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# In-Vivo Detection of Gaseous Microemboli during Aeromedical Evacuation using the Cardiohelp Extracorporeal Life Support System

***George Harea, BS<sup>1</sup>; Brendan Beely, RRT<sup>1,2</sup>; Vitali Karaliou MD<sup>1</sup>; Teryn Roberts, MS<sup>2,3</sup>; Jae-Hyek Choi, PhD, DvSC<sup>2</sup>; Andriy Batchinsky, MD<sup>2-3</sup>***

*<sup>1</sup>The Geneva Foundation, Tacoma, WA; <sup>2</sup>University of the Incarnate Word School of Osteopathic Medicine, San Antonio, TX; <sup>3</sup>Morsani College of Medicine, University of South Florida, Tampa, FL; <sup>4</sup>R Adams Cowley Shock Trauma Center, Baltimore, MD; <sup>5</sup>United States Army Institute of Surgical Research, JBSA Ft. Sam Houston, TX; <sup>6</sup>59<sup>th</sup> Medical Wing, Joint Base San Antonio, San Antonio, TX*

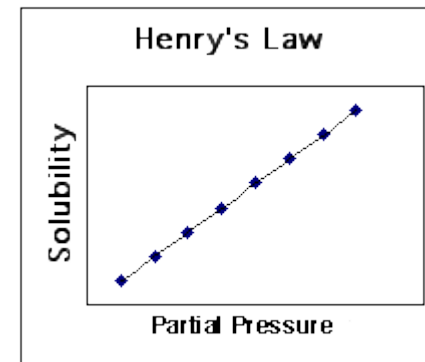
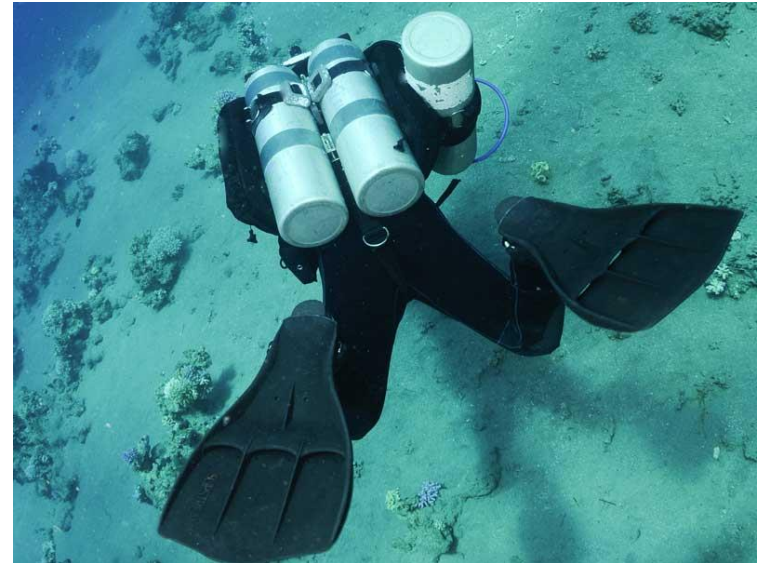
August, 2018  
Kissimmee, FL

*The views presented here are the private views of the author(s) and are not to be construed as the official views or policies of the U.S. Air Force, the U.S. Department of Defense, or The Geneva Foundation.*

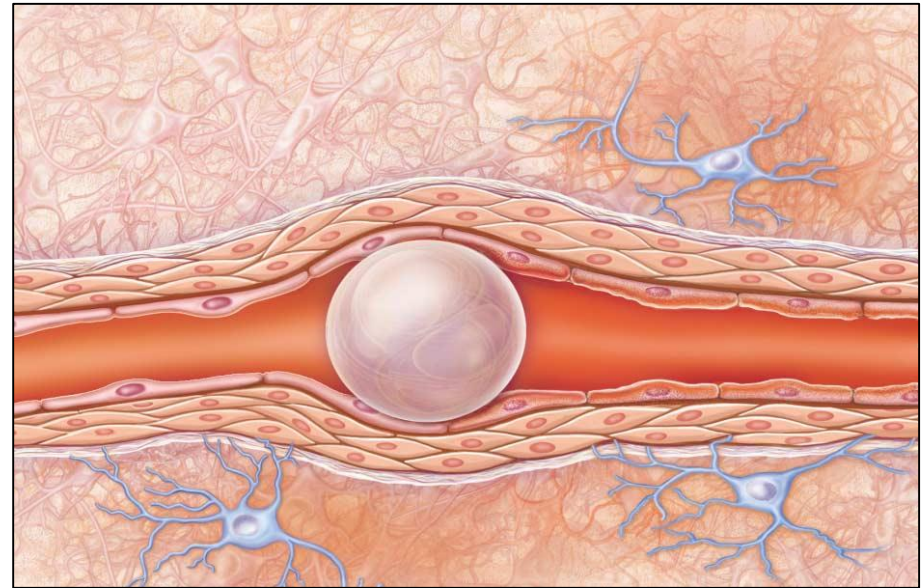
*This study was funded by the United States Air Force, and administered through the 59<sup>th</sup> MDW via The Geneva Foundation under Contract #FA8650-15-C-6692, PI Dr. Andriy Batchinsky, MD.*

*This study has been conducted in compliance with the Animal Welfare Act, the implementing Animal Welfare Regulations, and the principles of the Guide for the Care and Use of Laboratory Animals.*

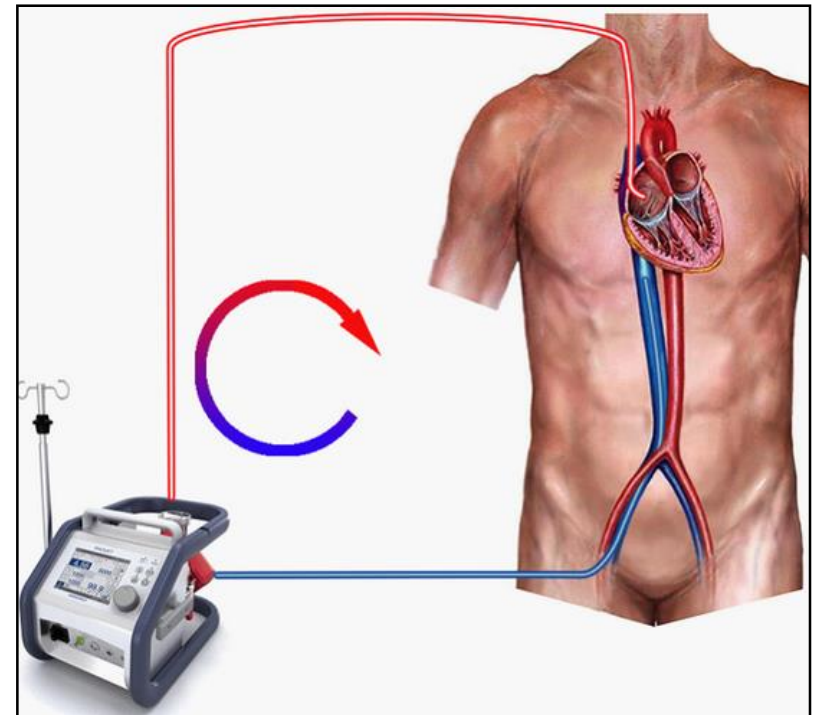
- Decompression Sickness
- “The Bends”
- Henry’s Law / Boyle’s Law
- Extracorporeal Life Support (ECLS) patients are also at risk for injuries caused by gaseous microemboli (GME or “bubbles”) at both ground level and at altitude
- Note: terms GME and bubbles are used interchangeably



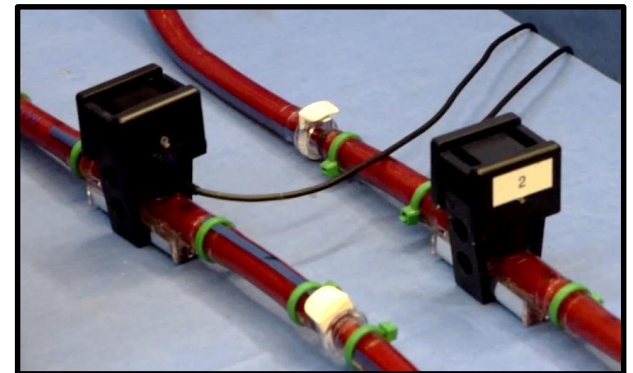
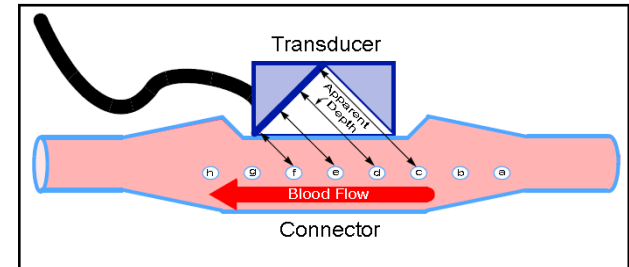
- Mechanical tissue damage
  - Embolisms
  - Gaps between endothelial cells
  - Increased thickness of arteries
  - Ischemia
- Activates coagulation cascade
  - Platelet aggregation
  - Thrombin production
- Inflammatory response



