New mathematics for next generation stent design

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Stents are mesh-like tubes which are used to prop diseased arteries open and restore normal blood flow, see Fig. 1 left. They have first been intro-

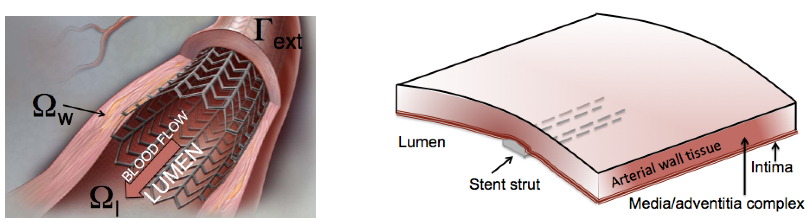

Figure 1: *Left: A sketch of an implanted stent. Right: A magnified view of a section of the arterial wall (multi-layered) containing a stent strut.*

duced in the late 1980's with the goal to help reduce the restenosis rates (re-narrowing of coronary arteries) associated with angioplasty procedure in the treatment of coronary artery disease. First generation stents were bare metal stents (BMS). BMS are still in use, although with various improved features, including the introduction of better materials, and improved topological and geometric features. BMS reduce the restenosis rates when compared to coronary angioplasty alone, but have been known to cause severe intravascular injuries (e.g., damaged endothelium and medial layer stretch leading to smooth muscle cell injury) often times leading to complications such as in-stent restenosis associated with proliferation of smooth muscle cells into the artery lumen. To further improve the restenosis rates, next generation stents were born in the late 1990's with the introduction of drug-eluting stents (DES). DES are stents coated with a polymer which incorporates an anti-proliferative drug. In 2006, a potential safety issue emerged with reports linking DES with the increased risk of late-stage stent thrombosis, associated with an inflammatory reaction to the polymer-based coating.

While DES are currently the state-of-the-art in stent design and usage, new ideas, which would circumvent the use of polymers, are emerging. For example, our collaborator T.A. Desai of UCSF, is working on *nano-engineered stents*, which are based on drug-free nanotechnology, in which the stent surface is nano-engineered in a way that promotes accelerated restoration of functional endothelium and provides a drug-free approach to keeping stents patent long-term [?].

Mathematical modeling and numerical simulations have been proven to be an indispensable tool in guiding optimal stent design [?]. Within the past twenty years, various studies discussing mechanical properties of stents, biodegradable stents and coating, optimal strategies in anti-inflamatory drug delivery, and stent impact on local and global blood flow and vascular wall, have been published. In addition to our group, the leaders in the field of mathematical stent modeling and simulation include Zunino, Migliavacca, Soares, Rajagopal, Wu, Gastaldi, J. Moore, Timmins, A. Marsden, McGinty, McKormick, Kiousis, Gasser, Holzapfel, to mention just a few.

As the models became more sophisticated, deeper mathematical questions had to be addressed to continue advancing the field. New mathematics in the area of fluid-structure interaction (FSI) involving elastic, viscoelastic, poroelastic and mesh-like structures had to be developed to capture the interaction between time-dependent blood flow, and stented vascular tissue.

Our group has been working on several aspects of FSI between blood flow and vascular walls treated with stents, including modeling, mathematical analysis and computations. While the development of computational methods for biological FSI has been a very active research area for the past forty years (see the works of Peskin, Griffith et al., Quarteroni et al., Hughes et al., Bazilevs et al., Shadden et al., Gerbeau et al., Aulisa and Gunzburger, to mention just a few), the **mathematical analysis** of solutions for this class of problems is still under development.

The problem consists of coupling the Navier-Stokes equations for an incompressible, viscous fluid modeling the blood flow, to a system of partial differential equations modeling the elastodynamics of an elastic structure. The equations of linearly and nonlinearly elastic membranes or shells have been used to model the thin intimal layer, while the equations of finite elasticity assuming linear or certain nonlinear hyperelastic models have been used to model the thick media/adventitia layer.

To model stents, several approaches have been proposed, mostly based on 3D approximations. They are known to be computationally expensive, since stent's components (stent struts) are slender/thin, see Fig. **??**. In 2010, a reduced, **1D stent net** model was developed (with Josip Tabača et al. [**?**]). This model provides significant computational savings, while approximating the full 3D model with high accuracy using a network of Antman-Cosserat 1D curved rods [**?**]. *The resulting stent net model is a system of 1D hyperbolic balance laws defined on a graph domain [**?**].* Coupling this model to arterial walls and fluid flow is very challenging from the mathematical standpoint, because it involves coupling PDEs of different dimensions [**?**]. Analysis of these problems has recently become an active research area (see e.g., K.A. Mardal, J. Nordbotten, M. Rognes, J. Tambača and P. Zunino).

Using this model, together with medical specialists Drs. Paniagua and Fish of Texas Heart Institute, we were able to suggest optimal design of a stent used in Transcatheter Aortic Valve Replacement (US patent US9125739 B2), now used in medical interventions involving Colibri Heart Valve.

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