study performed at our institution (Reference 1), this technique has not been investigated in high energy fracture patients that are at such risk for surgical site infections. Our study is a well powered multi-center randomized controlled trial investigating the use of supplemental perioperative oxygen to address the problem of infection in these at risk patients. Our hypothesis is that the use of supplemental perioperative oxygen for fractures at high risk for infection will reduce infection rates and therefore improve outcomes compared to treatment without this technique. The study population is patients with high energy tibial plateau, pilon (distal tibia), and calcaneus fractures. The results of this trial have the potential to reduce surgical site infection within both the military and civilian sectors and therefore improve patient outcomes from these potentially devastating injuries.

2. KEYWORDS:

Supplemental perioperative oxygen, surgical site infection, fracture fixation complications, complication reduction, pilon fracture, calcaneus fracture, tibial plateau fracture

3. OVERALL PROJECT SUMMARY:

The fourth year of the grant built on the success of the first three years. During the second year we rolled the study and began enrolling. In the fourth year we are now enrolling at 20 sites and have enrolled 624 patients (45% of those eligible). Follow up rates have been strong as the 3 month follow up rate is 94%. The rate is 87% at 6 months and 88% at 12 months. The study is performing well and there are no known barriers to study success at this time.

Specific Aim #1 Compare the proportion of surgical site infections within 6 months in patients treated with Supplemental Perioperative Oxygen compared to those treated without Supplemental Perioperative Oxygen.

1.1.Finalize Study Protocol

1. 1.1 Protocol Committee Creation

The Protocol Committee was successfully defined and formed during the first quarter of year one in keeping with METRC (Major Extremity Trauma Research Consortium) guidelines as described in previous reports. The committee for this study is detailed in Appendix 1. We designed to the committee to make sure it represents leaders in all fields that the study will involve. The committee for this study encompasses:

1. The P.I.
2. Orthopaedic Trauma Surgeons, from METRCg sites.
3. Infectious Disease Attendings, with expertise in orthopaedic infections
4. Two Anesthesiologists
5. Two PACU nurses
6. One Research Coordinators from Participating sites
7. One Research Coordinator from the PI's site
6. Two METRC Coordinating Center Staff (expertise in study design)
7. One METRC PI (Castillo)

The Protocol Committee members was defined, invited, and formed during the first quarter.

1.1.2. Protocol Development

Protocol Design:

During the first year the protocol was designed and finalized (included in Appendix 2 of first year report).

Protocol Approval History:

Protocol Committee Approval: The final protocol for IRB submission was approved by the protocol committee on January 2013.

METRC Steering Committee Approval: The protocol was circulated to the entire METRC Steering Committee. The final protocol for IRB submission was unanimously approved by METRC steering committee vote on February 2013.

1.2 Finalize/Adapt/Test Study Materials

CRF/SOP Development

CRF/SOP Design The Case Report Forms (CRFs) were developed in parallel to the protocol development along a similar timeline, leveraging previous METRC infrastructure to maintain uniformity with other METRC projects and leveraging on our experience with our pilot study (Reference 1) and other METRC studies.

CRF's were included in the annual report of year 1.

IRB Submission: The CRFs have been part of the IRB submission at sites that require it.

1.3 Train Study Coordinators

Study coordinator training occurred through both online live training (September 6, 2013) and in person training at the national meeting (October 9, 2013).

The presentation materials for local site training of anesthesia and recovery room nursing staff have been developed and completed by a subgroup of the protocol committee. This training will occur at each site just prior to first patient enrollment.

Additionally the PI and key personell from the protocol committee and METRC coordinating center contact each site and the local investigators for phone meetings once study enrollment begins to ensure that all questions are answered and to address any site specific issues.

1.4 IRB Approval at First Site (Milestone #1)

This task was accomplished in year one as detailed in prior reports.

IRB Approval at PI Site: The IRB submission was approved by University of Maryland School of Medicine on June 3rd 2013. A very minor modification required by the DOD IRB required IRB resubmission and this modification approval was received on October 15, 2013.

IRB Approval at METRC CC: The original IRB submission was approved by Johns Hopkins April 3, 2013. Revised protocol was approved on September 15, 2013 after modification for aforementioned minor changed required by DOD.

IRB Approval at DOD: DOD approval was obtained October 28, 2013.

DOD IRB Approval of PI Site: Pending

Assuming a relatively rapid approval of our IRB approved protocol by DOD, we are well positioned to begin enrollment at the first site soon.

1.5 IRB Approval at All Sites

The process of IRB approval at other sites has proceeded well in the past year. Of the 19 participating sites, 12 have local and DOD IRB approval and are currently enrolling, 4 are certified to begin enrollment, and 3 are in various stages of IRB approval process. We anticipated IRB approval at all sites in next quarter.

1.6 Enroll First Patient (Milestone #2)

The first milestone was accomplished during this last year on January 7, 2014 at the PI's site.

