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Cover Story

Better design of drug-eluting stents using computer modeling

Drug-eluting stents (DESs) have been successfully used for the last several years, and in the United States alone over a million patients receive DESs at costs in excess of a billion dollars each year. Despite early successes, uncertainty remains on the overall safety, especially the late in-stent thrombosis issue, of these devices. One of the main causes of the majority of problems experienced with DESs is healing-related [1]. The current drugs that are used for prevention of restenosis are non-specific, i.e., they can be also active against endothelial cells. It has been suggested that prolonged retention of a drug released from a DES may attribute to delayed endothelial coverage [1]. Thus, the efficacy and toxicity of DESs appear to depend on the local arterial drug levels. Despite ubiquitous use of DESs, however, there is still little understanding of the factors that govern local drug deposition and subsequent uptake into the arterial tissue. Nor is there an appreciation as to whether one stent is different from another. In particular, there has not been adequate consideration of the interaction of stent design and blood flow on observed patterns of drug distribution after controlled release.

A research article in this issue by Kolachalama et al. elucidates the extent to which various flow conditions alter arterial drug deposition after local release [2]. Employing computational fluid dynamics modeling tools, the authors explained that flow patterns within the milieu of the stent strut are significantly affected by net luminal flow and strut geometry. This study highlights the sensitivity of spatial drug targeting to intrinsic luminal flow and stent design. Design becomes increasingly important in determining drug distribution where the strut aspect ratio significantly modulates the relative contributions of contact-mediated drug diffusion and flow-mediated convective transport.

The clinical and device implications of this work are paradigmatic. The authors have explained that we must now resurrect consideration

of stent design rather than viewing drugs as leveling the playing field for all forms of endovascular implants. The implications of this work will change how we view composite drug devices, practice medicine and employ computational techniques. The paper beautifully illustrates why computational modeling can transform our understanding of the rational design, performance and regulatory evaluation of complex controlled release devices. Indeed, work like this illustrates why modeling is increasingly central to the FDA's Critical Path Initiative. Computational modeling becomes indispensable when experimental studies define areas of concern but cannot fully characterize them. Development of DESs to date has been focused on pharmacological agents, properties of the coating materials, and overall drug release kinetics. The current study by Kolachalama et al. provides a new, additional insight for further advances in developing truly safe and effective DESs.

References

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