- Cannulation procedure
- ECLS system
- Operator interventions on the ECLS patient
- Lung injury
- Environmental changes
  - Pressure - Boyle's Law / Henry's Law



- Detection in circulating fluids using ultrasound techniques
  - Ultrasound waves are scattered by particles in blood
  - Bubbles produce a stronger signal than blood cells
- Emboli Detection and Classification (EDAC) processes these signals and returns bubble counts and size ranges





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## OBJECTIVE



- Our objective was to assess in-vivo detection of GME in the Cardiohelp ECLS system during aeromedical evacuation using the Emboli Detection and Classification Quantifier (EDAC™)
- (Terumo Cardiovascular Systems Corp., Ann Arbor, MI)



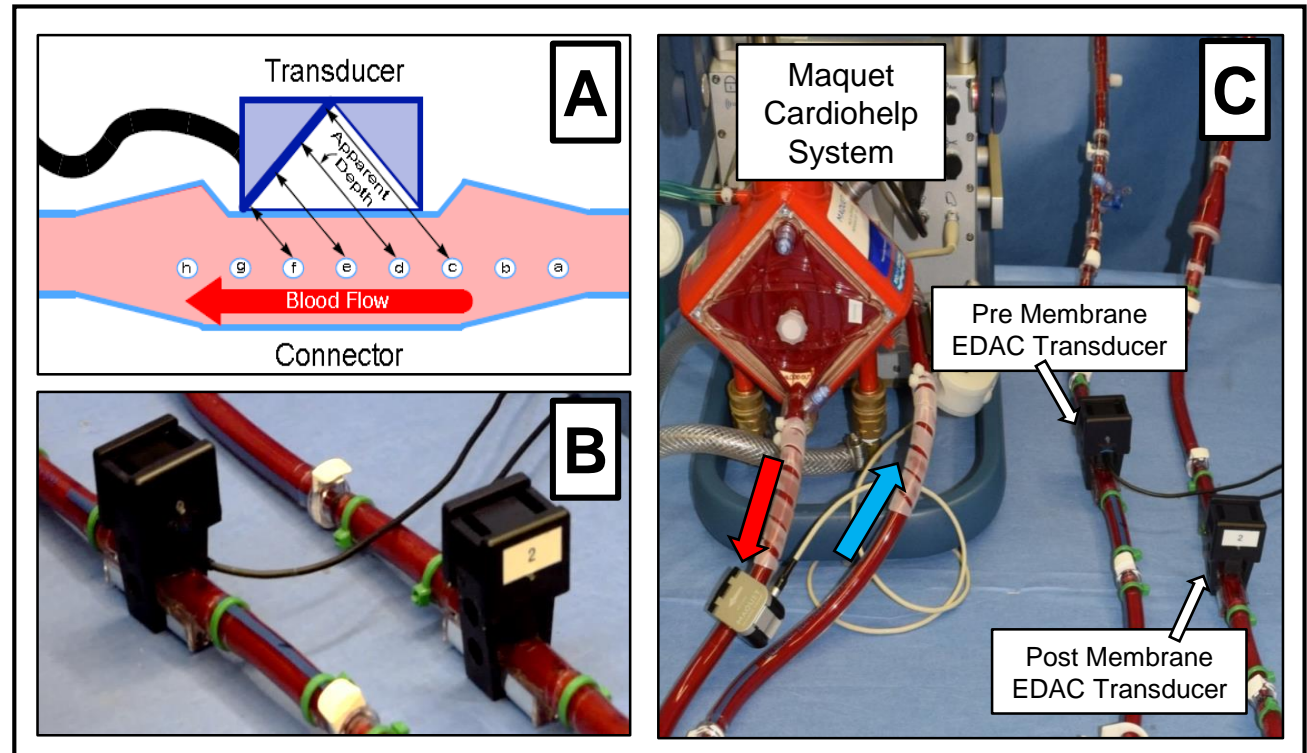
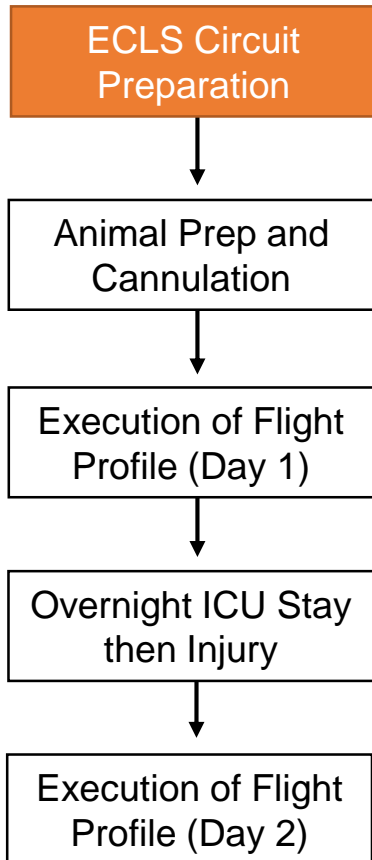
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# HYPOTHESIS



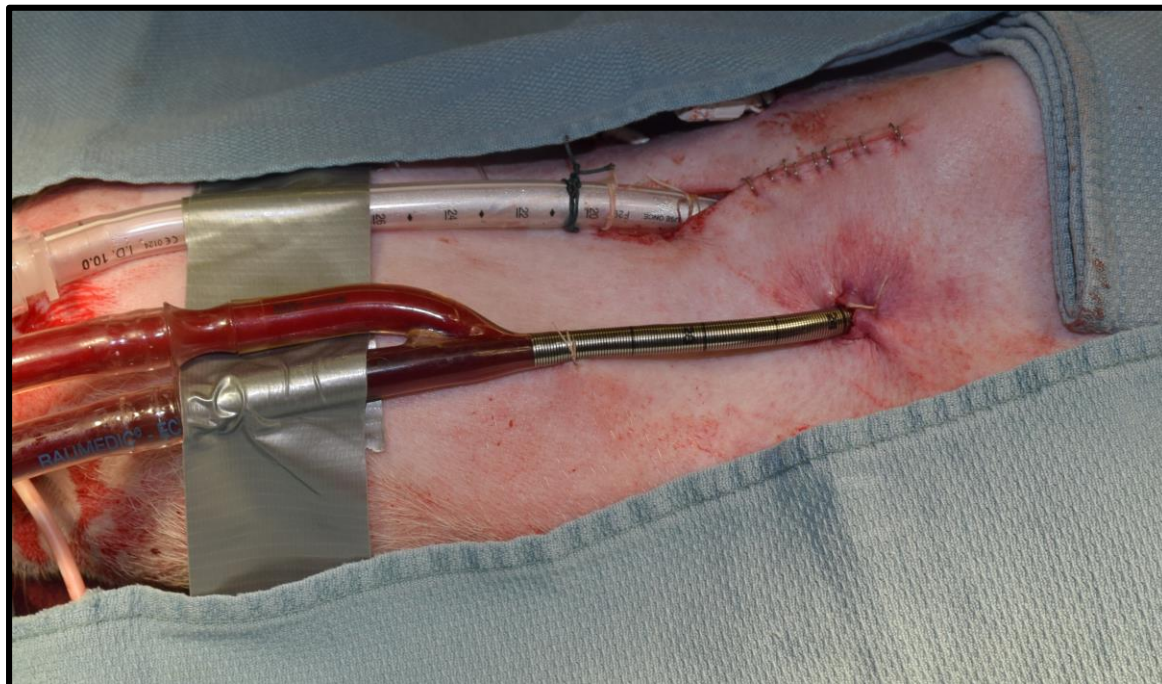
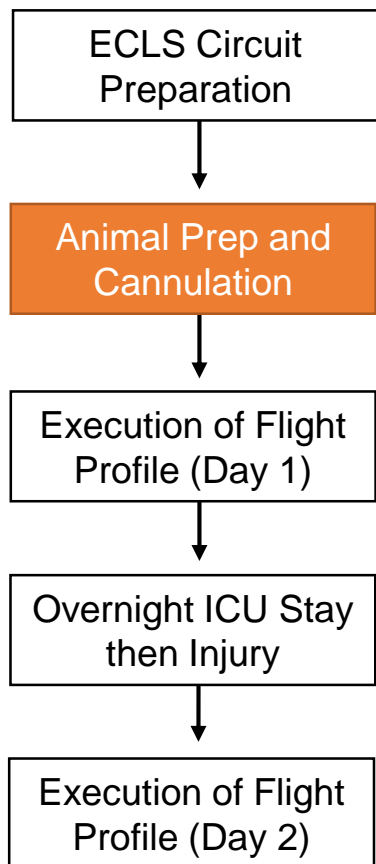
- We hypothesized that there will be an increase in GME counts as a result of trauma, changes in altitude and ECLS

