Exploring Mechanical Treatments to Reduce Calcification in Bioprosthetic Heart Valves

R. Ginley[1,2,a], L. Guerin[1,2], C. Lally[1,2,3]

[1]Trinity Center of Biomedical Engineering, Trinity Biomedical Sciences Institute, TCD, Dublin 2, Ireland
[2]Deparment of Mechanical, Manufacturing, and Biomedical Engineering, TCD, Dublin 2, Ireland
[3]Advanced Materials and Bioengineering Research Center (AMBER), TCD, Dublin 2, Ireland
[a]rginley@tcd.ie

Introduction

12.4% of the elderly population in developed nations suffer from Aortic Stenosis (AS). Patients with symptomatic AS have a 50% mortality rate after two years if left untreated [1, 2]. The only treatment for this disease is a replacement mechanical or bioprosthetic heart valve (BHV) [3]. BHVs are preferred for patients over the age of 65 [4], but suffer from two major failure mechanisms: mechanical degradation and calcification [5]. The tissue used in these devices, typically bovine or porcine pericardium (PP), contains calcium-binding sites, leading to tissue stiffening and device failure. We hypothesise that mechanical treatments can reduce calcification by limiting access to calcium-binding sites. This study explores tissue compression as a pre-assembly mechanical treatment for BHV tissue to reduce calcification.

Materials and Methods

A novel rolling-compression rig was developed to treat PP tissue using two methods: immediate and incremental compression. The immediate compression involved 10 compressions to a target thickness of 150 µm. The incremental method involved 3 compressions to 200 µm, 3 compressions to 175 µm, and then 4 compressions to 150 µm, shown in Fig 1. Both methods involved a total of 10 compressions, with a final target thickness of 150 µm. Thickness measurements, fibre alignment mapping (through small-angle light scattering (SALS) [6]), and scanning electron microscopy (SEM) were performed before and after compression. Calcification was tested under static and dynamic loading conditions. Static calcification involved submersion in calcification solution for 10 weeks, while dynamic calcification was tested using an in-house bidirectional bulge-inflation rig, which also provided mechanical and fatigue data [7,8]. The loaded samples were prepared with a black stochastic pattern and loaded to 150 mmHg (hypertensive equivalent), at a frequency of 3Hz for 15 million (M) cycles. Digital image correlation (DIC) was performed to track the Z-displacement across the surface of the samples after 0M, 5M, 10M, and 15M loading cycles, see Fig 2.

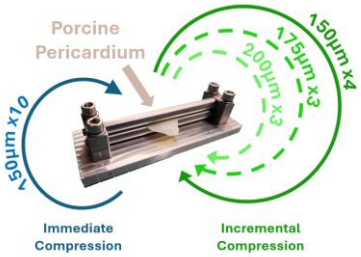

Figure 1. Diagram of rolling-compression rig showing immediate and incremental compression

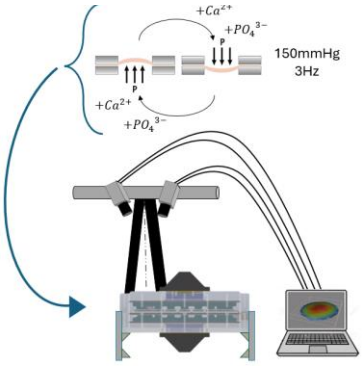

Figure 2. Diagram of bidirectional bulge inflation rig with calcification solution and DIC setup for mapping Z-displacement

Results

Both compression methods reduced tissue thickness; immediate compression reduced thickness for 1 week before regaining it, as seen in Fig 3a. Neither compression method significantly affected fibre alignment, nor did it have a noticeable effect on surface topography. Immediate compression significantly increased calcification percentage after both 10 weeks in static conditions and after 10M loading cycles (51.28% and 61.88%, respectively), while incremental compression did not seem to have any effect (32% and 25.73%, respectively), when compared to uncompressed (17.71% and 25.91%, respectively) under these same conditions, see Fig 3b & 3d. Similarly, at 10M loading cycles, the immediately compressed samples had significantly greater displacement (1.85mm) than the uncompressed samples (0.80mm) and three sample failures by 15M cycles, see Fig 3c. The incremental compression led to a reduced displacement and calcification (1.26mm and 30.37%, respectively) compared to the uncompressed case (1.51mm and 30.60%, respectively) after 15M loading cycles, though the differences were not significant. The incrementally compressed group also had no failed samples, compared with two failures in the uncompressed group.

