

Gzj kdkv'2007"

# **ADVANCES IN ANTICALCIFIC AND ANTIDEGENERATIVE TREATMENT OF HEART VALVE BIOPROSTHESES**

---

*Proceedings of the Fourth Scientific Meeting  
of the International Association  
for Cardiac Biological Implants*

**E D I T E D   B Y** \_\_\_\_\_

Shlomo Gabbay, M.D.  
Department of Cardiothoracic Surgery  
UMDNJ-New Jersey Medical School  
Newark, NJ

David J. Wheatley, M.D.  
Department of Cardiac Surgery  
University of Glasgow  
Glasgow, Scotland

# **ADVANCES IN ANTICALCIFIC AND ANTIDEGENERATIVE TREATMENT OF HEART VALVE BIOPROSTHESES**

---

*Proceedings of the Fourth Scientific Meeting  
of the International Association  
for Cardiac Biological Implants*

Held in Washington, D.C. on May 4, 1997.

Copyright © 1997.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without the prior written permission of the International Association for Cardiac Biological Implants or Silent Partners, Inc.

Printed in the United States of America.

ISBN 1-878353-42-X

Published by

Silent Partners, Inc.  
8727 Shoal Creek Blvd.  
Austin, TX 78757-6815 USA  
Telephone: 512-458-1191  
FAX: 512-458-1234

Advances in Anticalcific and Antidegenerative  
Treatment of Heart Valve Bioprostheses, First Edition,  
edited by Shlomo Gabbay, M.D., David J. Wheatley, M.D.  
Silent Partners, Inc., Austin • 1997

## CHAPTER 3

### **BIAXIAL MECHANICAL BEHAVIOR OF BIOPROSTHETIC HEART VALVE CUSPS SUBJECTED TO ACCELERATED TESTING**

M.S. Sacks, K.L. Billiar

Department of Biomedical Engineering  
University of Miami  
Coral Gables, Florida

#### **Abstract**

The effects of *in vivo* cyclic loading on the mechanical behavior of porcine bioprosthetic heart valves are largely unknown, and are undoubtedly related to their continued poor long-term durability. To elucidate the mechanisms that eventually produce failure in porcine bioprosthetic heart valves, tension-controlled biaxial mechanical tests were performed on the cuspal tissue following 0, 1.4, 5.7, 10.1, 50, 100, and 200 million cycles of accelerated testing. A microstructural constitutive model was employed to estimate the changes in the effective mechanical behavior of the collagen fibers. Under a 60-N/m equibiaxial tension state, a trend toward increasing circumferential extensibility was found, with no trend in the corresponding radial extension. Simulations using the microstructural model demonstrated that slight specimen misalignments with respect to the biaxial test axes can potentially cause large variations in the measured extensibilities. When the model was used to fit representative data from a nonfatigued and a 200 million cycle fatigued valve, the effective fiber stiffness for the fatigued specimen was markedly lower than the nonfatigued specimen. Histologic studies revealed delaminations but no evidence of damage to the collagen fiber structure, suggesting that tissue damage occurs on a subfibril structural level. Overall, our results imply that long-term cyclic loading produces a gradual weakening of the collagen fiber network, potentially facilitating calcification and ultimately valve failure.

#### **Introduction**

Although bioprosthetic heart valves remain a popular choice for heart valve replacement, they continue to suffer from limited long-term durability. The mechanisms of valve material degeneration, especially when related to calcification, are not well understood.<sup>1</sup> *In vivo* structural deterioration of porcine aortic valve

---

#### **FOR CORRESPONDENCE OR REPRINTS:**

Michael Sacks, Ph.D.  
Department of Biomedical Engineering  
University of Miami  
PO Box 248201

bioprostheses (PBHVs) is strongly time-dependent, decreasing rapidly after 10 years postimplantation.<sup>1,2</sup> Specially in bending, is believed to potentiate mineralization and valve deterioration.<sup>3,4</sup> Although the chemical aspects of mineralization and valve deterioration have been extensively studied,<sup>5-7</sup> little work has been completed on the cyclic loading of chemically treated valve tissue.<sup>8</sup>

At present, "adequate" fatigue life of an intact valve can only be determined by mechanical testing. In this procedure, the PBHV is cycled at 15°/s about its longitudinal axis until failure. The magnitude and loading pattern are believed to adequately simulate the physiological environment, with failure patterns generally similar to those observed in clinical studies of explanted tissue. In general, the study of the fatigue life of heart valves requires an understanding of the gradual mechanical changes that lead to complete valve failure. A study of the subfailure mechanics of heart valves can provide information on the progression with time (number of opening and closing cycles) of the damage that will establish a quantitative representation of the fatigue process. Such a study will elucidate the predominant mechanisms and mechanisms of failure.

Broom<sup>8-10</sup> completed a series of studies on the effects of cyclic loading on the tensile strength, extension and flexure on circumferential strips of glutaraldehyde-treated porcine mitral and porcine aortic valves. The circumferential strips were tested at 15°/s and failed markedly with as few as  $2.3 \times 10^6$  cycles, and the failure stress decreased with increased numbers of cycles.<sup>8</sup> Collagen disruption was observed at  $1.5 \times 10^6$  cycles, and pronounced flexure by  $300 \times 10^6$  cycles. In porcine aortic valves, the failure stress decreased with increased numbers of cycles and the failure stress was reduced to  $10^6$  cycles.<sup>9</sup> Low pressure fixed porcine aortic valves exhibited little damage, whereas high pressure fixed valves exhibited extensive damage similar to the mitral valve tissue. A crimp pattern was observed in all strips, and the native collagen fiber crimp was found in all but two strips in which the crimp pattern was already lost during the test.

These uniaxial studies provide the only information available on the fatigue behavior of heart valves under mechanical loading of heart valve tissue found in vivo. However, these studies, which used strips of tissue, however, cannot mimic the heterogeneity of the valve tissue or the combined loading sequences found in the physiological environment. In addition, the loading conditions used in these studies do not reflect the complex interactions between the axes of the valve. Accelerated testing preserves the 2-dimensional fiber network. Although the fatigue life of heart valves depends directly upon the individual valve geometry and testing conditions, the fatigue life of heart valves cannot be directly measured, the cuspal stresses more closely reflect the stresses experienced in vivo. Materials tests performed on heart valves subjected to realistic purely mechanical loading conditions can provide a better understanding of the fatigue behavior of heart valves over time. However, the gains of intact fatigue cycling, which reflects the mechanics of the intact valve tissue, are not predictable. Therefore, a series of tests is performed to assess the mechanical properties of the valve tissue.

# Explore Litigation Insights



Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

## Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

## Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

## Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

### API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

### LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

### FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

### E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.