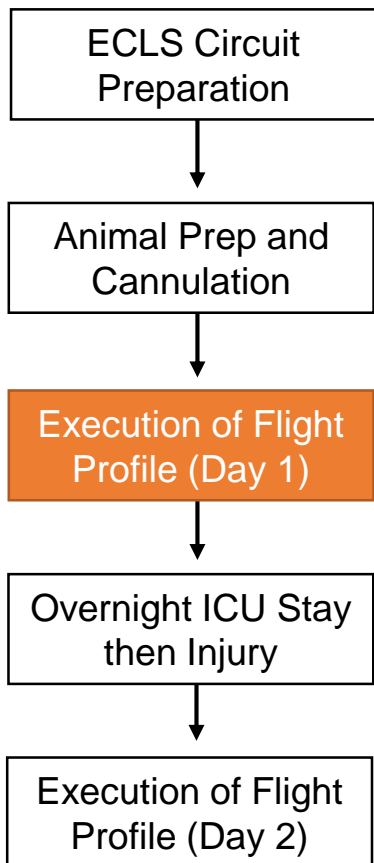
- Cardiohelp HLS Advanced 7.0 Set
- EDAC GME Detector



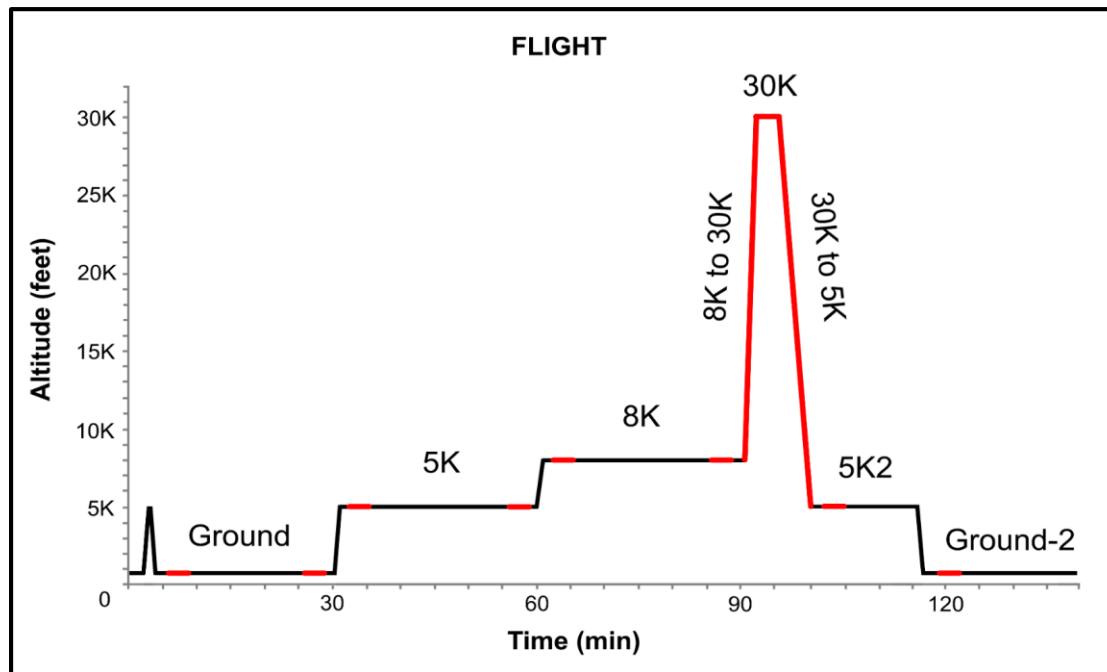


- Anesthetized swine received VV ECLS
- 23F veno-venous Avalon catheter in right jugular vein (n=13).
- No injury on 1<sup>st</sup> day.

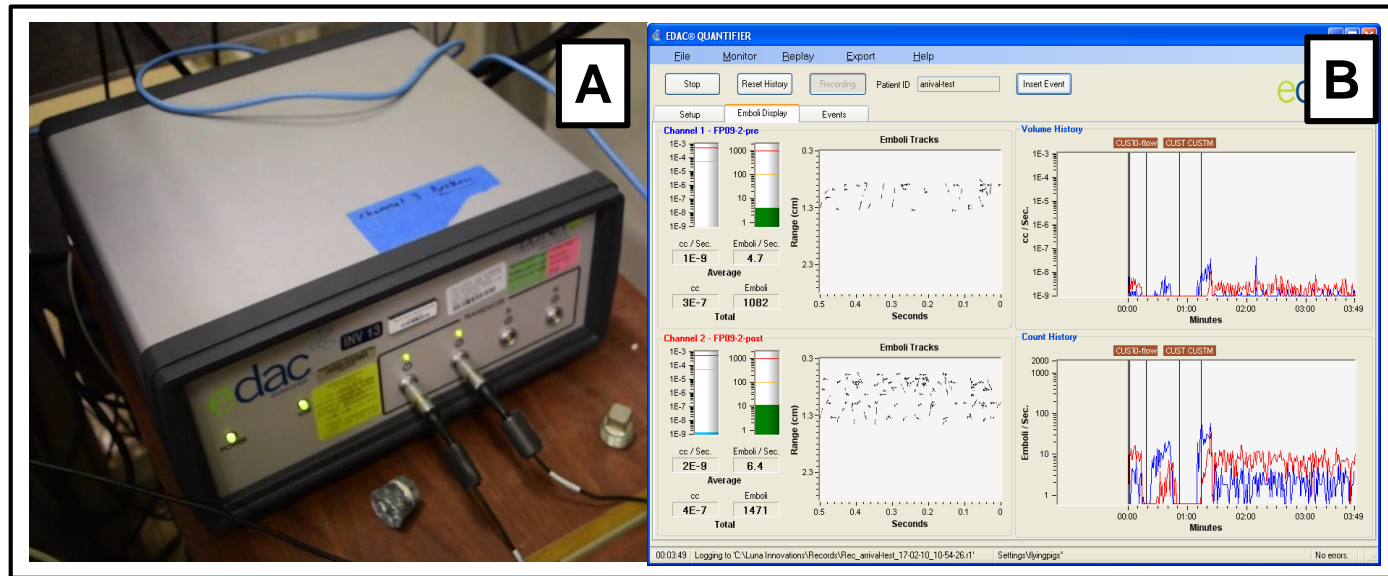
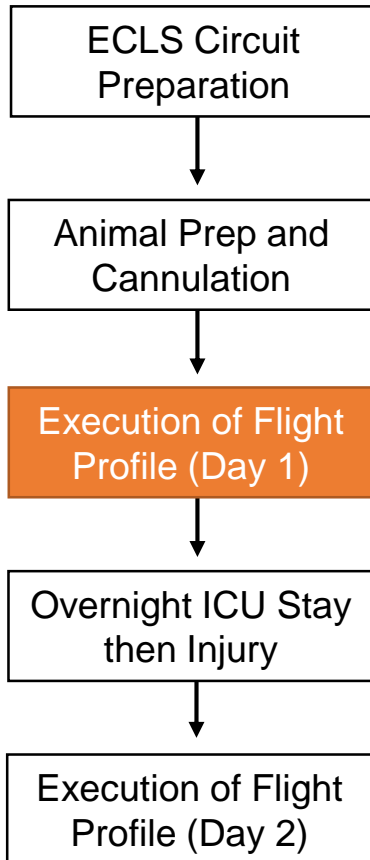




- Flight profile detailing operating altitudes
- Day 1 Flight is uninjured state
- EDAC measurements indicated by red highlights
- Two EDAC recordings per altitude level

