

Prolonged Zone I Partial REBOA Swine Model for Visceral Ischemia-Reperfusion Injury Therapeutic Evaluation

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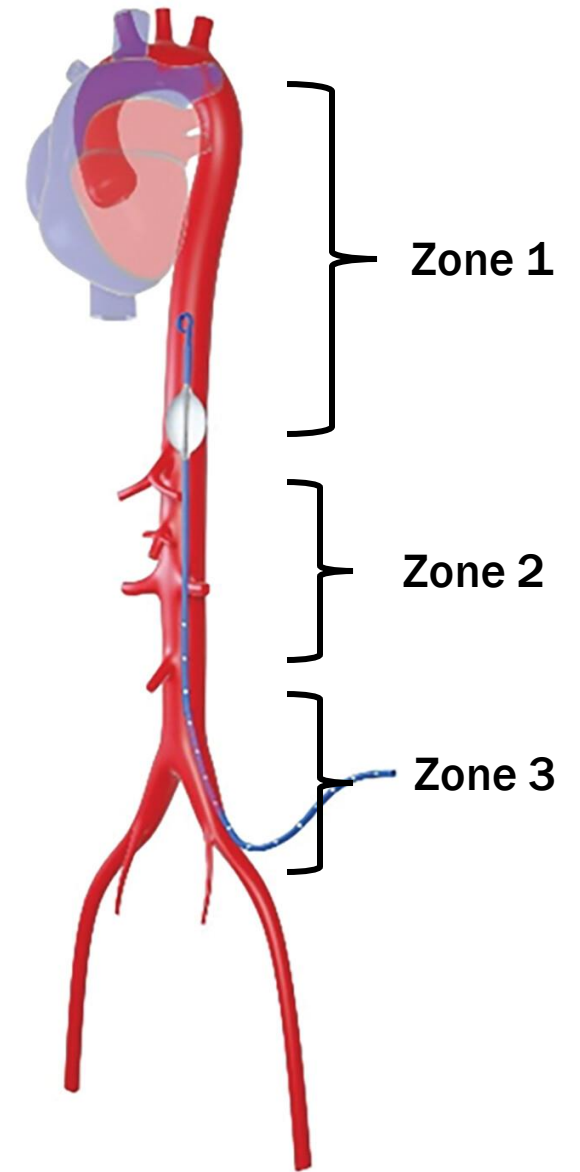
Battlefield Shock & Organ
Support Program (BSOS)

Non-Disclosure: The author has no conflicts of interest to disclose. The views expressed are those of the authors and do not necessarily reflect the official policy or position of the Department of Defense or the U.S. Government.

**Peer Reviewed Medical Research Program (PRMRP)
Award No. W81XWH-22-2-0034**

Clinical Problem

- Non-Compressible Torso Hemorrhage remains a leading cause of preventable death in civilian and military trauma
- Partial Resuscitative Endovascular Balloon Occlusion of the Aorta (pREBOA) of Zone 1 temporizes hemorrhage, maintains proximal perfusion, and allows some distal perfusion
- Future conflicts will likely be defined by prolonged field care and delayed evacuation - potentially necessitating longer use