1.7 Enrollment

Enrollment is underway and proceeding well. We have enrolled 624 patients to date (45% of eligible) with a 88% 12 month follow up rate (see Appendix 2). Site enrollment has reached a relative steady state (see Appendix 2); however we expect this enrollment rate to spike substantially in the back half of the year. This is because the METRC VANCO study competes for these same patients and runs at 35 METRC sites. The plan has always been to complete VANCO first (at current pace it should complete in 6 months) and then immediately switch those sites back to OXYGEN. The high volume sites already have IRB approval for OXYGEN so there should be no delay in switch and then the speed of enrollment will increase substantially allowing the study to be completed in a reasonable time.

2. Specific Aim #2 Compare bacterial species and antibacterial sensitivities of the bacteria in the patients who develop surgical site infections in study patients treated with Supplemental Perioperative Oxygen compared to those treated without Supplemental Perioperative Oxygen.

2.1 Finalize Study Protocol

The general progress and timing of the study protocol creation regarding specific aim #2 are identical to those described in specific aim above in section 1.

2.2 Finalize/Adapt/Test Study Materials

The general progress and timing of the creation of the study materials regarding specific aim #2 are identical to those described in specific aim above in section 1.

2.3 Train Study Coordinators

Identical to specific aims #1 as described above in section 1.

2.4 IRB Approval at First Site (Milestone #1)

Identical to specific aims #1 as described above in section 1.

2.5 IRB Approval at All Sites

Identical to specific aims #1 as described above in section 1.

2.6 Enroll First Patient (Milestone #2)

Identical to specific aims #1 as described above in section 1.

2.7 Enrollment

Identical to specific aims #1 as described above in section 1.

3. Specific Aim #3 Validate the previously developed risk prediction model for the development of surgical site infections after fracture surgery (Reference 2,3,4,5).

3.1 Interim Analysis/Final Analysis

One of the specific aims of this project is to validate a model to predict risk for infection after orthopaedic fracture surgery. We are basing this off our previous work and have done an analysis of our pilot data (different treatment but similar patient population [1]) to analyze risk factors for infection. This has now been published in J Trauma [2,3,4,5].

This work can only begin after patient enrollment has been completed.

4. Specific Aim #4 Measure and compare resource utilization and cost associated with surgical site infection in study patients treated with Supplemental Perioperative Oxygen compared to those treated without Supplemental Perioperative Oxygen

4.1 Interim Analysis/Final Analysis

One of the specific aims of this project is to evaluate this technique in terms of cost. Determining the “cost effectiveness” of this technique will be important in determining if it is appropriate for broader distribution. Our hypothesis is that it is such a low cost technique that even modest decreases in infection rate will be very cost effective.

This work can only begin after patient enrollment has been completed.

4. KEY RESEARCH ACCOMPLISHMENTS:

Our key research accomplishments during year two of the grant include:

1. 20 study sites are certified and have enrolled at least 1 patient.
2. 624 patients enrolled to date (November 1, 2015)
3. 88% follow-up rate at 12 month follow up.
4. No cost extension (EWOFF) applied for in July and we anticipate obtaining this soon.
5. Study is on pace to complete patient enrollment in a reasonable time frame.
6. Protocol paper draft completed, anticipate submission in next few months.

5. CONCLUSION

We believe that this project has significant potential to impact wounded warriors' and civilians' outcomes by reducing the rate of surgical site infection if our primary hypothesis is confirmed.

This past year demonstrates that we are clearly on track for study success. We are now enrolling patients at a high rate and with high follow up rates. There are no barriers to study success and we look forward to finishing enrollment in a reasonable time frame.

6. PUBLICATION, ABSTRACTS, AND PRESENTATIONS

Protocol paper draft completed and submission anticipated in the coming months.

7. INVENTIONS, PATENTS, AND LICENSES

Nothing to report

8. REPORTABLE OUTCOMES

Nothing to report

9. OTHER ACHIEVEMENTS

Nothing to report

10. REFERENCES:

1. Stall A, Paryavi E, Gupta R, Zadnik M, Hui E, O'Toole RV, "Perioperative supplemental oxygen to reduce surgical site infection after open fixation of high-risk fractures: A randomized controlled pilot trial" J Trauma Acute Care Surg 2013 Volume 75 Number 4 657-63.
2. Paryavi E, Stall A, Gupta R, Zadnik M, Hui E, Castillo RC, Scharfstein DO, O'Toole RV "A Predictive Model for Perioperative Assessment of Infection Risk in High Energy Lower Extremity Injuries" Podium Presentation at American Academy of Orthopaedic Surgeons, San Diego, CA, 2011.
3. Paryavi E, Stall A, Gupta R, Zadnik M, Hui E, Castillo RC, Scharfstein DO, O'Toole RV "A Predictive Model for Perioperative Assessment of Infection Risk After Surgery for High Energy Lower Extremity Injuries: Development of the Risk of Infection in Orthopaedic Trauma Surgery (RIOTS) Score" Podium Presentation at OREF Chesapeake Region Resident Research Symposium, December 2010.
4. Paryavi E, Stall A, Gupta R, Zadnik M, Hui E, Castillo RC, Scharfstein DO, O'Toole RV "A Predictive Model for Perioperative Assessment of Infection Risk in High Energy Lower Extremity Injuries" Poster Presentation 26th Annual Meeting of Orthopaedic Trauma Association, Baltimore, MD, October 2010.
5. Paravi E, Stall A, Gupta R, Scharfstein DO, Castillo RC, Zadnik M, Hui E, O'Toole RV, "Predictive model for surgical site infection risk after surgery for high-energy lower extremity fractures: Development of the Risk of Infection in Orthopedic Trauma Surgery Score" J Trauma Acute Care Surg 2013 Volume 74 Number 6 1521-27.

