# Systemic and Microcirculatory Effects of Severe Hemorrhage and Resuscitation Using a Hemoglobin-Based Oxygen Carrier (HBOC)

Bjorn K. Song, William H. Nugent. Song Biotechnologies LLC, Baltimore, MD, 21230

This study investigated the systemic (heart rate, mean arterial pressure) and microcirculatory (vasoactivity, interstitial fluid oxygenation - ISF $PO_2$) impact of two resuscitation fluids: a novel third generation HBOC (Sanguinate™; Prolong Pharmaceuticals™, South Plainfield, NJ), and a non-oxygen carrying colloid volume control (Hextend™; Hospira, Inc, Lake Forest, IL). Male Sprague-Dawley rats underwent a controlled 45% blood volume hemorrhage at 3.5 ml x $min^{-1}$ x $kg^{-1}$ through a cannulated carotid artery and were maintained in this hypovolemic, hemorrhagic shock phase for 30 minutes. Resuscitation fluids were infused at a rate of 3.5 ml x $min^{-1}$ x $kg^{-1}$ to a volume equal to 20% of the total estimated blood volume through a cannulated jugular vein. Systemic measurements were recorded via a cannulated femoral artery that was connected to a pressure transducer (MP150; Biopac Systems, Inc, Goleta, CA) while microcirculatory parameters were collected through phosphorescence quenching and intravital microscopic examination of the exteriorized spinotrapezius muscle. Compared to baseline, the 45% hemorrhage produced a significant reduction in heart rate, blood pressure, arterial diameter and ISF $PO_2$ in all animals. Resuscitation with either HBOC or Hextend™ animals improved the systemic parameters towards baseline, but only HBOC-treated animals showed an improvement in ISF $PO_2$. The impact of improved systemic variables was evident in mortality with untreated animals (sham) expiring an hour after hemorrhage, while Hextend resuscitated animals expired after 4 hours. HBOC animals survived for the entire 8 hour observation period. In addition to extended survival times, HBOC animals showed steady systemic and microcirculatory parameters. Hextend™ resuscitated animals, however, developed rigor mortis in their limbs at approximately 3 hours post-hemorrhage, which was concurrent with a rapid decline in systemic variables. These results demonstrate that while reestablishing blood pressure is acutely important

for post-hemorrhage survival, restoring oxygen delivery to peripheral tissues is critical for improving long-term outcomes.

Support: Prolong Pharmaceuticals™ Contract No. ???