Hemorrhage Control is Only Part of the Problem

B Kaplan-Meier survival estimates

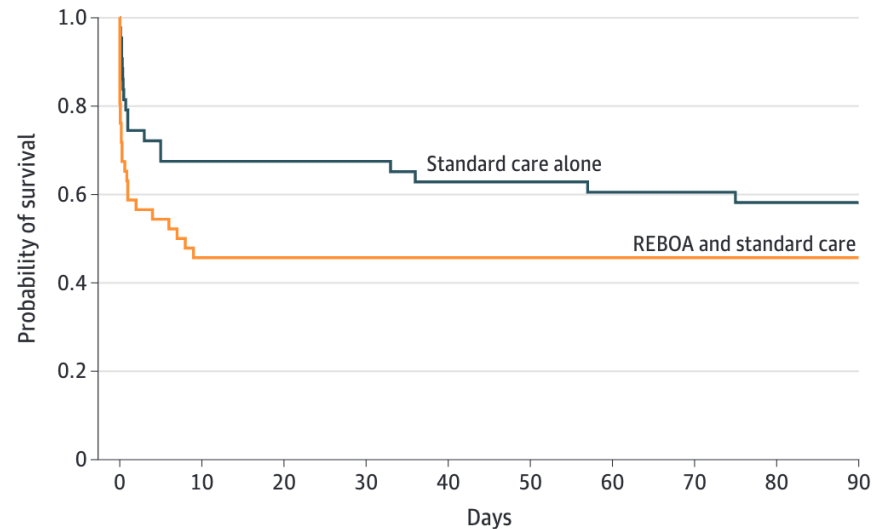
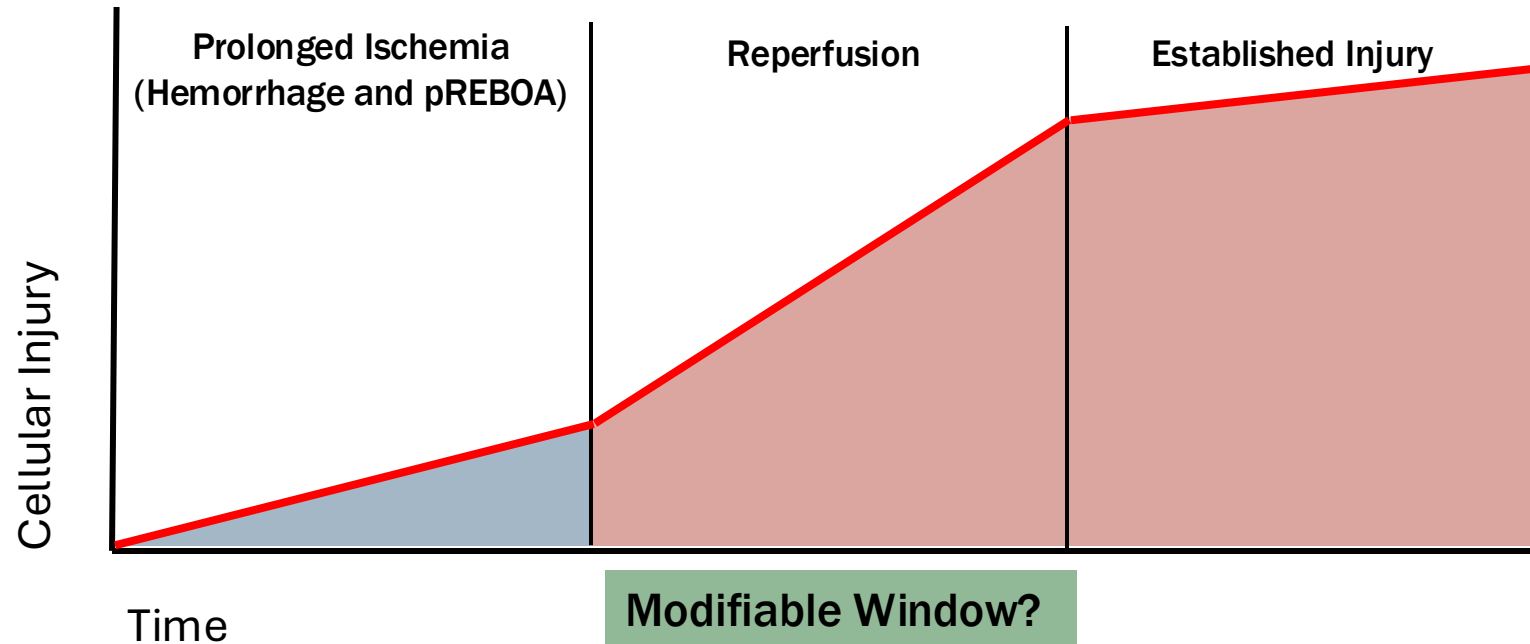


