MED DEVICE ONLINE

Application Note

Performance Of Bioprosthetic Heart Valves: Material Considerations

Source: DSM Biomedical

By Ben Kibalo

The treatment of severe cardiovascular disease has seen advancements which would have been considered impossible even 100 years ago, when the first surgical procedures were attempted. These advancements are a result of many lifetimes dedicated to furthering the understanding and treatment of cardiovascular disease. Modern developments in heart valve protheses have followed closely with advancements in available biomaterials[i].

The first artificial heart valve replacement was performed in 1960[i] with a mechanical ball valve. The materials utilized were durable but carried a high risk of inducing systemic thromboemboli mostly due to turbulent flow and, at that time, invasive open-heart surgery was required to implant the device. While there have been many iterations since then, recent designs focus on a minimally invasive trans-catheter approach, miniaturizing the device and the delivery system so they can be delivered through the femoral artery and steered through the vasculature to the implant site. These bioprosthetic valves must tolerate crimping, expansion when needed, and are required to function flawlessly with the first heartbeat.

Over the years, improved analytical methods have led to a better understanding of the failure modes associated with the current valves on the market. Bioprosthetic heart valves were developed to address some of these failure modes. These valves consist of cross-linked animal tissue assembled onto a supporting frame. The natural tissue mimics the blood flow patterns of the native valve, greatly reducing the risk for thrombosis compared to previous mechanical valves.[i]

While bioprosthetic valves overcome some of the failure modes, they have their own inherent challenges. The tissue needs to be cross-linked to stabilize the shape, inhibit enzymatic degradation, and prevent tissue remodeling. This cross-linking, however, can lead to mineralization of the valve leaflets over time.[ii] The rigid calcium deposits physically disrupt the function of the valve. In younger patients, this process is greatly accelerated, with a 10% failure rate seen over 4 years, and in elderly patients the total failure is the same over 10 years[iii]. Women who are pregnant also have additional risk factors[iv].

There are many known and hypothesized causes for this mineralization including: [ii, iii]

- Glutaraldehyde residues present in tissue following crosslinking
- Phosphorous-rich calcifiable structures present in the tissue (largely due to cellular phospholipid membrane remnants)
- Residual nucleic acids (DNA and RNA fragments)
- Host factors including calcium levels and metabolism
- Mechanical damage to the tissue providing a nucleation site for mineralization (cuspal wear, calcification-related stress, and manufacturing defects such as thickness variability, visual, and other physical defects)

By understanding the cause of mineralization, treatment methods have been developed to reduce the impact of each of these detractors. Improved tissue processing techniques performed prior to cross-linking can remove elements known to contribute to calcification including nonviable cells, phospholipids, and DNA fragments. Treatments applied after cross-linking can also remove residual cross-linking byproducts as well as minimize defect sites. Often, a combined approach is taken.

Decades-old, peer-reviewed publications and expired patents detail many processing options[v]. Historically, these techniques focus on post cross-linking techniques and, more recently, there has been a focus on improving tissue processing techniques. These pre-fixation techniques can range from simply improving rinsing to complex processes with enzymes and cleaning agents.

As new techniques for tissue processing are attempted, it is important to keep in mind that the inherent natural variability in tissue can be difficult to process repeatably. Additionally, tissue used in medical devices is required to adhere to strict sourcing controls and viral inactivation standards. These difficulties can be technically difficult and expensive to overcome. It is therefore advisable to partner with a manufacturer who has experience working with animal tissues.

DSM Biomedical has extensive experience in the sourcing and processing of bovine([vi],[vii],[viii],[ix]) and porcine([x],[xi],[xii],[xiii],[xiv]) tissues. Our proprietary processes have been developed to carefully remove specific components of the tissue, such as cellular remnants, DNA, and phospholipids; coupled with the preservation of native architecture, proteoglycans, and measurable biologic activity. DSM Biomedical also has readily available materials with a long history of clinical use that can be leveraged in developing new products. ([xv], [xvi],[xvii])

Future heart valve designs and materials will enable more efficacious therapies. DSM Biomedical's advanced biomaterials provide many options to consider as you design the next advancement in medical science.

