Curcumin-loaded bioresorbable stents based on internally coiled helix designs

Dasnurkar, A; Welch, T; Gampa, S; Chapman, C; Puthusseril, J; Su, S; Nguyen, K; Tang, L; Chuong C and Eberhart,R. Biomedical Engineering Program, University of Texas at Arlington and University of Texas Southwestern Medical Center at Dallas

Statement of Purpose:

We have developed a bioresorbable stent, fabricated from 0.1 mm poly(L-lactic acid) (PLLA) fibers, loaded with the anti-inflammatory agent curcumin and deployable by standard angioplasty catheter technique. We describe here the design, the composition and the experimental and numerical means employed to analyze the unique polymer fiber setting process upon angioplasty balloon expansion.

Methods:

The 1.5 mm furled stent is comprised of a series of internally wound coils that, upon 6 atm balloon expansion, convert to a 3.0 mm cylindrical helix with substantial compressive buckling resistance (14-210 KPa, depending upon fiber ply and internal helical coil size and number). The basis of stent strength is the torsional set of the fiber as the internal coils expand and convert to an open cylinder configuration. It is not necessary to thermally set the polymer to attain adequate strength for vascular applications. To demonstrate how the stent fibers undergo plastic deformation upon expansion, we created a 3-D model of the single ply coiled stent in SolidWorks that is exported into ANSYS for creation of the finite element model. The PLLA fiber has a Young's modulus of 7.04 (GPa) and a Poisson's ratio of 0.35. A nonlinear material analysis is used to simulate material behavior through plastic deformation, employing multilinear elastic properties in ANSYS. The von Mises stresses, the principal stresses, and the principal strains are analyzed to determine the yielding of the PLLA fiber [1]. We employed high MW polymer in the first stent constructions in order to ensure stent strength. However, multiple ply fiber designs were observed to strengthen these structures, permitting the use of high MW:low MW PLLA: PLLA blends (40:60-60:40) and PLLA:PDLA blends (50:50). These lowered the melting point and in turn permitted improved curcumin uptake in fibers upon melt extrusion [2]. The bioactivity of curcumin was evaluated in a series of *in vitro* and *in vivo* assays [3-5].

Results/Discussion:

Model predictions confirm the expansion of the stent at 6-14 atm, including the observation of plastic deformation of a short segment of the main coil of the helix at the site of final conversion of the inner coil (Fig 1. The model also predicts the lateral (axial) spread of the inner coil fiber upon expansion. In multiple ply configurations this may improve fiber grip on vessel walls. Stents constructed from these blends have considerable strength. Curcumin incorporation into PLLA fibers and blends (10 wt%) reduces fiber strength but does not destroy the stent structure. Eluted curcumin retains significant bioactivity as measured by reductions in activated neutrophil and macrophage adhesion to- and activity upon-curcuminated PLLA fibers ($p \leq 0.05$ in all comparisons), and in the observed absence of inflammation in the vicinity of fibers sutured into the rat aortic wall. Curcumin elution from fibers approximates a uniform rate and extends for well over one month.

Conclusions:

A series of biodegradable polymeric stents have been developed, based on PLLA and PLLA/PDLLA blends. The results of experimental and numerical mechanical analysis both indicate stable expansion configurations are obtained, including a local permanent "twist" to the fiber, without the need for extraneous set procedures. Various extrusion blends of PLLA and PDLA are suitable for stent construction, and also provide a wider range of melt extrusion conditions for curcumin incorporation.

References:

1. Dasnurkar, A, *MS Thesis.* U Texas-Arlington, (2005). 2. Welch, T, *MS Thesis.* U Texas-Arlington, (2005). 3. Su SH etal, *J. Biomater. Sci: Polymer Ed.* 16:353-370 (2005). 4. Nguyen, KT, etal. *Biomaterials.* 25:5333-5346 (2004). 5. Nguyen, KT, et al. *Biomaterials* 24:5191-5201 (2004).

Acknowledgements:

Supported in part by USPHS HL 53225.

*Biomedical Engineering Program, University of Texas at Arlington and University of Texas Southwestern Medical Center at Dallas.

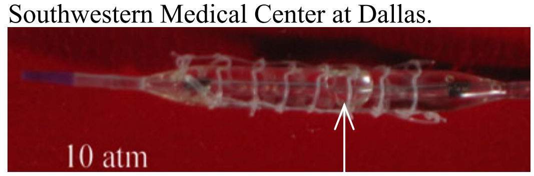

Fig 1. During expansion inner coils are extended axially and permanently twisted (arrow) since stresses in torsion exceed the elastic limit.