Table 2. Clinical Outcomes

Patient No. (sequential order)	Proximal hemodynamic response (mean arterial pressure)			Cardiac arrest		MODS, SOFA score at admission	Length of stay, d		Survival				CPC
	Pre-REBOA BP	Post-REBOA BP	Arrival at ED BP	Prehos- pital TCA	RT		Critical care	Hospital	3 h	24 h	30 d	90 d or Discharge	
Patients who underwent Z1 REBOA													
1 (1)	53/10 (21)	96/29 (51)	105/85 (94)	Yes	No	13	38	62	Yes	Yes	Yes	Yes	1
2 (2)	24/16 (20)	TCA, M ^a	66/41 (49)	Yes ^{b,c}	Yes ^{d,e}	13	<1	<1	Yes	No	No	No	NA
3 (3)	52/37 (30)	105/82 (89)	106/57 (90)	No	No	12	2	2	Yes	Yes	No	No	NA
4 (4)	42/13 (27)	79/53 (62)	110/66 (78)	No	No	4	12	12	Yes	Yes	No	No	NA
5 (9)	25/15 (19)	54/28 (37)	102/73 (79)	No	No	17	2	2	Yes	Yes	No	No	NA
6 (10)	40/28 (32)	67/48 (58)	131/71 (94)	No	No	12	2	2	Yes	Yes	No	No	NA
7 (11)	47/31 (38)	111/71 (84) ^f	99/46 (65) ^f	Yes ^b	No	13	11	11	Yes	Yes	No	No	NA
8 (12)	TCA, M ^a	114/38 (38) ^h	PLE	Yes ^{b,c}	No	PLE	0 ⁱ	0	No	No	No	No	NA
9 (14)	51/29 (34)	56/46 (52)	80/67 (75)	No	No	13	2	2	Yes	Yes	No	No	NA
10 (15)	TCA, M ^a	74/54 (64)	69/52 (58)	Yes ^{b,c}	Yes ^{d,j}	13	<1	<1	Yes	No	No	No	NA
11 (16)	48/39 (43)	104/78 (88)	100/81 (90)	No	No	12	39	76	Yes	Yes	Yes	Yes	1

Improving outcomes requires more than hemorrhage control...It requires understanding and mitigation of the down stream effects!

What Happens After Hemorrhage Control?