11. APPENDICES:

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Appendix 1. Protocol Committee

First Name	Last Name	Role	Site	
Robert	O'Toole	PI (Surgeon)	UMD	ROtoole@umoa.umm.edu
Renan	Castillo	MCC PI	JHU	rcastill@jhsph.edu
Mary	Zadnik	MCC Study Director	JHU	mzadnik@jhsph.edu
Anthony	Carlini	MCC IT Director	JHU	acarlini@jhsph.edu
Tara	Taylor	MCC Study Manager	JHU	tjtaylor@jhsph.edu
Degani	Yasmin	RC	UMD	AHolmes@umoa.umm.edu
Manjari	Joshi	ID	UMD	Manjarijoshi03@gmail.com
Robert	Sikorski	Anesthesiologist	UMD	rsikorski@umm.edu
Ebrahim	Paryavi	Surgeon, Stats	UMD	eparyavi@jhsph.edu ; eparyavi@umoa.umm.edu
Alec	Stall	Surgeon, Stats	UMD	alecstall@gmail.com
Nalini	Rao	ID	PIT	raon@upmc.edu
Arman	Dagal	Anesthesiologist	UWA	dagal@uw.edu
Milan	Sen	Surgeon	HOU	Milan.Sen@uth.tmc.edu
Madhav	Karunakar	Surgeon	CMC	madhav.karunakar@carolinashealthcare.org
Michael	Bosse	Surgeon	CMC	michael.bosse@carolinashealthcare.org
Josh	Gary	Surgeon	HOU	joshua.l.gary@uth.tmc.edu
Mike	Weaver	Surgeon		MJWEAVER@PARTNERS.ORG
Clinton	Murray	ID	BAM	clinton.murray@us.army.mil

Gregory	Altman	Surgeon	AGY	altmangregory@hotmail.com ; GALTMAN@wpahs.org
Andrew	Schmidt	Surgeon	HCM	schmi115@umn.edu
Thomas	Dipasquale	Surgeon	YRK	tdipasquale@wellspan.org
Jean Claude	D'Allyrand	Surgeon	WRD	ortho.traumatology@gmail.com
Pamela	Watkins	RC	UMD	pwatkins@umm.edu
Christa	Arndt	RC	UMD	carndt@umm.edu
Yasmin	Degani	RC	UMD	ydegani@umoa.umm.edu
Adrienne	Brandon	RC	YRK	abrandon@wellspan.org

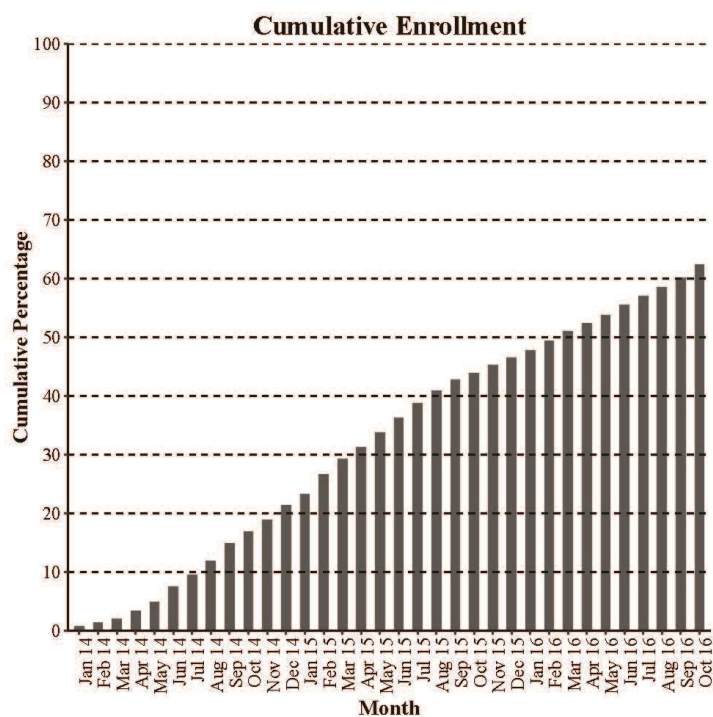
Appendix 2. Oxygen Monthly Report (November 1, 2016)



OXYGEN Monthly Report

Supplemental Oxygen to
Reduce Surgical Site Infection

Data as of November 1, 2016



Enrollment Updates

- There are 20 centers participating in this study (all centers are certified).
- 2563 patients have been screened for eligibility and of these, 1392 (54%) were eligible.
- 624 (45% of eligible) were consented and enrolled.
- We have now reached 62% of our total enrollment goal (see figure)
- 333 patients have completed the study.

