

# The Mechanical Environment of Peripheral Arteries

Advancing device design with improved mechanical testing and computational modeling.

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**T**he use of catheter-based interventions to treat cardiovascular diseases ranks among the most important recent technological advances in medicine. The ability to treat patients has expanded well beyond surgical interventions, resulting in reduced direct health care costs, including the indirect costs of lost productivity, as patient recovery is measured in days rather than weeks or months. Certainly, the largest degree of success has been made in the treatment of coronary artery atherosclerotic plaques. The development of more effective catheter and stent technologies (eg, drug-eluting designs) for this application has led to a great expansion in clinical usage. Drug-elution schemes have reduced restenosis rates in coronary applications and, consequently, inspired a desire to adapt similar technologies for use in peripheral arteries (Figure 1).

Unfortunately, restenosis rates in the periphery remain unacceptably high, hindering widespread adaptation and leaving patients with few treatment options. One impediment to success in treating the peripheral arteries is the complexity of the biomechanical environment, which is quite different from the environment that is found in the coronary arteries.

Arteries can have complex geometries, and although it is convenient to imagine them as static, unchanging vessels, they are in fact subjected to complex, dynamic loading on several different timescales and are capable of equally varied responses and adaptations. The pressure pulse (operating at approximately 1 Hz) is familiar to stent designers who, for regulatory purposes, must demonstrate a minimum simulated fatigue life of 10 years.

Artery walls also contain smooth muscle cells, with typical contraction/relaxation timescales of several seconds to minutes in response to changes in metabolic needs. Long-term adaptations, such as artery wall thickening in response to hypertension, are also frequently observed.<sup>1</sup>

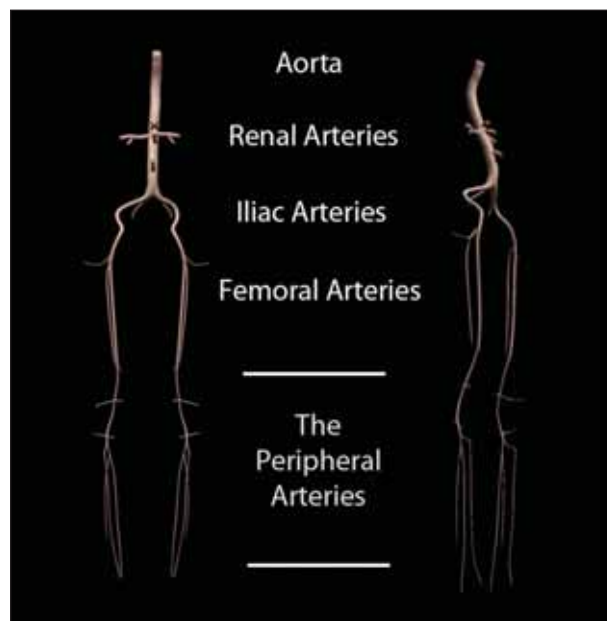


Figure 1. Stenting peripheral arteries poses unique challenges because vessel geometry and dynamic loading in this region can be relatively complex. In addition, drug-elution schemes have not realized the success in peripheral arteries that has been observed in coronary applications.

## VESSEL DEFORMATIONS DUE TO ADJACENT TISSUE MOVEMENT

An important biomechanical phenomenon with serious implications for implantable device durability involves the movement of adjacent tissues. Coronary arteries are subjected to significant deformations as a result of myocardial contraction. These deformations change following stent implantation<sup>2</sup> and may play a role in clinically observed stent strut fractures. Of more serious concern are the deformations associated with movement of the lower limbs. These are typically larger in magnitude and involve adjacent soft and hard tissue movement. The result is an extremely complex, dynamic mechanical environment from the distal aorta down to the smallest arteries of the legs into which stents are implanted.

