Acta Biomaterialia 45 (2016) 303–320

Contents lists available at ScienceDirect

Acta Biomaterialia

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

Full length article

Planar biaxial testing of heart valve cusp replacement biomaterials: Experiments, theory and material constants

Michel R. Labrosse [a,b,*,1], Reza Jafar [a,b,1], Janet Ngu [b], Munir Boodhwani [b]

[a] Department of Mechanical Engineering, University of Ottawa, 161 Louis Pasteur, Ottawa, Ontario K1N 6N5, Canada
[b] Division of Cardiac Surgery, University of Ottawa Heart Institute, 40 Ruskin Street, Ottawa, Ontario K1Y 4W7, Canada

ARTICLE INFO

Article history:
Received 29 March 2016
Received in revised form 22 July 2016
Accepted 19 August 2016
Available online 26 August 2016

Keywords:
Planar biaxial testing
Cusp replacement material
Strain energy function
Convexity

ABSTRACT

Objectives: Aortic valve (AV) repair has become an attractive option to correct aortic insufficiency. Yet, cusp reconstruction with various cusp replacement materials has been associated with greater long-term repair failures, and it is still unknown how such materials mechanically compare with native leaflets. We used planar biaxial testing to characterize six clinically relevant cusp replacement materials, along with native porcine AV leaflets, to ascertain which materials would be best suited for valve repair.
Methods: We tested at least six samples of: 1) fresh autologous porcine pericardium (APP), 2) glutaraldehyde fixed porcine pericardium (GPP), 3) St Jude Medical pericardial patch (SJM), 4) CardioCel patch (CC), 5) PeriGuard (PG), 6) Supple PeriGuard (SPG) and 7) fresh porcine AV leaflets (PC). We introduced efficient displacement-controlled testing protocols and processing, as well as advanced convexity requirements on the strain energy functions used to describe the mechanical response of the materials under loading.
Results: The proposed experimental and data processing pipeline allowed for a robust in-plane characterization of all the materials tested, with constants determined for two Fung-like hyperelastic, anisotropic strain energy models.
Conclusions: Overall, CC and SPG (respectively PG) patches ranked as the closest mechanical equivalents to young (respectively aged) AV leaflets. Because the native leaflets as well as CC, PG and SPG patches exhibit significant anisotropic behaviors, it is suggested that the fiber and cross-fiber directions of these replacement biomaterials be matched with those of the host AV leaflets.

Statement of Significance

The long-term performance of cusp replacement materials would ideally be evaluated in large animal models for AV disease and cusp repair, and over several months or more. Given the unavailability and impracticality of such models, detailed information on stress-strain behavior, as studied herein, and investigations of durability and valve dynamics will be the best surrogates, as they have been for prosthetic valves.
Overall, comparison with Fig. 3 suggests that CC and SPG (respectively PG) patches may be the closest mechanical equivalents to young (respectively aged) AV leaflets. Interestingly, the thicknesses of these materials are close to those reported for porcine and younger human AV leaflets, which may facilitate surgical implantation, by contrast to the thinner APP which has poor handling qualities. Because the native leaflets as well as CC, PG and SPG patches exhibit anisotropic behaviors, from a mechanistic perspective alone, it stands to reason that cardiac surgeons should seek to intraoperatively match the fiber and cross-fiber directions of these replacement biomaterials with those of the repaired AV leaflets.

1. Introduction

Native human aortic valve (AV) leaflets (or cusps) exhibit large deformations under comparatively small forces, and then undergo proportionally smaller deformations under larger forces (Fig. 1a) [1–3]. This mechanical response to loading, typical of soft biological tissues in general, is dependent on the direction of the load,

* Corresponding author at: University of Ottawa, Department of Mechanical Engineering, 161 Louis Pasteur, Colonel By Hall A213, Ottawa, Ontario K1N 6N5, Canada.
E-mail address: labrosse@eng.uottawa.ca (M.R. Labrosse).
[1] Both authors contributed equally.