Screening and Enrollment Summary
All Participating Sites

Facility	Days Certified	Expected Screened	Number Screened	Number Enrolled	Enrolled This Month	Completed	Discontinued
ALL			2563	624	22	333	41
UWA	686	532	307	120	12	42	8
UMD	1047	637	433	111	1	70	2
CMC	998	347	398	58	3	43	2
HRV	785	-	104	57	2	23	8
HOU	981	341	201	51	0	39	1
VMC	874	292	106	38	0	28	2
AGY	845	-	66	32	1	16	6
MTH	795	307	208	26	0	15	2
BMC	855	183	91	19	1	9	2
MIN ¹	811	138	63	18	0	9	0
ESK	776	-	70	17	1	5	0
YRK	816	-	20	17	0	8	3
PEN	741	-	39	12	0	0	1
USF	820	166	38	11	1	2	1
SPC ²	908	229	77	10	0	9	1
UOK	701	123	49	10	0	2	2
WFU	971	399	213	7	0	7	0
NSD	838	28	7	6	0	6	0
CAM	333	-	63	3	0	0	0
COR	60	-	10	1	0	0	0

¹ MIN is a dual site comprised of HCM and UMN, however only HCM was participating in this study. HCM withdrew from participating after becoming certified.

² SPC withdrew from participating after becoming certified.

Questions? Study Contacts:

- Study PI: Robert O'Toole, MD (ROtoole@umoa.umm.edu)
- MCC PI: Renan Castillo, PhD (rcastil1@jhu.edu)
- MCC Project Director: Anthony R. Carlini, MS (acarlini@jhu.edu)
- MCC Study Manager: Susan Collins, MSc (scollins@jhsph.edu)

Monthly Table 1
Number of Subjects Screened ³, Eligible, Enrolled, and Not Enrolled
Cumulative by Site

Facility	Days Certified	Expected Screened	Number Screened	Number Eligible	Among those Eligible (% Eligible)		
					Number Enrolled	Number Refused	Number Not Enrolled
ALL			2563	1392 (54%)	624 (45%)	192 (14%)	576 (41%)
AGY	845	-	66	40 (61%)	32 (80%)	5 (12%)	3 (8%)
BMC	855	183	91	24 (26%)	19 (79%)	2 (8%)	3 (12%)
CAM	333	-	63	53 (84%)	3 (6%)	9 (17%)	41 (77%)
CMC	998	347	398	248 (62%)	58 (23%)	52 (21%)	138 (56%)
COR	60	-	10	5 (50%)	1 (20%)	0 (0%)	4 (80%)
ESK	776	-	70	25 (36%)	17 (68%)	8 (32%)	0 (0%)
HOU	981	341	201	94 (47%)	51 (54%)	16 (17%)	27 (29%)
HRV	785	-	104	92 (88%)	57 (62%)	27 (29%)	8 (9%)
MIN	811	138	63	28 (44%)	18 (64%)	1 (4%)	9 (32%)
MTH	795	307	208	71 (34%)	26 (37%)	4 (6%)	41 (58%)
NSD	838	28	7	6 (86%)	6 (100%)	0 (0%)	0 (0%)
PEN	741	-	39	24 (62%)	12 (50%)	8 (33%)	4 (17%)
SPC	908	229	77	20 (26%)	10 (50%)	4 (20%)	6 (30%)
UMD	1047	637	433	265 (61%)	111 (42%)	23 (9%)	131 (49%)
UOK	701	123	49	30 (61%)	10 (33%)	6 (20%)	14 (47%)
USF	820	166	38	12 (32%)	11 (92%)	1 (8%)	0 (0%)
UWA	686	532	307	195 (64%)	120 (62%)	16 (8%)	59 (30%)
VMC	874	292	106	57 (54%)	38 (67%)	5 (9%)	14 (25%)
WFU	971	399	213	83 (39%)	7 (8%)	4 (5%)	72 (87%)
YRK	816	-	20	20 (100%)	17 (85%)	1 (5%)	2 (10%)

³ Number screened based on all patients with completed CRF00

Monthly Table 2
Number of Subjects Enrolled/Screened by Month of Participation and Site

