AWARD NUMBER: W81XWH-15-1-0025

TITLE: Clinical Study of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) for Severe Pelvic Fracture & Intra-Abdominal Hemorrhagic Shock using Continuous Vital Signs

PRINCIPAL INVESTIGATOR: Dr. Megan Brenner

CONTRACTING ORGANIZATION: University of Maryland
Baltimore, MD 21202

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Clinical Study of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) for Severe Pelvic Fracture & Intra-Abdominal Hemorrhagic Shock using Continuous Vital Signs

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6. AUTHOR(S)

Dr. Megan Brenner

E-Mail: mbrenner@umm.edu

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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

University of Maryland
22 S. Greene St.
Baltimore, MD 21202

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14. ABSTRACT

Hemorrhage remains a leading cause of death in military trauma settings. Reports from the battlefield have found that over 50%of potentially salvageable deaths are related to uncontrolled non compressible torso hemorrhage (NCTH). Severe pelvic injury with associated junctional femoral hemorrhage results in hemorrhagic shock. Endovascular techniques such as intra-aortic balloon occlusion have the potential to significantly decrease blood loss, improve physiologic parameters, and ultimately lead to increased survival in patients in hemorrhagic shock from severe pelvic injury.

15. SUBJECT TERMS

None listed

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRMC
U Unclassified	U Unclassified	U Unclassified	UU Unclassified	59	**19b. TELEPHONE NUMBER** *(include area code)*

TABLE OF CONTENTS

1. INTRODUCTION: Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

Resuscitative balloon occlusion of the aorta (REBOA) has been clinically demonstrated to stop bleeding below the diaphragm. It has the potential to significantly decrease blood loss thereby decreasing blood-product resuscitation requirements, improve physiologic parameters, and ultimately lead to increased survival in patients in hemorrhagic shock from severe torso injury. This is a simple endovascular technique which can be taught to forward deployed physicians and has over the past decade vastly improved the survival of ruptured abdominal aortic aneurysm patients. Although the technique is still in its infancy for trauma patients, we predict that the use of intra-aortic balloon occlusion will improve the survival of trauma patients and reduce morbidity. We have undertaken a 2 phase study to evaluate simulation-based REBOA training and the effectiveness of REBOA stabilization of severe intra-abdominal hemorrhagic shock and/or pelvic fracture patients. In phase I, a simulator based REBOA training curriculum was developed to train STC clinicians, and its efficacy will be evaluated. Phase 2 is a single center, prospective observational study in which patients with severe hemorrhagic shock and/or pelvic fracture admitted to the Trauma Resuscitation Unit of our level 1 trauma center are stabilized with REBOA. Our main objective was to assess the impact on mortality and morbidity after REBOA. We hypothesized that use of REBOA in cases of NCTH will decrease morbidity and mortality.

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

Trauma; Hemorrhage; Junctional Hemorrhage; Non-Compressible Torso Hemorrhage (NCTH); Combat Casualty Care; Aortic Occlusion; REBOA; Resuscitative Endovascular Occlusion of the Aorta; Thoracotomy; Aortic cross-clamp; Simulation; Virtual reality simulation; Endovascular

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Hypothesis 1: A simulator based learning platform is effective to train physicians who are already skilled in vascular access procedures, to place REBOA.

Specific Aim: Design and evaluate a comprehensive simulator based training program to train attending trauma surgeons, critical care faculty, trauma fellows, and chief residents to perform REBOA.

Hypothesis 2: Use of resuscitative endovascular balloon occlusion of the aorta (REBOA) in cases of non-compressible torso hemorrhage (NCTH) of the abdomen and pelvis will decrease the morbidity and mortality associated with this often fatal pattern of injury with improved physiological parameters, outcomes, and recovery periods and will allow time for vascular repair.

Specific Aim: Evaluate the ability of REBOA to improve survival and functional outcomes in patients with NCTH. Analysis of continuously recorded vital sign data will show that the use of REBOA will improve physiologic parameters in patients with NCTH.

What was accomplished under these goals?

Hypothesis 1: A simulator based learning platform was created to educate physicians to place REBOA. This training course initially incorporated utilizing the CODA® catheter to perform REBOA. After FDA approval of a new novel REBOA catheter (ER-REBOA^{TM} (Prytime Medical, Boerne, TX)) in October 2015, we incorporated this catheter into our practice in February 2016. Our REBOA training course (Basic Endovascular Skills in Trauma (BEST) course) and standard operating procedure was updated to incorporate this new catheter. The BEST course continues to be held and training of new trauma surgery fellows and new staff occurs. A modified BEST course was also held at the American College of Surgeons Clinical Congress (October 16–20, 2016, Washington, DC) and at the 30th Eastern Association for the Surgery of Trauma (EAST) Annual Scientific Assembly (January 10-14, 2017, in Hollywood, FL). See appendix A for a description and analysis of the BEST course. See #6 Products for a full listing of associated conference abstracts related to the training course.

Hypothesis 2: Multiple abstracts have been presented at various conferences (see #6 Products for a full listing of associated abstracts presented at conferences, and #6 for manuscripts currently accepted/published). We enrolled a total of 86 patients into an observational trial. See appendix B for a clinical description and analysis.

What opportunities for training and professional development has the project provided?

There have been multiple participants who work on this project who have been able to present different works as abstracts at various conferences (see #6 Products for a full listing). Participants have also had an opportunity to attend the various lectures and educational opportunities that are associated with each of these conferences.

The periodic performance of the BEST course also provides an opportunity for participants to continually practice their professional skillset as educators.

How were the results disseminated to communities of interest?

Information regarding scientific findings were disseminated at conferences. A full listing of abstracts and conferences can be found in the Products section (#6).

What do you plan to do during the next reporting period to accomplish the goals?

Nothing to report.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

This study has helped our institution with evidence based guidelines for the use of REBOA. This data is in various stages of presentation, or manuscript in preparation format.

What was the impact on other disciplines?

Nothing to report.

What was the impact on technology transfer?

Nothing to report.

What was the impact on society beyond science and technology?

Nothing to report.

5. CHANGES/PROBLEMS:

1. On November 9th, 2015, the University of Maryland transitioned their clinical electronic medical record to a new software package. This transition was anticipated, but our new electronic data tool had IT compatibility issues with the new software and was non-functional. Our backup procedures for paper documentation were re-initiated and continue currently.

2. The new electronic medical record, which necessitated a redesign of our electronic data tool. This is now complete and being used to enter and store study data.

3. Our CORE staff had unforeseen staffing issues on Thanksgiving Day 2015 and as a result, approximately 24 hours of prospective data collection time were lost. This did not affect our study as no patients matched screening criteria during this time.

4. Due to the riots during spring 2015, the city was closed to travel by all non-essential personnel. Our research staff was unable to report for work, resulting in a gap of 48 hours of prospective data collection. The clinical staff present in the Trauma Center assumed the responsibility of noting any REBOA placements. No placement occurred during this time and no data was lost.

5. On February 1, 2016, a newly FDA-approved device compatible with a smaller 7Fr sheath was available for clinical use. The SOP and data tool were updated in anticipation of these devices becoming available and were updated immediately.

6. Continuing IRB approval was obtained on May 4, 2016, extending approval for the project to May 3, 2017.

7. Continuing IRB approval was obtained on March 31, 2017, extending approval for the project to March 28, 2018. There have been no other new changes or problems during this reporting period.

Actual or anticipated problems or delays and actions or plans to resolve them

Nothing to report.

Changes that had a significant impact on expenditures

Nothing to report.

Significant changes in use or care of human subjects

Nothing to report.

Significant changes in use or care of vertebrate animals

Nothing to report.

Significant changes in use of biohazards and/or select agents

Nothing to report.

6. PRODUCTS:

- **Publications, conference papers, and presentations**

Journal publications.

1. Accepted for Publication in the Journal: Journal of Special Operations Medicine
   Title: Resuscitative Balloon Occlusion of the Aorta: Pushing care forward
   Authorship: W Teeter MD, A Romagnoli MD, J Glaser MD, A Fisher PA, J Pasley DO, B Scheele DO, M Hoehn MD, M Brenner MD

Books or other non-periodical, one-time publications.

Nothing to Report

Other publications, conference papers and presentations.

1th Annual Academic Surgical Congress Abstract Submission - February 2-4, 2016 in Jacksonville, FL

1. Virtual Reality Simulation for Residents: A Trainee Experience in Damage Control Endovascular Skills
   Authorship: William A. Teeter, MD, MS; Megan Brenner, MD, MS; Melanie Hoehn, MD; Deborah Stein, MD, MPH; Thomas Scalea, MD

39th Annual CONFERENCE ON SHOCK – June 11-14th, Austin, TX

2. REBOA IMPROVES MEAN BLOOD PRESSURE (MBP) AND SHOCK INDEX (SI) AS MEASURED BY CONTINUOUS VITAL SIGNS (CVS) EVEN IN PATIENTS ARRIVING IN ARREST
   Authorship: W Teeter MD, M Brenner MD, M Hoehn MD, P Hu PhD, S Yang PhD

24th Annual Military Health System Research Symposium Aug. 15-18, 2016, Kissimmee, FL

3. Resuscitative Balloon Occlusion of the Aorta: Pushing care forward
   Authorship: W Teeter MD, A Romagnoli MD, J Glaser MD, A Fisher PA, J Pasley DO, B Scheele DO, M Hoehn MD, M Brenner MD

75th Annual Meeting of AAST and Clinical Congress of Acute Care Surgery - September 14-17, 2016, Waikoloa, HI

4. Time to aortic occlusion: It's all about access
   Authorship: A Romagnoli MD, W Teeter MD, J Pasley DO, P Hu PhD, G Hagegeorge, D Stein MD, T Scalea MD, M Brenner MD

5. Age is just a number: REBOA can be performed in older patients at high risk for atherosclerotic vascular disease
   Authorship: M Ghneim MD, W Teeter MD, A Romagnoli MD, M Hoehn MD, P Hu PhD, T Scalea MD, M Brenner MD

American College of Surgeons Clinical Congress 2016 - October 16–20, 2016, Washington, DC

6. Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) Can Be Deployed Rapidly and Safely by Acute Care Surgeons
   Authorship: D HAMPTON MD, W TEETER MD, G HAGEGEORGE, M HOEHN MD, D STEIN MD, T SCALEA MD, M BRENNER MD

7. Paradigm shift in hemorrhagic traumatic arrest: REBOA is at least as effective as RTACC
   Authorship: W Teeter MD, A Romagnoli MD, H Li PhD, S Yang PhD, P Hu PhD, D Stein MD, T Scalea MD, M Brenner MD

American College of Emergency Physicians Annual Meeting 2016, October 15-20th, 2016, Las Vegas, NV

8. REBOA improves quality of resuscitation versus thoracotomy in patients in traumatic arrest.
   Authorship: William Teeter, MD MS, Anna Romagnoli, MD, Melanie Hoehn, MD, Jay Menaker, MD, Deborah Stein, MD MPH, Thomas Scalea MD, Megan Brenner MD MS.

9. Virtual Reality Simulation can help prepare Emergency Medicine physicians for REBOA
   Authorship: W. Teeter MD, A Romagnoli MD, M Hoehn MD, J Menaker MD, D Stein MD, T Scalea MD, M Brenner MD

Maryland Committee on Trauma Paper Competition November 4, 2016, Baltimore, MD

10. Life Over Limb: Lower Extremity Ischemia in the Setting of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA)
    Authorship: Philip J. Wasicek MD, William Teeter MD MS, Shiming Yang PhD, Peter Hu PhD, Melanie Hoehn MD, Deborah Stein MD MPH, Thomas Scalea MD, Megan Brenner MD MS

12th Annual Academic Surgical Congress February 7-9, 2017, Las Vegas, NV

11. Virtual Reality Simulation for Endovascular Skills for Trauma: Final Results of a Trainee Experience
    Authorship: P. Wasicek, W. Teeter, M. Hoehn, J. Pasley, D. Stein, T. Scalea, M. Brenner

88th Annual Meeting Pacific Coast Surgical Association February 17-20, 2017, Indian Wells, CA

12. Resuscitative endovascular balloon occlusion of the aorta (REBOA) is a feasible option for proximal aortic control in severe hemorrhage and arrest.
    Authorship: Brenner M, Teeter W, Romagnoli A, Hoehn M, Stein D, Scalea T.

Southeastern Surgical Congress Annual Meeting, February 25-28, 2017, Nashville, TN

13. Virtual Reality Simulation (VRS): Bringing Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) Closer to the Point of Injury
    Authorship: JD Pasley DO, W Teeter MD, W Gamble MD, P Wasicek MD, A Romagnoli MD, A Pasley DO, M Brenner MD, T Scalea MD.

14. Life Over Limb: Lower Extremity Ischemia in the Setting of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA)
    Authorship: Philip J. Wasicek MD, William Teeter MD MS, Shiming Yang PhD, Peter Hu PhD, Melanie Hoehn MD, Deborah Stein MD MPH, Thomas Scalea MD, Megan Brenner MD MS

15. REBOA is feasible in patients at risk for age-related vascular disease
    Authorship: Bryan Gamble MD, Mira Ghneim MD, William Teeter MD, Deborah Stein MD MPH, Thomas Scalea MD, Megan Brenner MD MS

16. Too much of a good thing? Prolonged aortic occlusion is associated with decreased survival.
    Authorship: M Hoehn MD, D Stein MD, P Wasicek MD, W Teeter MD, A Romagnoli MD, P Hu PhD, T Scalea MD, M Brenner MD

Military Health System Research Symposium (MHSRS) Annual Meeting, August 27-30, 2017

17. Life Over Limb: Lower Extremity Ischemia in the Setting of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA)
    Authorship: Philip J. Wasicek MD, William Teeter MD MS, Shiming Yang PhD, Peter Hu PhD, Melanie Hoehn MD, Deborah Stein MD MPH, Thomas Scalea MD, Megan Brenner MD MS

Accepted to be presented at the American College of Surgeons 103rd Annual Clinical Congress, Scientific Forum, San Diego, CA, October 2017.

18. **Assessment of Blood Flow Patterns Distal to Aortic Occlusion (AO) Using Computed Tomography (CT) in Patients with Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA)**
    Authorship: Philip J Wasicek MD, Kathirkamanathan Shanmuganathan MBBS, William A Teeter MD MS, William B Gamble MD, Peter Hu PhD, Deborah M Stein MD MPH FACS, Thomas M Scalea MD FACS, Megan L Brenner MD MS FACS

Website(s) or other Internet site(s)

Nothing to report.

- ### Technologies or techniques

Nothing to report.

- ### Inventions, patent applications, and/or licenses

Nothing to report.

- ### Other Products

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

Organization: *University of Maryland, Baltimore – Shock Trauma & Anesthesiology Research Organized Research Center (STA-ORC)*

Name: *Megan Brenner*
Project Role: *PI*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *0.18*
Contribution to Project: *Supervise and contribute to study design, manuscript revision, and data analysis.*

Name: *Thomas Scalea*
Project Role: *PI*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.01994*
Contribution to Project: *Dr. Scalea met with all other PIs and Co-Investigators to discussed clinical research logistics, data management and results.*

Name: *Fu M. Hu*
Project Role: *Co-In*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.294*
Contribution to Project: *Integrating the data collection system for this study. He also works in the development and analysis of the continuous VS and in working with Dr. Brenner to design the join prediction models.*
Name: *Hegang Chen*
Project Role: *Statistician*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *0.05*
Contribution to Project: *The design, analysis and interpretation of the data.*

Name: *Jennifer Kidd*
Project Role: *Epidemiological Assistant I*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.55*
Contribution to Project: *Assist the project coordinator with patient identification, data abstraction, audit and collection, follow up and reporting.*

Name: *Raymond Fang*
Project Role: *Co-In*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.15*
Contribution to Project: *Provides experience as health care providers for military severe pelvic fracture and intra-abdominal hemorrhagic shock victims to maximize the military relevance of the results and their interpretation*

Name: *Catriona Miller*
Project Role: *Co-In*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.15*
Contribution to Project: Assists with the study design, study coordination and reporting, data collection, data storage, and data analysis.

Name: *Melanie Hoehn*
Project Role: *Co-Investigator*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *0.037*
Contribution to Project: *Supervise and contribute to study design, manuscript revision, and data analysis.*

Name: *Christine Wade **
Project Role: *Manager, Clinical Research*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *0.50*
Contribution to Project: *She is responsible for overseeing the 24/7 coverage for the CORE Research Group.*

Name: *Eric Lund*
Project Role: *It Appt Int Engineer*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *0.05*
Contribution to Project: He was responsible for overseeing the 24/7 basis obtain pre-hospital and admit data on every admit to the STC.

Name: *Shiming Yang*
Project Role: *Research Associate*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.60*
Contribution to Project: Working Dr. Hu in the *acquisition, integrating, testing, and maintaining the trauma training center VS data collection system.*

Name: *Hsiao-Chi Li*
Project Role: *Graduate Research Assistant*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *1.0*
Contribution to Project: Assisting Dr. Hu with development and analysis of the continuous VS and other project data analysis.

Name: *Umang Shah*
Project Role: *General Associate*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *0.15*
Contribution to Project: Research assistant who screens and obtains pre-hospital and admit data on admissions in STC.

Name: *George Hagegeorge*
Project Role: *IT Support Associate*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.60*
Contribution to Project: Assisting in the acquisition, integrating, testing and maintaining the trauma training center VS and video data.

Name: *Keven Barnes **
Project Role: *Assistant*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.20*
Contribution to Project: Assist the project coordinator with patient identification, data collection, follow up and reporting.

Name: *Diandra Browne*
Project Role: *Research coordinator*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.50*
Contribution to Project: IRB task management, IT design and assist with reporting.
.
Name: *Ryne C. Jenkins*
Project Role: *Assistant*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.20*
Contribution to Project: Assist the project coordinator with patient identification, data collection, follow up and reporting.

Name: *Rajan Patel*
Project Role: *Graduate Research Assistant*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *1.0*
Contribution to Project: To matching the patient vital signs with the REBOA procedure time and duration based on the video review. Assist in calculating the VS features for the study.

Name: *Ashley Hargrove **
Project Role: *Res Asst, Clinical*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.33*
Contribution to Project: Contribution to Project: Assist the project coordinator with patient identification, data collection, follow up and reporting.

Name: *Brandon Bonds **
Project Role: *Post-doc Fellow*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.25*
Contribution to Project: Assisting in the integration, testing, and maintaining the trauma training center VS data collection system.

Name: *Hannah Huber**
Project Role: *Res Asst, Clinical*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.55*
Contribution to Project: The coordination of activities between patient identification, data collection, follow up and reporting.

Name: *Seeta Kallam*
Project Role: *Res Project Coordinator*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.025*
Contribution to Project: IRB preparation, submission, maintenance, and compliance.

Name: *Anthony Herrera **
Project Role: *Res Acct, Clinical*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.025*
Contribution to Project: Assist the project coordinator with patient identification, data collection, follow up and reporting.

Organization: University of Maryland Medical Center
Name: *William Teeter*
Project Role: *Research Resident*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *2.25*
Contribution to Project: Data management and QA review related to simulator training and clinical performance of REBOA.

Organization: University of Maryland Medical Center
Name: *Philip Wasicek*
Project Role: *Research Resident*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *2.25*
Contribution to Project: Data management and QA review related to simulator training and clinical performance of REBOA.

* indicates team member were involved outside of the current year.

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

Nothing to Report

What other organizations were involved as partners?

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

REBOA for Severe Pelvic Fracture and Intra-abdominal Hemorrhagic Shock

Log No. 13057166
W81XWH-15-1-0025

PI: Megan Brenner M.D. **Org: University of Maryland, Baltimore Award Amount: $999,999**

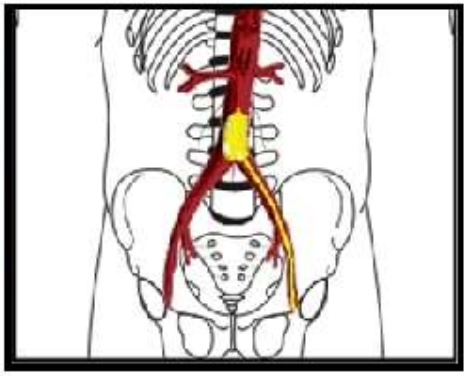
Problem: Pelvic fracture with shock represents a common form of non-compressible torso hemorrhage on the battlefield. Currently there are few rapidly deployable, hemorrhage control and resuscitative procedures for this complex injury pattern.

