

RESUSCITATIVE ENDOVASCULAR BALLOON OCCLUSION OF THE AORTA WITH TARGETED REPERFUSION INJURY MITIGATION (REBOA-TRIM)

A Multimodal Approach to Combat Reperfusion Injury Allowing for Longer Aortic Occlusion Periods and Decreasing Subsequent Multi-Organ Dysfunction

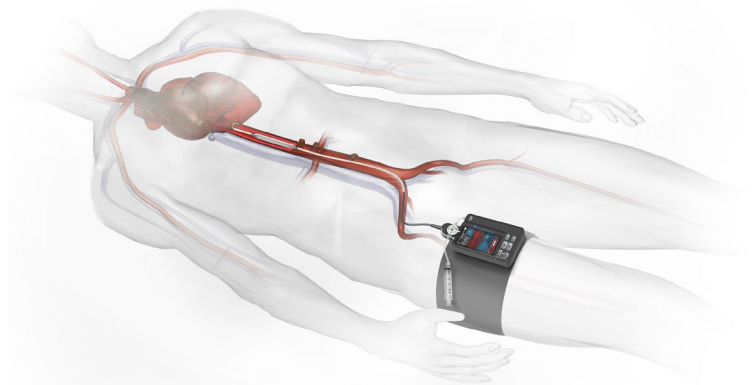
- **MISSION NEED:** Addresses the #1 preventable cause of combat death—non-compressible truncal hemorrhage—a time-limited problem particularly in prolonged care scenarios
- **CAPABILITY GAIN:** Targets ≥ 180 min safe zone 1 aortic occlusion by mitigating ischemia-reperfusion injury
- **MULTIMODAL MITOCHONDRIAL THERAPEUTIC COCKTAIL:** Repurposed FDA approved drugs + vetted experimental agents + transcutaneous vagus nerve stimulation

WHAT IS IT?

REBOA-TRIM is a next-generation damage-control strategy that transforms the standard Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) catheter into an active treatment platform. The project couples targeted distal infusion of a “mitochondrial cocktail” — a blend of repurposed FDA-approved agents and vetted experimental therapeutics that blunt the detrimental effects of reperfusion injury that occur with balloon deflation and return of blood flow — with non-invasive adjuncts such as transcutaneous vagus-nerve stimulation. Together, these pharmacologic and neuromodulatory interventions are designed to precondition ischemic tissues during prolonged aortic occlusion, treat detrimental effects of reperfusion, extend the safe balloon time beyond today’s 30-to-60-minute ceiling, and enable combat medics and surgical teams to successfully manage non-compressible truncal hemorrhage in austere, evacuation-delayed environments.

WHY IS IT IMPORTANT?

Non-compressible truncal hemorrhage (NCTH) is the leading cause of potentially preventable battlefield death. REBOA is a therapy to help decrease NCTH mortality, but current REBOA practice is a double-edged sword: after 30–60 minutes of full balloon inflation, reperfusion unleashes a surge of mitochondrial reactive oxygen species, delayed cellular death, and systemic inflammation that can convert a salvageable casualty into a mortality—paradoxically worsening outcomes the longer the aorta is occluded. Large-scale combat operations are expected to routinely exceed that time limit. REBOA-TRIM counters this liability by pharmacologically conditioning ischemic tissue, allowing safe extension of occlusion time and markedly reducing the injury that follows balloon deflation. The platform is designed to dovetail with emerging automated or algorithm-driven partial-occlusion and critical care systems.



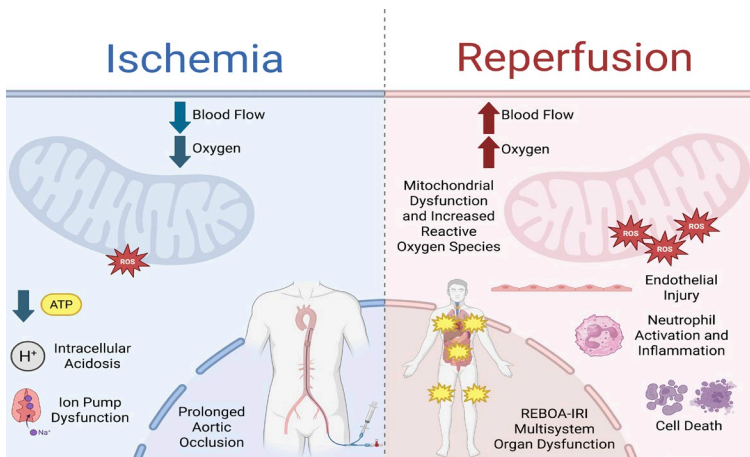
A next-generation automated REBOA catheter (Certus EVAC Catheter) that automatically titrates balloon inflation to allow for partial aortic occlusion. This technique can be further augmented with REBOA-TRIM.

Image by Certus Critical Care Inc. and used with permission (<https://www.certuscriticalcare.com/military>)

HOW DOES IT WORK?

REBOA-TRIM uses the access for the REBOA catheter as well as the flow from partial perfusion to deliver a targeted “mitochondrial cocktail” to at-risk ischemic tissues during occlusion and the first moments of reperfusion to decrease REBOA ischemia-reperfusion injury (IRI). The cocktail will be refined using two dual approaches—repurposed FDA-approved agents as well as experimental therapeutics and rheologic modifiers that are vetted in parallel in a military-civilian research consortium. Simultaneously, transcutaneous vagus-nerve stimulation (VNS) to modulate the cholinergic anti-inflammatory pathway and dampen systemic cytokine release will be tested as a synergistic noninvasive therapeutic modality. The drug cocktail will be designed to resuscitate at the mitochondrial level—beginning with oxidative stress—as well as the downstream deleterious effects of reperfusion injury that lead to life-threatening multisystem organ dysfunction.

This multidrug cocktail is a new approach to treating REBOA-IRI, as is synergizing with noninvasive therapies, ultimately allowing for more time that REBOA can be employed to allow for survival to definitive surgical intervention after NCTH.



Mitochondrial dysfunction and subsequent innate immune activation and endothelial dysfunction plays a critical role in REBOA-IRI.

Image created in BioRender. Walker, P. (2025) <https://BioRender.com/e9zlie7>

THE PATH FORWARD

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In the next 48 months, we will (1) rapidly downselect the mitochondrial cocktail and VNS parameters in swine REBOA models to confirm ≥ 120 min safe occlusion, (2) couple the leading regimen to a next-generation automated REBOA platform and (3) prepare an FDA submission (Investigational Device Exemption/Investigational New Drug as required). A small, civilian Level I trauma early-feasibility study will follow, running in parallel with Department of Defense (DoD) field evaluations, positioning REBOA-TRIM for pivotal trials and forward deployment in the DoD by the end of year four.

THE TAKEAWAY

REBOA-TRIM turns a lifesaving but time-limited therapy into an active, mitochondria-targeted resuscitation platform. By targeted access with a pharmacologic “mitochondrial cocktail” and battlefield-feasible vagus-nerve stimulation, it is poised to extend safe aortic occlusion well past the current 30-to-60-minute ceiling, decreasing mortality from NCTH despite prolonged care scenarios when air superiority is threatened. Fitting seamlessly into emerging automated partial-REBOA systems, REBOA-TRIM will target an agile, four-year development plan for rapid transition from bench to battlefield.

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