http://dx.doi.org/10.1016/j.actbio.2016.08.036
1742-7061/

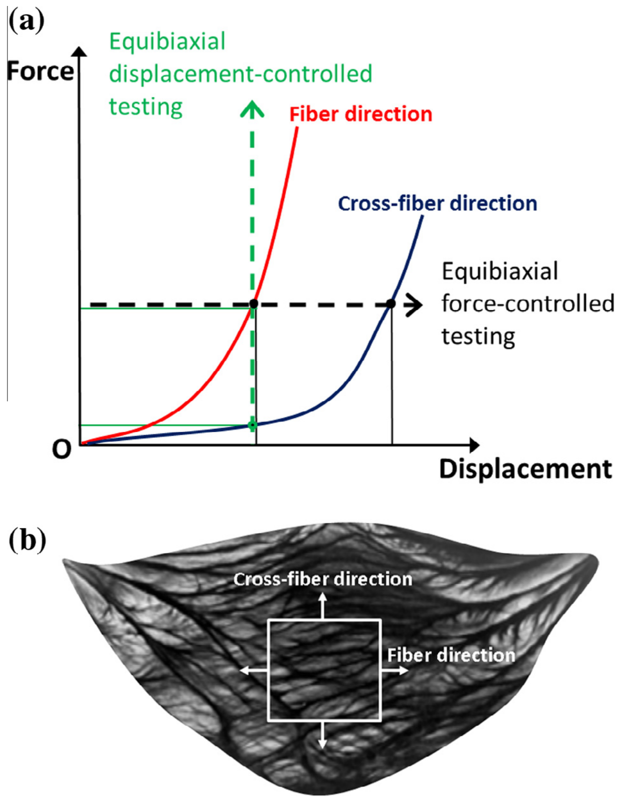

Fig. 1. (a) Typical force-displacement curves for a soft biological tissue. With equibiaxial displacement testing (green dashed line), it is possible to miss the upward turn in the curve for the softer direction of the material (and possibly that in the curve for the stiffer direction as well), if the range of displacements is not large enough, or if the capacity of the force gauge is too low in the axis of the stiffer direction of the material. With equibiaxial force testing (black dashed line), one could miss both upward turns if the applied force were not high enough; but if it is high enough, assuming that displacements are not restricted, the upward turns of the curves for both the softer and stiffer directions of the material are properly captured. (b) Schematic of an aortic valve leaflet showing the orientation of the collagen fiber bundles running mostly in the circumferential direction. The samples for mechanical testing were cut out of the belly region as shown by the white square. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

with the mostly circumferentially oriented collagen fiber bundles in the leaflet (Fig. 1a, b) accounting for the much larger stiffness observed in the circumferential direction compared to the radial direction [2]. Replacement of cusp tissue has occurred for decades with materials such as dura mater, fascia lata, and bovine pericardium [4]. Glutaraldehyde-treated bovine pericardium, as well as treated and untreated autologous human pericardial tissues, are common biomaterials used in both cardiac and vascular surgeries [5–7]. For instance, repair of cusp perforation due to healed endocarditis, or cusp restoration after resection of a calcified or restrictive raphe of a bicuspid AV, requires the placement of a biomaterial patch (patch repair). A patch can also be used to improve cusp coaptation in pediatric AV repair surgery, or to reconstruct a commissure when creating a bicuspid valve from a unicuspid AV, or a tricuspid valve from a bicuspid AV [6]. However, the use of a patch has been associated with an increased risk of long-term recurrent aortic insufficiency [6,8], a finding which may result from the limitations of the existing biomaterials available for cusp reconstruction. It is assumed here that the mechanical behavior of such materials may have a significant bearing on ease of implantation and durability, as elevated mechanical stresses have been reported to cause tears as well as to promote leaflet calcification [9,10]. Therefore, as new testing equipment made it possible to refine previous work by our group [11], the first objective of the present study was to identify the material properties of various commercially available cusp replacement biomaterials, and evaluate which one(s) may be the closest mechanical equivalent(s) to native AV leaflets.

As a tool for material characterization of rubber-like and biological membranes, planar biaxial testing has been used for decades, resulting from the understanding, grounded in continuum mechanics, that uniaxial testing is insufficient when one's goal is to characterize anisotropic materials [12,13]. Planar biaxial testing makes it possible to explore a wide range of loads, understood here as forces or displacements, applied at once in two orthogonal directions. The loads applied in both directions may the same (equibiaxial loading), may be kept in constant proportion between both directions (proportional loading), or independent from each other (general biaxial loading). The work from the pioneers of planar biaxial testing strongly supports that series of protocols including equibiaxial and proportional loadings should be used for best material characterization [12–15]. Unfortunately, most experimental set-ups used to date have been custom-designed, to the effect that a wide disparity in experimental conditions has been the norm (e.g. displacement vs. force controlled protocols; grip displacements vs. optical tracking for determination of strains; rigid grips vs. suture lines). With the advent of commercially available, integrated biaxial testing equipment specially designed for biological soft tissues, such as the Biotester (CellScale, Waterloo, Canada) used herein, it is timely to revisit the practice of planar biaxial testing [16]. This is the second objective of the present work.

First, we will go over the details of the materials and methods (both experimental and theoretical, with insights from continuum mechanics), and then will describe and discuss our findings in the contexts of aortic cusp repair in particular and biaxial testing in general. In an effort to share methods across laboratories, which is our third objective, the interest reader can send a request to M.R.L. for our specially created Matlab programs that can be used with the Biotester to set up the experimental protocols, expedite the sorting of relevant images before image processing for strain calculations and finally, determine material constants for two Fung-like material models.

2. Methods

2.1. Tissue preparation

Six potential cusp replacement biomaterials were included in the study: 1) fresh autologous porcine pericardium (APP), 2) glutaraldehyde fixed porcine pericardium (GPP), 3) St Jude Medical pericardial patch (SJM; St Jude Medical, St Paul, Minnesota, USA), 4) CardioCel patch (CC; Admedus, Minneapolis, Minnesota, USA), 5) PeriGuard (PG; Synovis, St Paul, Minnesota, USA) and 6) Supple PeriGuard (SPG; Synovis, St Paul, Minnesota, USA). APP and GPP were used as surrogates for the fresh or glutaraldehyde fixed autologous human pericardium samples that have been used in the operating room as cusp replacements [5,7,8]. The porcine tissues were harvested on hearts from adult pigs weighing approximately 105 kg obtained from a local abattoir within hours of slaughter, and stored in saline solution at 4 °C. The GPP samples were dipped in 0.6% glutaraldehyde for 20 min before testing [17].

We initially tested nine samples of each material. The samples were cut using parallel steel razor blades into $6.5 \times 6.5\ \mathrm{mm}^2$ squares whose sides were aligned with, or orthogonal to, the direction of fiber reinforcement, as determined by back-lighting and careful visual inspection. In addition, we tested the three AV leaflets in each of two porcine hearts. All the AV cusp samples (PC) were taken out of the belly region (Fig. 1b).