Military Relevance: Military research has identified high potential for Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) as a rapidly deployable adjunct to control hemorrhage and improve central aortic pressures in this setting.[1] Clinical study of REBOA for complex pelvic fracture and shock in the civilian setting has not been performed but stands to translate to military patterns of injury.

Hypothesis: Clinical use of REBOA with a commercially available balloon occlusion catheter can be and is safe and feasible using endovascular simulator to enhance skills and standardized operating procedures. Additionally application of REBOA results in reduced blood loss, improvement of central hemodynamics, fewer blood transfusion and less time to the operating room or Interventional angiography suite.

Approach/ Study Aim: Prospective observational trial of REBOA in level I civilian trauma center using commercially available devices

LR-RLBOA (Prytime Medical™)



[1]Morrison JJ, Percival TJ, Markov NP, Villamaria C, Spencer JR, Rasmussen TE. Aortic balloon occlusion is effective in controlling pelvic hemorrhage in porcine model. *J Surg Res* 2012; May 8

Timeline and Cost

Activities	CY 15	16	17
REBOA skills training standardization			
Standardize clinical performance of REBOA using simulator			
Prospective Enrollment			
Clinical data analysis and Interpretation			
Estimated Budget ($999,999)	**$544,233**	**$455,776**	

Updated: (Wasicek, Philip 11September17)

Goals/Milestones

CY15 Goal – System demonstration

- ☑ Standardized protocol for REBOA placement (1-2 m)
- ☑ VIST simulator training program curriculum (0-3 m)
- ☑ Enroll 30 subjects in simulator curriculum: COMPLETE
- ☑ Milestone: UMD and DOD IRB Approval (0-4 m)
- ☑ Retrospective Data Collection (**33 subjects** of 30 est. enrolled)
- ☑ Train clinical staff (3-12 M)
- ☑ Develop Study database (3-6 M)
- ☑ Prospectively enroll 24 patients (Complete)
  53 patients enrolled

Budget Expenditure to Date 08/31/17

Projected Expenditure:	$999,999
Actual Expenditure:	$999,999

9. APPENDICES:

Appendix A: Review of Educational Course and Simulator Based Learning Platform to Educate Physicians to Placed REBOA

Hypothesis 1:

A simulator based learning platform is effective to train physicians who are already skilled in vascular access procedures, to place REBOA.

Technical Objectives and Associated Specific Aims:

Standardized REBOA technique.

A standardized protocol for REBOA placement was established. The common femoral artery is accessed either directly via open cut-down or percutaneously using external landmarks only or using ultrasound guided placement. Once accessed, dilators are then utilized to upsize to the appropriate sized sheath (12 Fr sheath if using CODA® catheter (Cook Medical, Bloomington, IN), and 7 Fr sheath if using ER-REBOA™ (Prytime Medical, Boerne, TX)). Catheter insertion distance is then approximated using external morphometric landmarks. The catheter system (including wire for CODA® catheter) is then inserted to the appropriate distance. Radiographic confirmation of catheter placement is suggested prior to balloon inflation (although blind balloon inflation has been performed without complication during this study). The balloon should then be inflated and additional radiographic confirmation should be obtained. Standardized clinical performance of REBOA on the VIST Mentice simulator, as well as formal clinical standard operating procedure was created (see figure 1).

Development and Analysis of VIST Simulator Training Program by Knowledge Acquisition related to the REBOA Procedure and Performance on the VIST Simulator.

A VIST simulator training program with powerpoint lectures and hands-on training was established. A description of the indications for REBOA is given, as well as a detailed description of step-by-step method of performing REBOA. After the lecture, participants were then trained and allowed to practice the individual steps of performing REBOA on a VIST Mentice simulator (Mentice, Gothenberg, Sweden). A preliminary analysis of physician knowledge related to REBOA before and after didactic and simulator sessions was performed. 43 physicians participated in the pre- and post-test analysis. Physicians had a mean improvement of 2.7±1.6 questions (19±11%) correct in the post-test course (out of 14 questions). As seen in Figure 2-4, Most physicians had an improvement with the post-test score, and none had a decrease in their score (as seen in Figures 1 and 2, demonstrated distribution of differences in pre-and post-tests and their paired profiles. No physicians changed their answers from a correct answer on the pre-test to an incorrect answer on the post-test as seen in by an analysis of agreement between tests in Figure 4.

Figure 1: Clinical Standard Operating Procedure

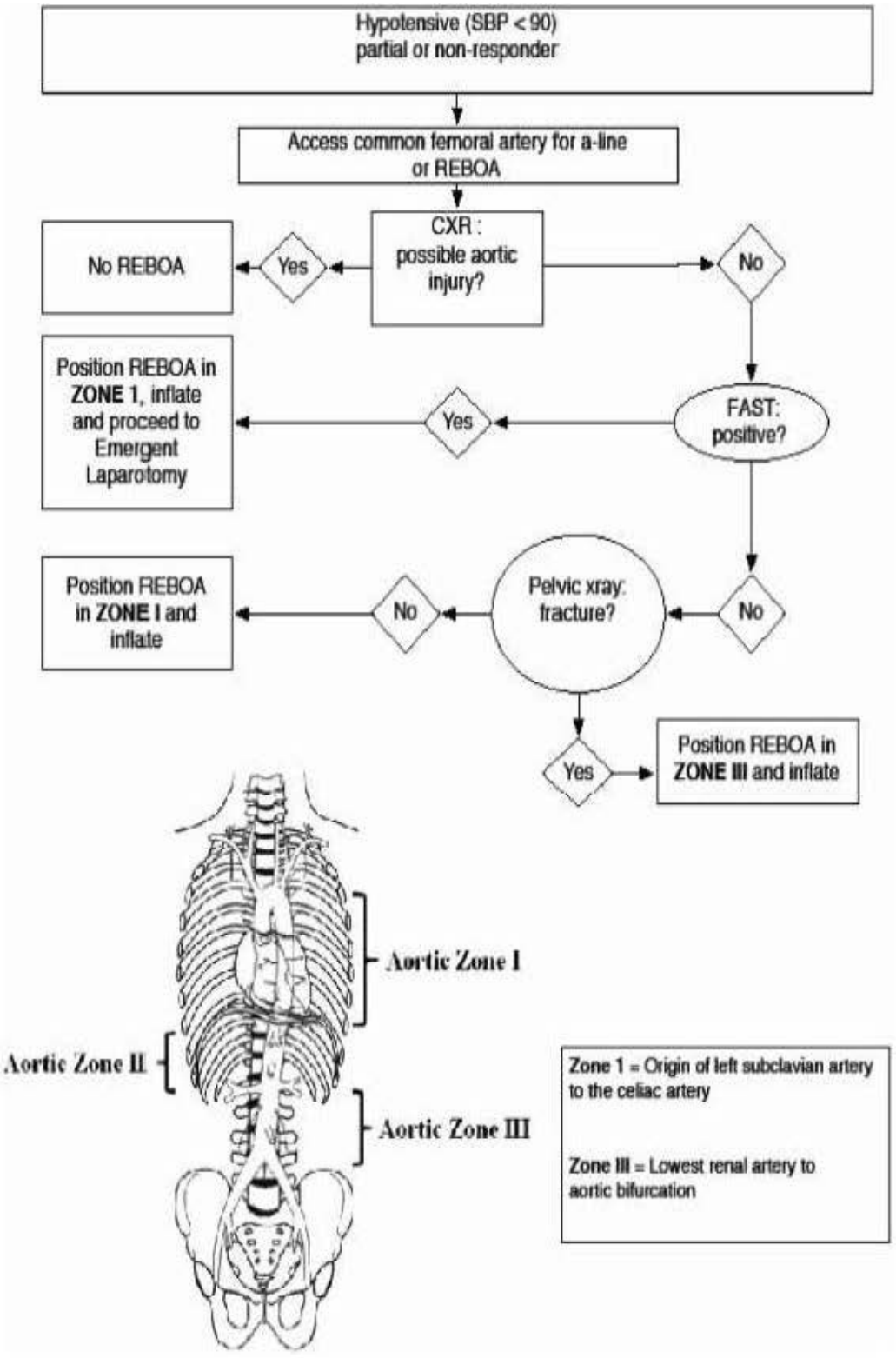


Figure 2: Improvement in Knowledge by Pre- and Post-Test Analysis, Distribution of Difference between Post-Test and Pre-Test

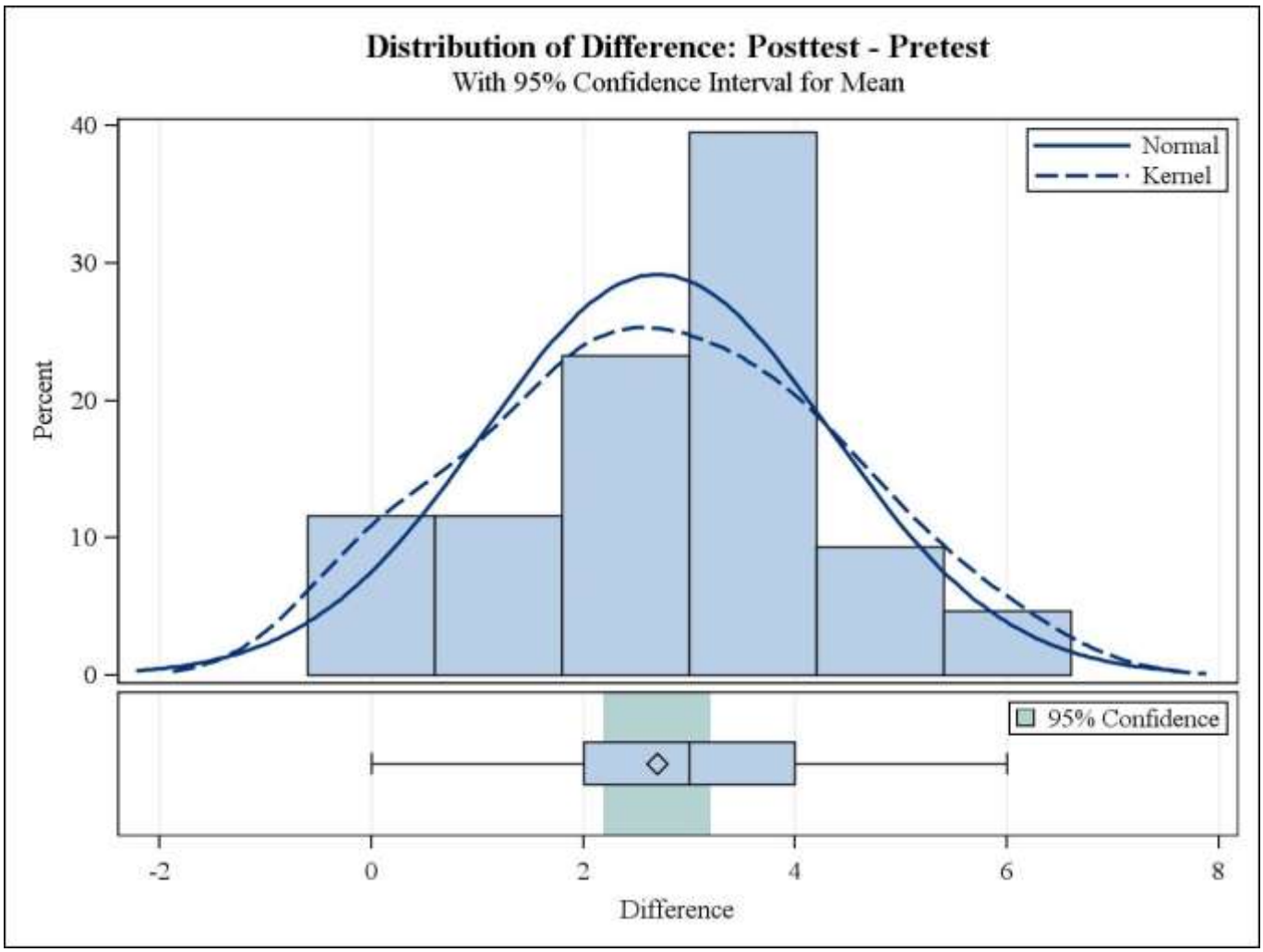


Figure 3: Paired Profiles of Post-Test and Pre-Test Performance and Improvement in Knowledge

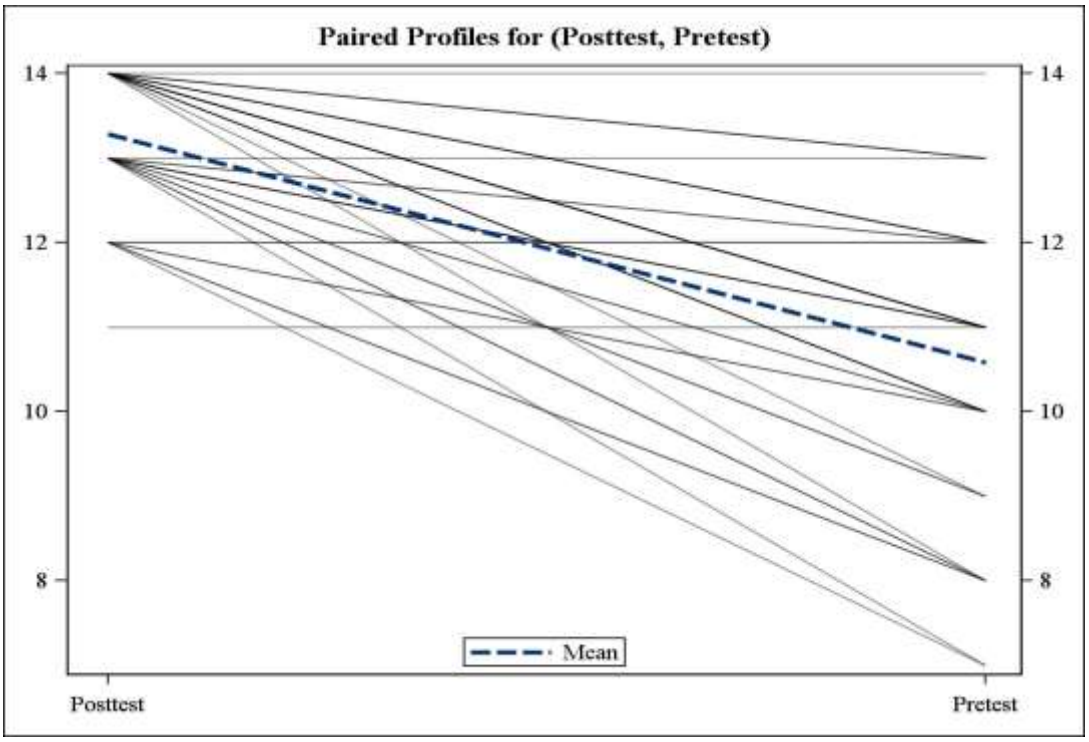
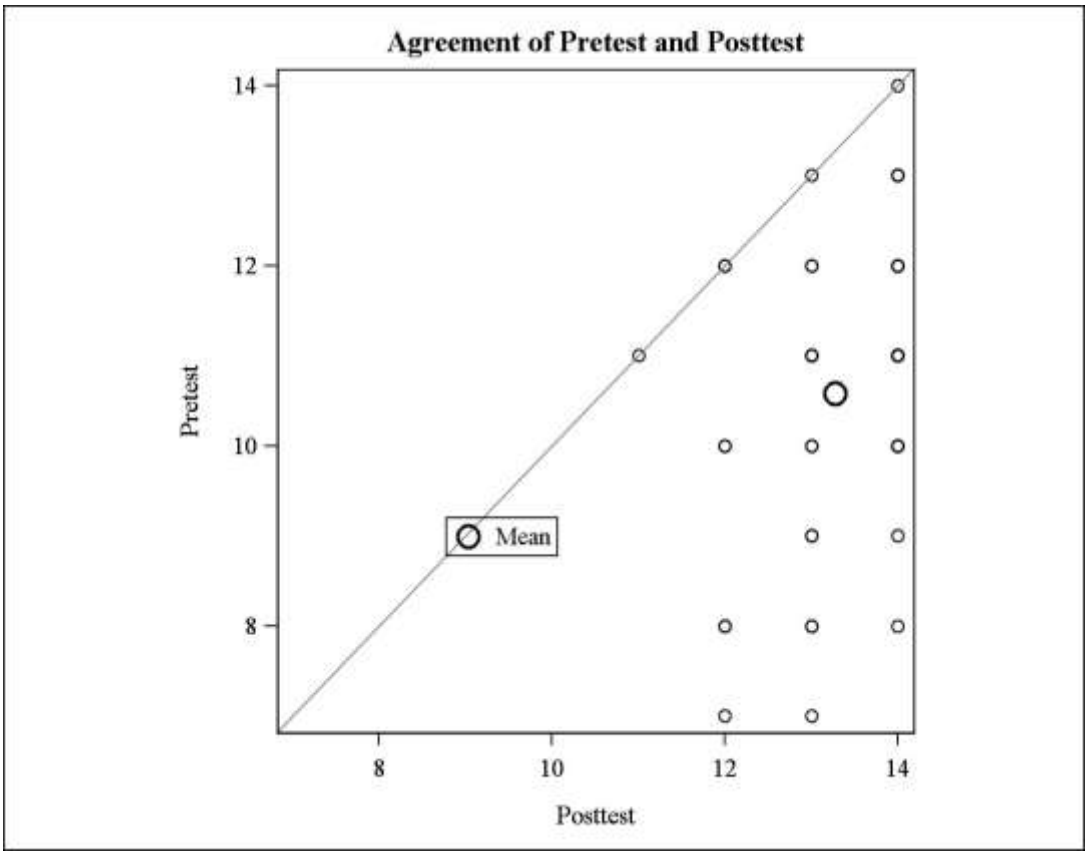


Figure 4: Analysis of Agreement of Pre-test and Post-test Answers



Using a VIST-Mentice® (Mentice, Gothenberg, Sweden) endovascular simulator, physicians were asked to perform REBOA. This simulator consists of a personal computer-based software coupled with a haptics unit through which devices are inserted and manipulated. Of note, this virtual reality simulator has vital sign monitoring that is responsive to complete aortic occlusion, as well as simulation of radiographic imaging. The simulator also provides tactile feedback with balloon inflation by simulating the pressure required to inflate the balloon. The procedure involved starting with arterial access already obtained with a 5 French arterial line in place and required the participants to upsize arterial access to the appropriately sized 12 French arterial sheath. Next, a wire is positioned at the appropriate distance using external morphometric landmarks of the simulator. Radiologic confirmation is obtained between each step. A CODA catheter is then inserted and the balloon inflated to achieve aortic occlusion. During the procedure, evaluators did not provide assistance for tool selection, suggesting steps for task progression, or assisting with procedural tasks. Each physician performed this task six times. Participants improved the time to perform the task from the first attempt to the sixth attempt a mean of 120±36 seconds. The distribution of improvement can be seen in Figure 5. An examination of paired profiles (Figure 6), agreement (Figure 7), and q-q plot (Figure 8) demonstrate that all participants improved their times from the first attempt to the last (sixth) attempt.