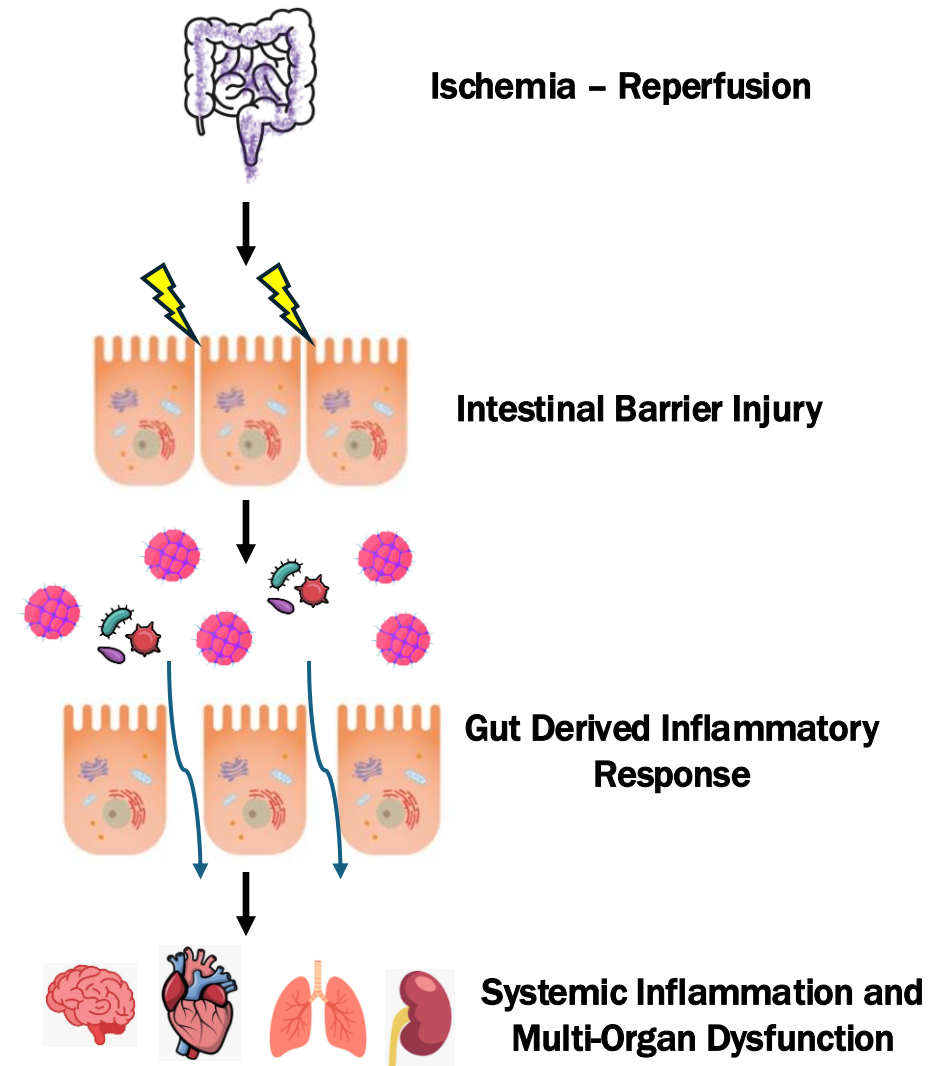


Although ischemia is unavoidable during REBOA, reperfusion injury may represent a modifiable phase of total organ injury!

Why Focus on Bowel?

- Cardiac and renal IRI have been extensively studied
- Bowel is highly susceptible to IRI
- Critical Barrier Organ

Objective: Develop a reproducible, survivable prolonged Zone I pREBOA model that generates clinically relevant intestinal ischemia-reperfusion injury and serves as a platform for evaluating reperfusion-directed therapies.



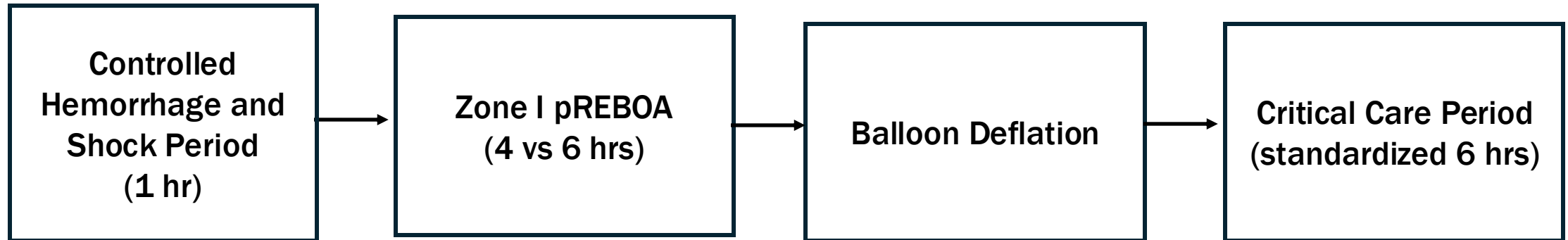
Methods

6-hr pREBOA

- 40% EBV hemorrhage
- dSBP 20–30 mm Hg
- n=8

4-hr pREBOA

- 25% EBV hemorrhage
- dSBP 30–40 mm Hg
- n=6



→ Blood samples collected every hour

→ Intestinal samples collected at baseline, end of shock, and every 2 hours afterward

