



UNIVERSITY OF NOTRE DAME

AEROSPACE AND MECHANICAL ENGINEERING

SEMINAR ANNOUNCEMENT

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TOPIC: Insights into Aortic Valve Calcification: A Mechanobiological Study

DATE: Thursday, February 28, 2008

TIME: 3:30 p.m.

PLACE: 138 DeBartolo Hall

Abstract

The aortic valve (AV) is a sophisticated anatomical structure that interacts closely with its surrounding hemodynamic environment. Studies indicate that pathologic hemodynamics lead to AV disease characterized by inflammation, calcification and ultimate failure. Unfortunately, the events involved in these processes are not well characterized. In order to address this knowledge gap, this study aims at investigating the effects of normal and altered shear stress conditions on the initiation of aortic valve inflammation, and characterizing the respective role of transforming growth factor- β 1 (TGF- β 1) and bone morphogenic proteins (BMPs) in this response.

The physiologic shear stress waveforms experienced by the ventricular and aortic sides of AV leaflets were characterized computationally. An *ex vivo* tissue culture system was designed to subject each surface of porcine AV leaflets to both waveforms for 48 hours. Three culture media were used: standard culture medium, medium supplemented with TGF- β 1, and medium supplemented with the BMP antagonist noggin. Immunohistochemistry was performed to detect expressions of two well-known inflammatory markers VCAM-1 and ICAM-1, and the novel marker BMP-4. The results showed an increased inflammatory activity of the aortic surface exposed to pulsatile shear stress (altered hemodynamics) as compared to fresh tissue (four-fold increase in ICAM-1 and VCAM-1 expressions, six-fold increase in BMP-4 expression). Under similar hemodynamics, the use of osteogenic medium resulted in a eight-fold increase in BMP-4 expression as compared to fresh tissue, while noggin significantly reduced the inflammatory response observed with standard and osteogenic media.

The results demonstrate that altered hemodynamics regulates the inflammatory response of AV leaflets in a TGF- β 1- and BMP-dependent manner. A detailed characterization of AV response to physiologic and non-physiologic hemodynamics will improve our understanding of AV disease progression and enable the development of culture systems for the mechanical stimulation of tissue engineered heart valves.