Acta Biomaterialia 8 (2012) 2722–2729

Contents lists available at SciVerse ScienceDirect

Acta Biomaterialia

journal homepage: www.elsevier.com/locate/actabiomat

Effects of cryopreservation, decellularization and novel extracellular matrix conditioning on the quasi-static and time-dependent properties of the pulmonary valve leaflet

Gabriel L. Converse *, Matt Armstrong, Rachael W. Quinn, Eric E. Buse, Michael L. Cromwell, Sara J. Moriarty, Gary K. Lofland, Stephen L. Hilbert, Richard A. Hopkins

Cardiac Surgery Research Laboratories of the Ward Family Center for Congenital Heart Disease, Children's Mercy Hospital and Clinics, 2401 Gillham Road, Kansas City, MO 64108, USA

ARTICLE INFO

Article history:
Received 22 November 2011
Received in revised form 28 February 2012
Accepted 28 March 2012
Available online 4 April 2012

Keywords:
Pulmonary heart valve
Leaflet
Viscoelasticity
Biaxial
Decellularization

ABSTRACT

Decellularized allografts offer potential as heart valve substitutes and scaffolds for cell seeding. The effects of decellularization on the quasi-static and time-dependent mechanical behavior of the pulmonary valve leaflet under biaxial loading conditions have not previously been reported in the literature. In the current study, the stress–strain, relaxation and creep behaviors of the ovine pulmonary valve leaflet were investigated under planar-biaxial loading conditions to determine the effects of decellularization and a novel post-decellularization extracellular matrix (ECM) conditioning process. As expected, decellularization resulted in increased stretch along the loading axes. A reduction in relaxation was observed following decellularization. This was accompanied by a reduction in glycosaminoglycan (GAG) content. Based on previous implant studies, these changes may be of little functional consequence in the short term; however, the long term effects of decreased relaxation and GAG content remain unknown. Some restoration of relaxation was observed following ECM conditioning, especially in the circumferential specimen direction, which may help mitigate any detrimental effects due to decellularization. Regardless of processing, creep under biaxial loading was negligible.

1. Introduction

A variety of options are available for heart valve replacement, including mechanical valves, bioprosthetic xenografts and cryopreserved homografts. While all function well under the right circumstances, the ideal valve substitute, especially for the pediatric population, has yet to be developed. Mechanical valve substitutes require lifelong anticoagulation therapy, while the durability of bioprosthetic valves in adults is limited due to calcification or structural fatigue [1–5]. The service life of bioprosthetic valves is further reduced in children due to accelerated calcification [3,4]. Cryopreserved allograft valves offer excellent hemodynamics but are susceptible to fibrosis and calcification [6] and, as with other valve replacements currently available, are not capable of somatic growth [3,6]. Thus, the development of a tissue engineered heart valve capable of tissue remodeling and growth would mark a significant advancement in the treatment of valve disorders, especially in the pediatric population [7–11].

Decellularized heart valve conduits have also been used clinically for heart valve replacement [12–15]. These offer the hemodynamic advantages of the cryopreserved homograft, while reducing the propensity for calcification due to the removal of antigenic material [3,16]. The decellularized valve also serves as a potential cell seeding scaffold for the tissue engineered heart valve (TEHV) [16–22]. However, even as a scaffold for cell seeding, the mechanical behavior of the decellularized valve leaflet must be such that the in vivo valve function is not impacted in the event that a viable cell population is not maintained after implantation.

The quasi-static mechanical behavior of the decellularized leaflet has been described previously, though limited reports are available [17,23–25]. Under uniaxial loading conditions, the reported effects of leaflet decellularization are minimal. Following decellularization with sodium dodecyl sulfate (SDS), Korossis et al. found increased extensibility and failure strain in the circumferential specimen direction but ultimate tensile strength was not affected in either the circumferential or radial specimen directions [23]. Spina et al. reported similar mild effects on the tensile behavior following decellularization with Triton X-100 or n-cetylpyridinium. Both protocols resulted in slightly increased extensibility and reduced stiffness in the circumferential direction [17]; however, the properties of radial samples were not affected. Liao et al. investigated the effects of multiple detergent-based decellularization protocols (SDS, Trypsin or Triton X-100) on the mechanical

* Corresponding author. Tel.: +1 816 983 6509; fax: +1 816 983 6308.
E-mail address: glconverse@cmh.edu (G.L. Converse).

1742-7061/$ - see front matter © 2012 Acta Materialia Inc. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.actbio.2012.03.047