Degradation of PLLA Tubes in a Pulsatile Flow Loop as a Model for Cardiovascular Stent Degradation

Maureen L. Dreher, PhD[1], Srinidhi Nagaraja PhD[1], Qijin Lu PhD[1], Richard Malinauskas PhD[1], Benjamin Batchelor[2]
[1] US FDA/Center for Devices and Radiological Health/Office of Science & Engineering Laboratories/ Division of Applied Mechanics; [2] University of Texas at Dallas, Department of Chemistry

Statement of Purpose: In order to mitigate the risk of late stent thrombosis, cardiovascular stents fabricated from fully absorbable polymers are being developed and evaluated in clinical trials. Performance of these devices is highly dependent on degradation time and loss of mechanical properties. While the primary mechanism of degradation is expected to be hydrolysis, cardiovascular stents are also exposed to continuous fluid flow and cyclic deformation from blood pressure *in vivo*. Since mechanical forces can affect polymer degradation [1], exposure of stents to cyclic deformation may affect the degradation rate and transient mechanical performance. In this study, we developed a custom pulsatile flow loop to model cardiovascular stent degradation under physiologic conditions. The degradation of an absorbable stent substitute in the loop was compared to static immersion conditions.

Methods: A custom 8-channel pulsatile flow loop was designed to simulate physiologic coronary flow and pressure effects. The loop was used as a model for degradation of fully absorbable cardiovascular stents by delivering phosphate buffered saline (PBS) at 37°C to stent substitutes in each channel. The stent substitute consisted of a poly(L-lactide), i.e. PLLA (Purac PL38), extruded tube (3.5mm OD, 0.25mm wall thickness) in a silicone mock vessel (3.2mm ID, 3-5% compliant). Control PLLA tubes inside of a mock vessel ("MV control") or without a mock vessel ("control") were also degraded under immersion conditions in PBS at 37°C (Fig 1). pH was monitored and the PBS exchanged weekly; at no time did the pH drop below 7.2. Samples (n=6/group) were analyzed for molecular weight using gel permeation chromatography and % crystallinity using differential scanning calorimetry after 2, 4, or 6 months of degradation.

Results: The flow loop maintained an average flow rate of 120±2.8ml/min to each channel. Similarly, the pressure pulse was consistent throughout the experiment, with an average systolic pressure of 131±5mmHg and a diastolic pressure of 87±3 mmHg, which is consistent with Stage 1 hypertension.

At each timepoint, partially degraded control PLLA tubes (with or without a mock vessel) exhibited nearly equivalent changes in molecular weight and % crystallinity (Fig 2). In contrast, PLLA tubes in the flow loop exhibited statistically slower loss of molecular weight than control specimens (Fig 2, $p<0.05$) at all timepoints. Crystallinity was significantly reduced for tubes degraded in the flow loop as compared to controls.

Conclusions: The current study demonstrates that PLLA tubes degraded in a mock pulsatile flow loop exhibit a statistically different degradation pattern than tubes degraded under control conditions. The slower loss in molecular weight for samples in the flow loop may be explained by the constant removal of low molecular weight oligomers from the interior tube surface, whereas the small volume of fluid inside the control tubes does not allow for constant removal of oligomers, thus creating potential for some localized degradation. This potential for localized degradation inside of the tube may occur even though the total volume of degradation solution for control samples aligned with ASTM recommendations for simulating degradation in absorbable medical devices [2]. The lower % crystallinity for specimens degraded in the flow loop may be explained by relaxation of the polymer chains in the presence of pulsating flow due to a sensitivity of PLLA mechanical properties to temperature, plasticization, and frequency. In conclusion, the results suggest that the more physiologic degradation conditions incorporating pulsating fluid flow can significantly affect the degradation pattern when using tubes as a model for stents.

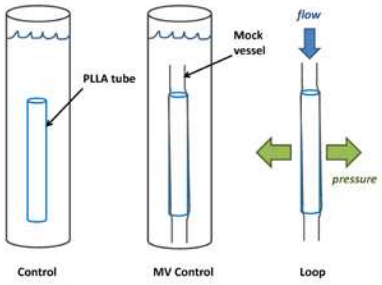

Fig 1: PLLA tubes were degraded in PBS (control), in a mock vessel in PBS (MV control), or in a mock vessel in the pulsating flow loop (Loop).

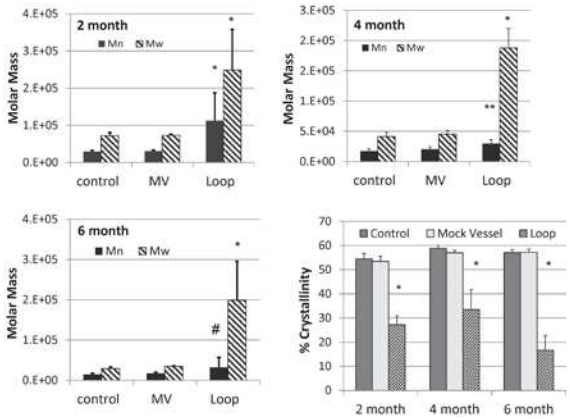

Fig 2: Degradation in flow loop ("Loop") vs specimens under immersion ("Control") and in a mock vessel under immersion but not in the loop ("MV"). *p<0.01, **p<0.05, #p<0.10 vs control and MV groups (ANOVA).

References: [1] Dreher ML et al, J Biomed Mater B, 2014 doi: 10.1002/jbm.b.33248. [2] ASTM International, F1635, Standard Test Method for in vitro Degradation Testing of Hydrolytically Degradable Polymer Resins and Fabricated Forms for Surgical Implants.

Acknowledgements: This study was funded by CDRH's Critical Path Initiative.