Figure 5: Distribution of Difference Between First and Sixth Attempt

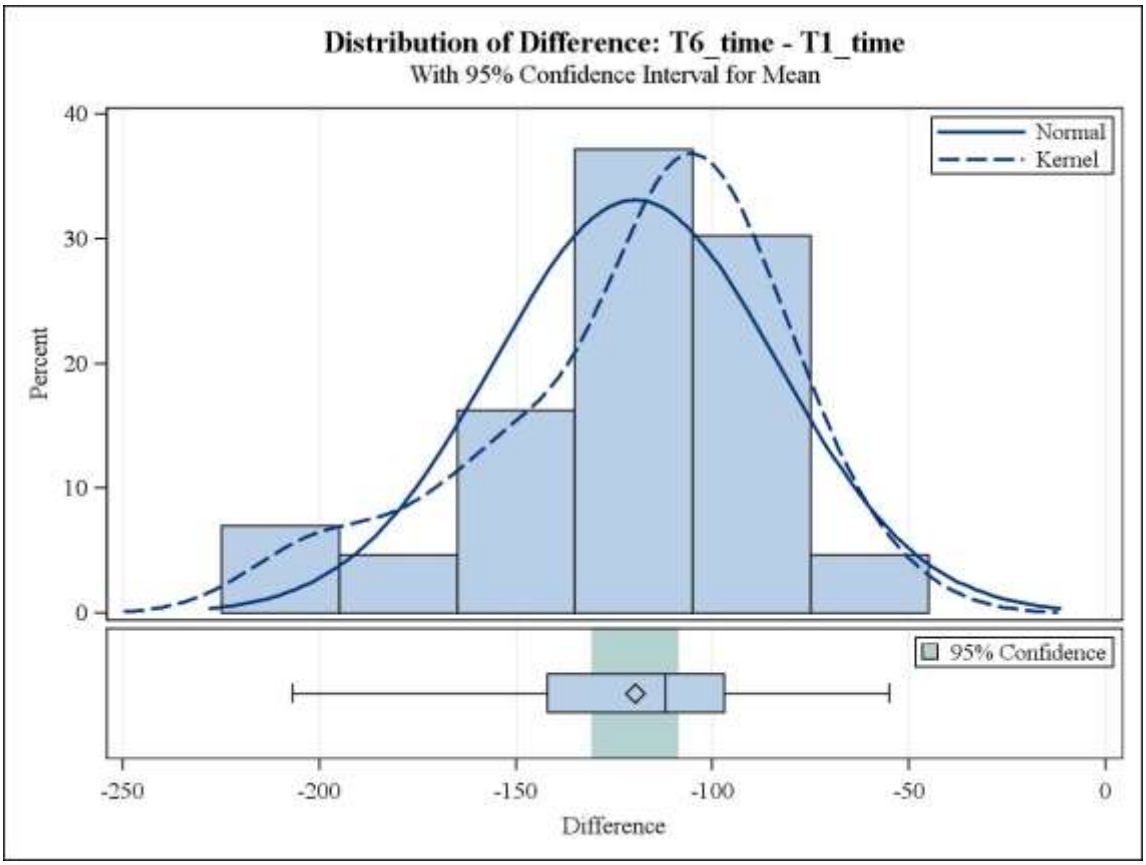


Figure 6: Paired Analyses of Improvement Between First and Sixth Attempt

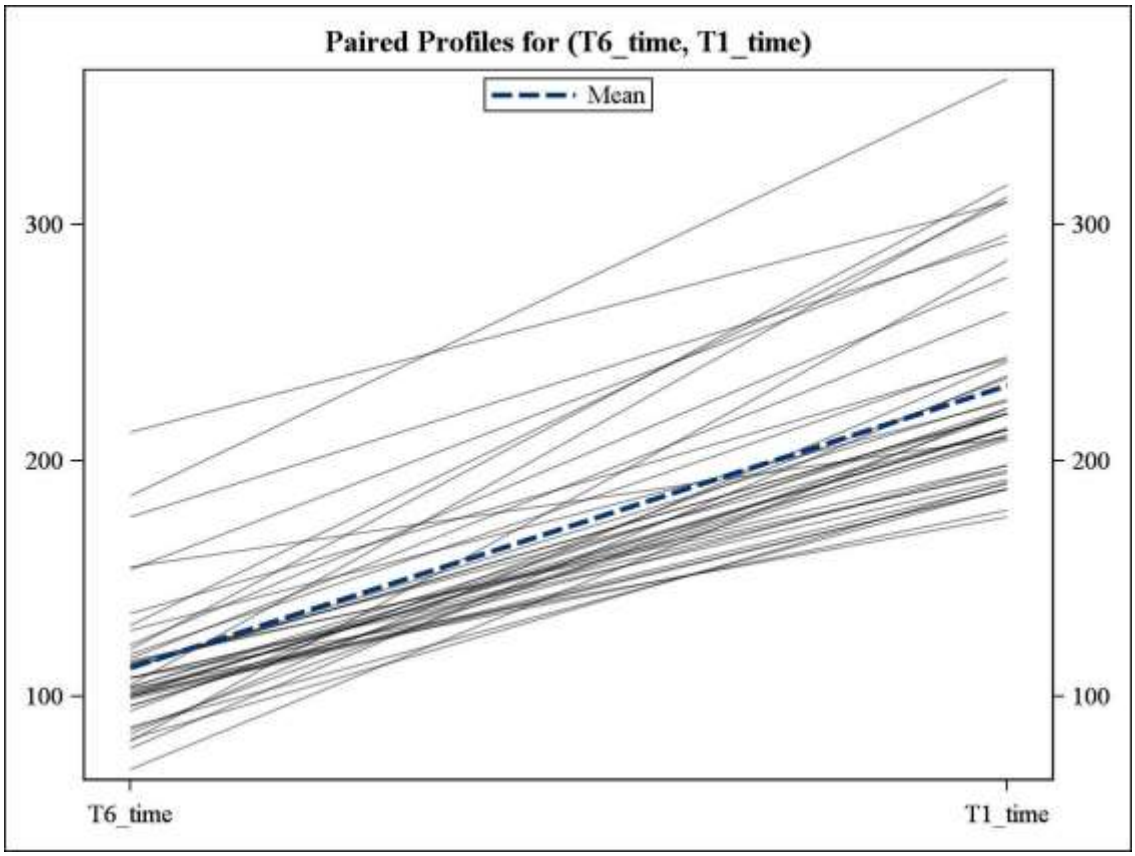


Figure 7: Agreement Plot of Improvement from First to Sixth Attempt

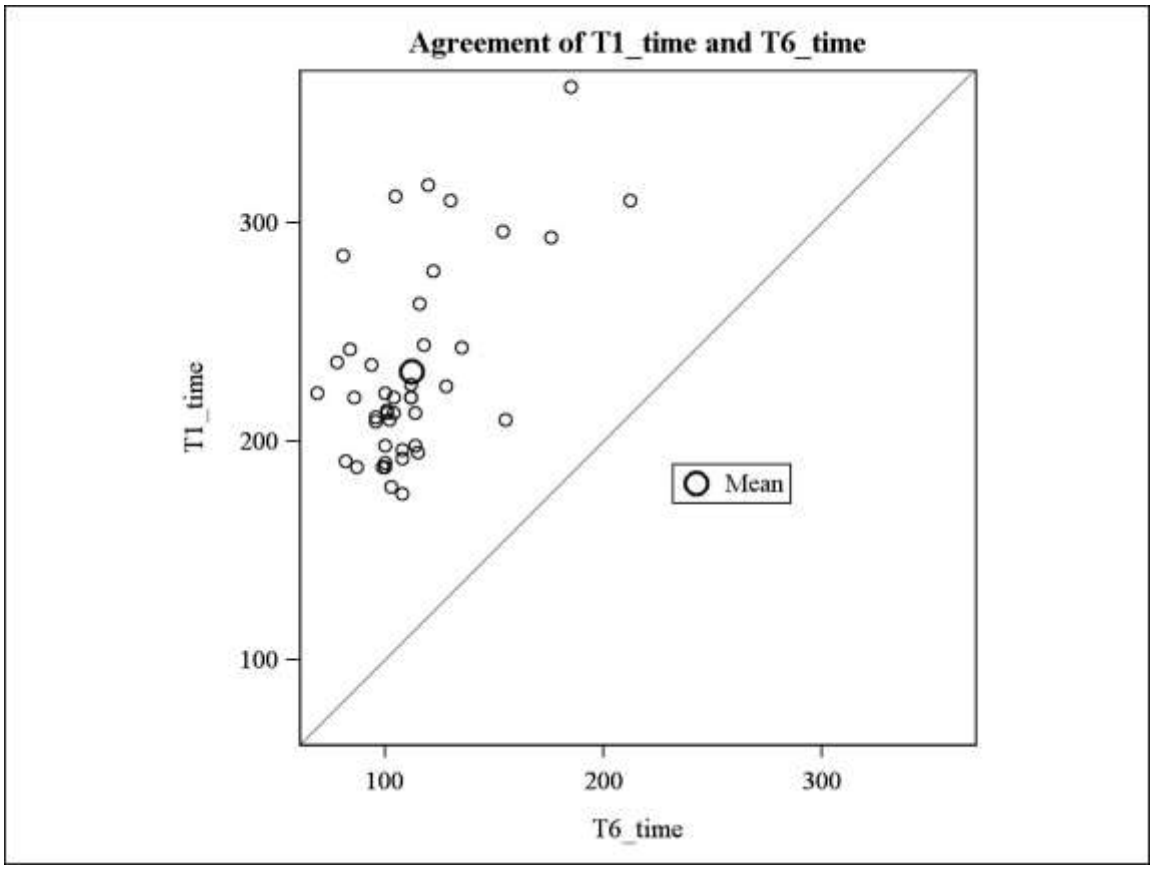
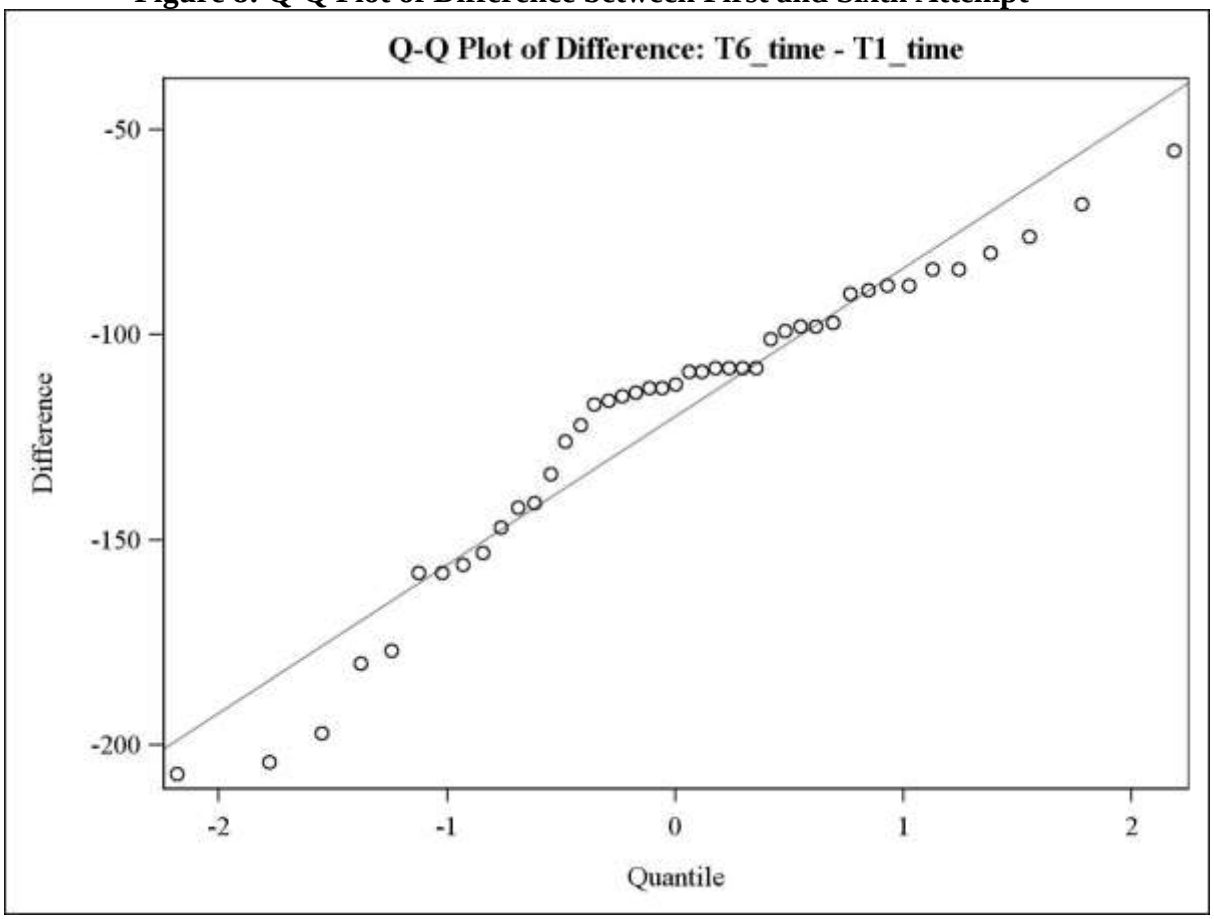


Figure 8: Q-Q Plot of Difference between First and Sixth Attempt



A validated REBOA placement training program.

An abstract of the findings was written and presented at the Annual Meeting of American College of Surgeons, October 16-20, 2016, and was presented at the World Congress of Trauma in Basil, Switzerland in 8/2017. A manuscript is currently in process.

RESUSCITATIVE ENDOVASCULAR BALLOON OCCLUSION OF THE AORTA (REBOA) CAN BE DEPLOYED RAPIDLY AND SAFELY BY ACUTE CARE SURGEONS

DAVID HAMPTON MD, MENG, WILLIAM TEETER MD, GEORGE HAGEGEORGE, MELANIE HOEHN MD, DEBORAH STEIN MD, MPH, THOMAS SCALEA MD, MEGAN BRENNER MD, MS

Introduction: REBOA is an emergent procedure requiring endovascular skills. We hypothesized there was no difference in REBOA deployment times or complications between acute care surgeons (ACS) trained in endovascular procedures during residency (ACS-EP) and those who did not (ACS-NEP), and ACS virtual reality simulation (VRS) and clinical procedural times did not differ.

Methods: Patient demographics, vital signs, and trauma statistics were obtained. ACS professional training and surgical case history were documented. All ACS completed a 1-day REBOA VRS course. The procedural time was defined as the interval from common femoral arterial access to balloon inflation. Published VRS results were compared to clinical performance. Intra-group ACS and patient comparisons were made using chi squared and student t-tests. Significance was $p < 0.05$.

Results: Twenty-eight REBOAs were performed: ACS-EP (n=11) vs. ACS-NEP (n=17). There was no difference in admission SBP, HR, ISS, or BMI between patients treated by either group. There was no difference in intra-group procedure times (ACS-EP: 303 seconds (SD:±100) and ACS-NEP: 315 seconds (SD:±105), p=0.46). There was no difference in ACS REBOA procedure times as compared to VRS training (ACS: 310 seconds (SD:±102) versus VRS: 277 seconds (SD:±55), p=0.18). There were no REBOA-related complications. Sixty-eight percent of patients arrived in arrest, and 30-day survival was 11%.

Conclusion: There was no difference in REBOA deployment times or complications between the two groups. ACS-NEPs can perform REBOA rapidly and safely after completion of a 1-day VRS course. This is the first study to validate transfer of skills from VRS to clinical performance of REBOA.

Appendix B: Clinical Summary and Review of Data Capture Process: Continuous Vital Signs (VS) and Videography

Hypothesis 2:

Use of resuscitative endovascular balloon occlusion of the aorta (REBOA) in cases of non-compressible torso hemorrhage (NCTH) of the abdomen and pelvis will decrease the morbidity and mortality associated with this often fatal pattern of injury with improved physiological parameters, outcomes, and recovery periods and will allow time for vascular repair.

Technical Objectives and Associated Specific Aims:

1.) Evaluate the ability of REBOA to improve survival and functional outcomes in patients with NCTH. Analysis of continuously recorded vital sign data will show that the use of REBOA will improve physiologic parameters in patients with NCTH.

Descriptive Characteristics of Population

		n	Mean ± SD
Total Patients		86	
Race	Black	45	
	White	38	
	Asian	1	
	Hispanic	2	
Gender	Male	72	
	Female	14	
Mechanism	Penetrating	29	
	Blunt	57	
Zone 1		69	
Zone 3		17	
ISS			37 ± 15
GCS			6 ± 5
SBP on Admission (for those not in Cardiac Arrest)			111 ± 37
HR on Admission (for those not in Cardiac Arrest)			112 ± 30

	n	Mortality (%)
Patients with No CPR	28	36%
Patients with CPR before Aortic Occlusion (AO) only	13	69%
Patients with CPR at time of AO	7	86%
Patients with CPR including after AO	14	93%
Patients with CPR without ROSC	24	100%

Brief Clinical Summary

During the study period, 86 patients had REBOA for severe non-compressible hemorrhage and traumatic arrest. Mean age was 40±18 years. Mean admission GCS was 6±5 and mean ISS 37±15. Mean admission SBP and HR was 111±37 and 112±30, respectively for those patients with vital signs. The distal thoracic aorta (Zone 1) was occluded in 80% of patients and 20% had distal abdominal aortic occlusion (Zone 3). Mean time to aortic occlusion (including cannulation—after delay correction) was 511±264s and femoral artery cannulation was 309±314s. Percutaneous access was used in 43%, and groin cutdown used in 57%, including 74% of those in arrest. Overall mortality was 72%, which included 36% for hemorrhage patients, 69% in patients who had cardiac arrest and CPR performed before aortic occlusion (AO), 86% in patients who had cardiac arrest and CPR at time of AO (and may have had CPR before AO), 93% in patients who were in cardiac arrest and CPR performed after AO (and may have had CPR before and/or at time of AO), and 100% in patients who were in cardiac arrest and never had return of spontaneous circulation (ROSC). Of the patients in cardiac arrest, 48% were resuscitated and went to the operating room. Four patients had femoral arterial shunts placed three with 12 Fr sheath, one with 7 Fr sheath) with one patient surviving to definitive repair (requiring femoral bifurcation reconstruction). Two femoral arteries required repair with patch angioplasty (both with 12 Fr sheaths). Three balloon ruptures occurred without sequelae after REBOA use. One patient developed mesenteric ischemia that was directly attributed to prolonged aortic occlusion time (209 minutes). No aortoiliac injury occurred from REBOA use.

Real-time Continuous Vital Signs and video recording and archiving system

The need to adequately interpret vitals trends and subsequently respond rapidly to patient physiology and resuscitative needs is particularly paramount following trauma. Large quantities of real-time patient monitoring data are now available through hospital vital signs monitoring systems, yet vital signs are typically recorded manually periodically by clinical staff. Non-invasive continuous vital signs monitoring provides accurate real-time displays of continuous hemodynamic and perfusion data and trends that might provide for early detection of circulatory deficits that can contribute to both significant organ dysfunction and death. Continuous monitoring may both allow early recognition of pathologic processes which require intervention and may give clinicians feedback on the pathophysiological processes present in the patient before and after intervention.

Our goal is to apply this sophisticated data collection tool in order to provide real time data regarding the physiologic consequences of REBOA. By capturing heart rate, heart rate variability, pulse oximetry, temperature, end tidal CO2, respiratory rate, and systolic blood pressure and MAP (if arterial line present) on REBOA patients, we will be able to quantify the physiologic changes associated with REBOA in a linear fashion as they relate to time and length of balloon occlusion rate, and systolic blood pressure and MAP (if arterial line present).

Theoretically, the continuous monitoring of patient vital signs during balloon inflation should allow for assessment of time to hemodynamic stability, the degree of stability, and what happens to the patient physiologically when the balloon is deflated. Such detailed data will allow us to fine tune and perfect our technique. In addition to the real time, time stamped continuous vital signs data, all trauma bays and operating rooms at STC are recorded by video cameras from multiple angles, which gives us the ability to thoroughly document the exact time course of resuscitation efforts.

Continuous vital signs collection:

Real-time patient VS data feed is collected (Bed Master) every 2 seconds and recorded for future analysis. Raw real-time VS waveforms, trends, and alarms are compressed more than 90%, transferred to a centralized VSDR server through the secure hospital intranet, and stored securely for linkage with demographic, injury-specific clinical, imaging, and general laboratory data for subsequent analysis. VSDR collects over 80 VS variables from conventional vital signs and physiologic parameters—SpO2, etc., shock index (systolic blood pressure divided by heart rate), continuous electrocardiogram, oxygen saturation, and end-tidal carbon dioxide waveforms at 240 Hz. The numerical values of heart rate, blood pressure, intracranial pressure, cerebral perfusion pressure, respiratory rate, and temperature, are recorded every 2 seconds. Data rates after compression averaged 76.4 KB/h for numerical and 12.3MB/h for waveforms. The VSDR server is interfaced with the Shock Trauma Research Registry, which provides patient demographic,

admission assessment, laboratory, and outcome data. Custom processing and viewing programs, previously developed by our team, are used for real-time patient data abstraction, artifact removal, 5- to 60-minute time-window averaging, VS variability, and summary data output to both computer automatic processing and human reviewing.