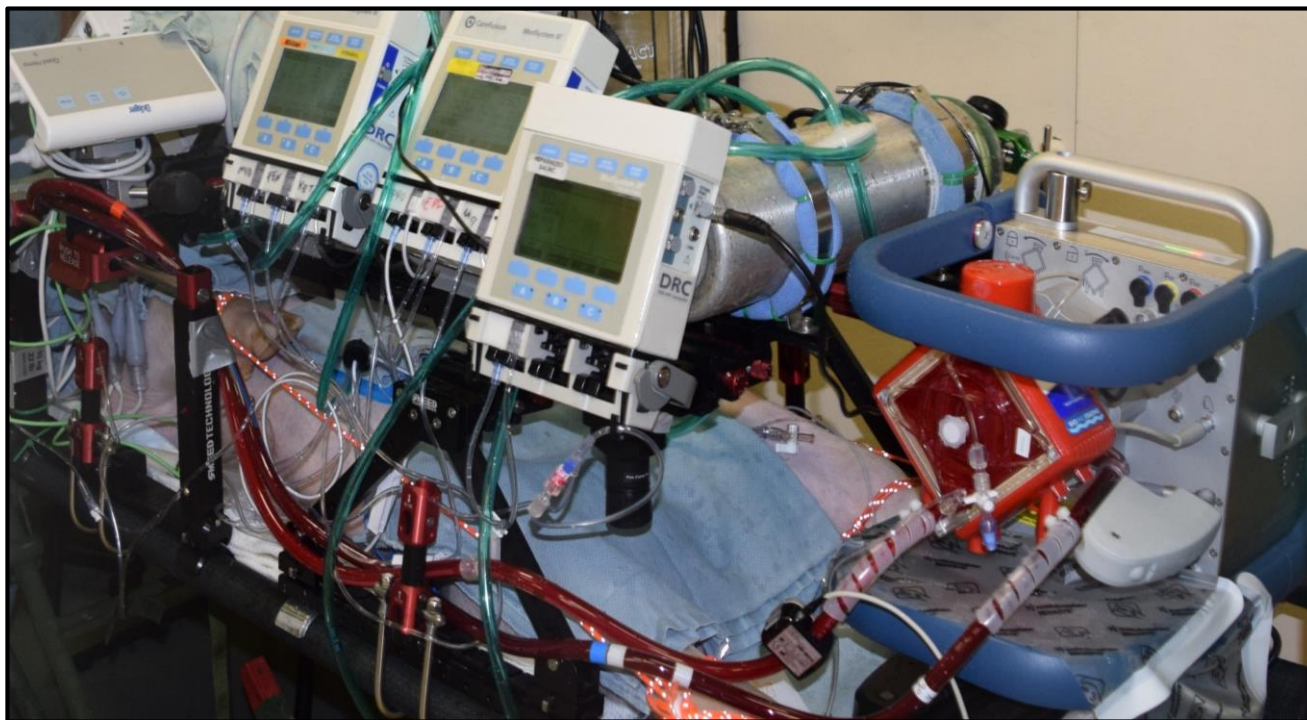
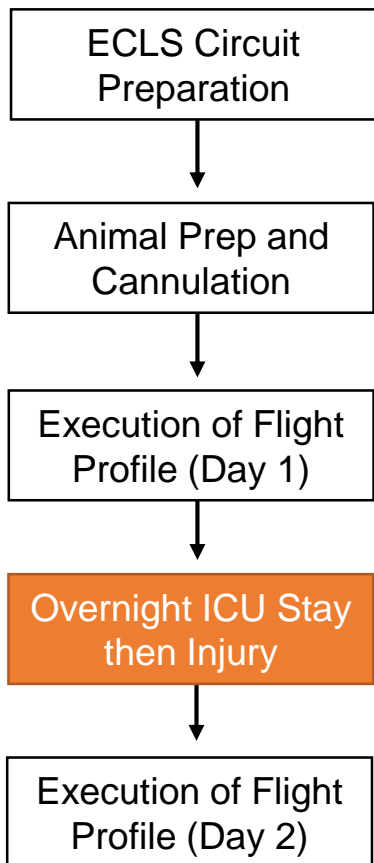


- Flight profile detailing operating altitudes
- Day 1 Flight is uninjured state
- EDAC GME Detector (A) with two transducers: pre-ML- upper panel and post ML- lower panel (B).

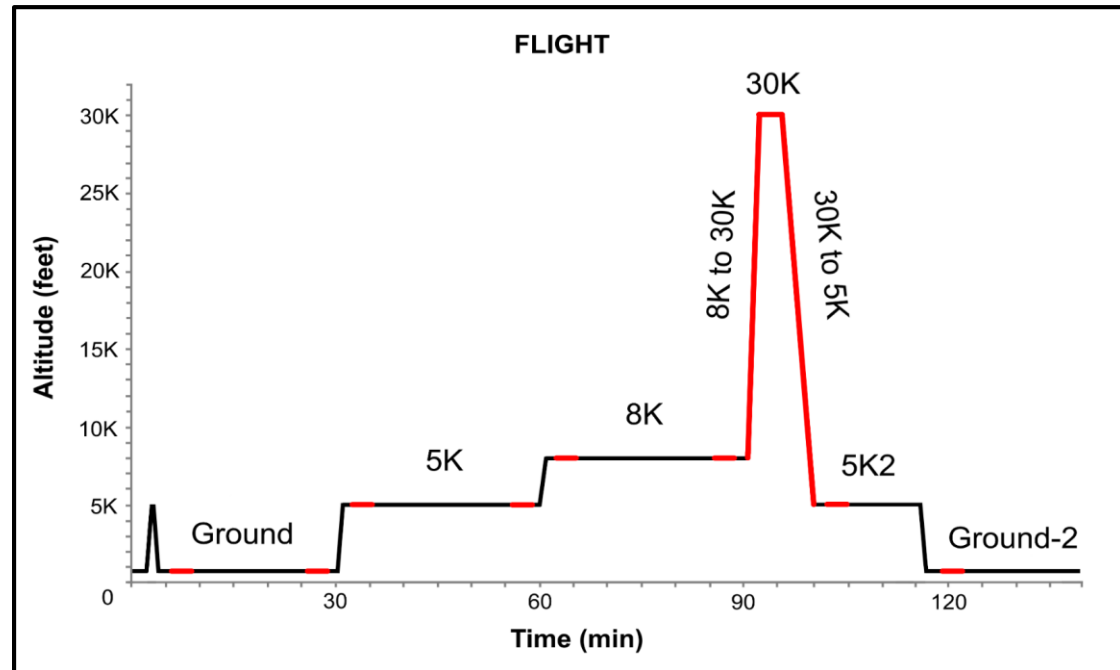
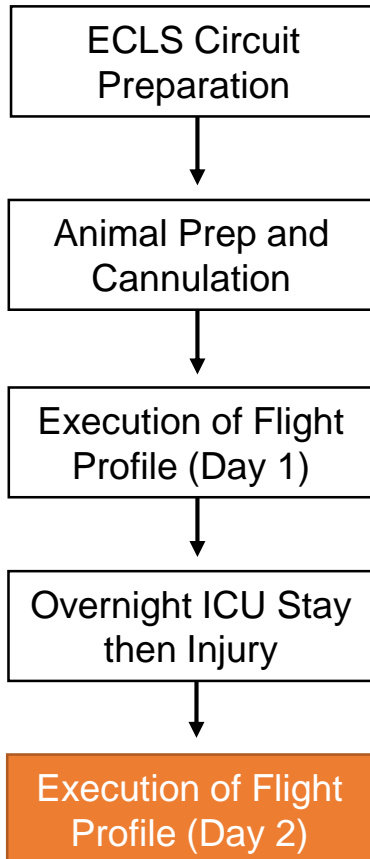




- After flight, transport back to ICU for overnight stay
- Morning of Day 2, animal receives bilateral pulmonary contusion using modified captive bolt stunner
- Transport back to altitude chambers



- Day 2
- Flight repeated with animal in injured state
- EDAC measurements indicated by red highlights



