# Strategies to Increase the Longevity of Bioprosthetic Heart Valves

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## 1. Abstract

Pathological conditions of heart valves result in more than 300,000 operations annually to replace diseased valves with artificial valves. Mechanical heart valves, which consist of artificial materials, were the first devices developed for heart valve replacements, but with further research, bioprosthetic heart valves, which are manufactured from biological tissues, were developed as a viable alternative. Mechanical valves have good endurance life, but require lifelong anticoagulative therapy. Bioprosthetic valves show better biocompatibility and anatomical accuracy and do not require anticoagulative therapy, but have a significantly decreased service life. Bioprosthetic valves fail when their leaflets tear, allowing regurgitation of blood flow, or the valve stenoses, and this is typically caused by tissue degradation or calcification of the valves. After providing a brief background on natural heart valve anatomy, mechanical heart valves, and bioprosthetic valves, this review will analyze the specific mechanisms that contribute to leaflet tearing or stenosis in bioprosthetic valves, and will present and evaluate current strategies that are being investigated as a means to prevent these failure mechanisms.

## 2. Introduction

### *2.1 Heart Valve Anatomy and Pathology*

In order to optimize the efficiency of the work done by the heart with each pump, four passive valves ensure unidirectional blood flow from the atria to the ventricles, and from the ventricles to the arteries leading from the heart [1]. Many pathological conditions can occur in the valves, such as congenital defects, build-up of mineral deposits on the tissue, or degradation of the tissue from aging or drugs [2]. These conditions result in compromised cardiac efficiency or output through incomplete opening or closing of the valves [3]. In some cases, such as valve prolapse, replacement with a prosthetic valve is the best treatment option. Such valve replacement procedures are performed worldwide in over 300,000 patients annually [4], creating a demand for high performance prosthetic heart valves.

The native heart valves consist of either two or three leaflets, or cusps, and the leaflets are composed are a three-tiered ultrastructure (Fig.1) [2]. Starting at the “bottom” of the valve, and moving “up” in the direction of the blood outflow, the bottom layer consists of primarily elastin and is known as the ventricularis. The topmost layer is the fibrosa, and is comprised of primarily collagen, which provides the structural support of the valve [4]. The middle layer, known as the spongiosa, consists primarily of