Testing a Survivable Model

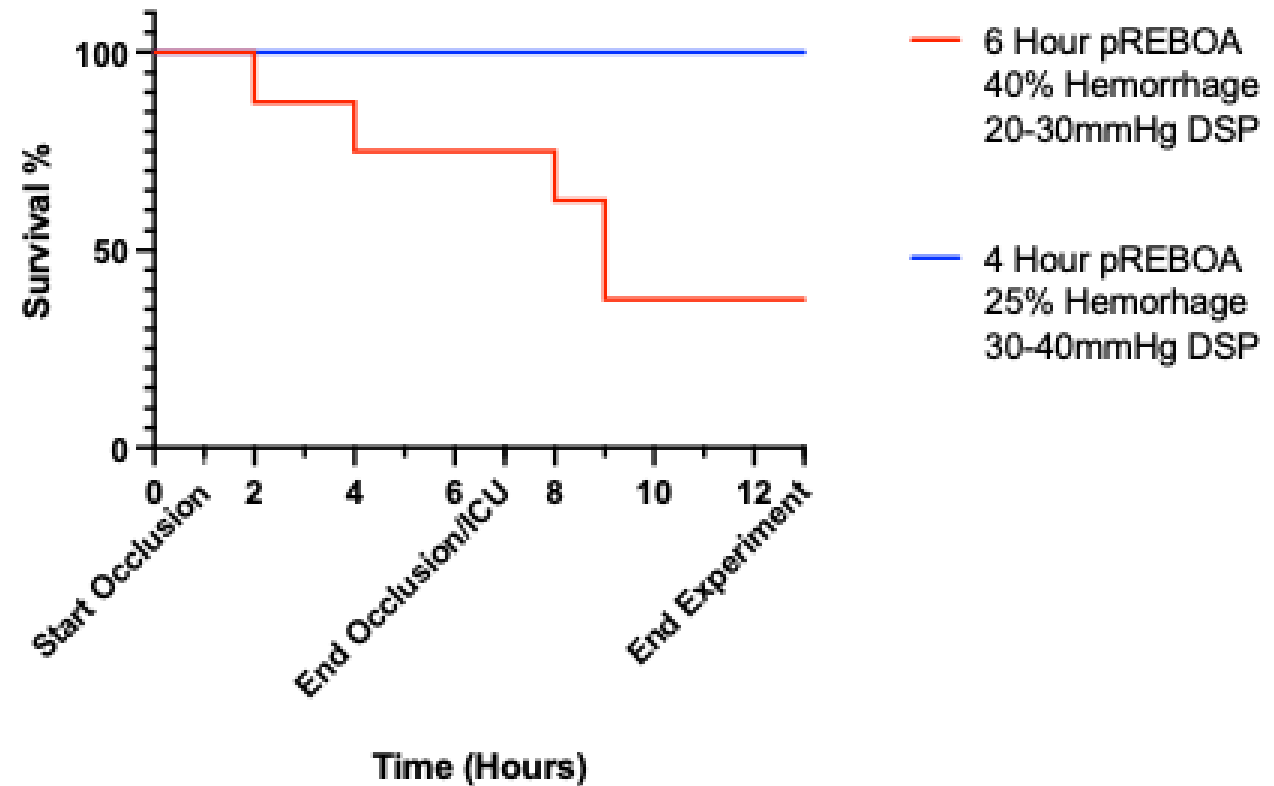
6hr pREBOA / 40% EBV / 20-30mm Hg dSBP

- 3/8 survived
- 2 deaths during occlusion
- 3 deaths during critical care period/reperfusion