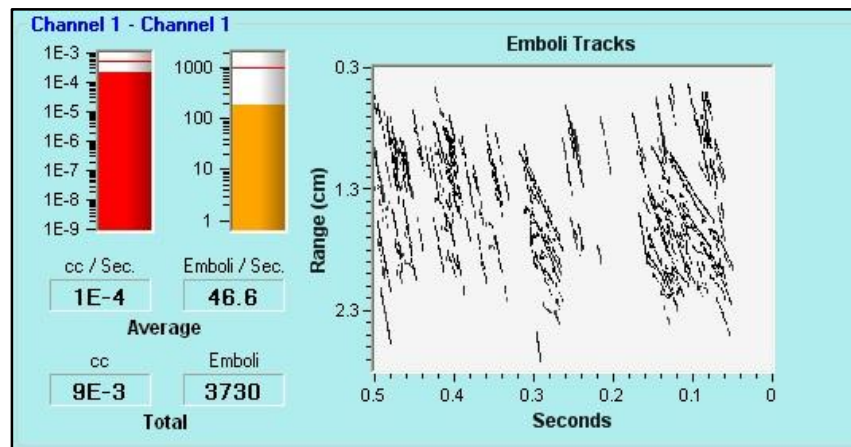


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# METHODS



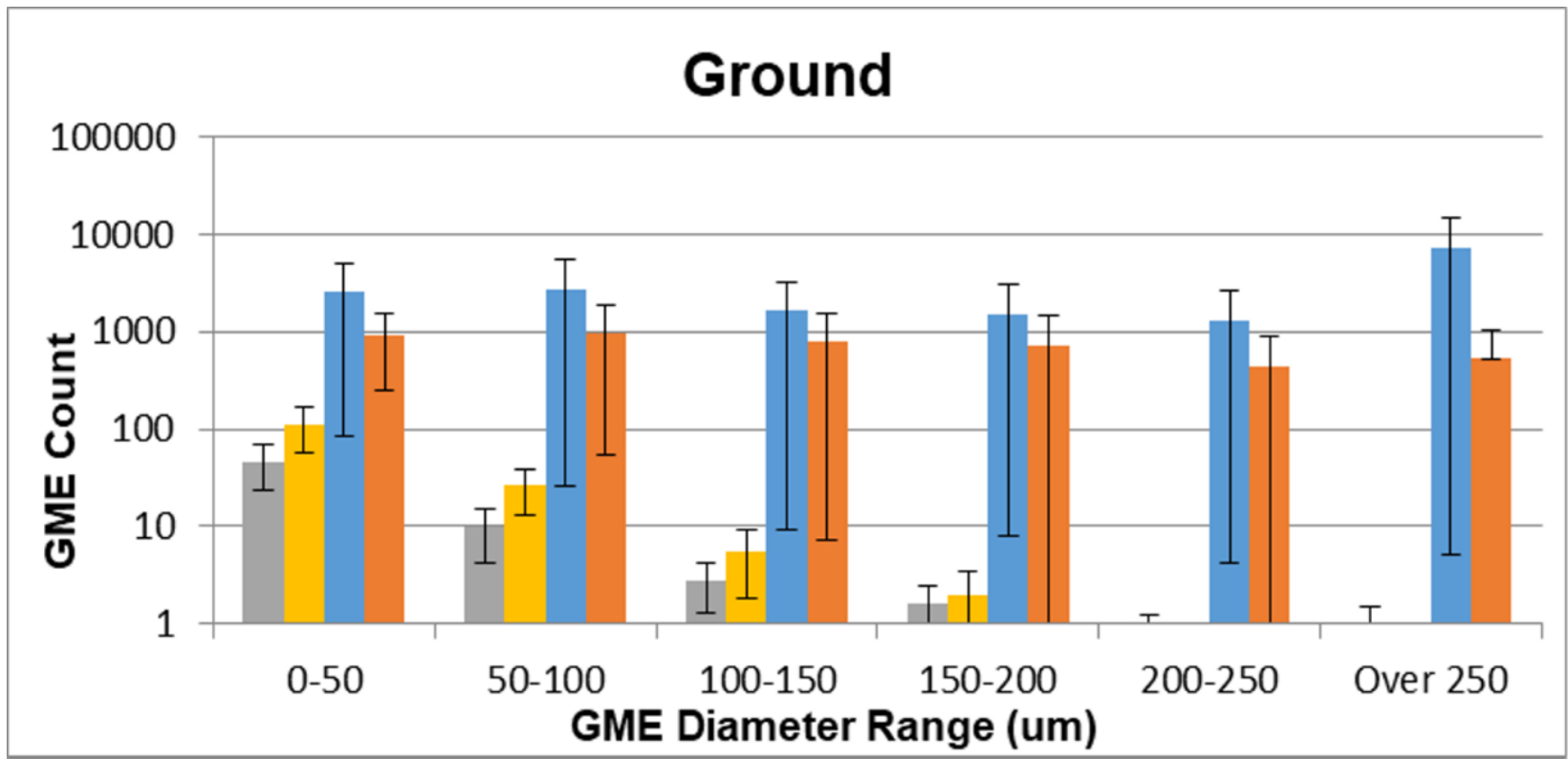
Phase 1	Phase 2	Phase 3	Phase 4	Phase 5	Reset	
<b>EDAC</b>	Disconnected	Connected	Connected	Connected	Connected	Disconnected
<b>Flow Rate</b>	2 liters/min	0 liters/min	2 liters/min	2 liters/min	2 liters/min	2 liters/min
<b>Recording Time</b>	3 minutes Pre and Post	3 minutes Pre and Post	3 minutes Pre and Post	3 minutes Pre and Post	3 minutes Pre and Post	
<b>Expected Results</b>	0 bubbles	0 bubbles	Some bubbles	<b>A lot of bubbles due to injection</b>	Fewer bubbles	



- Statistics
- Using SAS 9.3 (Cary, NC) and an alpha of 0.05 for significance, a Two Sample test for equivalence was conducted comparing pre- and post-membrane bubble counts for each phase
- Followed by an independent variable test to compare between groups for each pre- and post-membrane measurement at each bubble size range.

Ground	5K	8K	8K to 30K	30K	30K to 5K	5K-2	Ground-2
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- No difference between uninjured and injured conditions
- No difference between pre and post membrane for any size ranges

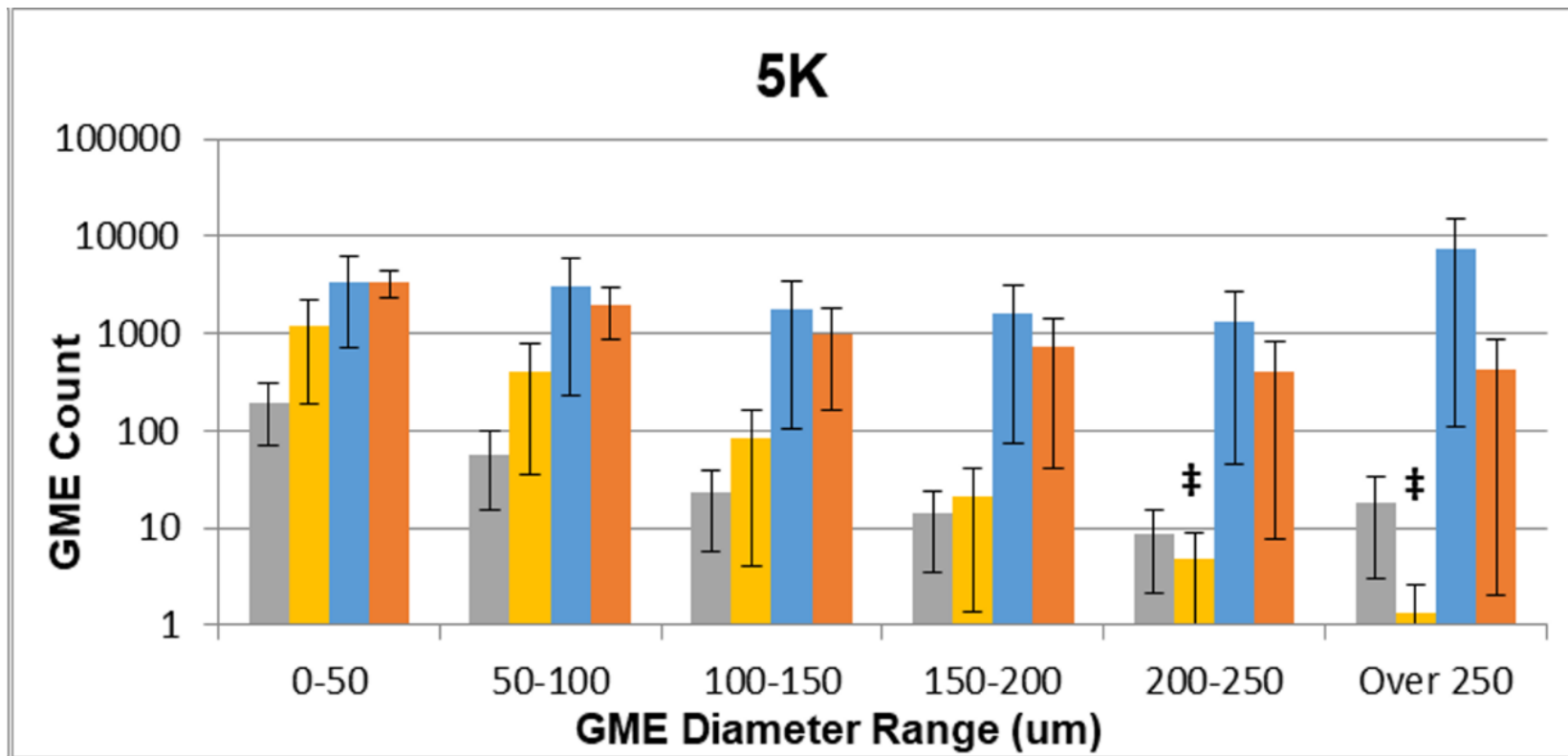


<span style="display: inline-block; width: 15px; height: 15px; background-color: grey; border: 1px solid black; margin-right: 5px;"></span> Uninjured Pre-Membrane	<span style="display: inline-block; width: 15px; height: 15px; background-color: yellow; border: 1px solid black; margin-right: 5px;"></span> Uninjured Post-Membrane
<span style="display: inline-block; width: 15px; height: 15px; background-color: blue; border: 1px solid black; margin-right: 5px;"></span> Injured Pre-Membrane	<span style="display: inline-block; width: 15px; height: 15px; background-color: orange; border: 1px solid black; margin-right: 5px;"></span> Injured Post-Membrane

\* difference from baseline within the same injury group  
 † difference between pre- and post- detector locations  
 ‡ difference between uninjured and injured  
 § difference from previous altitude

Ground	5K	8K	8K to 30K	30K	30K to 5K	5K-2	Ground-2
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- Injured animals show increase in post-membrane GME compared to uninjured above 200um GME diameter

