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Low Shear and Thromboresistance in the Synchronous Pulsatile Adult and Pediatric TORVAD

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Study: The TORVAD is a positive-displacement ventricular assist device that synchronizes with the cardiac cycle to deliver full support to a failing heart with either a 30 ml (adult) or 15-ml (pediatric) counterpulse ejection. Pumping is achieved by rotating two pistons within a toroidal chamber on ceramic hydrodynamic bearings. The design achieves low-shear pumping by virtue of controlled gaps and low rotational speeds (60–140 rpm). The adult device has undergone chronic animal experiments and the initial prototype of the pediatric device has undergone bench top and acute animal testing. Previous chronic animal studies with the adult pump revealed a problematic seam that produced thrombus. Additional chronic animal studies were performed to assess the performance of the TORVAD with the seam corrected by laser welding.
Methods: Two sheep were implanted with laser-welded adult devices for a target study duration of two months. Anticoagulation was discontinued on postoperative day (POD) 1. Blood samples were taken throughout the study for assessment of hemolysis and von Willebrand Factor (vWF) multimeric analysis. Densitometry analysis was used to quantify high and low molecular weight vWF multimers with respect to baseline values.
Results: The first animal was euthanized on POD 3 for non-device related complications. The second animal reached the study endpoint. At necropsy the pump was carefully disassembled and inspected and showed no sign of thrombus, most notably in the region of the previously problematic pump seam. Hemolysis remained low throughout the study with a mean value of 4.1 ± 2.0 mg/dl. High and low molecular weight vWF returned to baseline levels by POD 28 following an initial period of operative trauma. These results reaffirm low-shear pumping as seen in previous benchtop and chronic animal experiments and validates that laser-welding the pump seam eliminates thrombus formation in the TORVAD.

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Metabolites Associated with Improved Survival in Alcoholic Hepatitis Patients are Enriched in ELAD-treated Subjects

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Study: Metabolomics shows promise in identifying potential prognostic disease biomarkers and was performed on severe alcoholic hepatitis (sAH) subjects' plasma samples to identify potential biomarkers suggesting clinical benefit due to the ELAD System, an investigational human hepatic cell-based liver treatment.
Methods: Plasma and/or plasma ultrafiltrate (UF) samples from 16 subjects surviving ≥91 d (ELAD VTI-208 clinical study; 8 controls, 8 treated) were retrospectively analyzed by global, unbiased metabolomics profiling. *In vitro* cell-based studies exposed primary human hepatocytes (PHH) and endothelial cells (EC) to oxidative stress-inducing factors ± ELAD C3A cell cartridges conditioned media (CM) and measured intracellular levels of glutathione.
Results: Biochemical targets in plasma UF changed within 24 h on ELAD treatment, consistent with active VTL C3A cell metabolism. ELAD-treated subjects' plasma was enriched in metabolites of o-cresol sulfate (suggesting improved liver detoxifying function) and glutathione metabolism (suggesting anti-oxidative function). Co-treatment of PHH or EC with ELAD CM during challenge with known oxidative stress inducers (e.g. alcohol and H_2O_2) resulted in higher molar intracellular ratios of reduced:oxidized glutathione. Enriched metabolites associated with improved survival in sAH subjects (e.g. 3-OH-isobutyrate and N1-methyladenosine) were also enriched in the ELAD-treated subjects. Aromatic amino acids (e.g. phenylalanine and tyrosine), which can increase in sAH subjects due to systemic inflammation, were reduced in the ELAD-treated group. Metabolomics profiling of ELAD subject samples revealed several metabolites/biomolecules that are associated with less severe disease. Cell-based experiments further identified that increasing reduced glutathione intracellular reservoirs may be a contributing mechanism to potential treatment benefit.