Month	ALL	UMD	CMC	HOU	WFU	SPC	VMC	BMC	AGY	NSD	USF	YRK	HCM	MTH	HRV	ESK	PEN	UOK	UWA	CAM	COR
Dec 2013	0/0	0/0																			
Jan 2014	7/11	7/11																			
Feb 2014	6/8	6/8	0/0	0/0																	
Mar 2014	7/14	6/9	1/4	0/0	0/0																
Apr 2014	14/28	4/8	1/3	9/16	0/0																
May 2014	14/36	6/12	4/9	3/9	1/1	0/3															
Jun 2014	27/57	14/21	6/14	4/11	1/4	2/4	0/0	0/0													
Jul 2014	20/65	3/11	4/8	2/6	2/7	2/15	0/0	5/7	2/3	0/0											
Aug 2014	24/62	8/11	4/14	4/12	0/5	2/5	0/0	1/1	2/3	0/0	0/3	0/0	3/8	0/0							
Sep 2014	30/71	9/16	5/12	4/13	1/6	1/7	2/2	0/2	2/2	0/0	1/3	1/3	1/1	3/4	0/0	0/0					
Oct 2014	19/74	4/19	5/16	2/6	0/5	0/12	3/5	0/0	2/4	0/0	0/0	0/0	0/0	3/7	0/0	0/0	0/0				
Nov 2014	21/63	6/10	2/12	1/5	0/3	0/12	4/5	1/1	2/3	0/0	0/0	0/0	0/3	2/3	2/5	0/0	1/1				
Dec 2014	25/65	8/17	2/8	2/9	0/4	1/5	4/7	0/1	1/1	0/0	1/1	1/1	0/0	1/2	3/3	1/6	0/0	0/0	0/0		
Jan 2015	18/68	1/11	4/9	1/8	0/9	0/5	4/8	0/4	2/2	2/2	0/2	0/0	0/0	1/2	3/3	0/2	0/0	0/0	0/1		
Feb 2015	34/83	2/5	5/12	3/12	2/6	1/3	3/5	0/2	2/5	0/0	1/3	2/2	2/2	1/2	3/5	1/3	0/0	3/5	3/11		
Mar 2015	27/90	1/12	1/13	7/9	0/5	1/5	3/6	1/3	0/1	0/0	1/1	0/1	0/0	2/3	3/5	1/4	0/9	0/2	6/11		
Apr 2015	20/78	0/8	0/9	3/11	0/10	0/1	0/0	0/4	1/3	0/0	0/0	4/4	0/0	2/5	4/4	0/3	0/3	0/3	6/10		
May 2015	24/86	2/16	0/13	1/5	0/10	0/0	4/4	1/4	0/1	1/1	1/2	1/1	0/2	0/4	3/5	1/1	1/1	0/2	8/14		
Jun 2015	26/103	3/16	1/16	0/3	0/14	0/0	5/5	0/3	2/4	0/0	1/1	1/1	2/4	0/6	2/5	0/0	1/1	1/2	7/22		
Jul 2015	25/95	1/11	1/16	1/5	0/4	0/0	5/8	0/3	0/2	0/1	0/2	2/2	1/3	0/8	4/5	0/0	2/3	0/2	8/20		
Aug 2015	21/105	3/22	1/11	1/12	0/6	0/0	0/0	1/5	0/1	2/2	0/3	0/0	2/7	0/5	3/5	1/2	0/1	0/5	7/18		
Sep 2015	18/82	2/11	1/5	1/8	0/0	0/0	1/1	0/3	2/3	1/1	0/0	0/0	0/1	2/16	2/7	2/2	0/0	1/3	3/21		
Oct 2015	12/85	0/6	1/13	0/6	0/9	0/0	0/0	0/3	3/4	0/0	0/1	0/0	3/6	1/19	1/2	0/1	0/0	1/4	2/11		
Nov 2015	14/83	2/12	0/14	1/10	0/12	0/0	0/0	0/1	0/2	0/0	0/3	1/1	1/1	0/7	0/2	1/4	0/0	0/3	8/11		
Dec 2015	12/91	1/13	1/18	0/6	0/7	0/0	0/0	2/3	1/1	0/0	0/0	0/0	0/0	0/15	1/2	1/1	1/3	1/3	3/8	0/11	
Jan 2016	13/73	0/7	0/13	0/7	0/7	0/0	0/0	0/4	1/2	0/0	0/0	3/3	0/1	2/6	2/3	1/5	1/3	0/2	3/4	0/6	

