Mechanical Characterization and Preclinical Evaluation of a Bioengineered Human Acellular Vessel for Vascular Patch Applications

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Statement of Purpose: Reconstruction and repair of blood vessels by implantation of a vascular patch is often performed following carotid or femoral endarterectomies, oncologic resection, iatrogenic or traumatic injury, or to correct congenital defects. The types of commercially available biomaterials currently utilized as vascular patches includes synthetic polymers such as expanded polytetrafluorethylene (ePTFE) or polyethylene terephthalate (PET or Dacron®), xenografts created from treated animal tissues like small intestine submucosa (SIS) or pericardium, and allografts such as cryopreserved human veins.[1] While vascular patches need sufficient mechanical strength, mismatch in compliance between graft and native vessels can precipitate loss of patency.[2] Humacyte, Inc. has developed a bioengineered Human Acellular Vessel (HAV) currently under clinical evaluation for vascular repair after traumatic injury, bypass for peripheral artery disease, and access for hemodialysis in patients with renal failure. In this study, we mechanically evaluate the HAV in a planar configuration compared to other commercially available vascular patch materials and implant the HAV patch in a sheep model of carotid endarterectomy.

Methods: Vascular patch materials for mechanical testing included two synthetics: ePTFE (Gore-Tex Cardiovascular Patch) and Dacron® (Maquet Hemashield Platinum Finesse), two xenografts: porcine SIS (CorMatrix ECM for Vascular Repair) and bovine pericardium (LeMaitre XenoSure Biologic Patch), and the tissue-engineered 6mm diameter HAV (Humacyte, Inc.) which was cultured and decellularized as previously described.[3] Materials were cut to appropriate sample sizes for mechanical characterization studies performed in accordance with ANSI/ISO 7198 guidelines. Probe burst as well as suture retention and tensile strength, performed in longitudinal and circumferential sample axes, was conducted using the eXpert 7600 single column testing machine (ADMET, Norwood, MA). Compliance of tubular HAV and ePTFE was measured using a custom designed luminal pressurization circuit with high-resolution imaging. For in vivo evaluation, an HAV patch was used to repair a sheep carotid arteriotomy and examined at 2 weeks using angiography and histology.

Results: The suture retention strength of the HAV (n=27) in the longitudinal (243±41g) and circumferential (260±39g) direction was higher than that of native human vessels[4] and less than that of the tested synthetic and xenogenic patch materials (all n=9). Quantification of the circumferential elastic modulus of the HAV patch (858±279 PSI) showed it was slightly more stiff than the woven PET patch (709±31 PSI), but less stiff than bovine pericardium (4543±1205 PSI), porcine SIS (1965±781 PSI), and ePTFE (4138±891 PSI). Measurement of diametrical compliance in tubular HAV and ePTFE showed that the HAV was significantly more compliant than ePTFE and closer to that of native arteries and veins.[5] A pilot animal study showed that the tubular 6mm diameter HAV could be cut into a patch, used for closure of a carotid arteriotomy, and support patency with mechanical integrity and tissue integration in a 2 week sheep model (**Figure 1**).

Conclusions: In a planar patch configuration, the HAV demonstrated in vitro mechanical properties that were overall more consistent and similar to native blood vessels than that of the tested synthetic and xenogenic patch materials. In addition to its native-like human extracellular matrix and having off-the-shelf availability, the HAV has shown resistance to infection and evolves to become living tissue after implantation through host cellular remodeling.[3] While more studies are needed, these attributes along with its demonstrated mechanical and functional utility may support use of the HAV as a vascular patch material on appropriately sized arteries.

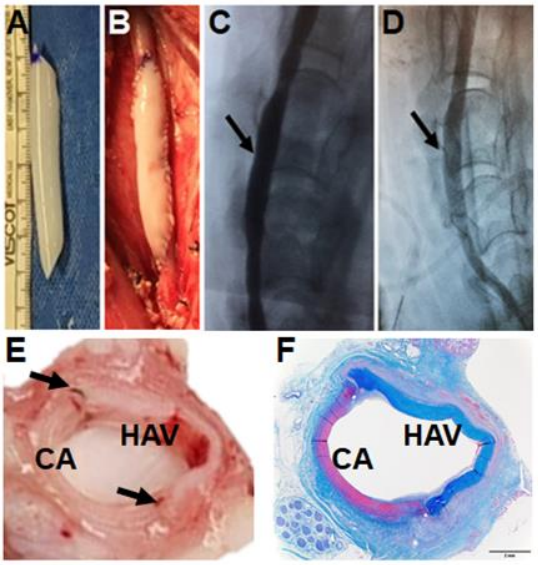

Figure 1: HAV Patch Implantation in Sheep Model. After cutting the HAV into a 6cm-long x 1.3cm-wide patch (A), it was sutured onto a right carotid arteriotomy (B). Angiography confirmed patency of patched artery (black arrow) post-operatively (C) and at 14 day end-point (D). Explanted tissue (E, suture at black arrows) and Trichrome stained cross-section (F) show integration of HAV and carotid artery (CA).

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