An *In Situ* Self-Expanding Polyurethane Foam for the Treatment of Noncompressible Abdominal Hemorrhage

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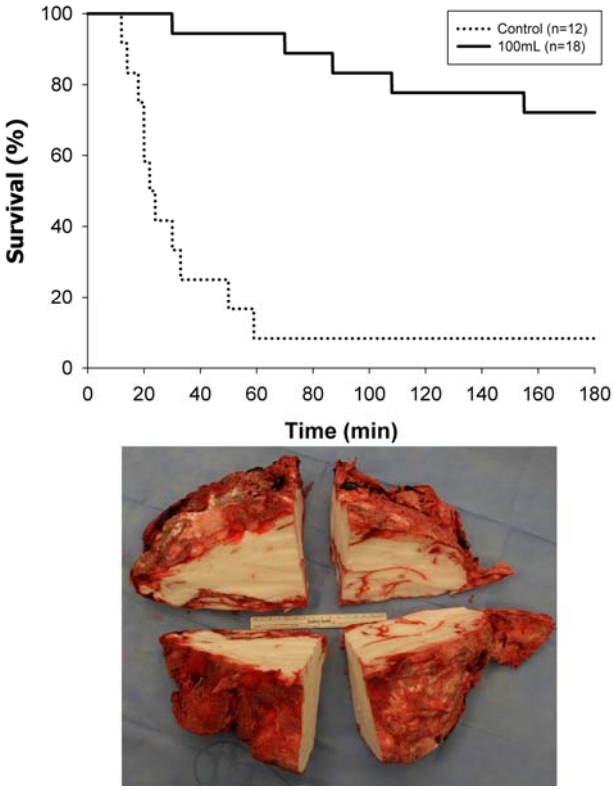
Statement of Purpose:
Noncompressible abdominal hemorrhage is a significant cause of preventable death in military and civilian trauma.[1, 2] There are no available pre-hospital treatments other than rapid transport to definitive surgical care, and many die before reaching a surgeon.[3] Previous concepts for treating this injury have been ineffective when tested in relevant animal models.[4, 5] We have developed an *in situ* self-expanding polyurethane foam as a prehospital, bridge-to-surgery intervention for severely injured, high-risk patients. We hypothesized that this material could improve survival relative to the current standard of care.

Methods: We developed a library of over 1,300 novel, self-expanding polyurethane foams by systematically varying key properties such as expansion ratio, hydrophobicity, viscosity, and compressive strength. A subgroup of formulations was tested in a swine model to determine key properties for transport within the abdominal cavity in order to select a lead.

This formulation was subsequently tested in two animal models to evaluate efficacy and safety: (1) hepatic-portal injury, (2) non-lethal splenic injury/chronic survival. Model 1: Strategic wire placement was used to create a lethal, closed-cavity hepato-portal injury. Foam was administered at a range of doses and compared to a control group with resuscitation alone. Model 2: A low grade splenic injury was created, and animals received fluids (control) or foam. Foam was removed at three hours and animals were monitored for 28 days.

Results: Exploratory work revealed that high expansion ratio coupled with low blood absorption is optimal for foam transport through pooled blood and contact with bleeding tissue. The optimized formulation was subsequently tested in two swine models to determine efficacy, safety, and dose. Model 1(hepatoportal injury)[6]: Administration of foam improved survival in a lethal model. Survival was 94% at one hour and 72% at three hours compared to 8.3% in the control group at both time points ($p<0.001$) at the selected dose (100 mL). Hemorrhage rate from injury was significantly reduced in the foam group compared to controls (0.51 ± 0.50 vs. 3.0 ± 1.3 g/kg/min; $p<0.001$). The use of foam resulted in a transient increase in intraabdominal pressure and immediate rebound in arterial pressure and cardiac output. Model 2 (chronic survival)[7]: After splenic injury and recovery, animals survived without impaired organ function, differences in serum chemistry, or significant complications to 28-days after simulated use. Foam conformation to bowel resulted in ecchymotic lesions that were repaired prior to recovery. Remnant foam particles were encapsulated within a thin fibrotic layer, with an inflammatory response similar to absorbable suture. The treatment was not associated with unacceptable adhesions.



Kaplan-Meier curve demonstrating survival improvement in a severe liver injury model (top)[6], and a representative image of the foam after being cut into four pieces (bottom)[7].

Conclusions: Significant pre-clinical work has demonstrated the efficacy and safety of our *in situ* forming polyurethane foam. While further translational research is required, this intervention can provide a prehospital "hemostatic bridge" for severely bleeding casualties, who would otherwise bleed to death in the field, enabling them to arrive alive to a surgical treatment facility

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