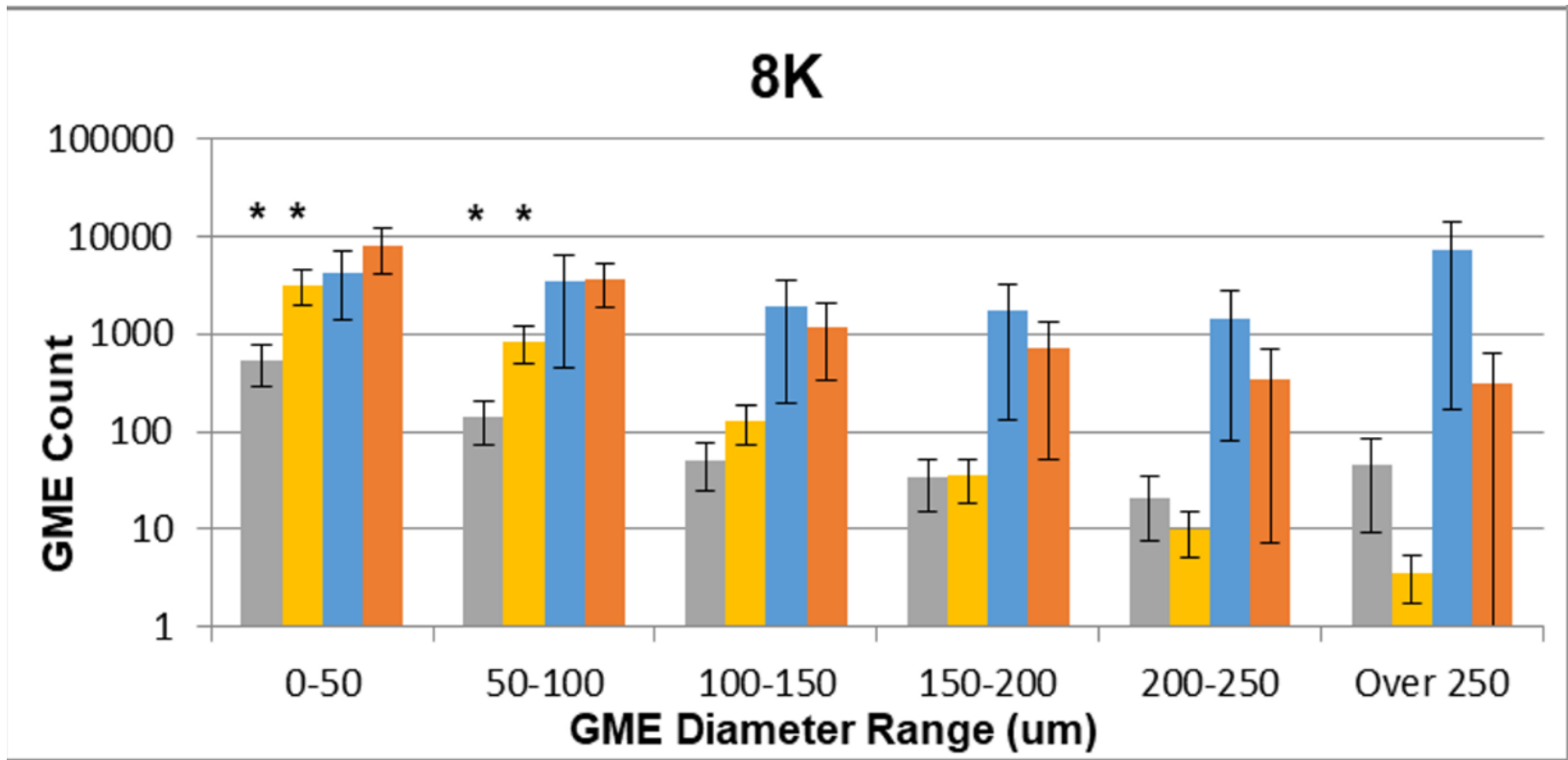


Uninjured Pre-Membrane
  Uninjured Post-Membrane  
 Injured Pre-Membrane
  Injured Post-Membrane

\* difference from baseline within the same injury group  
 † difference between pre- and post- detector locations  
 ‡ difference between uninjured and injured  
 § difference from previous altitude

Ground	5K	8K	8K to 30K	30K	30K to 5K	5K-2	Ground-2
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- 10-fold GME increase vs. Ground level for uninjured animals in the smallest two size ranges

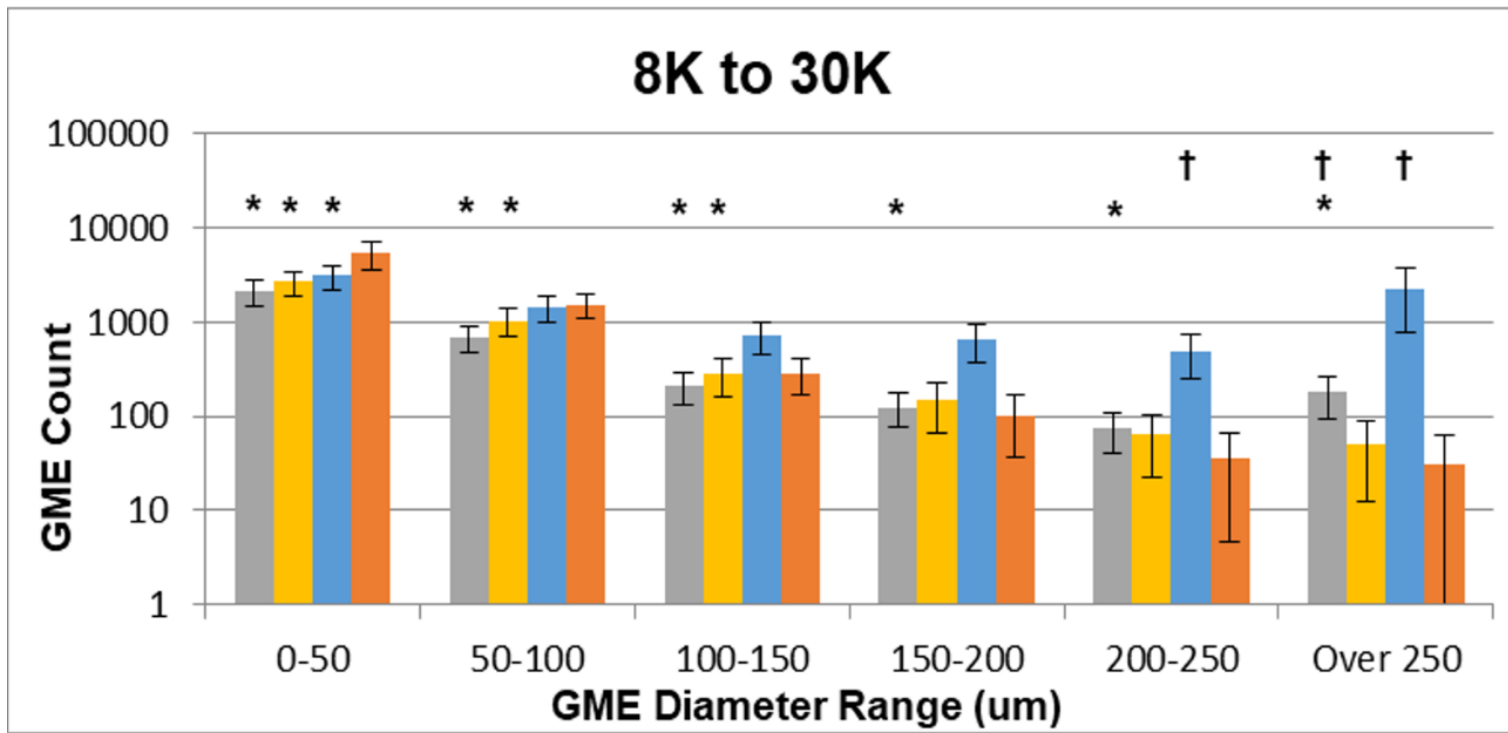


Uninjured Pre-Membrane   
  Uninjured Post-Membrane  
 Injured Pre-Membrane   
  Injured Post-Membrane

\* difference from baseline within the same injury group  
 † difference between pre- and post- detector locations  
 ‡ difference between uninjured and injured  
 § difference from previous altitude

Ground	5K	8K	8K to 30K	30K	30K to 5K	5K-2	Ground-2
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- 10-fold increase in GME vs. Ground level for uninjured pre-membrane at all size ranges
- Similar increase seen in uninjured post membrane but only for the smallest 3 size ranges
- Reduction in GME counts post membrane for GME sizes larger than 200um