The use of continuous data collection allows linear, episodic data to be converted to 2-dimentional analysis. Our goal is to apply this sophisticated data collection tool in order to provide data regarding the physiologic consequences of REBOA. By capturing heart rate, heart rate variability, pulse oximetry, temperature, end tidal CO2, respiratory rate, and systolic blood pressure and MAP (if arterial line present) on REBOA patients, we will be able to quantify the physiologic changes associated with REBOA in a linear fashion as they relate to time and length of balloon occlusion. The work proposed here will be based on mean and standard deviations of the every-6-second raw data over the course of the balloon inflation. We will calculate the dose of time spent above and below certain vital sign thresholds or cut offs and record the minimum and maximal values. Vital signs before, during, and after REBOA placement will be assessed and compared. The stability of vital signs readings during REBOA placement will be compared to patient outcomes.

Triple redundant VS collection system and real-time Monitor of monitors for ensuring reliable data collection

In order to capture all the unscheduled and emergency REBOA cases, it is critical to develop a real-time patient vital signs collection network which will **capture all patient VS at anytime, anywhere** (13 TRU and 10 ORs).

STC has implemented a single VS collection server-based VSDR system in the past 10 years. The effective real-time data collection rate is between 60% to 80% for all 13 TRU and 10 ORs. The missing VS data collection was mainly due to hardware and software failure and no real-time notification of collection failure and user errors.

To ensure anytime, anywhere reliability (>99% collection rate) of real-time VS data collection, we designed and implemented a **triple redundant VS** collection system and real-time **Monitor of monitors (MoMs)** for live VS collection status notification.

Fig. 9 illustrates the triple redundant VSDR and MoMs system architecture.

BM1, 2, 3 are the VS trend data collection server and BMA,B,C are the waveform (240Hz) and alarm status collection server. All triple-redundant data servers including 3 vital signs trend data collectors (blue dots in Fig 9) and 3 waveform collectors (green dots in Fig 9), send the latest data with timestamps to the MoMs Sever. Fig. 10 shows a snippet of the MoMs system. Each data server is represented by a large block (Fig 10). Each bed unit collected by such server is represented by a colored small box. If a bed unit is online in the last 5 minutes, the box shows in green, with the admission status (admitted or discharged) and the last heart rate value. If a bed unit is offline for longer than 5 minutes, the box is colored as yellow. It turns red, if the bed unit has been offline longer than 6 hours.

Vital signs data of each one minute median are submitted to three independent MoMs servers (red dots). The MoMs server processes the data and provides the patient VS data collection status in real-time to any remote MoM viewer inside the hospital intranet (for security purposes).

With the implementations of the above system we have been able to improve our data collection rate to >99% for all patient beds.

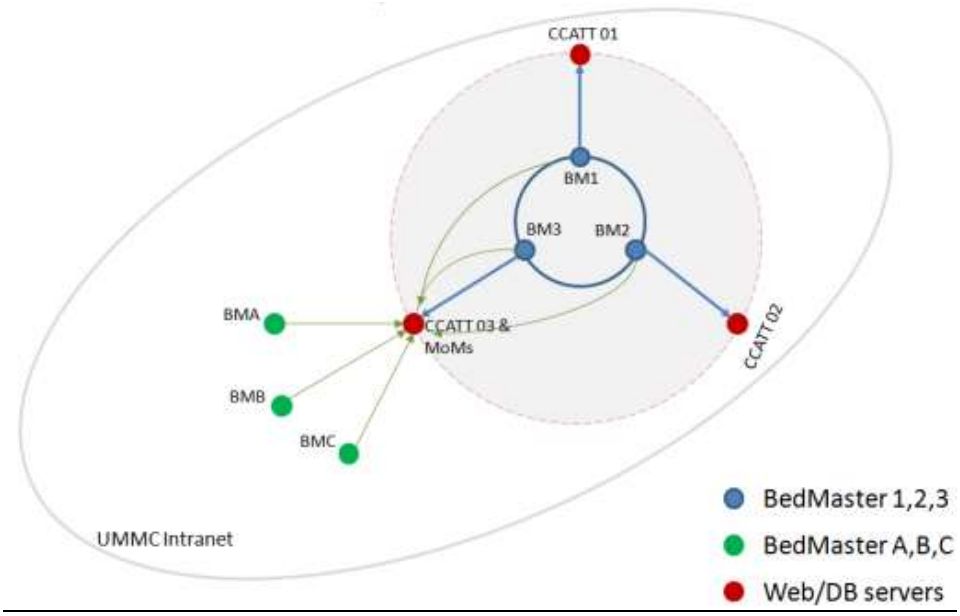


Fig. 9 Illustration of VSDR and MoMs system architecture

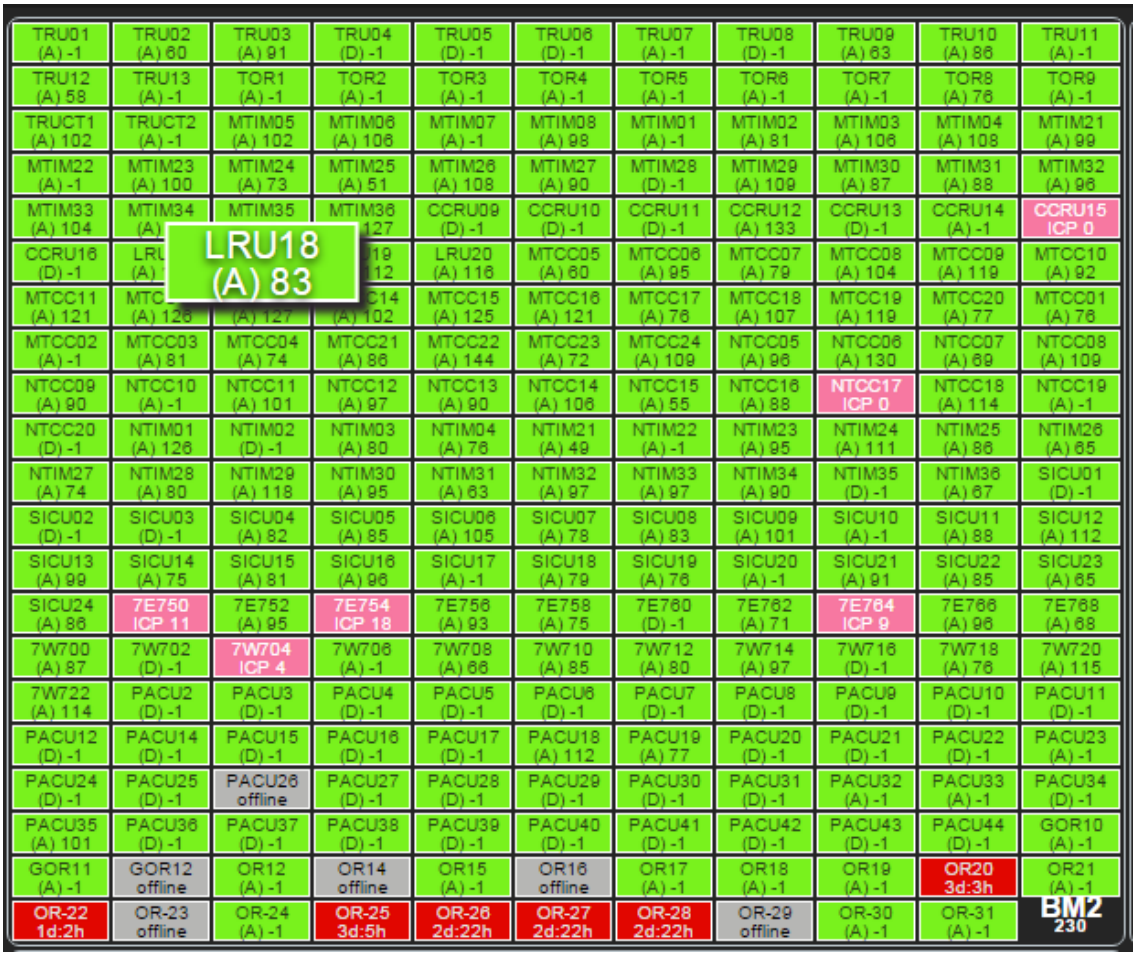


Fig. 10 A snippet of MoMs system of 230 bed units in one data server

Vital Signs data abstraction software.

The Vital Signs data abstraction software was developed to accurately match the vital signs for feature abstraction and statistical analysis. Based on the REBOA patient admission and insertion time (abstracted from videography), we are able to match vital signs data to REBOA performance metrics and aortic occlusion time with high accuracy.

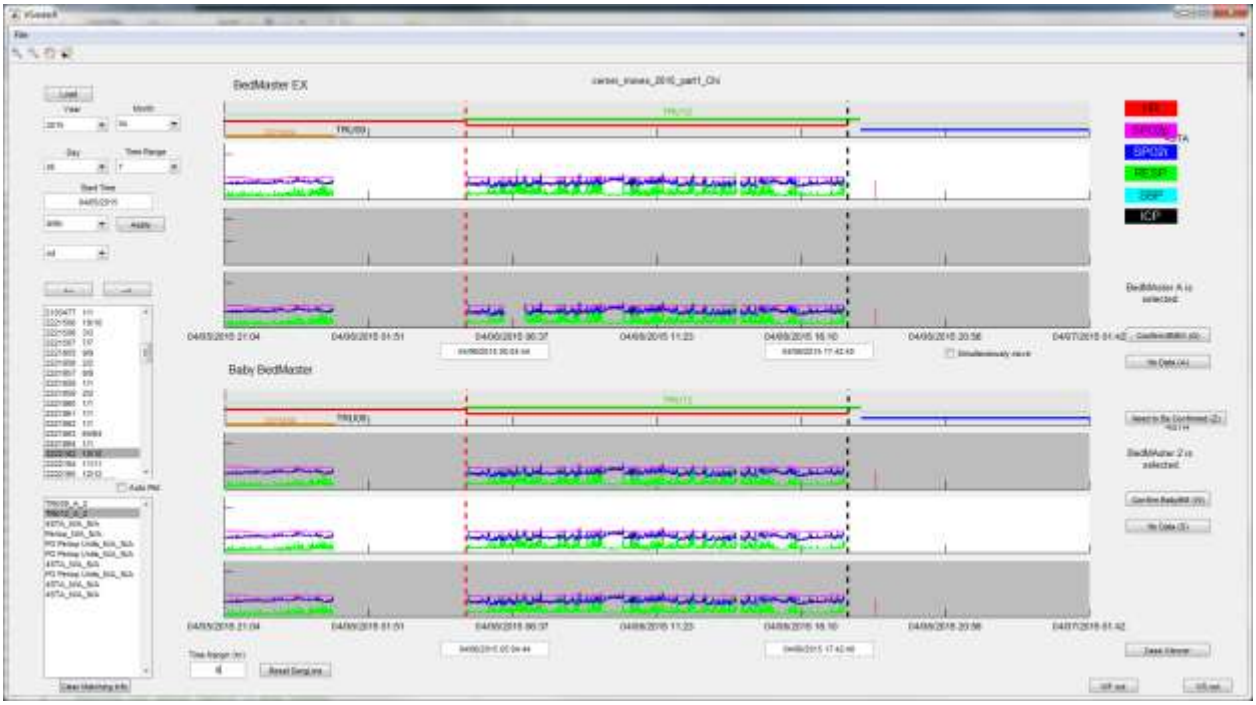


Figure 11. Vital Sign Matching Software

REBOA Vital Signs Viewer

The REBOA Vital Signs Viewer was developed to provide the detailed evaluation of the physiological changes pre and post REBOA procedure (Figure 12).

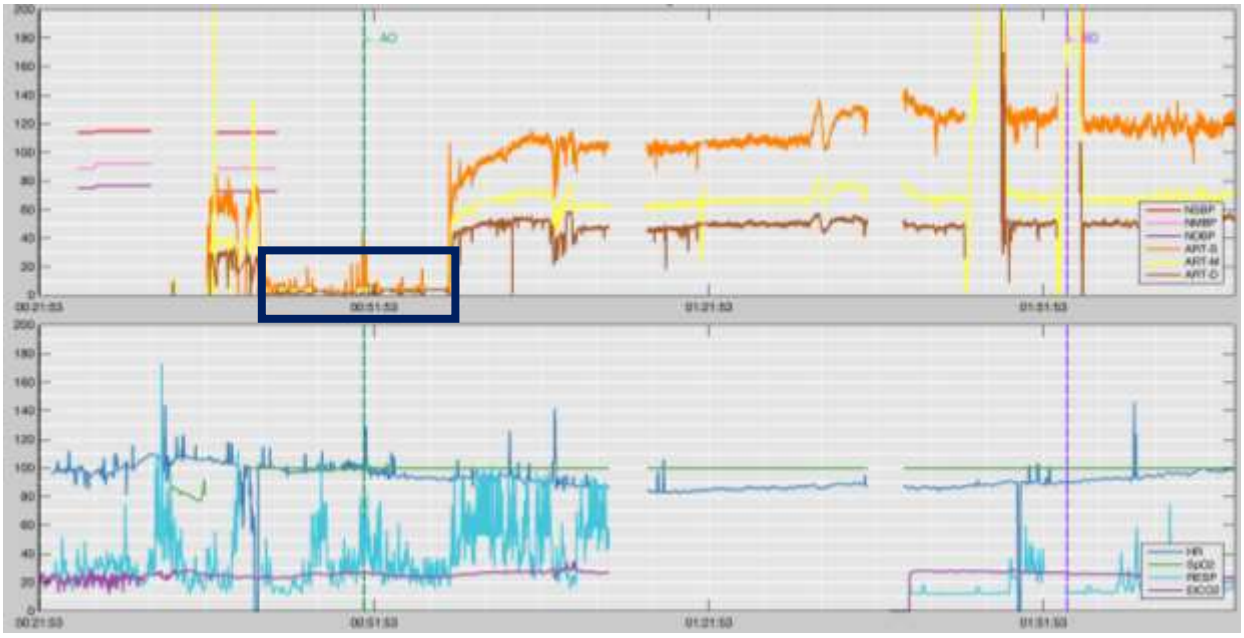


Figure 12. REBOA case viewer with example case with REBOA performed (AO-Aortic Occlusion (green dashed line), BD-Balloon Deflation (purple dashed line))

Vital Signs Data Processing

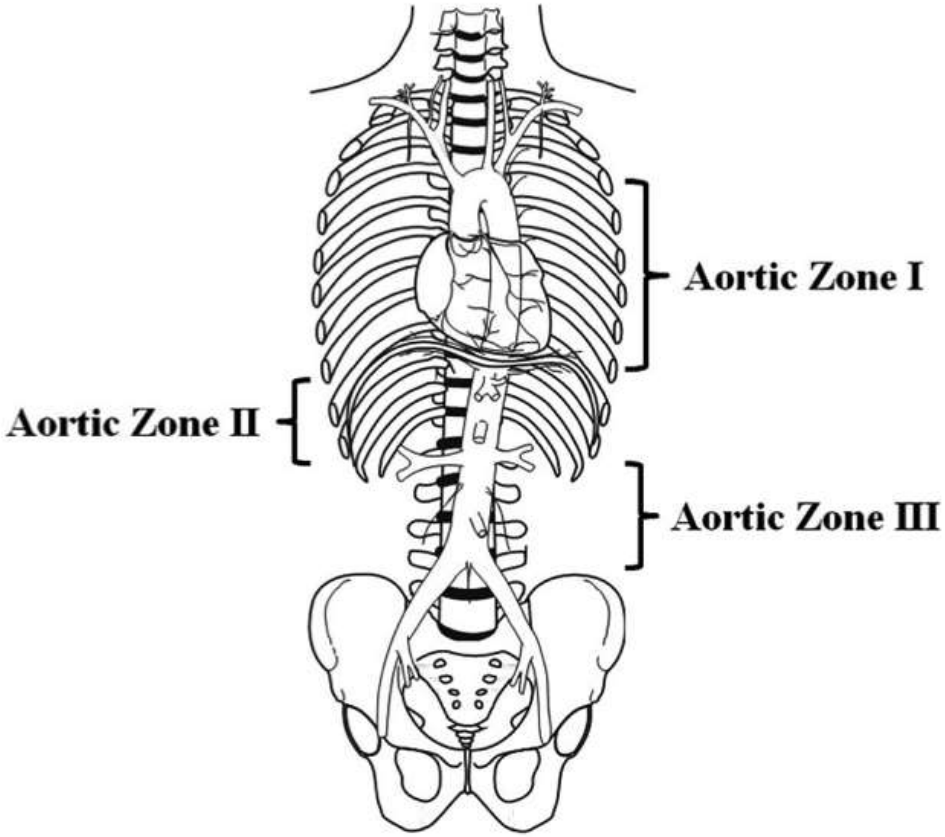
During analysis and interpretation of hemodynamic data, it was noted that there was raw data abstracted from continuous vital sign recording that did not represent physiologic data from the patient. An example of this included recording and continued data capture of arterial line tracing while the arterial line was disconnected from the patient and was being upsized for sheath insertion prior to REBOA deployment (this is represented by the black box in Figure 12 around time of AO-aortic occlusion). An additional example of inaccurate data included artifact/interference created by cardio-pulmonary resuscitation and chest compressions on heart rate recording. Cases were reviewed by a clinician and data was compared to the medical record and available videography. A clinician then determined and annotated what data should be excluded, when CPR was being performed, and which form of blood pressure measurement (non-invasive cuff or arterial line) should be used at specific time points for data analysis.

VS feature abstraction and statistical analysis.

A total 62 cases are included in the current analysis out of 86 enrolled. Patients who arrived to the hospital in cardiac arrest and never had return of spontaneous circulation were excluded (24 cases). Continuous vital signs with 0.5 Hz sample rate were collected for REBOA cases. Given recorded and videography-verified aortic occlusion time, the mean of the systolic blood pressure and heart rate for 10 minute blocks were taken before (up to 30 minutes pre-AO), and after (up to 120 minutes after AO). When continuous vital sign monitoring data was absent, vital sign data from the medical chart and anesthesia records was included; however, there were periods of time in which there were no recorded vital signs (such as during travel from the resuscitation bay to the operating room) and periods of time where there were no blood pressure recordings but other hemodynamic data was recorded (e.g. heart rate). For patients who had the

location of their AO changed (from zone 1(supra-celiac) to zone 3 (infra-renal) or vice versa), the time was noted and additional analysis of hemodynamics past the initial AO location change were not included in the analysis. Blood pressure measurements during CPR were excluded. Based on the location of REBOA inflation (Zone 1 is at the diaphragm and Zone 3 just proximal to the iliac bifurcation **[See illustration below])** and presence vs absence of pulse on arrival to the TRU, the study cases are grouped into eight categories:

1. Zone 1 group 1 are patients with REBOA performed in Zone 1 without CPR (N=18).
2. Zone 1 group 2 are patients with REBOA performed in Zone 1 with CPR before AO (N=11).
3. Zone 1 group 3 are patients with REBOA performed in Zone 1 with CPR around the time of AO. (N=6).
4. Zone 1 group 4 are patients with REBOA performed in Zone 1 with CPR after AO (N=11).
5. Zone 3 group 1 are patients with REBOA performed in Zone 3 without CPR (N=10).
6. Zone 3 group 2 are patients with REBOA performed in Zone 3 with CPR before AO (N=2).
7. Zone 3 group 3 are patients with REBOA performed in Zone 3 with CPR around the time of AO. (N=1).
8. Zone 3 group 4 are patients with REBOA performed in Zone 3 with CPR after AO (N=3).



We analyzed the median systolic blood pressure and heart rate values of 10 minute blocks up to 30 minutes prior to aortic occlusion and throughout aortic occlusion. We then aggregated these values for each time point and reported them as a box plot (with mean, IQR, and 2^{nd} and 98^{th} percentiles) as a composite of the entire group. Data was not available for all cases within each time point, so the number of cases analyzed is reported underneath each box plot. In addition, aortic occlusion times varied, so the number of cases available to analyze decreased with increasing time after aortic occlusion.

For zone 1: within group 1, the mean aggregated blood pressure increased after aortic occlusion for up to 30 minutes after aortic occlusion, and then slowly decreased, but did not reach pre-AO levels by 120 minutes post-aortic occlusion (Figure 13). In addition, heart rate initially decreased, but then gradually increased (Figure 14). Within group 2, the mean blood pressure increased after aortic occlusion (Figure 15), and the heart rate stayed relatively elevated immediately after aortic occlusion before decreasing at 20-40 minutes after AO (Figure 16). Group 3 (Figure 17 and 18) and group 4 (Figure 19 and 20) displayed similar trends, with an increase in blood pressure after aortic occlusion and an increase initially in heart rate after aortic occlusion.

