Effects of Fatigue Loading on Absorbable Stent Sub-Unit Degradation

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Statement of Purpose: While absorbable materials have been used in medical devices for decades, only recently have they been investigated for applications where they are expected to provide structural support and must withstand cyclic loading, e.g., as a tissue engineered scaffold or a cardiovascular stent [1, 2]. Understanding the interaction between fatigue and degradation for absorbable medical devices is critical for assessing their performance and predicting their degradation. In this study, we investigated the fatigue behavior and effect of fatigue on degradation rate for a model medical device. Due to the important mechanical function of cardiovascular stents in maintaining vessel patency while being exposed to long term loading, sub-units of a model cardiovascular stent was chosen for this study.

Methods: Custom sub-units based on the geometry used in previous fatigue studies for stents [3] were manufactured from poly(L-lactide), i.e., PLLA. The geometry consisted of two stent v - shapes with tabs at the top and bottom to facilitate loading (Fig 1). Cyclic axial displacement of this stent sub-unit results in bending at the corner v's, similar to motions expected to occur in stents under radial pulsatile loading *in vivo*.

A subset of stent sub-units underwent S-N testing in order to determine a cyclic displacement level that would not result in fracture over the course of 1 year of simulated loading. S-N testing demonstrated that higher amplitudes of cyclic displacement decreased the survival of PLLA stent sub-units, and that a plateau at ~0.2mm can be reached beyond 10 million cycles (Fig 2). Therefore, 0.2mm of cyclic displacement was used for long term degradation during fatigue.

The remaining stent sub-units underwent simulated degradation in phosphate buffered saline using a temperature (i.e., 42°C) that was expected to accelerate degradation by a factor of 2, based on preliminary experiments. Degradation proceeded under static immersion according to ASTM F1635 (i.e., "control", n=12) or in combination with fatigue loading (i.e., "fatigue", n=12, 2.4Hz). The test frequency ensured that fatigue cycles would be synchronized with degradation kinetics. Samples were removed from degradation after a simulated 6 (20 million cycles) or 12 months (40 million cycles). These samples were then tested for mechanical properties, molecular weight as measured by gel permeation chromatography, and crystallinity assessment as measured by differential scanning calorimetry.

Results: Due to the dual elbows in the design of this stent sub-unit, mechanical testing exhibited 2 fracture points (1st break & separation). Fatigue loading during degradation significantly increased the stiffness after 40 million cycles as compared to control specimens (Fig 3). The force at 1st break and at separation was lower for specimens degraded under fatigue conditions, though this only reached statistical significance at 20 million cycles for the 1st break (Fig 3).

Chemical analyses demonstrated that fatigue loading resulted in a transient statistically significant increase in the molecular weight loss at 20 million cycles (i.e., 6 months of simulated degradation) (Table 1). However, fatigue loading was not found to have a significant effect on the % crystallinity at either time point (Table 2).

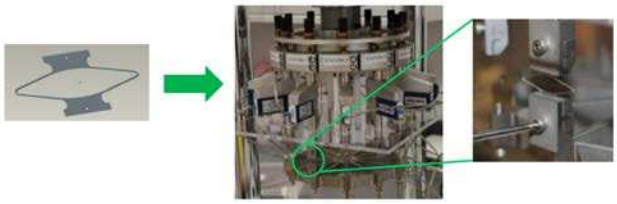

Fig 1: Stent sub-unit geometry (left); Stent sub-units into multi-station fatigue tester (middle) with zoomed in image (right).

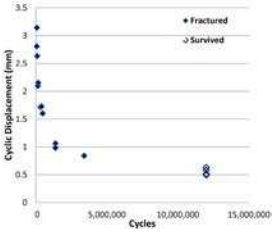

Fig 2: S-N testing of PLLA stent sub-units showing that a plateau is reached between 5 and 10 million cycles

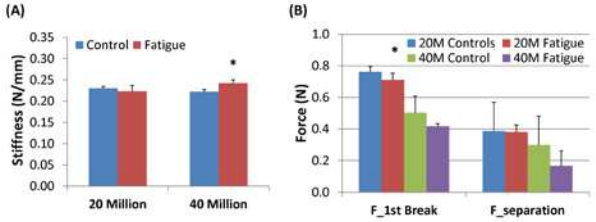

Fig 3: Stiffness (A) and break properties (B) after simulated degradation for 6 months (20 million) or 1 year (40 million). *p<0.05, different from control group, T-test.

	6 months - 20M		1 year - 40M	
	Control	**Fatigue**	**Control**	**Fatigue**
Mn (kDa)	156 ± 11	143 ± 6.9 *	105 ±14	153 ± 22
Mw (kDa)	377 ± 41	309 ± 13 *	97.3 ± 7.1	137 ± 9.2
% crystallinity	51.6 ± 4.4	53.9 ±10	54.0 ± 7.5	63.5 ± 19

Table 1: Chemical properties after simulated degradation for 6 months (20 million cycles) or 1 year (40 million cycles). * p<0.05, as compared to the control group, ttest

Conclusions: This study demonstrates that fatigue loading during degradation can affect both the mechanical properties and the chemical degradation rate. The results are important for defining appropriate *in vitro* degradation conditions for absorbable stent preclinical evaluation.

References: [1] Gloria A et al. J Appl Biomater Biomech 2010;8:57-67. [2] Gonzalo N et al. Vasc Health Risk Manag 2012; 8: 125-132. [3] Pelton A et al. J Mech Behav Biomed Mater 2008; 1: 153-164.

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