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Editorial

Dynamic Blood Vessels and Implications for Medical Devices

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Abstract

The primary function of most vascular stents is to resist radial constriction after angioplasty, and the majority of stent grafts are meant to exclude aneurysms or dissected false lumens. These functions require radial force, however, these devices must also survive vascular deformations. Vascular deformation used to be an afterthought since experts once believed blood vessels had no significant movement aside from cardiac-induced radial pulsatility, but it is now known to be a critical consideration for medical device development. The main drivers of vascular deformation can include cardiac pulsatility, respiration, musculoskeletal motion, and external influences. Since long term implant durability came to the forefront of concern in the early 2000s, it is now entangled into device design, regulation, product positioning, marketing, sales, and corporate strategy. Investment in defining anatomic boundary conditions during the early stages of product development will improve product design and save time and money in the long run.

Primary Function vs. Accommodation

A design engineer is tasked with designing tires for a car. He is given the dimensions of the wheel, the weight of the car, and the range of terrains the car will drive upon. He spends a year designing a tire that fits the wheel perfectly, can be installed easily with simple tools, and can more than accommodate for the weight of the car. In addition, he designs an innovative tread that can drive equally well on paved road under dry conditions or with rain, snow, or sleet. On initial road tests, the tire performs well and the product undergoes production for limited distribution. Within six months of commercialization, complaints of thinning treads and losing traction in rain and snow pile in. In some rare cases, the tires thin so much that they rupture on the road. After some failure investigations, engineers realize that costumers do not always drive on nicely paved roads, and that cracks, potholes, and gravel wear the tires much faster than originally anticipated. The company needs to recall all the tires and redesign for durability in real-life driving conditions.

The above scenario is basically what happened in the world of vascular stents and stent grafts for the first twenty years of stenting, while only in the past decade has the industry begun to design holistically for durability beyond just primary function. The majority of arterial stents are produced for atherosclerotic occlusive disease, where stents are meant to fight the elastic recoil of the artery after angioplasty. This means that the primary function of the stent is to supply sufficient resistance to radial compression while not substantially compromising the flow lumen area. This is exactly the reason why manufacturers make stents that provide high radial resistive force, and are also thin in order to not take up substantial luminal cross-sectional area.

While arterial stents primarily need to resist radial compression, they also have to be implanted precisely at lesions safely and easily, which requires low-profile catheters that can deploy stents with reliable position and length. These additional requirements are assisted by the addition of longitudinal stiffness in the form of axial bridges, which also aids in the manufacturing of the device (Figure 1). In addition, this axial "connectedness" enhances *in situ* stability by preventing stent tilting and ensuring good wall apposition. With many stent designs, longitudinal stiffness, which may be incompatible with the mechanics of the artery, is concomitant with stiffness in the bending and twisting directions, which can make accommodation of the biomechanical and physiologic environment of the artery even more problematic.

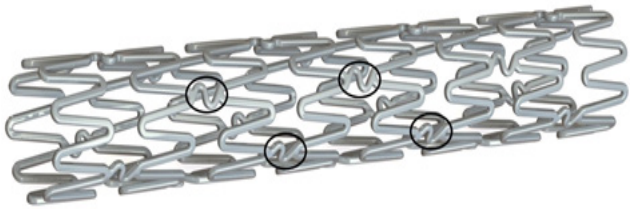

Figure 1. Balloon-expandable stent with axial bridges (circled) to enable consistent delivery and ease of manufacturing.

Figure adapted from commons.wikimedia.org

While radial pulsatility in arteries is well described due to the obvious pulse pressure between diastole and systole, deformations in the axial, bending, and twisting directions are more difficult to quantify. For example, it took dedicated imaging studies of patients during straight and flexed-leg positions to quantify the shortening, twisting, and bending of the femoropopliteal artery that occur with every cycle of hip and knee flexion[1-7]. It is now known that these deformations are transferred to implanted stents and can vary substantially with arterial tension, stent design, stented length, and implant location, and can cause high rates of stent fatigue and fracture. Furthermore, in many cases, stent fractures are clinically important as they are correlated with restenosis and less durable clinical outcomes[8-10].

Similarly, for aortic stent grafts, the devices are meant to seal the aneurysm sac from blood pressure and create a new flow channel, or in the case of dissection, to close off the false lumen to encourage blood to flow in the true lumen. While both of these functions require a certain amount of radial force (e.g. outward force for device anchoring and aneurysm sealing, and outward force for closing the entry tear and pushing the dissected intima towards the rest of the wall), other functional requirements are more elusive. There is evidence that radial, longitudinal, and bending stiffness of stent grafts and branch devices can cause a host of potential durability issues[11-14].

Variety of Vascular Deformations

We now know that the vasculature deforms in complex ways due to cardiac pulsatility, respiration, musculoskeletal movement, and external influences, and that these motions can lead to device fracture. Furthermore, the added stiffness of an implant causes concentration of vascular deformation at the native vessel adjacent to the ends of the implant. This concentration of deformation can cause chronic tissue irritation, intimal hyperplasia, compromised hemodynamics, and eventually thrombosis, occlusion, aneurysm, or dissection. In the case of aortic endografts and venous implants, where anchoring can be tenuous, complete fracture can increase susceptibility to fragmentation and migration.