These peripheral arteries are subjected to pulsatile distention, pressure-induced changes in length, radius of curvature (in multiple planes), and torsion (ie, deformation in all degrees of freedom) (Figures 2 and 3). Choi et al reported human iliac artery deformations during motion from the supine to fetal positions.<sup>3</sup> The degree of axial shortening was  $5.2\% \pm 4.6\%$ , whereas the change in curvature was  $85\% \pm 44\%$ , and axial twist was measured at  $18^\circ \pm 10^\circ$ . Measurements of the deformations that are encountered in normal human superficial femoral arteries indicate shortening in length (from 5.9% in the proximal superficial femoral artery to 8.1% in the distal portion), changes in curvature that exceeded three times the supine curvature value, and twist rates of up to 2.1 deg/cm.<sup>4</sup>

In terms of animal models, a recent study has quantified porcine iliac artery deformation during the range of motion from full extension to full flexion (axial shortening,  $11.8\% \pm 2.3\%$ ; change in curvature,  $87.5\% \pm 36\%$ ; axial twist,  $27.5^\circ \pm 4.8^\circ$  over the length of the vessel).<sup>5</sup> So, although animal models exhibit vessel deformation, the magnitude and types of deformation may have little correlation with those encountered in humans. Moreover, ani-

mal models are impractical for long-term fatigue testing, where in vitro accelerated testing is preferred.

Changes in coronary artery curvature are smaller than the changes in curvature observed in the arteries of the lower limbs and are periodic with the cardiac cycle.<sup>6,7</sup> Furthermore, large periodic variations in axial twisting are mainly observed in distal regions of the left anterior descending/right coronary artery, where stents are not commonly deployed. Thus, deformations in the coronary arteries do not resemble those in the peripheral vasculature for multiple reasons.

Despite clear indications that the in vivo mechanical environment is more complex, current fatigue testing of implantable cardiovascular devices typically includes only cycling pressure in a straight, compliant tube. This is generally true whether the testing is done experimentally or computationally. The US Food and Drug Administration (FDA) has recognized the need for more realistic modeling of the in vivo situation and has organized multiple workshops on improving computational modeling. These workshops have provided an excellent forum for interactions between the regulatory agencies, device manufacturers, and academicians. They have also played a role in the establishment of new funding mechanisms such as the National Institutes of Health's Advancing Regulatory Science Through Novel Research and Science-Based Technologies grant.<sup>8</sup>

## IMPROVING IN VITRO TESTING

Although knowledge of the in vivo mechanical environment is improving, there is a lag in the adaptation of this knowledge to in vitro testing regimens. For example, the first testing apparatus that apply bending to existing fatigue tests have arrived on the market (Figure 4); however, given the simple nature in which bending is applied, the mechanical environment still lacks realism. Whether or not this simplified bending method is sufficient for device test-

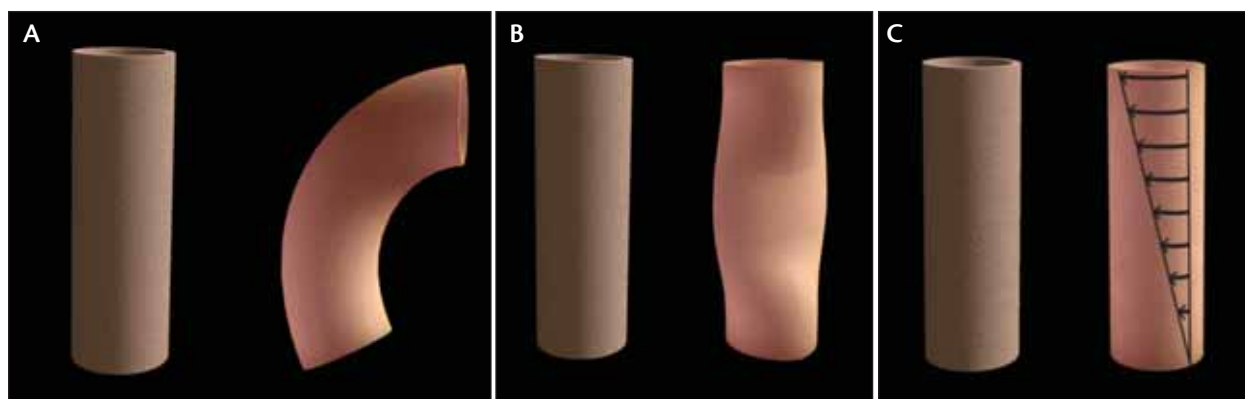
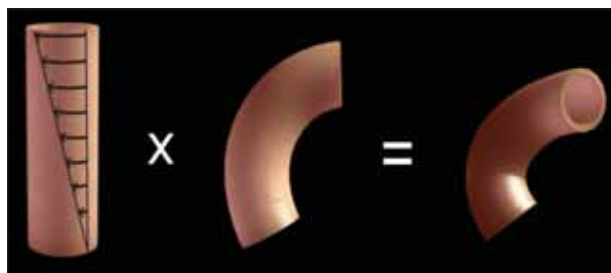


Figure 2. Simple arterial deformations: bending (A), lateral impingement (B), and torsion (C). These basic deformations can be static or dynamic, changing with cyclic pressure loading, and can be combined to form more complex deformations (see Figure 3).