For zone 3: within group 1, the mean aggregated blood pressure increased after aortic occlusion and then stays relatively stable, without a large amount of variation (Figure 21). Similarly, heart rate decreases after aortic occlusion and remains relatively stable (Figure 22). Groups 2 and 4 (Figures 23 and 24, and Figures 27 and 28, respectively) only had a few patients per group, but show an initial increase in blood pressure and minimal change in heart rate after AO. Group 3 contained only 1 patient, so the individual case was presented, instead of an aggregate of patients. The case in group 3 (Figures 25 and 26) shows a decline in heart rate; and after return of spontaneous circulation after AO, the patient was severely hypotensive for the majority of time.

Figure 13: Zone 1 Group 1 Systolic Blood Pressure Aggregate of Mean 10-Minute Intervals

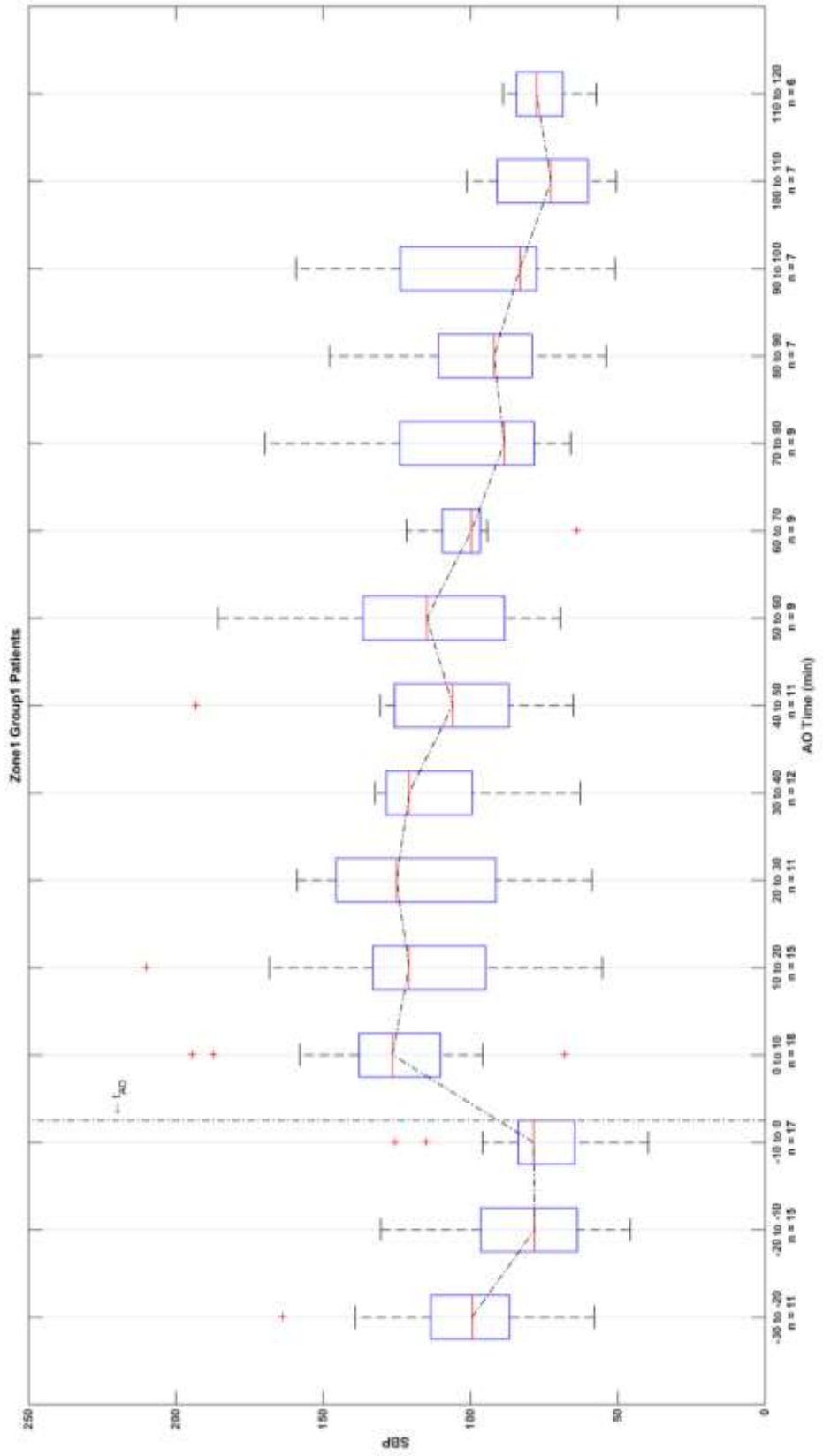


Figure 14: Zone 1 Group 1 Heart Rate Aggregate of Mean 10-Minute Intervals

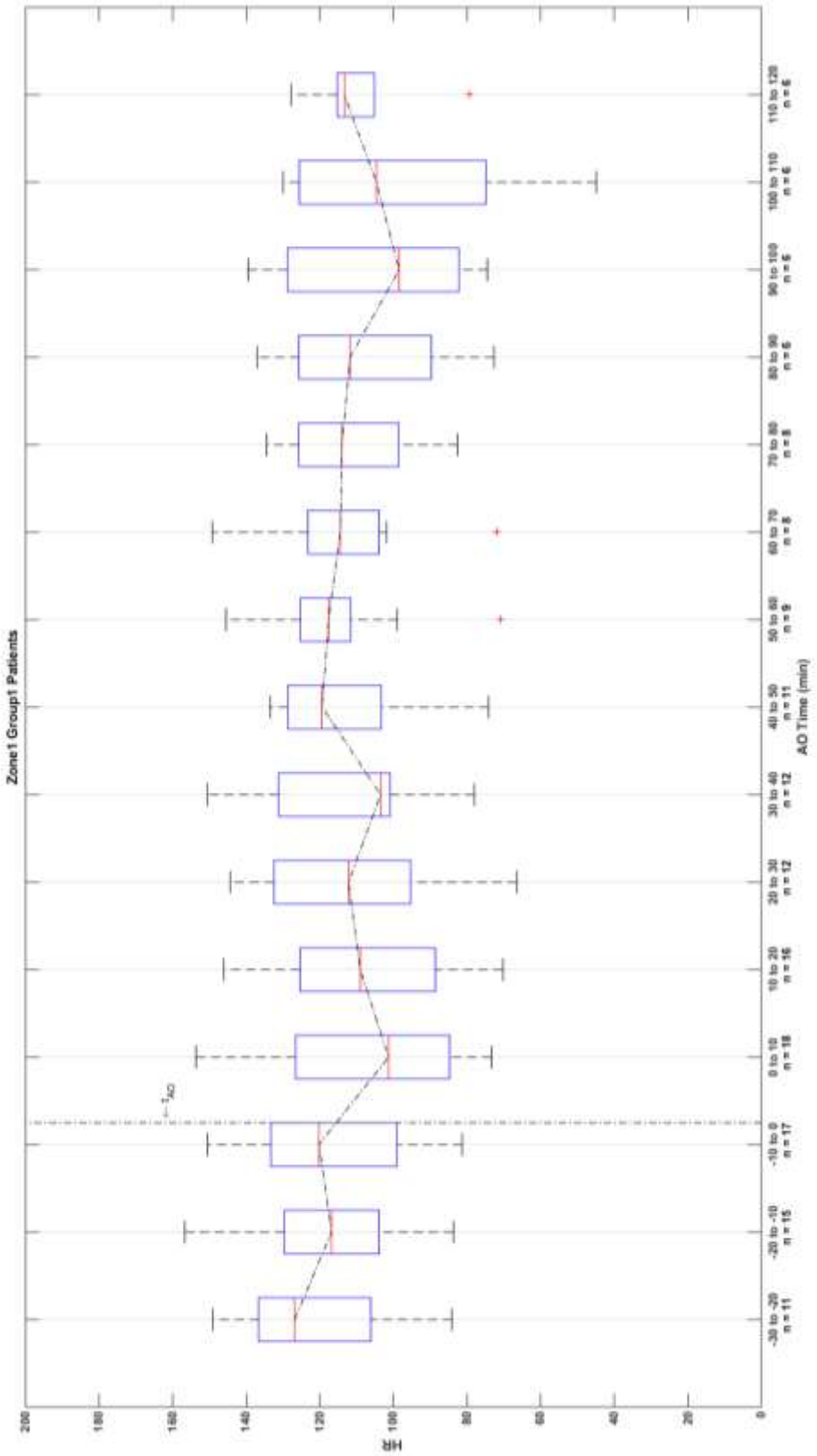


Figure 15: Zone 1 Group 2 Systolic Blood Pressure Aggregate of Mean 10-Minute Intervals

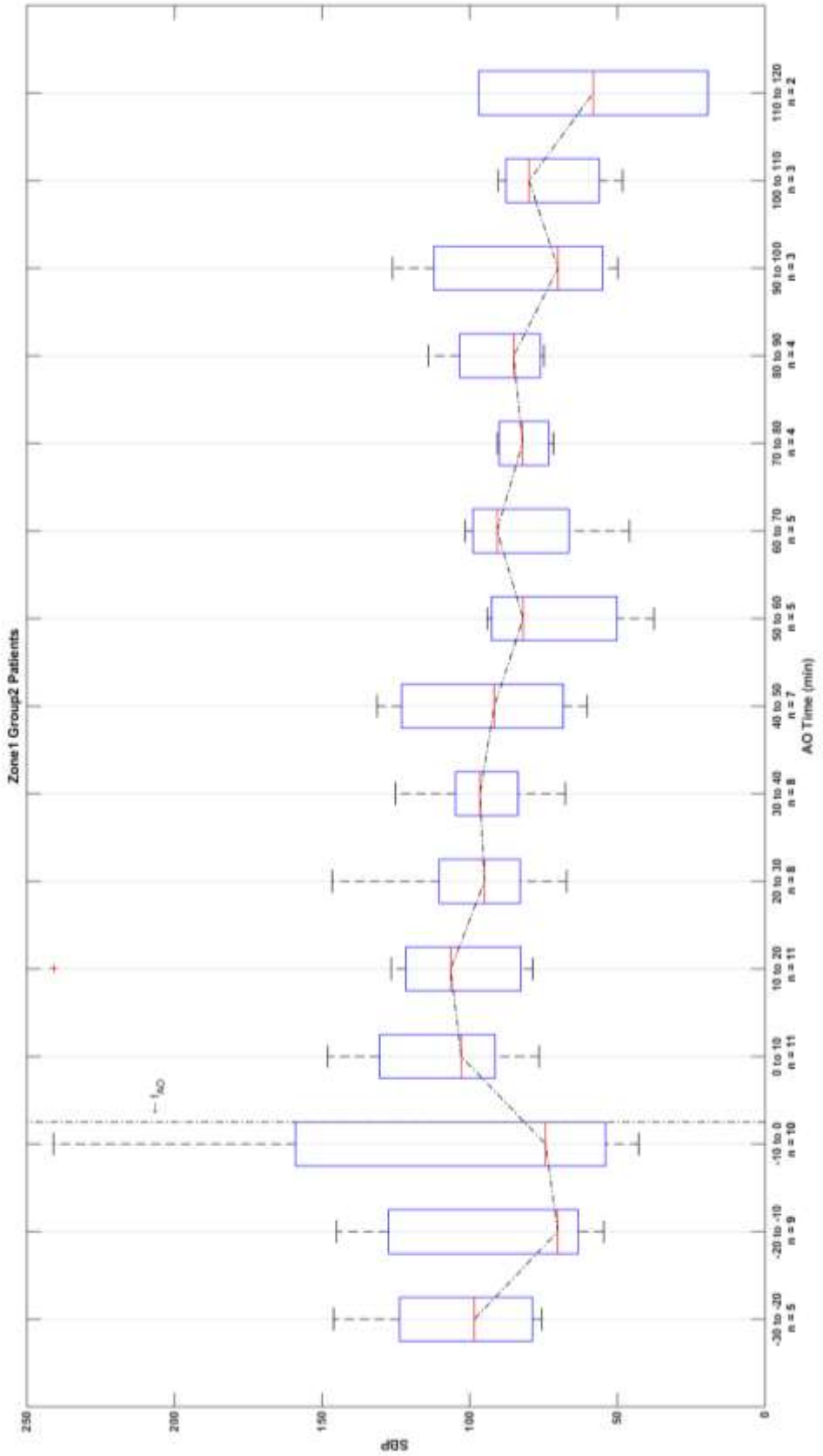


Figure 16: Zone 1 Group 2 Heart Rate Aggregate of Mean 10-Minute Intervals

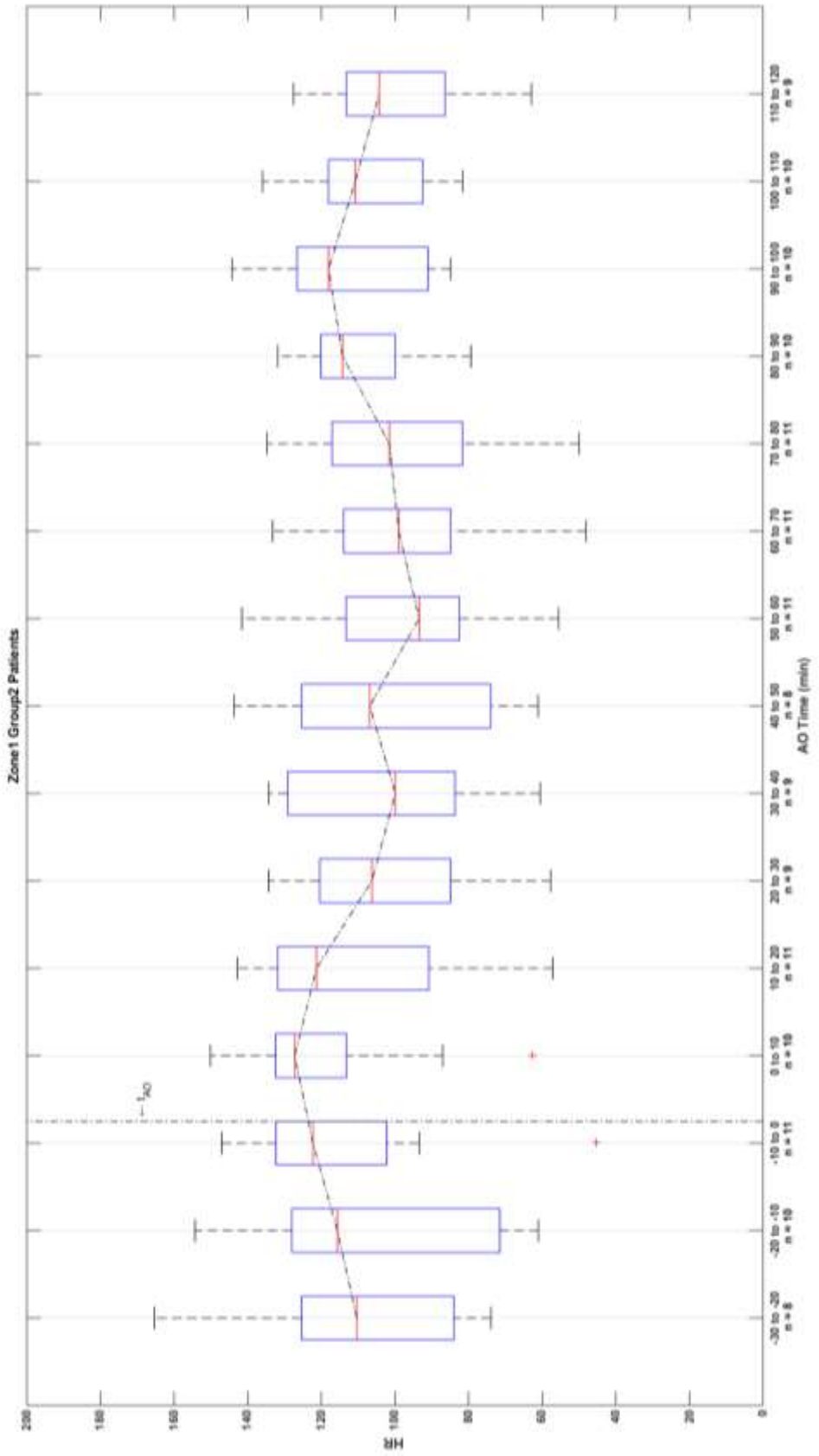


Figure 17: Zone 1 Group 3 Systolic Blood Pressure Aggregate of Mean 10-Minute Intervals