The first step in defining the deformations of a particular vascular environment is to understand the patient population. The patient group can vary from very sick elderly patients with limited mobility, to children with a treatable congenital heart defect who are otherwise healthy. Not only does defining the indication drive design requirements, it also sets mechanical durability criteria for device testing.

Next, understanding the source of deformation is paramount for quantifying the boundary conditions for design and durability testing. Cardiac pulsatility most simply manifests as the radial expansion and recoil during systole and diastole, respectively. The exact timing of radial expansion and narrowing varies along the body due to finite pressure pulse propagation speed. Larger arteries and those closer to the heart tend to experience greater radial pulsatility than small arteries further away from the heart due to greater tissue elasticity and less constraint from surrounding musculature. And in certain circumstances, cardiac-driven pulsatility can manifest in other directions, such as axial length change, bending, or twist. For example, in a highly curved artery, the high pressure pulse and increased flow during systole can cause the artery to lengthen and/or increase in curvature.

Respiration can cause blood vessel deformation by direct expansion and collapse of the thorax and abdomen, or by changes in intrathoracic and intraabdominal pressure. During inspiration, the thoracic cavity expands and the abdominal cavity is compressed from the descending diaphragm. This means that the abdominal organs and associated blood vessels can be pushed downward during inspiration, instigating changes in blood vessel length, branch angles, and curvature (Figure 2). In parallel, during inspiration, intrathoracic pressure decreases while intraabdominal pressure increases, causing increased venous return from the abdomen towards the thorax and accompanying cross-sectional area changes of the inferior vena cava. Related physiologic phenomenon, such as Valsalva maneuver, can cause even greater cross-sectional deformations due to more dramatic swings in intraabdominal pressure.

Musculoskeletal movement induces blood vessel deformations by pure geometric constraints rather than through hemodynamics. For example, blood vessels that cross joints can bend and straighten with joint flexion and extension, and muscle contraction and relaxation can pull and push on blood vessels even in the absence of a skeletal joint. Blood vessels can also deform by alterations in path length and tension, e.g. a vessel that is originally under tension will begin to bend if it shortens past the point of slack. These deformations can be exacerbated at localized areas when adjacent segments are mechanically restricted by surrounding muscle (e.g. adductor canal) or stiff implants.

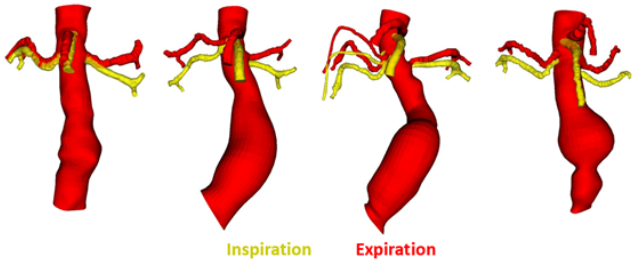

Figure 2. Three- dimensional geometric models built from computed tomography angiograms of small abdominal aortic aneurysms.

Note that the visceral arteries are deflected inferiorly (yellow) as compared to expiration (red).

Attention to Vascular Deformation Pays Off

Through concerted effort, a lot of headway has been made in quantifying vascular deformations, and stent and stent graft design has benefitted greatly. Many second generation stent designs are more harmonious with the vascular environment, such as the Supera® (Abbott Laboratories, Abbott Park, Illinois), Viabahn® VBX (W.L. Gore & Associates, Flagstaff, Arizona), and BioMimics 3D (Veryan Medical, West Sussex, United Kingdom).

However, more attention is needed. It is all too common for a development program to be halted, even in the late stages of a pivotal clinical trial, due to device fractures that result from unforeseen vascular deformations. Discovering high fracture rates in a clinical trial could jeopardize the commercialization of a product, or conversely, if boundary conditions are chosen to be too rigorous, mechanical testing may yield false negative results, potentially halting development of a benefical product. Any company developing vascular implants can tell you how much more expensive it is to redesign midway through a clinical trial vs. before clinical testing. It just requires some early investment and patience to acquire the necessary biomechanical design boundary conditions.

In many cases, it is not necessary to reinvent the wheel. Sometimes a strategic, thorough literature search will suffice. In other cases, cadaver studies, especially those where vascular

deformations are quantified before and after stent implantation, will yield sufficient mechanical boundary condition data. In cases where *in vivo* patient imaging studies are warranted, even studying a small population of 10-20 patients is much better than developing in the dark. This is where collaborative efforts between companies and hospitals are valuable.

When evaluating the mechanical durability of medical devices, there are three main efforts: 1) Quantifying anatomic boundary conditions including deformations and number of cycles, 2) Quantifying stresses and strains of the implant based on these deformations, and 3) Interpreting fatigue performance based on material properties, stresses and strains, and number of cycles. While a lot of attention has been paid to steps 2 and 3, step 1 has historically been relatively ignored or handled in an ad hoc manner. Investing into step 1 is good bang for the buck. Furthermore, fundamental understanding of dynamic vascular anatomy has been shown to be valuable for disease evaluation, diagnostics, and may spur new ideas for novel treatments.

Conflicts of interest

None.

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