4hr pREBOA / 25% EBV / 30-40mm Hg dSBP

- 6/6 survived

Logrank $p = 0.02$



Distinct Systemic Injury During Ischemia and Reperfusion

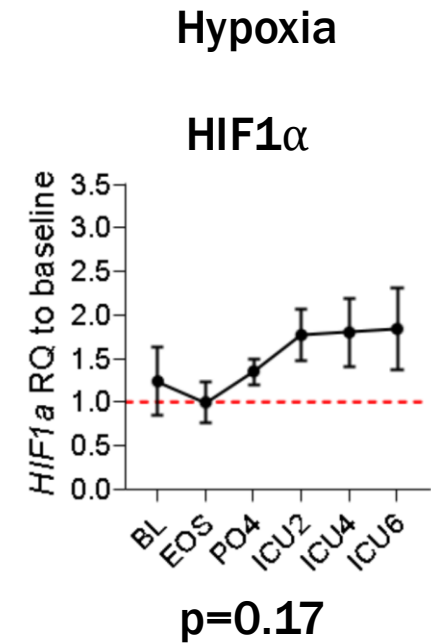
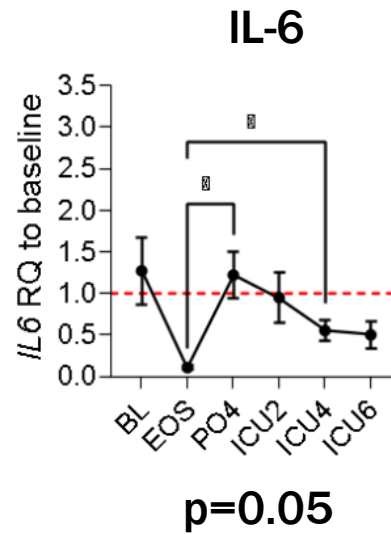
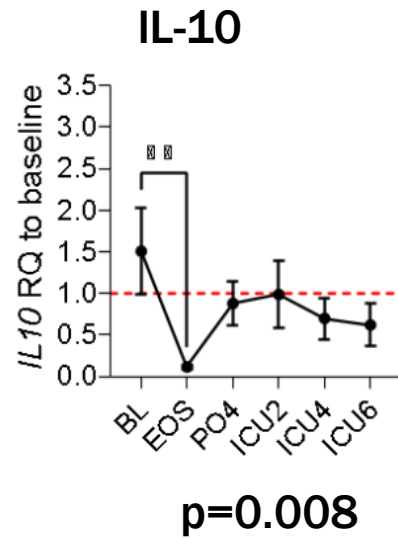
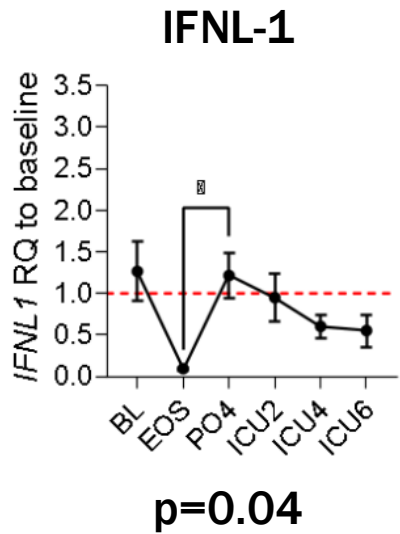
* = Difference from Baseline

** = Difference from End of Occlusion to End of Experiment

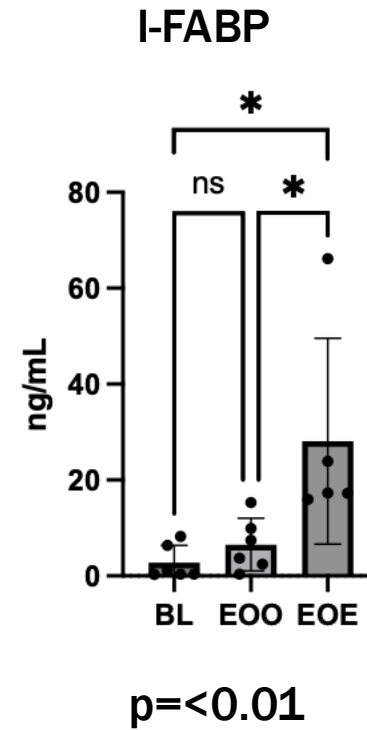
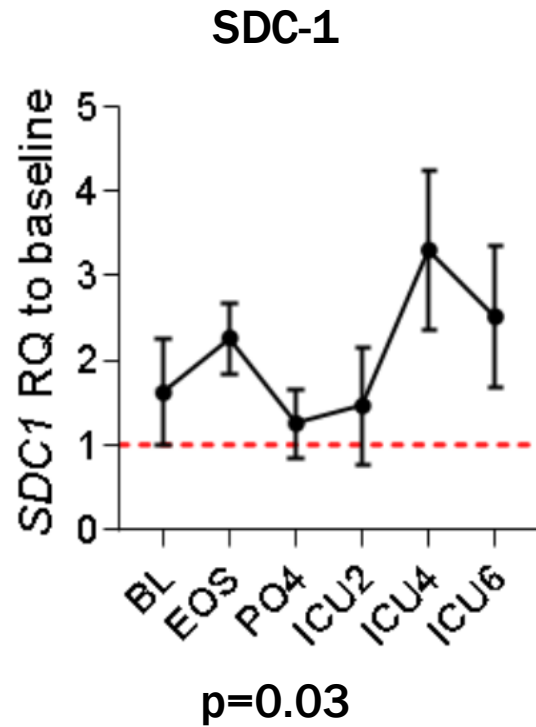
Marker	Baseline	End of Occlusion	End of Experiment	p-value
→→ Potassium (mmol/L)	3.7 ± 0.1	4.7 ± 0.4 *	6.1 ± 0.7 *, **	<0.001
→ Lactate (mmol/L)	3.7 ± 1.9	12.8 ± 4.0 *	11.6 ± 6.7	0.007
→ Creatinine (mg/dL)	1.7 ± 0.3	3.3 ± 0.4 *	4.0 ± 1.0 *	<0.001
BUN mg/dL	6.9 ± 2.6	11.3 ± 2.7 *	19.2 ± 5.2 *, **	<0.001
AST (U/L)	45 ± 26	150 ± 99 *	1156 ± 854 *	0.023
ALT (U/L)	31 ± 5	41 ± 9	65 ± 27	0.030
→ LDH (U/L)	506 ± 57	720 ± 278	3400 ± 1941 *, **	0.014
→ CK (U/L)	828 ± 294	1803 ± 938	17967 ± 12277 *, **	0.019