Month	ALL	UMD	CMC	HOU	WFU	SPC	VMC	BMC	AGY	NSD	USF	YRK	HCM	MTH	HRV	ESK	PEN	UOK	UWA	CAM	COR
Feb 2016	16/68	2/6	0/5	0/5	0/5	0/0	0/0	0/2	2/4	0/0	1/4	1/1	2/4	1/12	1/2	0/0	1/2	2/2	3/8	0/6	
Mar 2016	16/83	1/15	0/13	0/1	0/9	0/0	0/0	0/9	0/0	0/0	1/1	0/0	0/1	2/12	3/4	2/3	2/2	0/1	5/8	0/4	
Apr 2016	14/81	1/9	0/14	0/0	0/8	0/0	0/0	0/1	1/4	0/0	0/0	0/0	0/1	2/13	1/2	1/3	0/1	1/1	6/17	1/7	
May 2016	13/81	1/5	2/18	0/1	0/6	0/0	0/0	4/8	0/2	0/0	0/0	0/0	1/3	0/9	3/5	0/2	0/0	0/3	2/14	0/5	
Jun 2016	18/98	2/26	0/12	0/0	0/6	0/0	0/0	0/0	1/1	0/0	0/1	0/0	0/0	0/10	6/9	0/5	0/7	0/2	9/17	0/2	
Jul 2016	15/97	2/18	1/14	0/3	0/8	0/0	0/9	0/6	0/0	0/0	1/3	0/0	0/0	1/9	1/5	0/7	0/0	0/1	9/10	0/4	
Aug 2016	15/152	1/16	1/21	0/1	0/20	0/0	0/24	0/2	0/2	0/0	1/3	0/0	0/0	0/11	2/5	2/8	2/2	0/1	6/34	0/2	
Sep 2016	17/122	1/25	1/22	1/1	0/7	0/0	0/6	2/6	2/4	0/0	0/0	0/0	0/0	0/7	2/6	1/6	0/0	0/0	4/13	2/13	1/6
Oct 2016	22/105	1/10	3/17	0/0	0/10	0/0	0/11	1/3	1/2	0/0	1/1	0/0	0/0	0/11	2/5	1/2	0/0	0/2	12/24	0/3	0/4

Monthly Table 3
Number of Expected⁴, Completed⁵, and Missed⁶ Visits by Study Visit

Facility	Enrolled	2 week			3 month			6 month			12 month		
		E	C	M	E	C	M	E	C	M	E	C	M
ALL	624	587	583 (99%)	1 (0%)	549	517 (94%)	22 (4%)	502	436 (87%)	46 (9%)	407	357 (88%)	10 (2%)
AGY	32	31	31 (100%)	0 (0%)	29	26 (90%)	3 (10%)	25	21 (84%)	4 (16%)	18	16 (89%)	1 (6%)
BMC	19	17	16 (94%)	0 (0%)	15	15 (100%)	0 (0%)	13	13 (100%)	0 (0%)	10	9 (90%)	1 (10%)
CAM	3	3	3 (100%)	0 (0%)	1	1 (100%)	0 (0%)	1	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)
CMC	58	55	55 (100%)	0 (0%)	53	52 (98%)	1 (2%)	49	47 (96%)	1 (2%)	47	46 (98%)	1 (2%)
COR	1	1	1 (100%)	0 (0%)	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)
ESK	17	17	17 (100%)	0 (0%)	13	11 (85%)	2 (15%)	13	11 (85%)	1 (8%)	7	6 (86%)	0 (0%)
MIN	18	18	18 (100%)	0 (0%)	18	18 (100%)	0 (0%)	17	13 (76%)	1 (6%)	12	9 (75%)	0 (0%)
HOU	51	51	51 (100%)	0 (0%)	50	46 (92%)	3 (6%)	50	38 (76%)	5 (10%)	49	40 (82%)	1 (2%)
HRV	57	52	50 (96%)	0 (0%)	45	43 (96%)	2 (4%)	34	31 (91%)	3 (9%)	26	24 (92%)	1 (4%)
MTH	26	24	24 (100%)	0 (0%)	24	23 (96%)	1 (4%)	23	21 (91%)	2 (9%)	16	15 (94%)	0 (0%)
NSD	6	6	6 (100%)	0 (0%)	6	6 (100%)	0 (0%)	6	6 (100%)	0 (0%)	6	6 (100%)	0 (0%)
PEN	12	11	10 (91%)	1 (9%)	10	8 (80%)	0 (0%)	10	7 (70%)	1 (10%)	5	3 (60%)	0 (0%)
SPC	10	10	10 (100%)	0 (0%)	10	10 (100%)	0 (0%)	10	10 (100%)	0 (0%)	9	9 (100%)	0 (0%)
UMD	111	110	110 (100%)	0 (0%)	107	100 (93%)	6 (6%)	102	86 (84%)	16 (16%)	95	83 (87%)	1 (1%)
UOK	10	9	9 (100%)	0 (0%)	9	9 (100%)	0 (0%)	9	8 (89%)	1 (11%)	4	2 (50%)	0 (0%)
USF	11	8	8 (100%)	0 (0%)	7	6 (86%)	0 (0%)	7	3 (43%)	2 (29%)	5	4 (80%)	1 (20%)
UWA	120	104	104 (100%)	0 (0%)	92	86 (93%)	1 (1%)	74	65 (88%)	6 (8%)	47	42 (89%)	2 (4%)
VMC	38	37	37 (100%)	0 (0%)	37	35 (95%)	2 (5%)	36	34 (94%)	2 (6%)	35	28 (80%)	0 (0%)
WFU	7	7	7 (100%)	0 (0%)	7	6 (86%)	1 (14%)	7	7 (100%)	0 (0%)	7	7 (100%)	0 (0%)
YRK	17	16	16 (100%)	0 (0%)	16	16 (100%)	0 (0%)	16	15 (94%)	1 (6%)	9	8 (89%)	1 (11%)

E = Expected, C = Completed, M = Missed

⁴ A visit is counted as complete (i.e. fully or partially completed) if at least one field in the CRFs to be completed for the visit has been keyed and this visit has not been indicated as missed on AF03. All out of window visits count as completed for the purpose of this report.