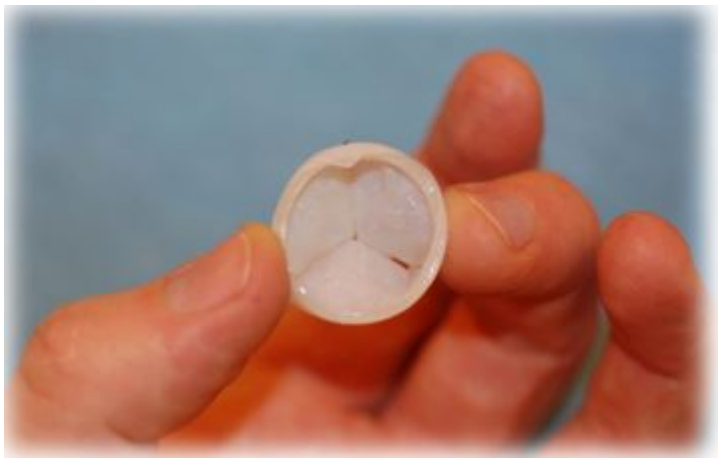

Figure 1: Stented, bioprosthetic heart valve, non-TAVR, in-vivo feasibility prototype. Constructed using DSM Biomedical porcine peritoneum ECM material for leaflets

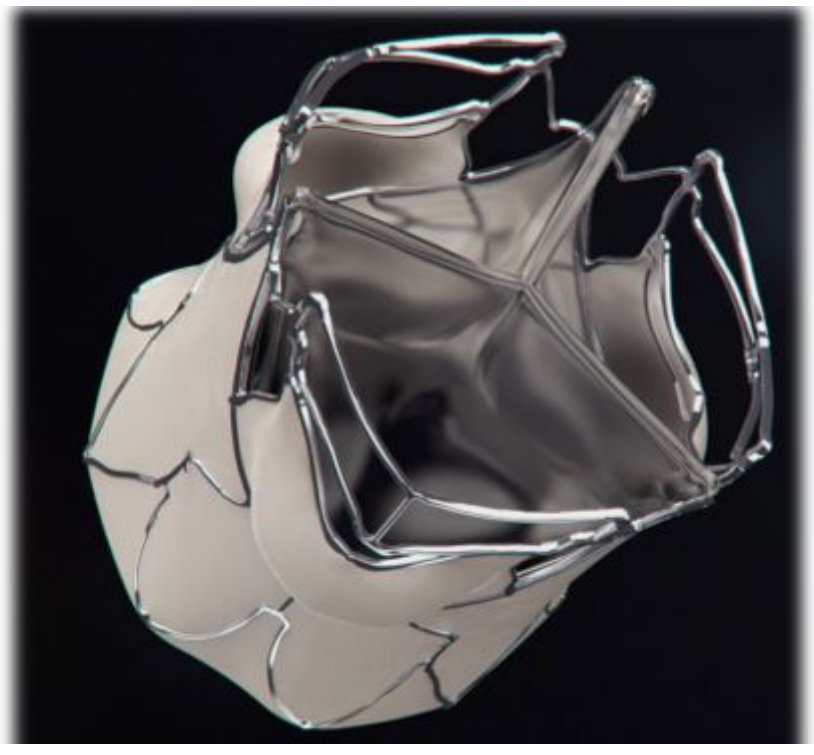

Figure 2: All-synthetic bioprosthetic heart valve designed by Strait Access Technologies (SAT) using DSM Biomedical's Carbosil® Thermoplastic Silicone-Polycarbonate-urethane (TSPCU) polymer for leaflets and in the electrospun skirt.

About the Author

Ben Kibalo is a Senior ADTS at DSM Biomedical supporting the natural materials technology portfolio. He has more than 20 years of experience working in biotechnology, primarily focused on soft tissue reconstruction with synthetic and animal-derived materials. Ben has extensive experience in medical device commercialization from early feasibility prototyping, design control requirements, process scale-up, and animal-tissue sourcing. If you would like more information about this topic or considerations related to natural materials and the potential for use in your medical product, Ben can be reached at Benjamin.Kibalo@dsm.com or through LinkedIn (insert Ben's LinkedIn profile information - Link Here).

DSM Biomedical is the world's unrivaled biomaterials expert and committed partner driving sustainable innovation in healthcare. For 30+ years, their solutions have been recognized for their unmatched quality, consistency and performance, ultimately supporting their company-wide vision of solving the world's healthcare needs through sustainable science. To learn more, visit DSMBiomedical.com.

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