**Figure 3. Complex deformation as the product of two or more simple deformations. In this example, torsion is combined with bending to produce a more complex deformation, bending that is “out of plane” (see Figure 5).**

ing is unknown. Unfortunately, although systems that incorporate bending represent a substantial improvement over previous systems, which merely cycle pressure, the use of these testing systems and methods is not prevalent.

It is important to determine if devices tested in a given system exhibit the same failure modes as those observed in vivo. This would motivate more widespread use of these systems and potentially provide important insight for device design improvements. Note that this approach would apply whether the in vitro tests are experimental or computational. In fact, it is likely that a combination of these two approaches would improve testing technologies more efficiently. It is quite typical in many fields that computational techniques provide the opportunity for quicker design iteration, whereas potentially time-consuming experiments are used more for verification and validation of computational models.

Arteries have complex geometries such that, once deployed, an implantable device may be subjected to a measurable static strain; that is, devices are typically constructed as straight tubes that are ultimately deployed in tapered, curved, and/or tortuous vessels. Dynamic loading associated with pulsatile pressure and flow is then superimposed on the static strains imposed by the vessel geometry. Fatigue testing using straight compliant tubes neglects the strains that may be imposed on the device as it conforms to the vessel geometry.

The previous in vivo measurements of iliac artery deformations with limb movement were clearly three-dimensional. In a first pass, applying bending in a single plane seems reasonable. Indeed, this will likely reveal some weak points in device design. However, neither devices nor in vivo deformations are axisymmetric, implying that single-plane bending experiments should be repeated at different relative positions of the device and bending plane (Figure 5).

The combination of bending or torsion with pressure pulsations at cardiac pulse frequency places a high

demand on either experimental or computational attempts at reproduction. Limb movements occur at irregular intervals that have no relation to the cardiac pulse. Some scaling of frequencies, which is particularly important in the design of accelerated fatigue experiments, is required. For example, one might propose to employ a frequency of bending proportional to the average number of steps taken in a day, ignoring variations that occur throughout the day. Again, such first-pass approaches are likely to reveal weak points in device design, thus satisfying the principal criterion of making devices safer for patients. More realistic simulations would include duty cycles representative of the intermittent nature of daily activities.

The presence of large-scale deformations in vivo has hugely important implications on the application of individually applied deformations in assessing device design. It is certainly tempting to simplify testing by applying radial deformations in one experiment and bending/torsion in another. In the realm of small deformations (eg, < 1% strain), such an approach of superposition has a rational basis. Commonly employed in the design of metallic structures such as buildings and bridges, this approach relies on the fact that the addition of small strains from various kinds of loading results in a total deformation that is “close enough” for design purposes.

For large deformations such as those found in peripheral arteries, the inaccuracies brought about by superposition are considerable. For example, linear superposition of strains < 0.1% results in an error of < 0.05% relative to true strain. Linear superposition of physiologic strains (eg, 20% strain) results in an error of at least 10%, which could seriously compromise the applicability of individually performed fatigue tests. Iterations in design brought about by



**Figure 4. Testing device designed to apply bending forces. Systems capable of applying bending, such as this, offer improvements to designs that only cycle pressure. However, further improvements are required to better replicate the in vivo mechanical environment.**

making such assumptions should eventually be tested using a comprehensive approach.