Reperfusion Alters Intestinal Molecular Response

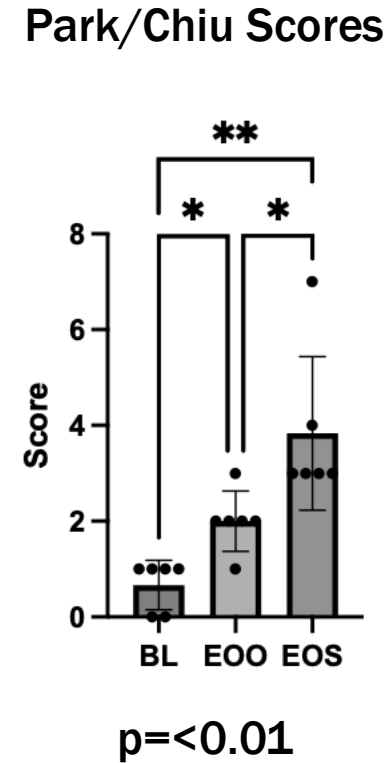
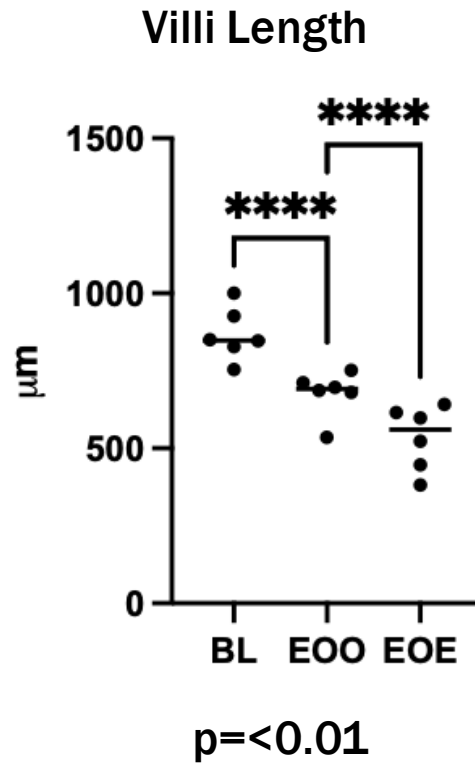
Cytokines/Inflammatory Markers