⁵ A visit is counted as expected when the visit has been completed (as defined above) or when the visit window has been closed for 7 days and no forms have been keyed.

⁶ Patients who withdraw/ are lost to follow up are kept in as incomplete visits. Deaths are censored at time of death. Patients inappropriately enrolled are removed from all totals. Patients for whom Time Zero (e.g. date of injury) is incomplete are excluded from this report.

A visit is counted as missed based on AF03. Patients with no AF03 or no data entered into REDCap will be listed in Query 2.

Monthly Table 4
Evaluate Oxygen treatment adherence by Site ⁷
By Average Absolute Deviation ⁸, % Observations Within Range 1 ⁹ and % Observations Within Range 2 ¹⁰

Facility	Data	Average Absolute Deviation			% of Observations within Range 1			% Observations within Range 2		
		Mean $\pm$ SD	Median	Range	Mean $\pm$ SD	Median	Range	Mean $\pm$ SD	Median	Range
ALL	553	7.5 $\pm$ 19.6	2.9	(0.0, 280.4)	80.6 $\pm$ 30.9	93.8	(0.0, 100.0)	85.9 $\pm$ 27.2	100.0	(0.0, 100.0)
UMD	108	7.7 $\pm$ 12.9	2.3	(0.0, 64.0)	79.0 $\pm$ 37.3	100.0	(0.0, 100.0)	82.6 $\pm$ 34.0	100.0	(0.0, 100.0)
UWA	100	5.4 $\pm$ 8.7	3.2	(0.0, 49.4)	86.6 $\pm$ 22.4	94.1	(0.0, 100.0)	90.1 $\pm$ 19.5	96.8	(0.0, 100.0)
CMC	52	6.2 $\pm$ 8.7	2.4	(0.0, 36.2)	79.8 $\pm$ 28.0	90.7	(0.0, 100.0)	85.5 $\pm$ 26.6	100.0	(0.0, 100.0)
HOU	49	3.3 $\pm$ 8.1	1.0	(0.0, 50.0)	89.3 $\pm$ 23.7	100.0	(0.0, 100.0)	90.4 $\pm$ 23.8	100.0	(0.0, 100.0)
HRV	48	13.9 $\pm$ 44.3	2.8	(0.5, 280.4)	76.7 $\pm$ 32.2	92.3	(0.0, 100.0)	82.5 $\pm$ 30.3	98.1	(0.0, 100.0)
VMC	36	8.1 $\pm$ 9.0	5.7	(0.0, 52.4)	63.9 $\pm$ 35.6	78.9	(0.0, 100.0)	76.8 $\pm$ 30.0	88.6	(0.0, 100.0)
AGY	23	7.8 $\pm$ 12.8	1.6	(0.0, 42.8)	77.7 $\pm$ 32.4	92.3	(0.0, 100.0)	80.9 $\pm$ 32.7	100.0	(0.0, 100.0)
MTH	23	6.0 $\pm$ 7.6	2.7	(0.0, 34.5)	68.9 $\pm$ 40.1	90.0	(0.0, 100.0)	86.3 $\pm$ 26.9	100.0	(0.0, 100.0)
HCM	18	4.9 $\pm$ 3.0	4.3	(1.2, 11.9)	90.6 $\pm$ 23.7	100.0	(0.0, 100.0)	91.5 $\pm$ 23.9	100.0	(0.0, 100.0)
ESK	17	5.1 $\pm$ 7.7	0.9	(0.0, 26.6)	88.7 $\pm$ 24.6	100.0	(0.0, 100.0)	89.6 $\pm$ 24.8	100.0	(0.0, 100.0)
BMC	16	4.1 $\pm$ 4.5	2.7	(0.6, 16.7)	90.8 $\pm$ 11.0	91.1	(57.1, 100.0)	92.5 $\pm$ 11.2	97.5	(57.1, 100.0)
YRK	14	6.6 $\pm$ 5.9	4.5	(1.5, 18.2)	73.5 $\pm$ 40.3	97.6	(0.0, 100.0)	88.9 $\pm$ 24.8	100.0	(12.5, 100.0)
PEN	9	7.1 $\pm$ 9.1	2.9	(0.9, 26.2)	78.9 $\pm$ 32.2	90.9	(0.0, 100.0)	89.8 $\pm$ 14.1	100.0	(62.5, 100.0)
SFC	9	3.3 $\pm$ 3.8	1.2	(0.3, 10.9)	95.7 $\pm$ 6.8	100.0	(83.3, 100.0)	96.1 $\pm$ 6.7	100.0	(83.3, 100.0)
USF	8	3.1 $\pm$ 3.0	2.1	(1.0, 10.0)	92.3 $\pm$ 8.0	94.1	(73.7, 100.0)	94.7 $\pm$ 9.3	100.0	(73.7, 100.0)
UOK	7	53.6 $\pm$ 97.5	5.4	(1.3, 262.8)	65.1 $\pm$ 46.4	93.3	(0.0, 100.0)	82.1 $\pm$ 37.4	100.0	(0.0, 100.0)
WFO	7	10.4 $\pm$ 9.0	7.1	(1.1, 23.5)	71.8 $\pm$ 26.1	77.8	(23.1, 100.0)	75.8 $\pm$ 28.0	80.0	(23.1, 100.0)
NSD	6	14.0 $\pm$ 14.1	6.4	(2.6, 36.3)	58.7 $\pm$ 37.2	74.2	(4.2, 90.5)	66.9 $\pm$ 43.1	88.6	(4.2, 100.0)

