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Title: Treatment of noncompressible intraabdominal hemorrhage with resorbable foam supplemented with clotting factors

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Background
An effective field treatment for stabilizing injured warfighters with noncompressible torso hemorrhage is not available. The objective of this study was to test the efficacy of an expansile, resorbable foam supplemented with clotting factors on survival and other endpoints in a porcine model of noncompressible intraabdominal (torso) hemorrhage.

Methods
Anesthetized domestic swine (barrows, age 3 months, 30-35 kg; N = 58) underwent neck line placement, were splenectomized through a midline incision with placement of an intraabdominal pressure monitor, and then underwent resection of the left medial liver lobe (15-20% of hepatic mass). The abdomen was closed with towel clips, and treatment was injected intraabdominally through a cannula inserted in a separate stab incision, in four groups: (1) calcium alginate foam (CAF) + fibrin sealant (FS = plasma-derived fibrinogen + recombinant thrombin (rFII) and Factor XIII (rFXIII)); (2) CAF + rFII + rFXIII; (3) CAF alone; or (4) no treatment. The engineered foam injector nozzle produced a dual-phase foam that expanded within the abdomen. CAF constituted the inner bulk phase, and was coated with a thin-layer of biologic-based foam. Warm Lactated Ringer's solution was given IV post-injury at 10 mL/min for mean arterial pressure (MAP) <80% of pre-injury MAP. Subjects were monitored (vitals signs and labs) for 3 h or death, followed by necropsy with blood loss measurement.

Results
Pre-injury data (body mass, splenic mass, blood loss, vital signs, hematology and coagulation testing, arterial blood gases) were not different among treatment groups. Intraabdominal pressure in groups 1-3 rose to ≤35 mm Hg during treatment injection, but then decreased gradually to <10 mm Hg by 30 min. Survival among groups 1-4 was 10/11, 10/12, 9/14, and 14/21, respectively ($p = 0.006$, ANOVA); final Hb (3h or imminent death) was 7.7±2.1, 9.1±2.1, 9.6±1.8, and 7.2±2.2 g/dL, respectively (mean±sd; $p = 0.01$). There were no significant differences in final MAP, final blood loss, liver weights (main organ or resection specimen), or number of transected hepatic and portal veins.

Conclusion
Treatment of noncompressible torso hemorrhage in swine with an resorbable expansile foam supplemented with clotting factors provided a survival advantage compared to no treatment or foam treatment without factors. The efficacious treatment provided a combination of intraabdominal tamponade plus exogenously enhanced clotting. This technology will be intended for field deployment in order to obtain early and rapid stabilization of critically injured warfighters with life-threatening noncompressible torso hemorrhage, for which there currently is no effective pre-hospital treatment.

[below Table not included with MHSRS submission; web form would not allow Tables. But this is how data originally was compiled.]

Table 1. fibrin sealant-foam treatment of noncompressible hemorrhage in swine.

Endpoint	(1) CAF + FS	(2) CAF + rFII + rFXIII	(3) CAF	(4) No Rx	p-value*
Survival, x/N (%)	10/11 (91%)	10/12 (83%)	9/14 (64%)	14/21 (67%)	**0.006**
Blood loss (mL)	1567 ± 457	1174 ± 372	1176 ± 370	1213 ± 552	0.126
Final Hb (g/dL)	7.7 ± 2.1	9.1 ± 2.1	9.6 ± 1.8	7.2 ± 2.2	**0.010**
Final MAP (mm Hg)	40 ± 20	66 ± 35	40 ± 26	40 ± 29	0.061

*Survival = Fisher exact test, all others = ANOVA.