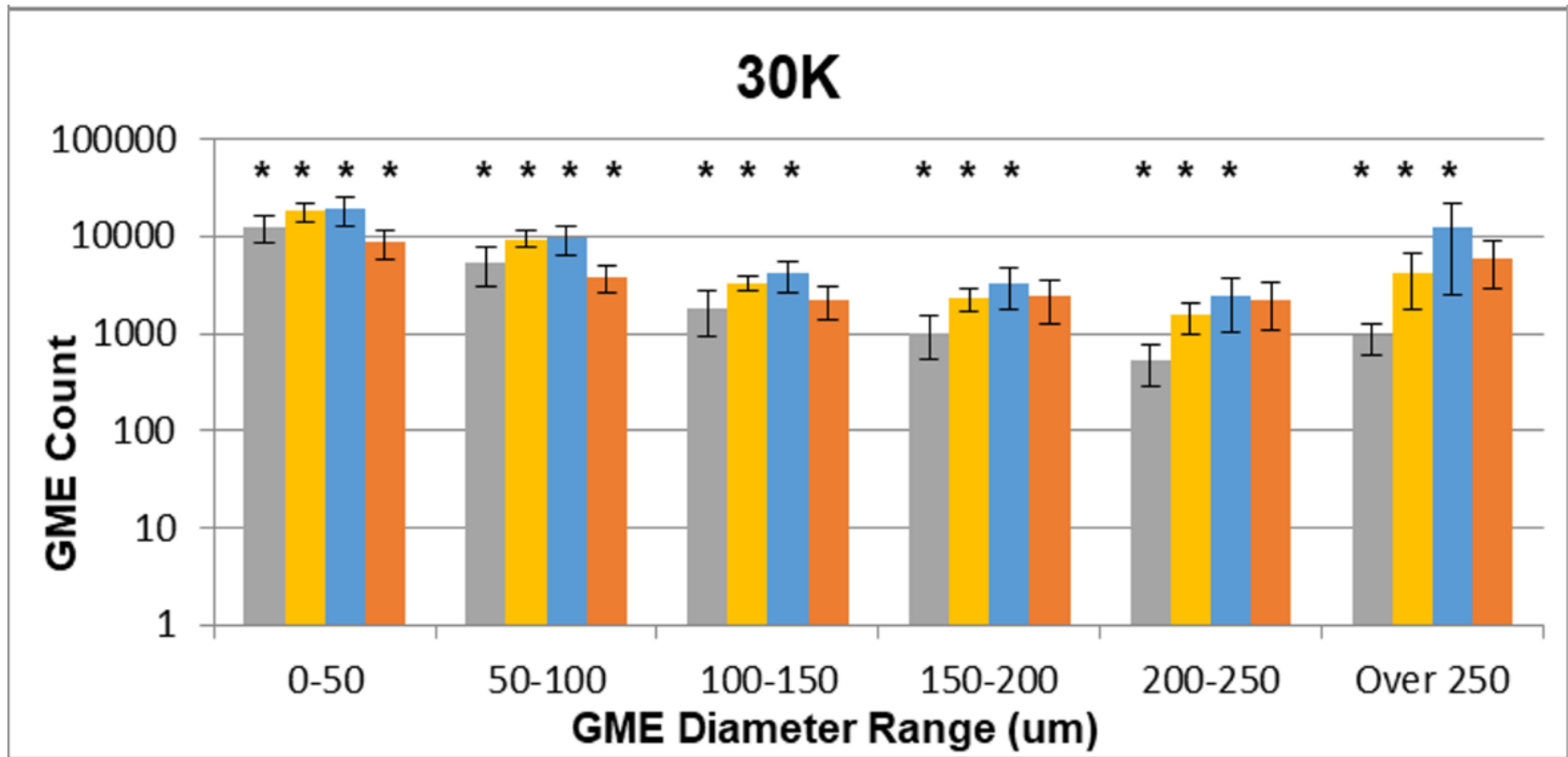


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\* difference from baseline within the same injury group  
 † difference between pre- and post- detector locations  
 ‡ difference between uninjured and injured  
 § difference from previous altitude

Ground	5K	8K	8K to 30K	30K	30K to 5K	5K-2	Ground-2
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- 10- to 100-fold increase in GME counts for all diameter ranges vs Ground

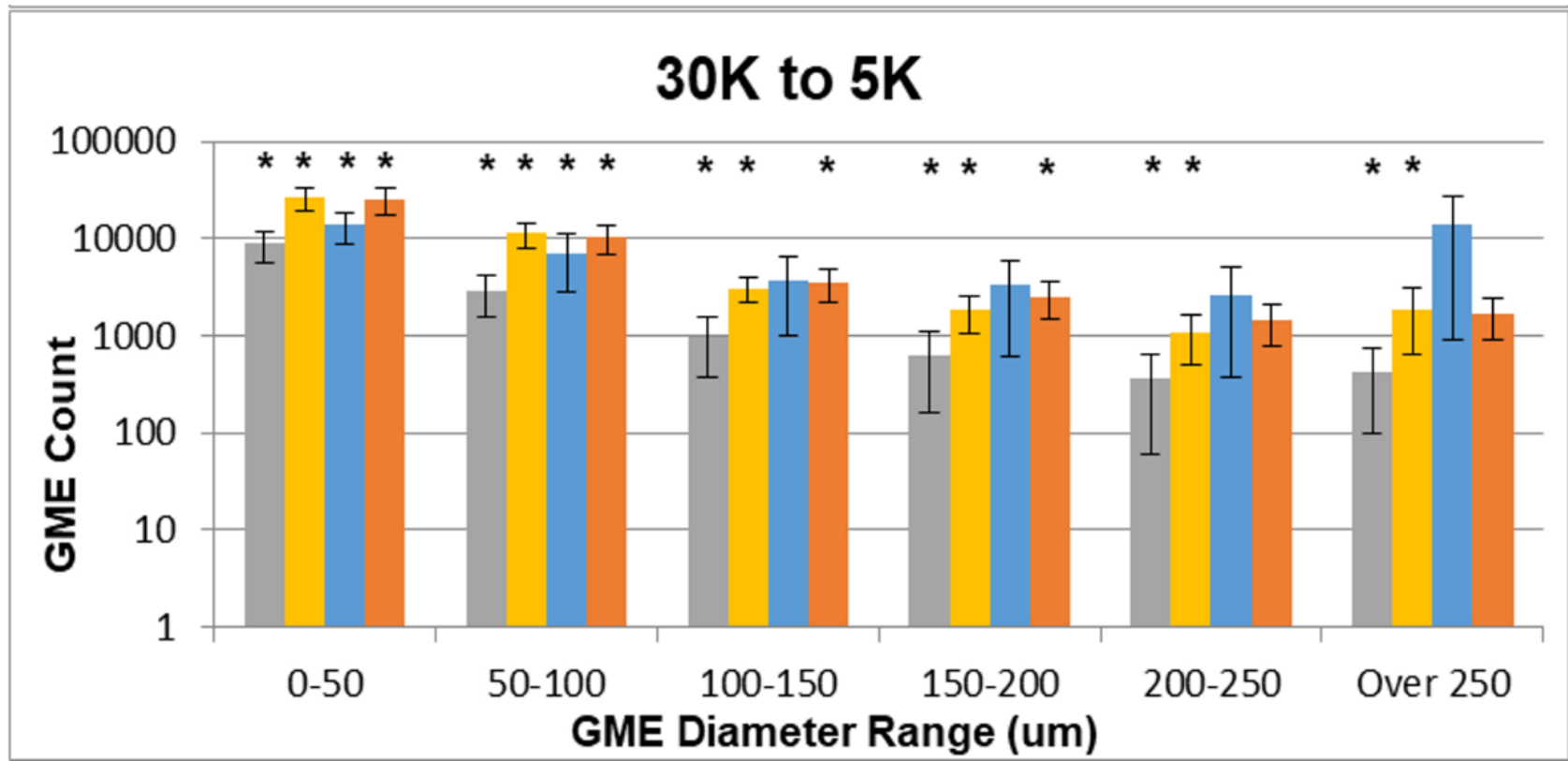


Uninjured Pre-Membrane    
  Uninjured Post-Membrane  
 Injured Pre-Membrane    
  Injured Post-Membrane

\* difference from baseline within the same injury group  
 † difference between pre- and post- detector locations  
 ‡ difference between uninjured and injured  
 § difference from previous altitude

Ground	5K	8K	8K to 30K	30K	30K to 5K	5K-2	Ground-2
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- 10- to 100-fold increase in GME counts for all diameter ranges vs Ground

