

Cardiovascular disease remains the leading cause of death in developed countries, with **coronary artery disease (CAD)** as a primary contributor. The introduction of stents revolutionized the treatment of CAD, enabling effective percutaneous coronary revascularization. Over time, coronary stents have advanced from bare metal designs to drug-eluting stents (DES) that integrate pharmacological therapies. While stents address some limitations of balloon angioplasty, they also trigger acute thrombus formation and neointimal hyperplasia. First-generation DES significantly reduced in-stent restenosis but delayed healing, increasing the risk of late stent thrombosis and long-term clinical complications. Despite these improvements, stents still face fundamental issues of incompatibility with vascular tissue, which remain inadequately addressed. Tissue engineering provides a potential solution to these limitations. The project combines the usage of several naturally derived polymers of outstanding mechanical properties, biodegradability, biocompatibility and synthetic polymers which significantly improves the stability and mechanical properties of the scaffolds. Incorporation of anti-inflammatory, antibacterial, anti-thrombotic agents will reduce the risk of infection, hyperplasia and acute thrombosis is another advantage of the project.

This project aims to design, synthesize, and fabricate **biocompatible, slowly degradable stents** that support the **adhesion and maintenance of an endothelial cell monolayer**. The proposed material will be cast using a custom-built casting system, with detailed fluid dynamics simulations to optimize flow performance. Advanced physicochemical analyses, including **solid-state Nuclear Magnetic Resonance (NMR) spectroscopy** **mechanical properties** (rheology, dynamic mechanical analysis, compression and tensile properties) and **surface properties** will assess and fine-tuned with the that of the native tissue . Moreover, potential free radical generation during polymerization as well as nitric oxide release from the stents will be studied using Electron Paramagnetic Resonance (EPR) spectroscopy. In the final stages, the feasibility of depositing a bioactive (γ) layer (consisting of anti-bacterial, anti-thrombotic and anti-inflammatory drugs) inside the stent lumen using a novel volumetric bioprinter will be evaluated. **Drug release studies** and **the anti-bacterial potential** will be performed on different *Staphylococcus* species. The biological interactions between the **biomaterial, stent, and perfusion system** will also be thoroughly investigated. Moreover, the simulations will be performed using the physiological properties of developed DES and will be compared with the real time scenario created using perfusion systems. The simulation and real-time data will be compared and a model for *in silico* testing will be delivered which can be potentially utilized for future studies.

The primary goal is to establish conditions for developing mechanically stable, casted or 3D-casted/printed stents capable releasing drugs while supporting endothelial cell layer maintenance. The research hypothesis proposes that the resulting 3D bioactive stents will serve as optimal, biocompatible scaffolds for **endothelial cell** growth, with potential applications in **cardiac tissue engineering**.

The detailed effect of solvent casted or 3D printed stents on cell growth, behavior and the interactions among **endothelial cells** will be examined at *in vitro* and *ex vivo* conditions in the custom made device imitating blood flow. Comprehensive biomechanical properties will be carefully investigated to enable proper, long-term stability. Final step of the project is *in vivo* stent evaluation on pig model. The obtained results will demonstrate the design of novel biocompatible stents for tissue integration that can be useful for designing devices for treating cardiovascular diseases.