⁷ This table describes adherence to the randomized oxygen concentrations (30% or 80% F_{iO_2}). To preserve blinding, sites with at least 5 patients enrolled are included on this table. There are three sets of means, medians, and ranges in the table. They represent:

⁸ Average Absolute Deviation: This set of mean, median, and range measures the distance of each observation recorded on CRF15 from either 30% or 80%, depending on which group the patient was randomized to, and excluding the 1st and last observations recorded. The mean shown here is a mean of the means, and the median is the median of several means. A higher median in this cluster indicates "worse" protocol adherence.

⁹ % Observations Within Range 1: This set of mean, median, and range measures the percent of observations recorded on CRF15 that fall within either 20–35% or 70–85%, depending on which group the patient was randomized to, and excluding the 1st and last observations recorded. This is our more stringent definition of protocol adherence. A higher median in this cluster indicates "better" protocol adherence.

¹⁰ % of Observations Within Range 2: This set of mean, median, and range measures the percent of observations recorded on CRF15 that are < 35% or > 70%, depending on which group the patient was randomized to, and excluding the 1st and last observations recorded. This is our more lenient definition of protocol adherence. A higher median in this cluster indicates "better" protocol adherence.

Appendix 3. Oxygen Quad Chart

Supplemental Perioperative Oxygen to Reduce Surgical Site Infection After High Energy Fracture Surgery

OR110123 (W81XWH-12-1-0588)

PI: Robert V. O'Toole, MD

Org: Department of Orthopaedic Surgery, Univ of Maryland Award Amount: \$2.447M (Directs only)



Study/Product Aim(s)

Our hypothesis is that the use of supplemental perioperative oxygen for fractures at high risk for infection will reduce infection rates and therefore improve outcomes compared to treatment without this technique.

- Infection rates will be lower in the treatment arm
- There will be no difference in bacterial susceptibilities in the treatment arm
- Validate our previous RIOTS model that predicts infection

Approach

The study uses the DOD-funded METRC infrastructure for a multicenter randomized controlled treatment trial. The study population is patients with high energy tibial plateau, pilon (distal tibia), and calcaneus fractures. The study is guided by a pilot study already completed of 250 fractures at our center. We plan to enroll 1000 patients.



Surgical Site infection (left) in orthopaedic trauma is thought to be affected by biofilm formation (Right). General surgery clinical literature suggests that supplemental perioperative oxygen might limit surgical site infection. The effect on orthopaedic trauma surgery awaits the outcome of this trial.

Accomplishment: We finalized the protocol, CRFs, study sites, and have IRB approval and site certification at 20 sites. 624 patients have been enrolled with f/u rate of 88% at one year.

Timeline and Cost

Activities	CY	13	14	15	16+
Develop and Approve Protocol					
IRB approval at Multiple sites					
Enroll/Follow Patients					
Analysis					
Estimated Budget (\$K)		\$ 165,127	\$741,645	\$1,741,138	\$0

Updated: (11/22/2016)

Goals/Milestones

Year 1: CY13-14 Goal –Protocol Development/Implementation/IRB

- ☒ Develop protocol and gain approval of METRC steering committee
- ☒ IRB approval at METRC Coordinating center and DOD
- ☒ IRB approval at PI site
- ☒ Perform site education program for research coordinators
- ☒ Develop site educational and study materials

Year 2: CY14-15 Goals – Patient enrollment

- ☒ Begin patient enrollment
- ☒ IRB/DOD approval at all study sites (20/20 completed to date)

Year 3: CY14-17 Goals – Enrollment completion

- ☐ Complete patient enrollment & study analysis

Comments/Challenges/Issues/Concerns

- Patient enrollment is >12 months behind due to IRB delays.

Budget Expenditure to Date

Projected Expenditure: \$ 1,276,199 (including JHU sub payments)

Actual Expenditure: \$ 1,371,711 (including JHU sub payments)