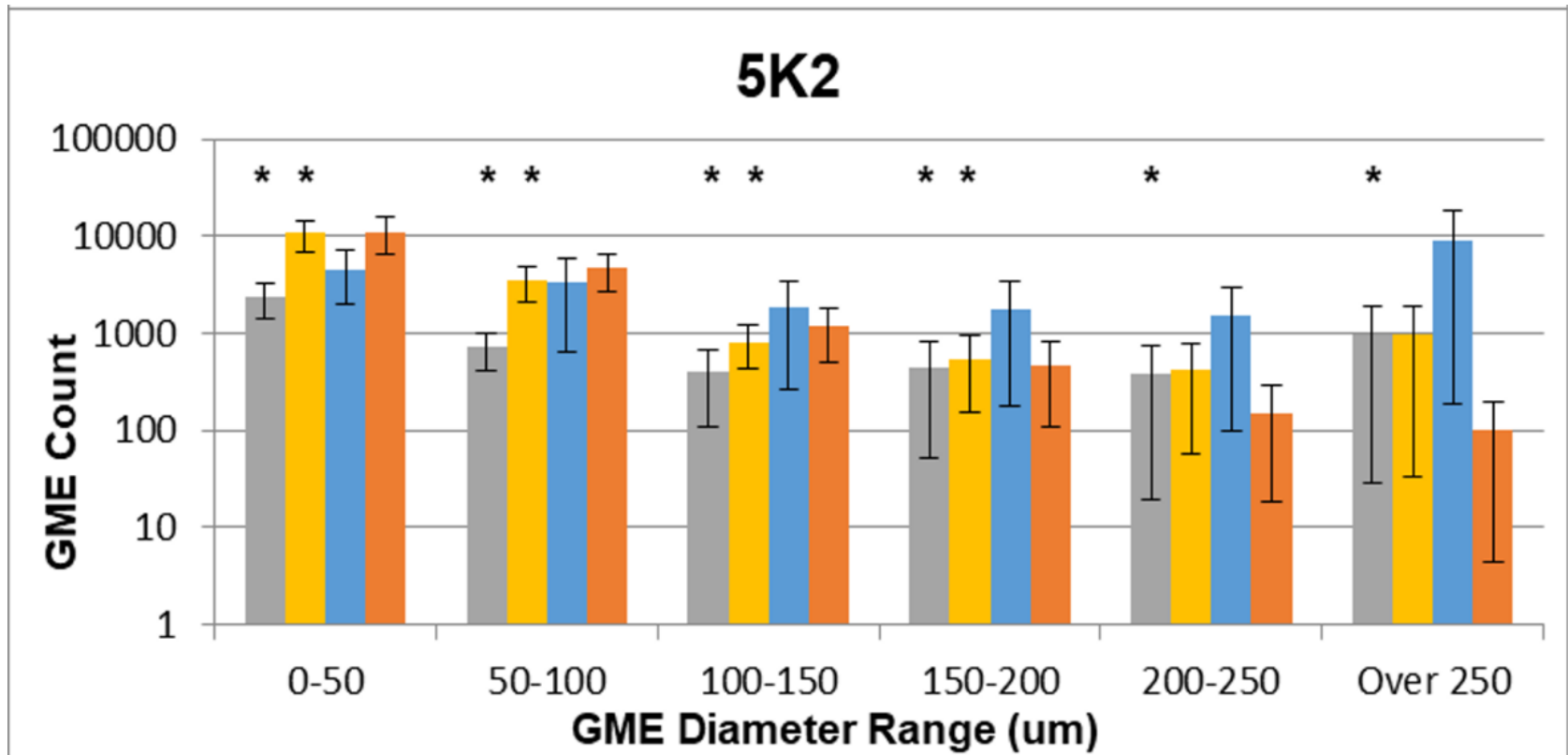


Uninjured Pre-Membrane    
  Uninjured Post-Membrane  
 Injured Pre-Membrane    
  Injured Post-Membrane

\* difference from baseline within the same injury group  
 † difference between pre- and post- detector locations  
 ‡ difference between uninjured and injured  
 § difference from previous altitude

Ground	5K	8K	8K to 30K	30K	30K to 5K	5K-2	Ground-2
--------	----	----	-----------	-----	-----------	------	----------

- GME counts for uninjured pre-membrane at all size ranges, and uninjured post membrane under 200um remain elevated vs. Ground

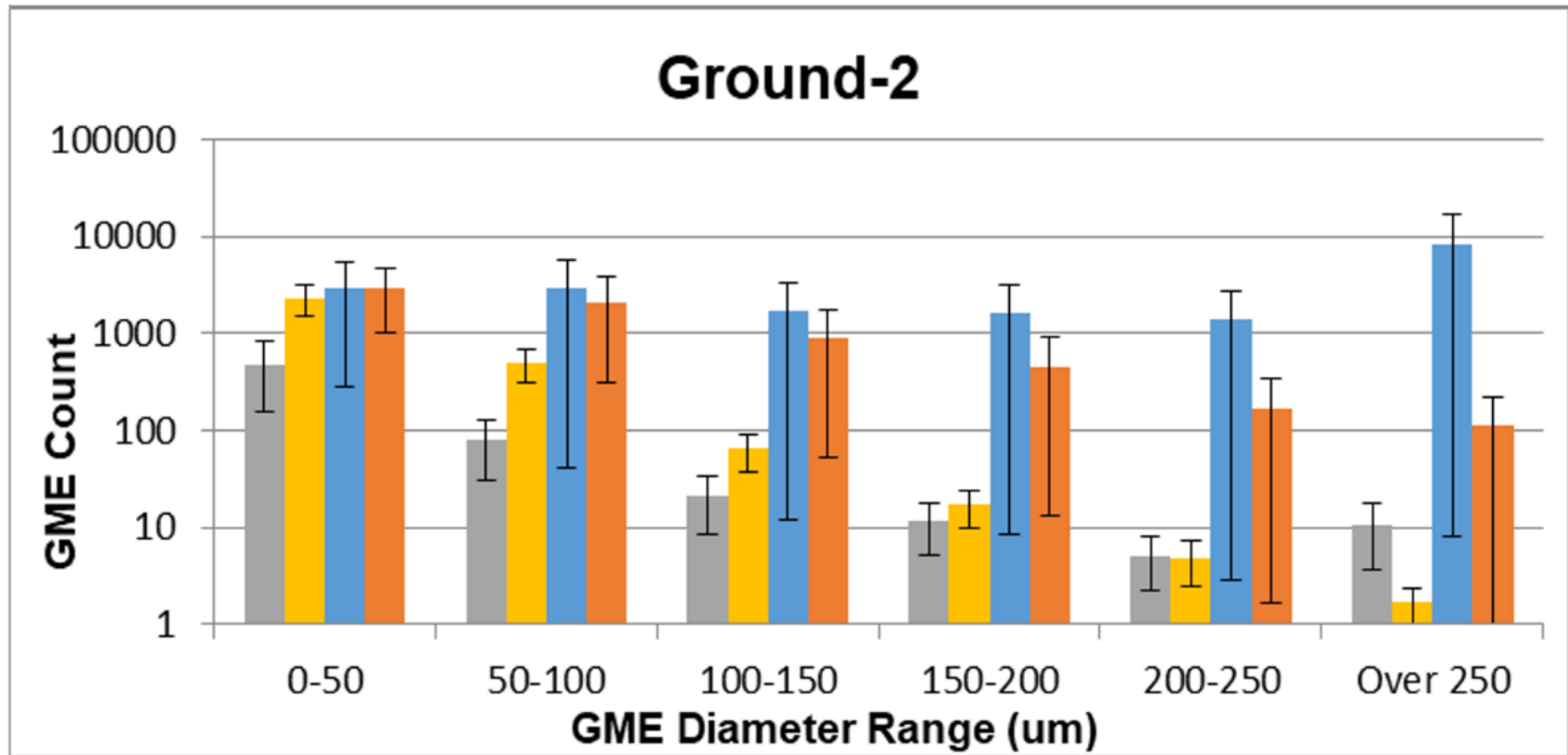


Uninjured Pre-Membrane  
 Uninjured Post-Membrane  
 Injured Pre-Membrane  
 Injured Post-Membrane

\* difference from baseline within the same injury group  
 † difference between pre- and post- detector locations  
 ‡ difference between uninjured and injured  
 § difference from previous altitude

Ground	5K	8K	8K to 30K	30K	30K to 5K	5K-2	Ground-2
--------	----	----	-----------	-----	-----------	------	----------

- No differences between Ground and Ground-2 in both uninjured and injured animals in all ranges



<span style="display: inline-block; width: 15px; height: 15px; background-color: grey; border: 1px solid black; margin-right: 5px;"></span> Uninjured Pre-Membrane	<span style="display: inline-block; width: 15px; height: 15px; background-color: yellow; border: 1px solid black; margin-right: 5px;"></span> Uninjured Post-Membrane
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\* difference from baseline within the same injury group  
 † difference between pre- and post- detector locations  
 ‡ difference between uninjured and injured  
 § difference from previous altitude



## CONCLUSION

- This is the first report of GME detection in a modern ECLS device during aeromedical evacuation of subjects with ARDS at ground and various altitudes
- Ascent to 8 and more so to 30K led to sustained elevation of GME levels in all ranges vs. ground level
- There was no significant difference in GME counts between uninjured and injured states
- GME  $\geq 100\mu\text{m}$  were not significantly increased possibly due to the presence of the ML
- ML may trap larger GME and prevent them from re-entering the animal's systemic circulation
- GME may be an important contributor to end organ damage during transport of subjects at altitudes above 8K feet



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# QUESTIONS