Discussion

The results here show that immediate compression is not a viable method for reducing calcification in PP. It appears that immediate compression may damage the collagen fibres, leading to reduced performance and an increase in calcium-binding sites. However, this does not entirely rule out compression as a method.

Incremental compression, while not proven to reduce calcification, could still potentially provide benefits to the tissue. Although the results were not statistically significant, incrementally compressed samples outperformed uncompressed samples under dynamic testing. This suggests that compression could still yield beneficial results and warrants further investigation.

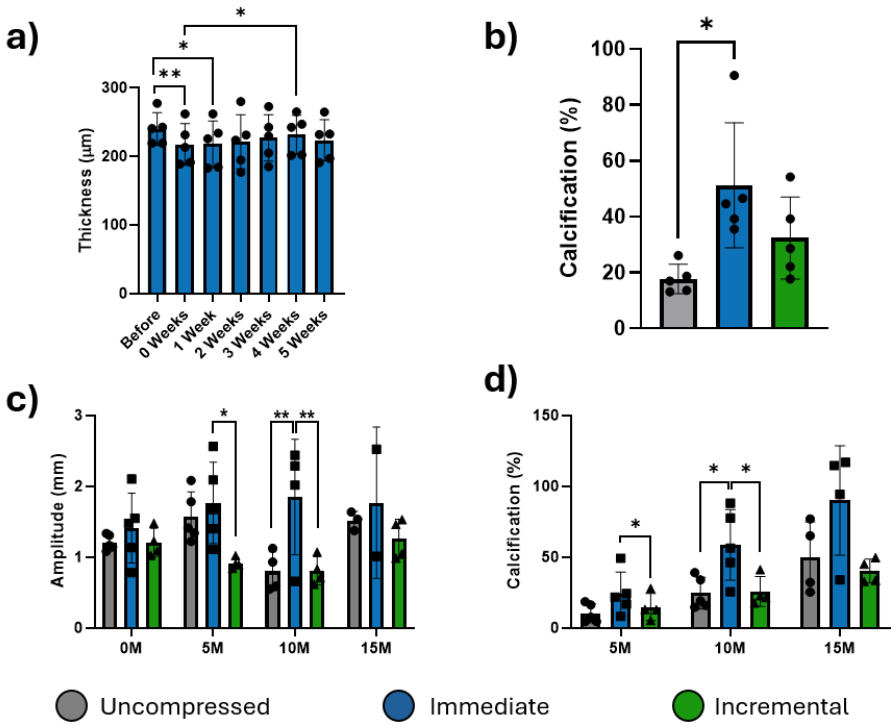

Figure 3. Results showing a) thickness recovery of immediately compressed samples, b) calcification of samples under static conditions, c) displacement amplitude over the course of 15M loading cycles, and d) calcification of samples over the course of 15M cycles.

Conclusion

Mechanical treatments have the potential to improve the lifetime of BHVs by reducing both calcification and structural damage. Incremental compression has shown potential as a treatment method for porcine pericardium, showing a non-significant reduction in calcification and fatigue failure. This requires further investigation to elucidate its effect on the tissue. Mechanical treatments to reduce calcification would be a major benefit to current devices, as they could be easily applied to devices on the market without introducing new chemicals, thereby reducing the regulatory approvals required.

Future Works

An alternative stamping-compression method is being explored to address the issues found in rolling-compression methods. The stamping method is designed to provide a mechanism similar to that of previous crimping studies, which appeared to locally reduce calcification in the region compressed by a strut. By applying a similar compression method across the entire tissue, the accumulation of local effects may reduce overall calcification. This method will be tested with the same procedures described here.

References

[1] Osnabrugge (et al.), Journal of American College Cardiology 62: 1002-1012, 2013
[2] Otto (et al.), New England Journal of Medicine 371: 744-756, 2014
[3] Pawade (et al.), Journal of American College Cardiology 66: 561-577, 2015
[4] Bonow (et al.), Circulation 144, e188-e189, 2006
[5] Kataruka, A., Journal of Thoracic Disease 10: S3629-S3636, 2018
[6] Gaul (et al), Journal of Mechanical Behavior of Biomedical Materials 75: 359-368, 2017
[7] Whelan (et al.), Journal of the Mechanical Behavior of Biomedical Materials 121: 2-8, 2021
[8] Guerin (et al.), Acta Biomaterialia 210: 82-94, 2026