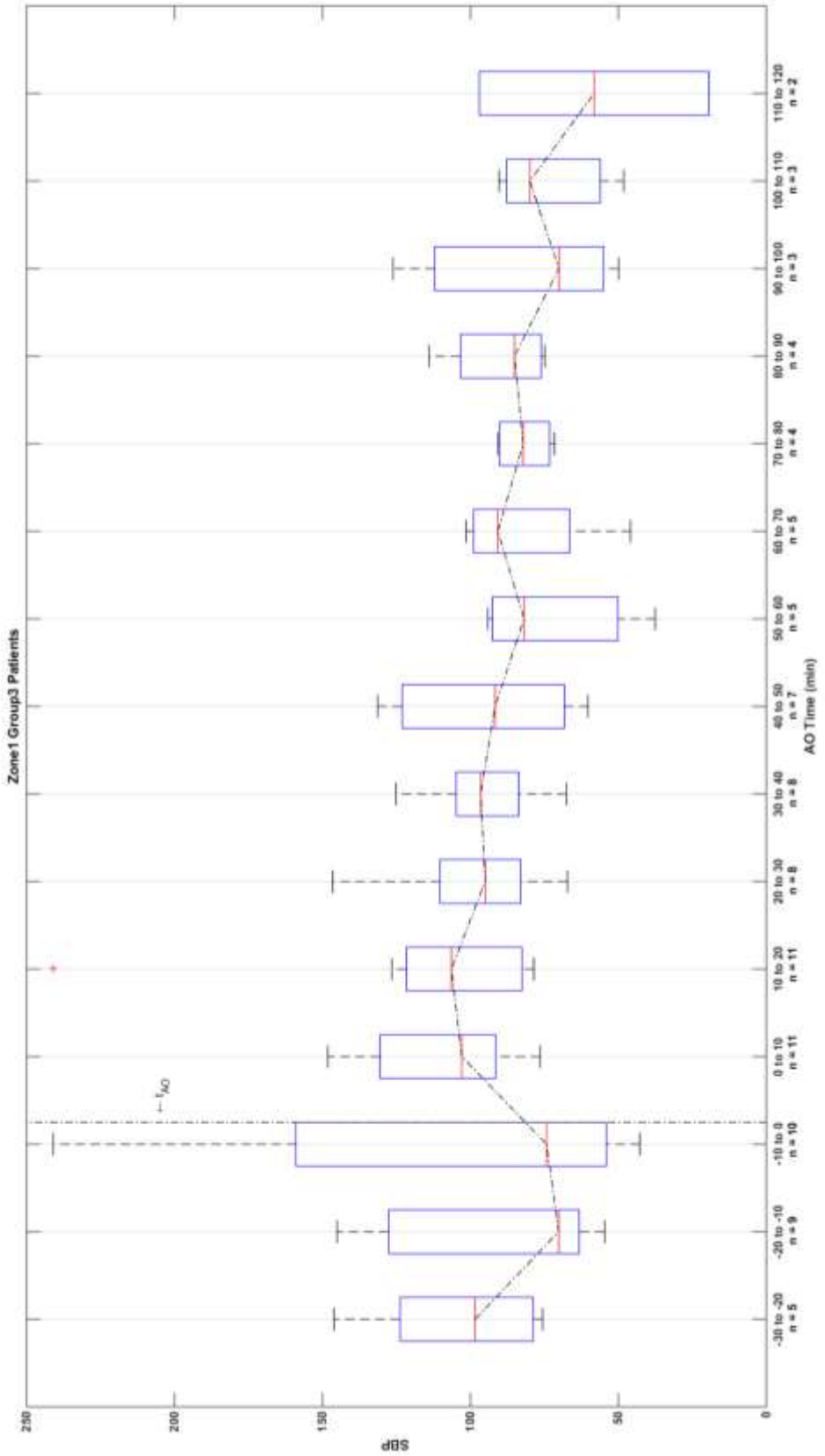


Figure 18: Zone 1 Group 3 Heart Rate Aggregate of Mean 10-Minute Intervals

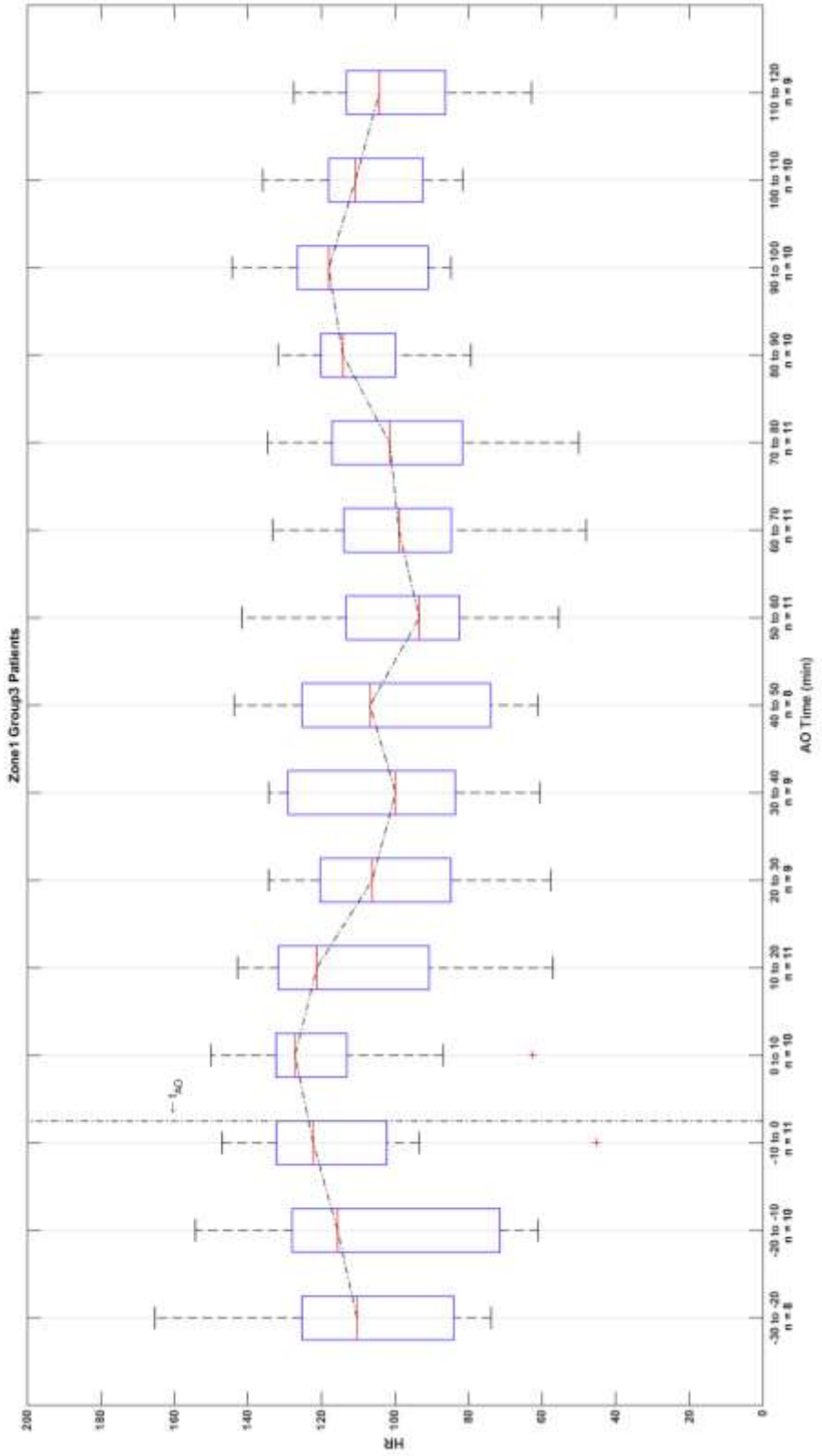


Figure 19: Zone 1 Group 4 Systolic Blood Pressure Aggregate of Mean 10-Minute Intervals

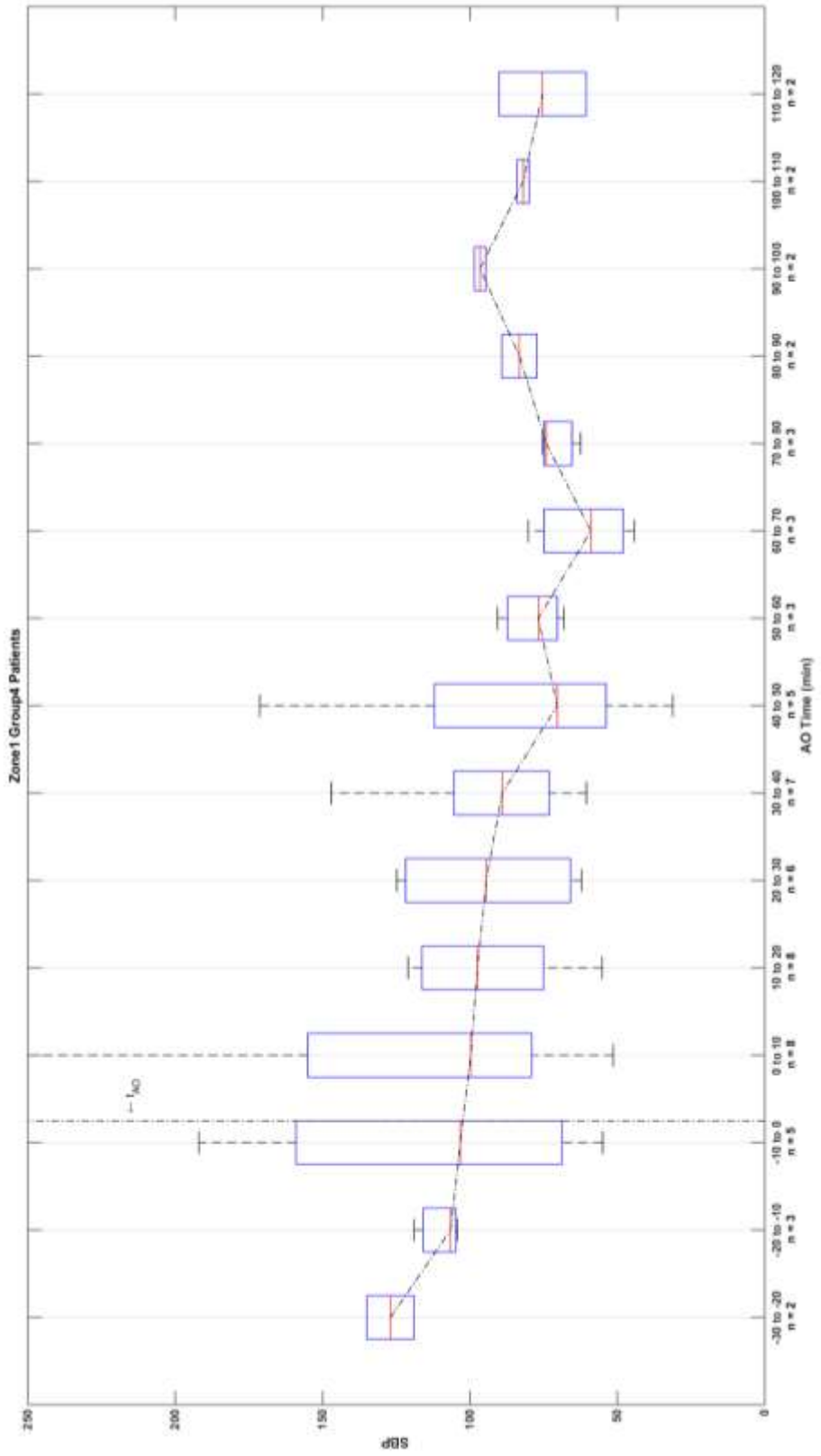


Figure 20: Zone 1 Group 4 Heart Rate Aggregate of Mean 10-Minute Intervals

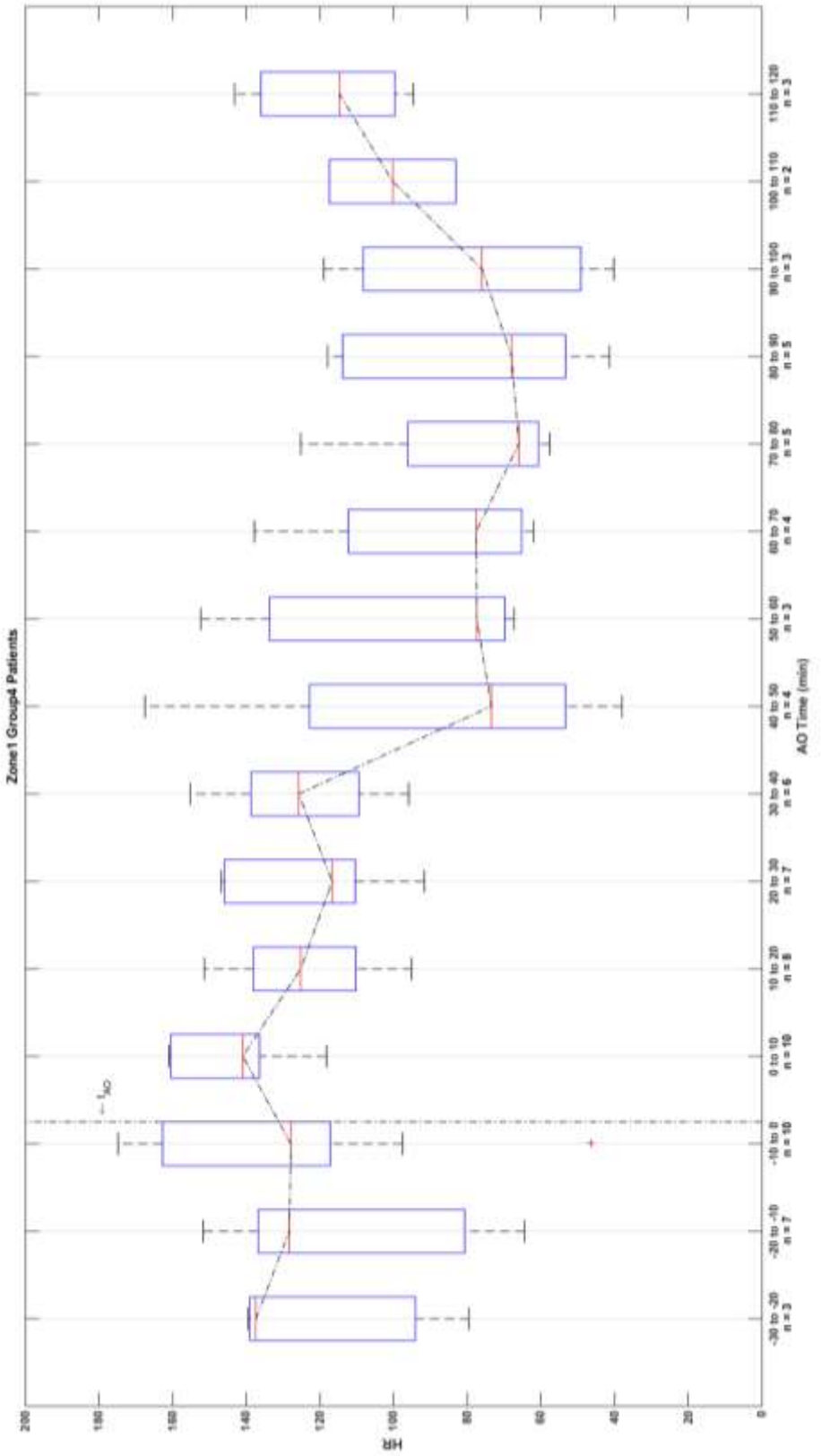


Figure 21: Zone 3 Group 1 Systolic Blood Pressure Aggregate of Mean 10-Minute Intervals

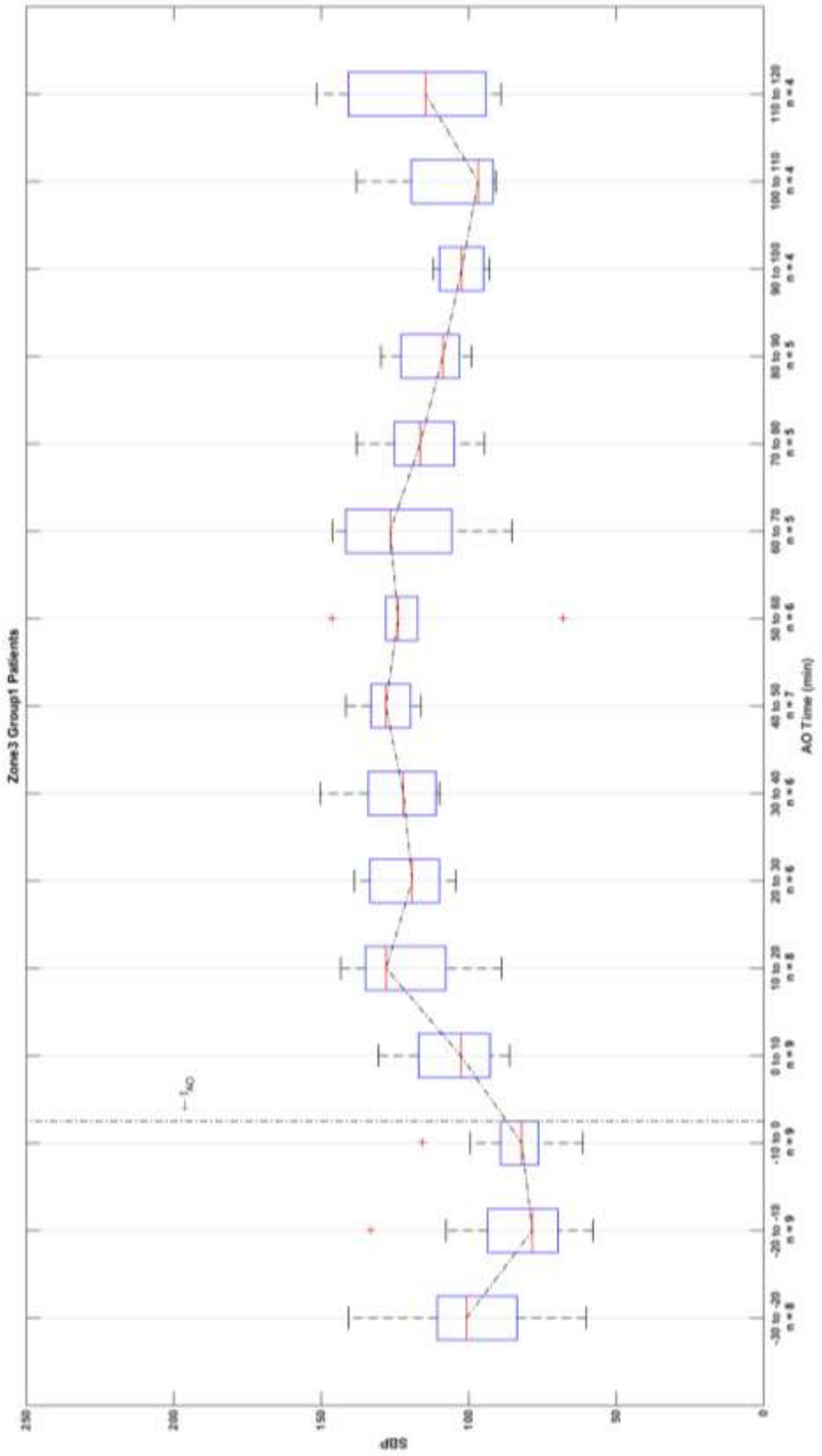


Figure 22: Zone 3 Group 1 Heart Rate Aggregate of Mean 10-Minute Intervals

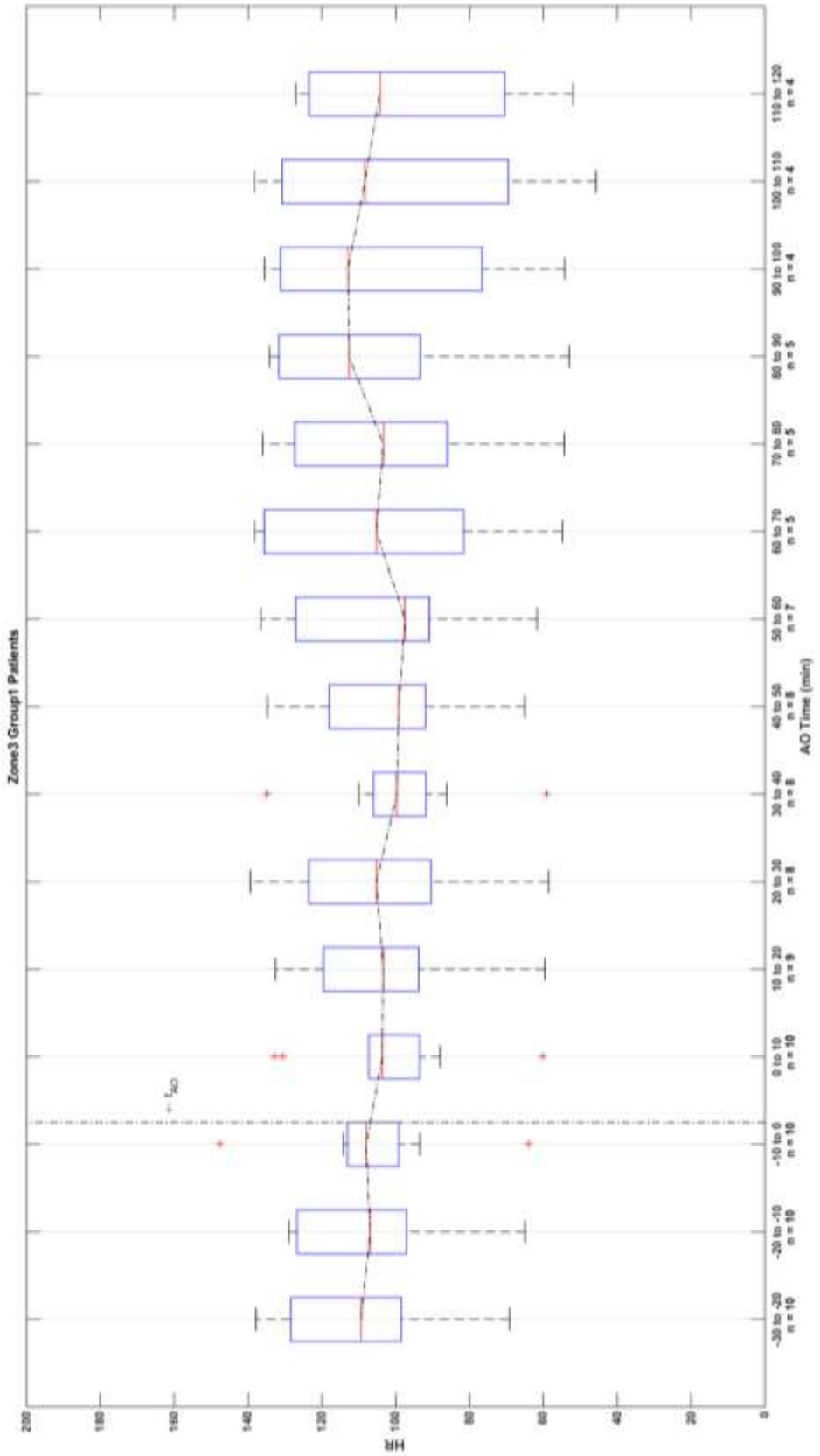


Figure 23: Zone 3 Group 2 Systolic Blood Pressure Aggregate of Mean 10-Minute Intervals