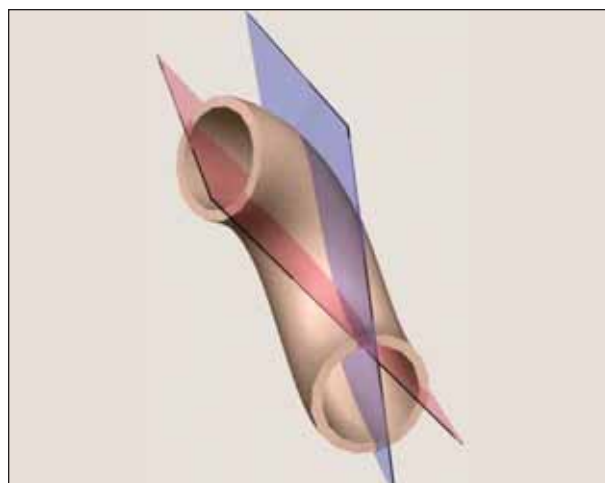
### A PROPOSED PATHWAY TO ESTABLISHING DEVICE SAFETY IN PERIPHERAL ARTERIES

Clearly, there is a need to establish criteria for testing cardiovascular devices under realistic conditions that are representative of peripheral arteries. The market for such devices, while currently about an order of magnitude smaller than the coronary market, could grow considerably if more reliable devices were available. The following is a recommended strategy for accomplishing this task.

The deformations imposed on implantable devices must be realistically quantified. Although measurements of vessel deformations are important, the implantation of stents or endografts will alter this picture. The problem falls into the category of contact mechanics, in which two elastic bodies with opposing tendencies to deform are opposed. With purely radial deformation, the stent pushes out on the artery that tends toward a smaller diameter, deforming both the artery and the stent from their relaxed configurations. The field of mechanics is well developed in this regard, although the presence of large deformations and complex material properties renders computational analysis a tall challenge.<sup>9</sup>

In peripheral arteries, the picture is complicated by complex perivascular structures such as bone and soft tissues of varying properties. Indeed, the field of biomechanics has yet to address this situation fully. The fact that the final state of deformation will depend on the characteristics of the device itself is an additional complication. Clearly, there is a need to advance computational biomechanical modeling to the point where a database of physiologic deformations can be established. Furthermore, there is a need to improve the *in vitro* testing capabilities for cross-validation of computational models. Although animal models are effective for short-term testing, long-term or accelerated fatigue testing requires experimental systems that are designed to accurately reproduce the human biomechanical environment, including the use of realistic mock artery geometries and physiologic dynamic loading.

Given a more complete picture of *in vivo* deformations, both experimental and computational simulations can be pursued to identify weak points in device design. Despite the previously outlined indications that superposition is not appropriate, testing devices under isolated deformation modes is a logical first approach. The degree to which these individual experiments are reliable will be revealed with the advent of capabilities to reproduce fully physiologic three-dimensional deformations of varying frequencies. This will be an important step in establishing the



**Figure 5. Out-of-plane bending.** Bending of arterial segments may be out-of-plane. Current systems designed to apply bending to vascular devices only provide bending that is in-plane.

required complexity of fatigue and wear testing equipment and computational abilities.

The design of completely physiologic loading equipment or boundary conditions for computations will be challenging. Part of the challenge lies in the question for which there is no exact answer: What is physiologic? This depends on patient anatomy, metabolic needs, level of activity, etc. Employing traditional engineering design techniques, an appropriate strategy would be to establish an envelope of typical deformations encountered and then incorporate an appropriate safety factor. This in itself is a delicate balance because the use of excessive safety factors will result in devices that are not deployable or occlude an unacceptably high portion of the lumen after deployment. Physician acceptance is also crucial. The criteria for success of implantable devices are many, varied, and not always quantifiable.

### CONCLUSION

Despite recent advances in medical device manufacturing (including design, materials, and manufacturing techniques) and biomechanics research, it remains a challenge to design stents and endografts that are reliable in peripheral artery applications. The rush to market devices for these applications has certainly not progressed in total disregard of the complications presented by the biomechanical environment, but rather on the hope that the devices will survive sufficiently for long-term clinical benefit. Clearly, this strategy is due for an update. The way forward will require the cooperation of various partners. Indeed, even rival medical device manufacturers have expressed



the need for cooperative efforts to establish relevant in vivo criteria. Biomechanics researchers in academia also have an important role to play, as advanced modeling techniques being employed on a daily basis will be required to fully elucidate the loads applied to devices in vivo.

Last, but certainly not least, is the role of government agencies. Regulatory agencies such as the FDA have made great strides in understanding in vivo biomechanics and their effects on devices. This knowledge is, of course, crucial in judging the validity of any tests presented in application of regulatory approval. Funding agencies such as the National Institutes of Health and the National Science Foundation also have an important role to play because the FDA is extremely limited in its ability to encourage researchers to pursue biomechanical studies of the appropriate level of complexity. ■

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