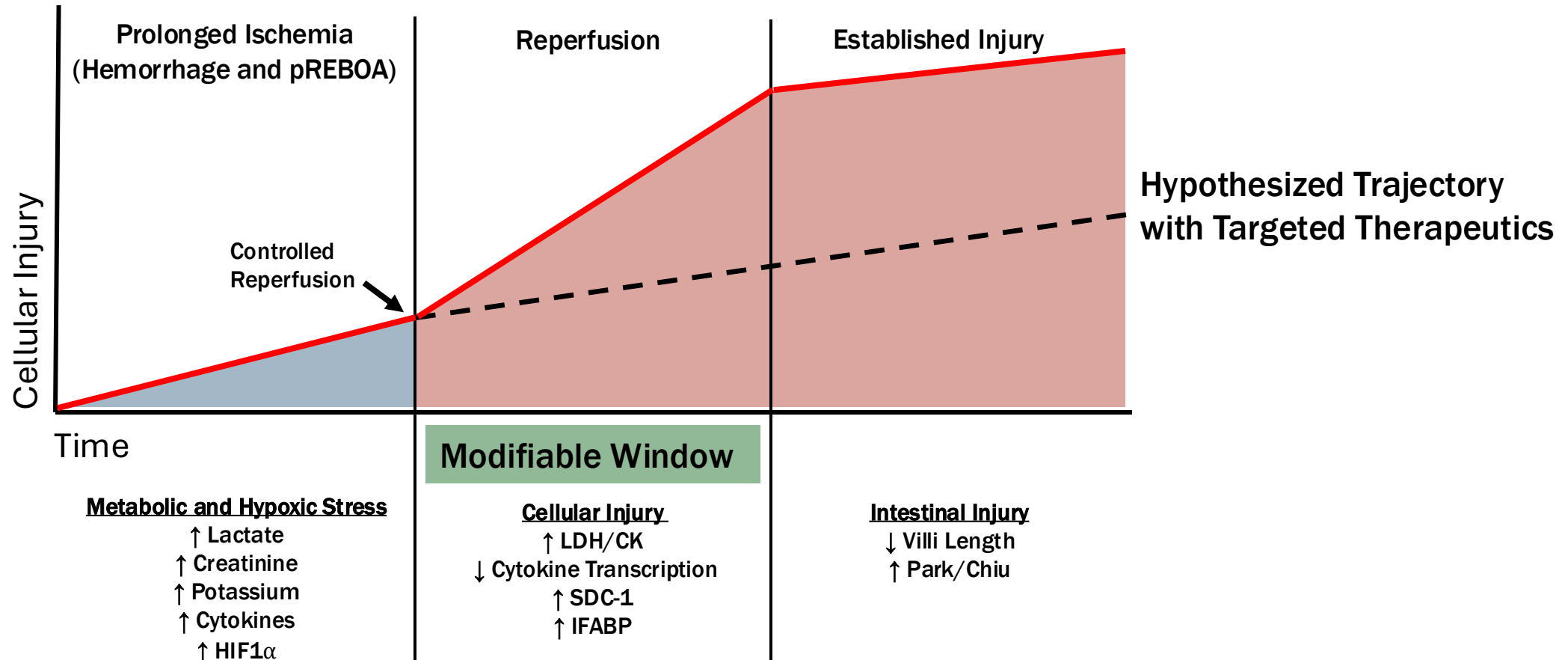
Intestinal Barrier Disruption Progresses Following Reperfusion



Structural Intestinal Injury Progresses During Reperfusion



Reperfusion Defines a Potential Therapeutic Window



Conclusion

A refined 4 hour, 25 % EBV, 30-40 mm Hg targeted dSBP provides a reproducible and survivable platform for pREBOA-associated IRI therapeutic testing

→ Intestinal barrier dysfunction and mucosal injury progress following reperfusion

→ This distinct pattern will enable controlled testing of reperfusion targeted therapeutics

Acknowledgements: BSOS Team

Dr. Patrick F. Walker
Dr. Matthew J. Bradley
Dr. David Burmeister
Dr. Eric A. Elster
Dr. Woo Do
Dr. Jonathan Morrison
Dr. Amy Wang
Dr. Ben Scott
Dr. Saman Qadri
Dr. Joseph Bozzay
Dr. David Schectman
Dr. John T. Green
Dr. Elizabeth Powell
Dr. Jason Radowsky
John Mares
Justin Hutzler

THANK YOU!

Questions?