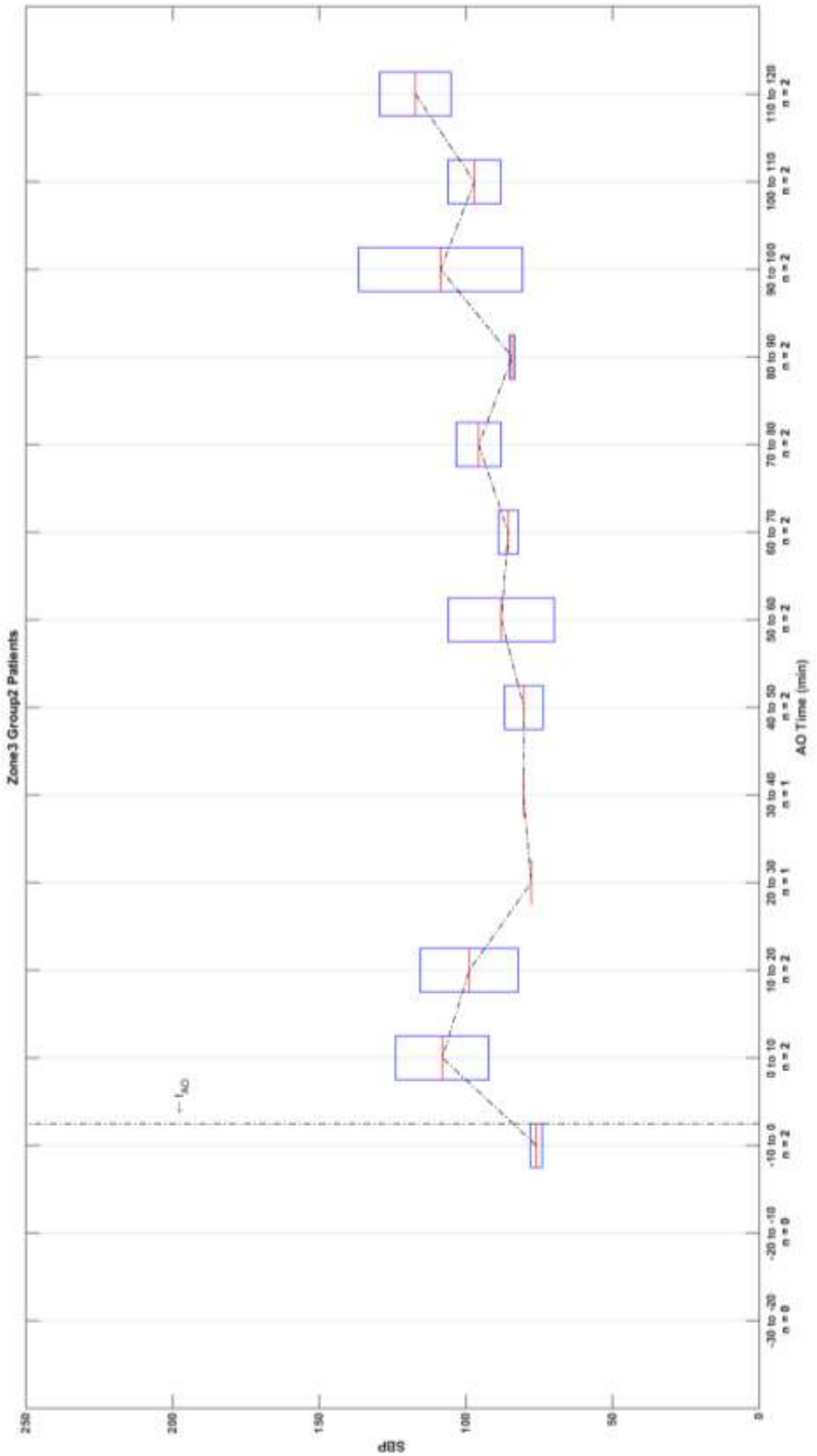


Figure 24: Zone 3 Group 2 Heart Rate Aggregate of Mean 10-Minute Intervals

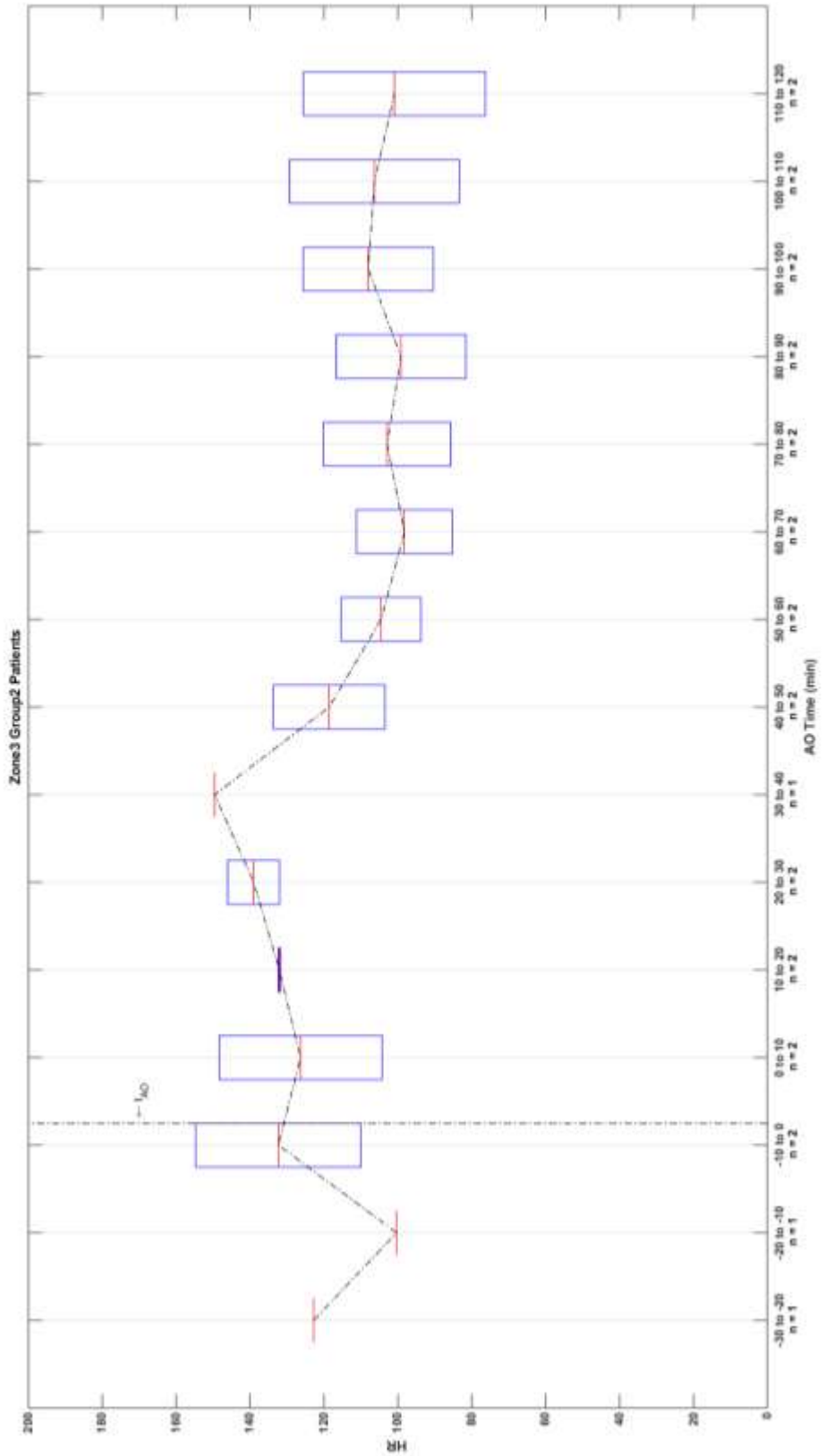


Figure 25: Zone 3 Group 3 Systolic Blood Pressure Aggregate of Mean 10-Minute Intervals

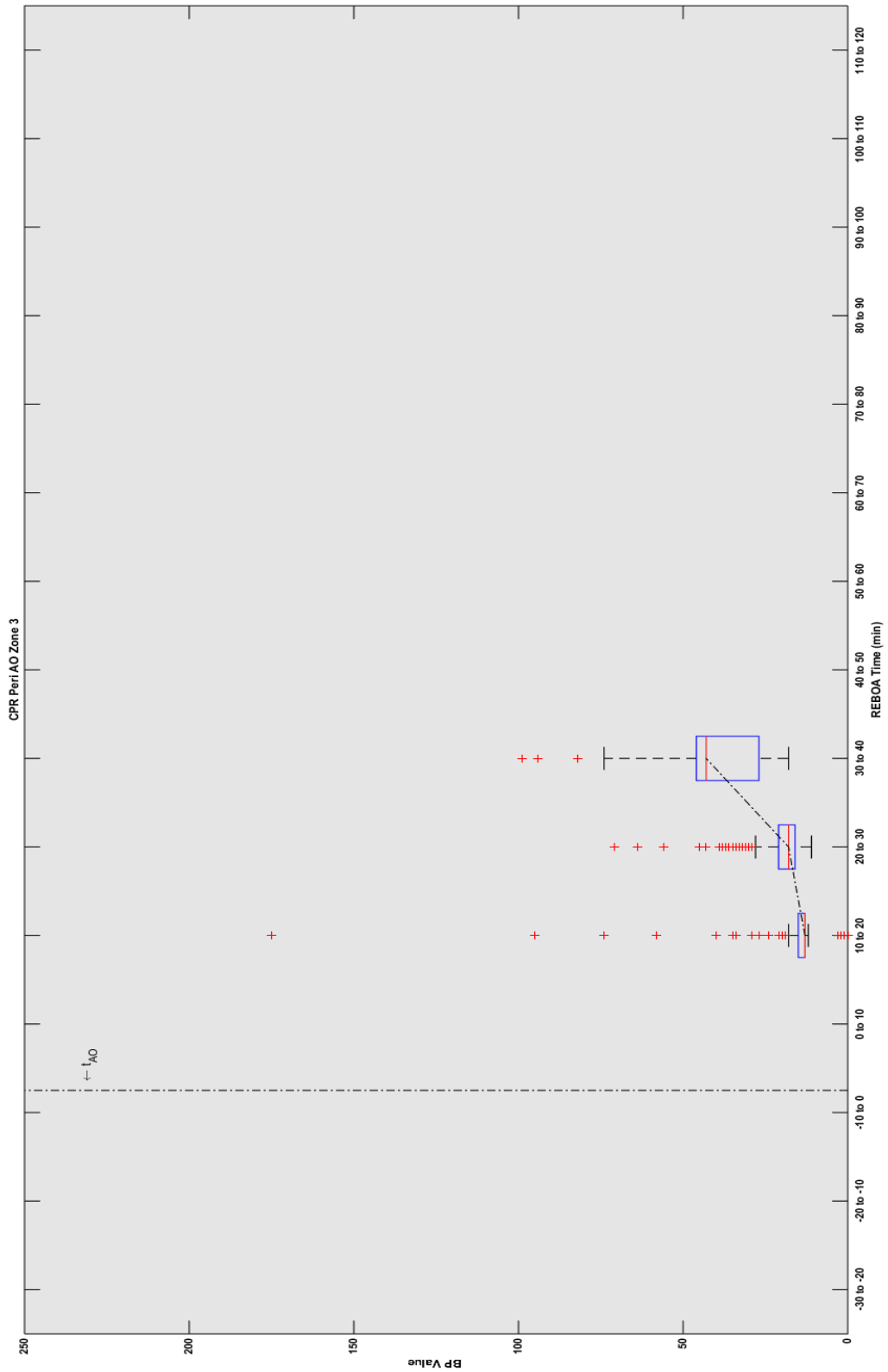


Figure 26: Zone 3 Group 3 Heart Rate Aggregate of Mean 10-Minute Intervals

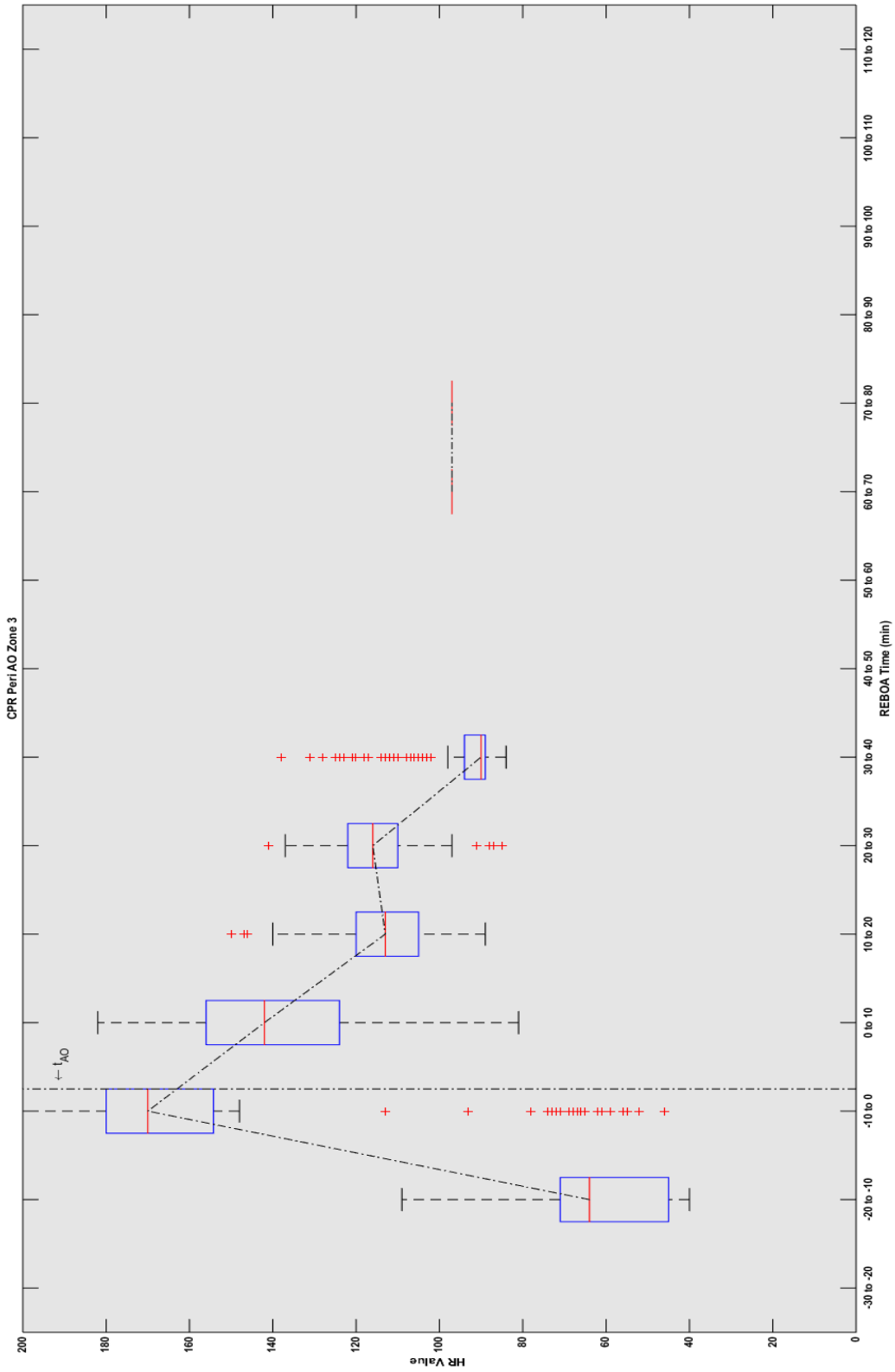


Figure 27: Zone 3 Group 4 Systolic Blood Pressure Aggregate of Mean 10-Minute Intervals

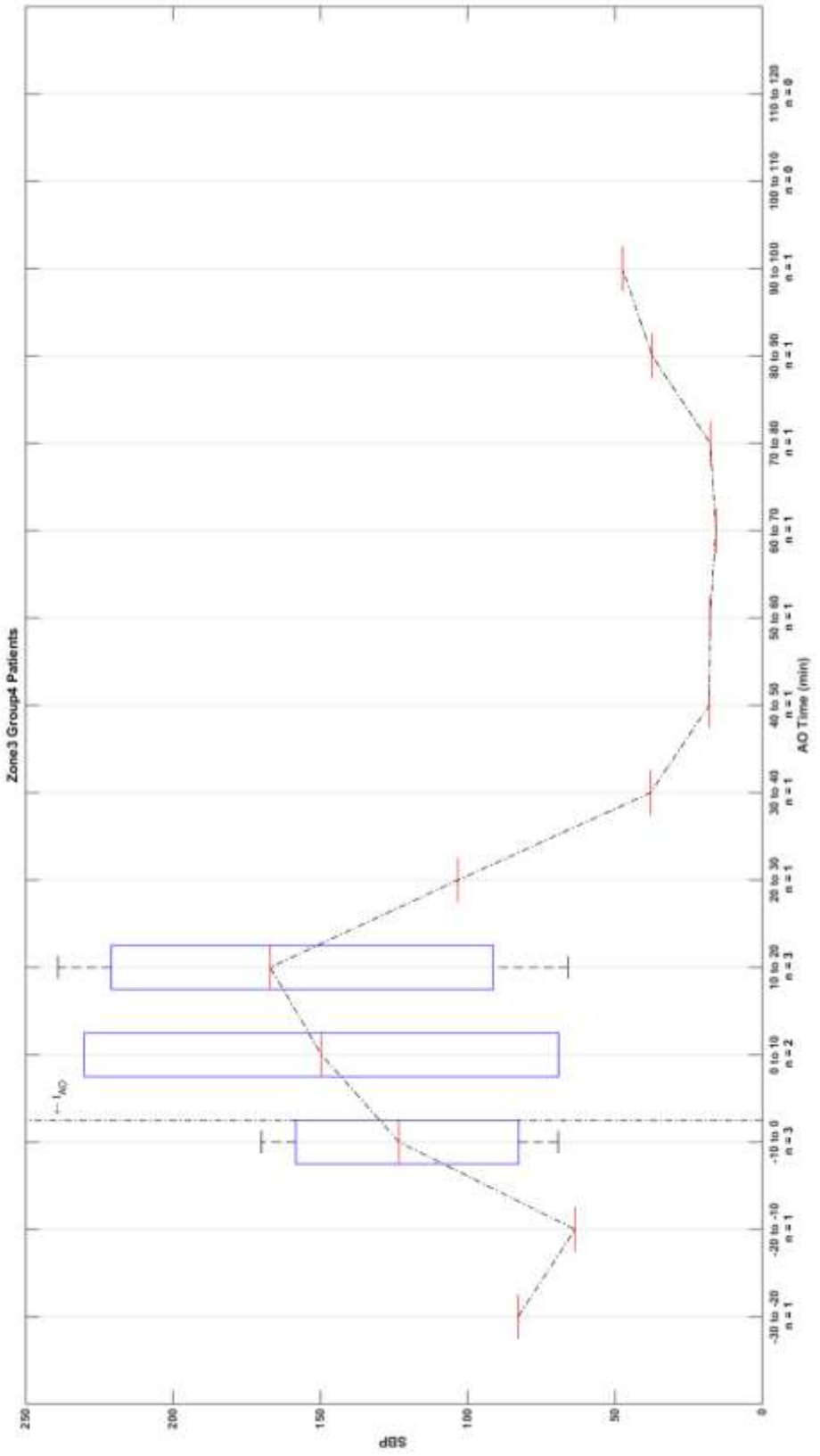
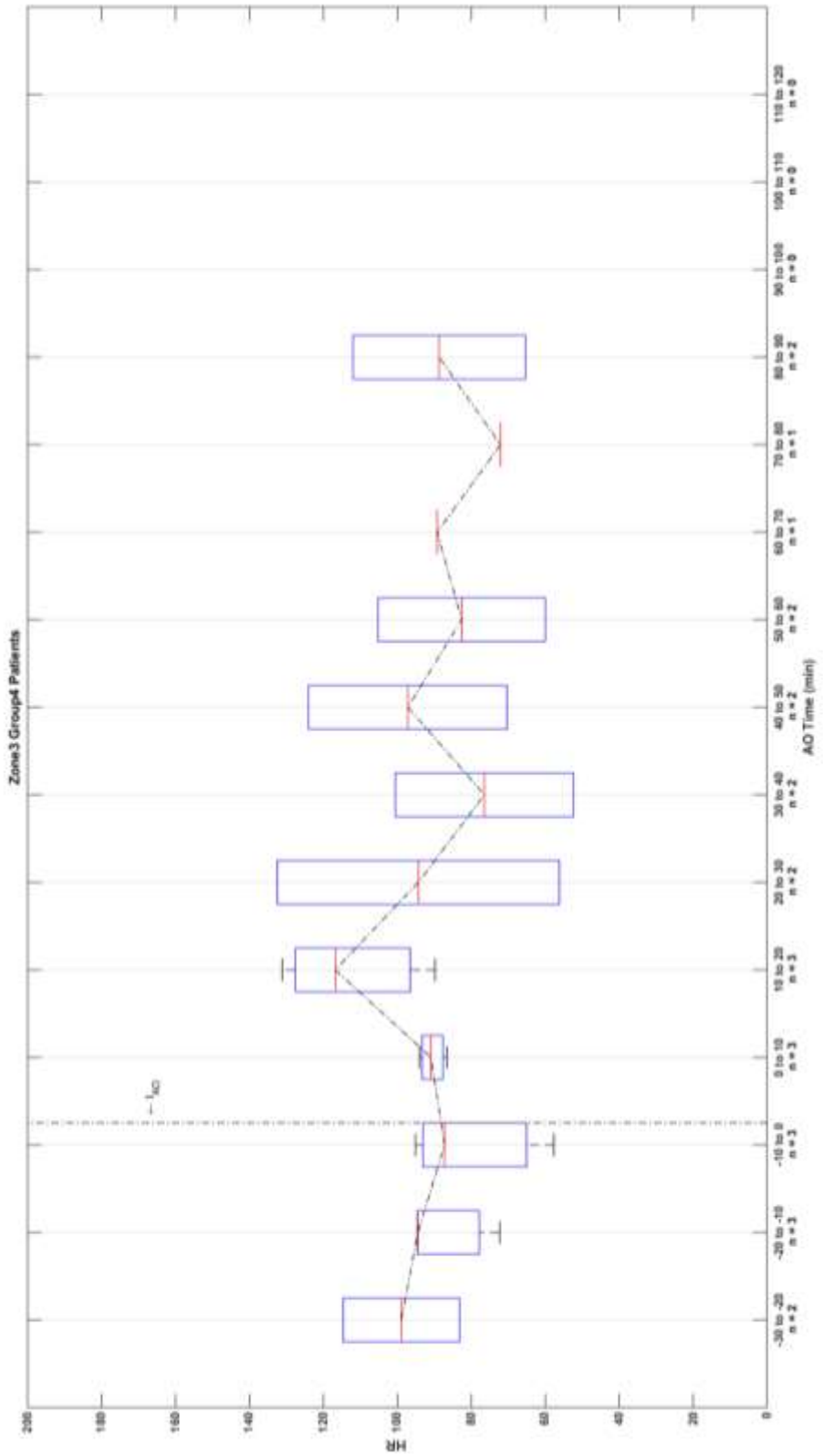


Figure 28: Zone 3 Group 4 Heart Rate Aggregate of Mean 10-Minute Intervals



Arterial Line Monitoring Characteristics Around the Time of Aortic Occlusion

Figure 29: Demonstration of Four Generalized Patterns of Blood Pressure Data Acquisition Around Time of AO. In graph A, no recordable blood pressure (arterial line or noninvasive cuff pressure) is obtained before AO but a "palpable pulse" is documented and an arterial line is established after AO. In graph B, blood pressure data is obtained with a noninvasive cuff with arterial line established after AO. In graph C, a femoral arterial line is obtained before AO, but is then sacrificed to be upsized for a sheath for REBOA, and then an arterial line is established after AO. In graph D, a radial arterial line or the ER-REBOA arterial line monitoring port is in place before the decision to perform REBOA is made and arterial line data is present throughout.

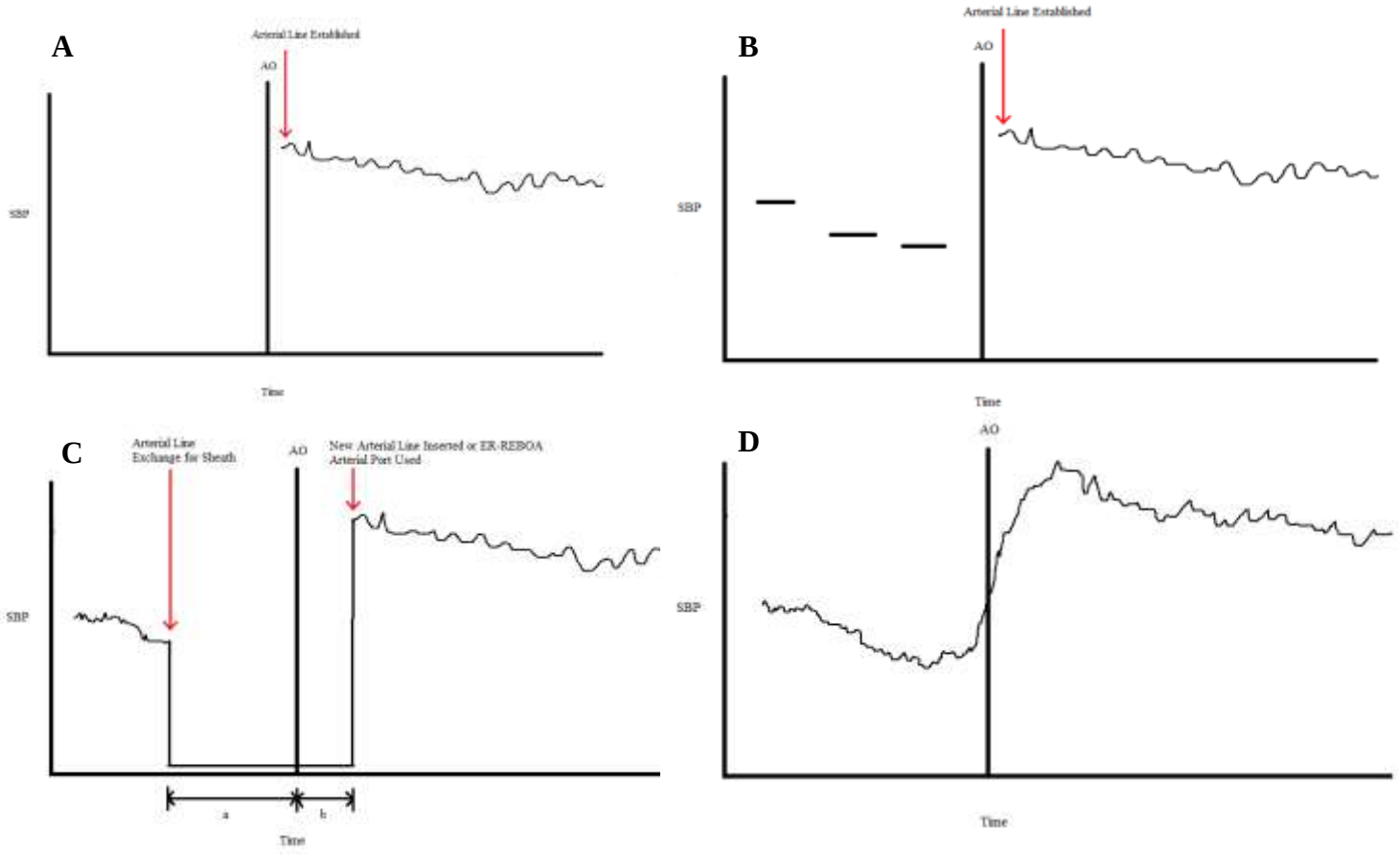
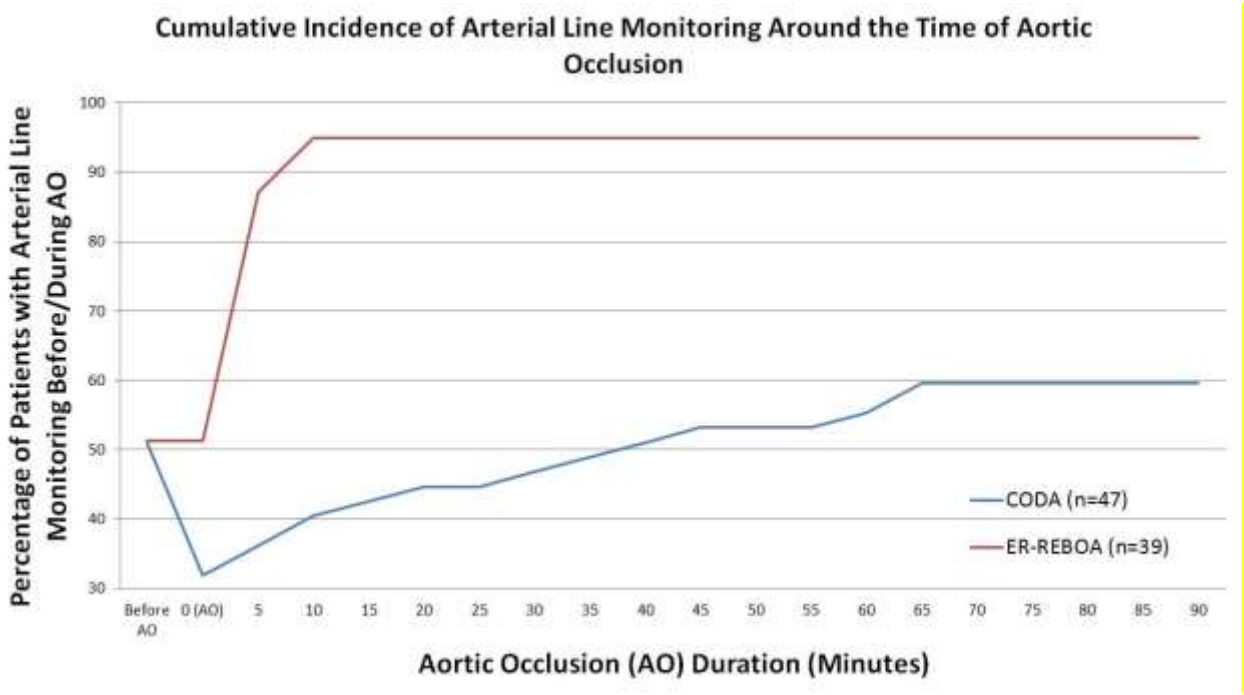


Figure 30: Cumulative Incidence of Arterial Line Monitoring Around the Time of Aortic Occlusion



The timing and presence of arterial line transduction in relation to AO was compared between the CODA® and ER-REBOA™ catheters given the fact that the ER-REBOA™ catheter has an arterial line monitoring port above the level of the balloon while the CODA® catheter does not. Before AO, 94% of patients who had REBOA performed using the CODA® catheter had arterial line monitoring, with 35% having only a femoral arterial line and 59% having a radial arterial line in place. The patients with only femoral arterial lines had the arterial lines sacrificed to upsize for REBOA, with only 59% of patients with the CODA® catheter having arterial line monitoring in place at time of AO. Over time new radial arterial lines were placed in patients after AO. In comparison, 100% of patients who had REBOA performed using the ER-REBOA™ catheter had arterial line monitoring in place before AO with 73% with femoral arterial lines which were later sacrificed for sheath upsizing, 9% (1 patient) who had the ER-REBOA™ placed and used for arterial line monitoring without any other arterial lines, and 18% with radial arterial lines. 82% (9 out of 11) had the ER-REBOA™ catheter arterial line monitoring port utilized and transduced. The two patients who did not have the catheter arterial line monitoring port utilized already had radial arterial lines in place before REBOA. As seen in Figure II, the cumulative incidence of arterial line monitoring before AO was similar between both catheters. Immediately upon AO, there was a higher incidence of arterial line monitoring with patients with the ER-REBOA™ catheter compared to the CODA® catheter. Eventually arterial line monitoring was accomplished for all patients after AO, but was accomplished dramatically sooner in more patients with the ER-REBOA™ catheter.

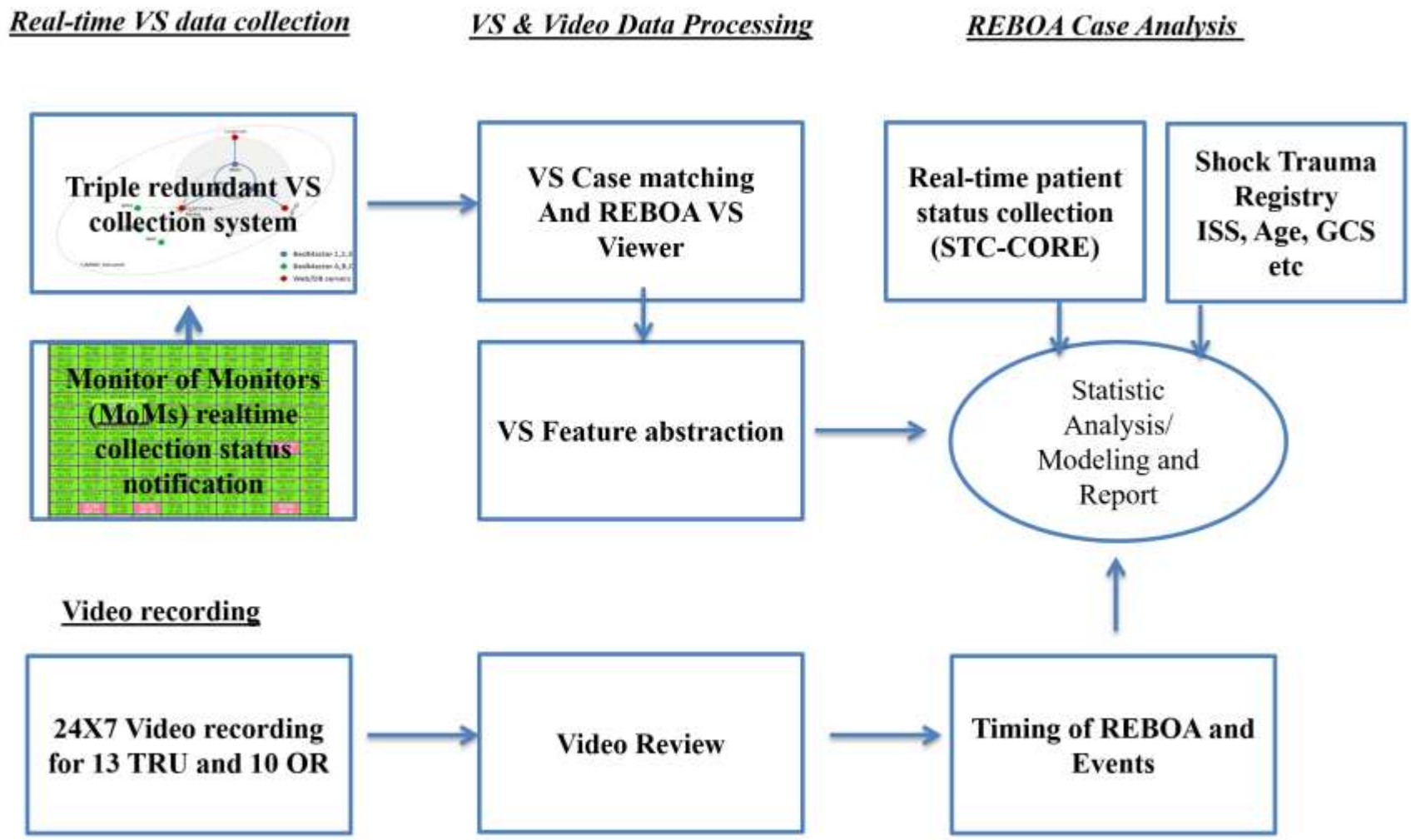
Realtime Video Recording System Infrastructure and Video Review:

The trauma bays in the STC TRU (trauma resuscitation unit) and the operating rooms have integrated audio-visual recording capability and are recorded continuously from multiple angles. This video capability will allow us to obtain exact timelines of REBOA placement and other resuscitation efforts during REBOA placement as necessary to ensure accuracy. Video is stored for 48 hours prior to being deleted without appropriate IRB approvals.

The TRU bays are video recorded by three cameras pointed toward the patient resuscitation area at each bay. The camera over the lower extremity of the patient is the Axis P5534 Pan/Tilt/Zoom IP camera. The camera behind the head area of the patient and also the camera located outside the bay are fixed position Axis P3344-6MM.

Capture of all video signals (including other patient care units) are distributed across five HP PowerEdge R310 servers, Intel Xeon 2.27GHz processors with 4 GB RAM running an embedded version of Windows. Videos are rendered via Vision Client 7.2.1 and output in AVI format utilizing H.264/MPEG-4 AVC video codec for playback on common media players.

Prospective REBOA Data Collection and Analysis



Appendix C: IRB Approval Letter

University of Maryland, Baltimore
Institutional Review Board (IRB)
Phone: (410) 706-5037
Fax: (410) 706-4189
Email: hrpo@umaryland.edu

APPROVAL OF RESEARCH NOTIFICATION

Date: March 31, 2017

To: Megan Brenner
RE: HCR-HP-00061192-2
Type of Submission: Continuing Review
Type of IRB Review: Expedited

Approval for this project is valid from 3/29/2017 to 3/28/2018

This is to certify that the University of Maryland, Baltimore (UMB) Institutional Review Board (IRB) approved the continuing review report for the above referenced protocol entitled, "*Clinical Study of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) for Severe Pelvic Fracture and Intra-abdominal Hemorrhagic Shock using Continuous Vital Signs*".

The IRB has determined that this protocol qualifies for expedited review pursuant to Federal regulations 45 CFR 46.110, 21 CFR 56.110, & 38 CRF 16.110 category(ies):
(5) - Research involving materials (data, documents, records, or specimens) that have been collected for any purpose, or will be collected solely for non-research purposes.

The IRB made the following determinations regarding this submission:
- A waiver of consent has been approved per 45 CFR 46.116(d).
- A waiver of HIPAA authorization for release of the PHI identified in the CICERO application has been reviewed and approved for this research study.

Below is a list of the documents attached to your application that have been approved:
Eligibility Checklist for HP-00061192 v3-24-2015-1427219238785
bibliography
10-14-15 REBOA data collection tool Revised.docx
10-14-15 REBOA data collection tool Revised.docx
P. Wasicek HIPAA 201
K. Fioretti HIPAA 125
P. Wasicek CITI
C. Feather CITI Completion Certificate
C. Feather HIPAA 125.pdf
J. Kidd HIPAA 125
M. Scarboro HIPAA 201
J. Kidd HIPAA 201
R. Jenkins HIPAA 201
A. Romagnoli HIPAA 125_pdf.mht
P. Wasicek HIPAA 125
R. Jenkins HIPAA 125

10-14-15 REBOA data collection tool Revised.docx
M. Scarboro CITI Completion Certificate
K. Fioretti HIPAA 201
C. Feather HIPAA 201.pdf
A. Romagnoli HIPAA 201_pdf.mht
K. Volpini CITI Completion Certificate
M. Scarboro HIPAA 125

In conducting this research you are required to follow the requirements listed in the INVESTIGATOR MANUAL. Investigators are reminded that the IRB must be notified of any changes in the study. In addition, the PI is responsible for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(4)(iii)). The PI must also inform the IRB of any new and significant information that may impact a research participants' safety or willingness to continue in the study and any unanticipated problems involving risks to participants or others.

DHHS regulations at 45 CFR 46.109 (e) require that **continuing review** of research be conducted by the IRB at intervals appropriate to the degree of risk and **not less than once per year.** The regulations make **no provision for any grace period extending the conduct of the research beyond 3/28/2018.** You will receive continuing review email reminder notices prior to this date; however, it is your responsibility to submit your continuing review report in a timely manner to allow adequate time for substantive and meaningful IRB review and assure that this study is not conducted beyond **3/28/2018**. Investigators should submit continuing review reports in the electronic system at least six weeks prior to this date.

Research activity in which the VA Maryland Healthcare System (VAMHCS) is a recruitment site or in which VA resources (i.e., space, equipment, personnel, funding, data) are otherwise involved, must also be approved by the VAMHCS Research and Development Committee prior to initiation at the VAMHCS. Contact the VA Research Office at 410-605-7000 ext. 6568 for assistance.

The UMB IRB is organized and operated according to guidelines of the International Council on Harmonization, the United States Office for Human Research Protections and the United States Code of Federal Regulations and operates under Federal Wide Assurance No. FWA00007145.

If you have any questions about this review or questions, concerns, and/or suggestions regarding the Human Research Protection Program (HRPP), please do not hesitate to contact the Human Research Protections Office (HRPO) at (410) 706-5037 or HRPO@umaryland.edu.