CAN THE GEOMETRY OF THE ATHEROMA PLAQUE INFLUENCE ON DRUG TRANSMURAL TRANSPORT ON DRUG ELUTING STENTS?

Estefanía Peña (1,2), Javier Escuer (1), Estela Pina (1), Miguel A. Martínez (1,2)

1 Aragón Institute of Engineering Research (I3A), University of Zaragoza, Spain. 2 Biomedical Research Networking Center in Bioengineering, Biomaterials and Nanomedicine, Spain

Introduction

Coronary angioplasty with stenting is currently the most widely used treatment for advanced atherosclerotic lesions. The introduction of drug-eluting stents (DES), which deliver antiproliferative substances to the arterial wall, has contributed to the improvement of in-stent restenosis (ISR). Despite the improvement achieved with DES compared to bare metal stents, ISR remains a major clinical and technological challenge in the design of these intravascular devices. The development of computational models has led to great advances in the understanding of drug transport on DES, but they usually represent simplified healthy straight geometries or highly simplified plaques that do not reproduce the characteristic geometry and composition of them. However, there is growing evidence that plaque composition may well have an impact on drug distribution within diseased tissue.

Methods

In an attempt to address some of the limitations of the previously computational models, we perform a series of computational drug transport models to analyse and understand the effect of atheroma plaque composition and structure on spatio-temporal drug uptake within the tissue. To this end, a finite element model of an idealised coronary artery under conditions of atherosclerotic disease between DES and healthy tissue is performed, and the effect of plaque composition and structure on global drug distribution is investigated. Of all the geometric factors to be analysed, we focus on the thickness of the fibrous cap, the total length of the plaque and the length and thickness of the necrotic core and percentage stenosis.

Results and Discussion

The results clearly demonstrate that the spatio-temporal distribution of drug is highly dependent on the geometrical variables analysed. The composition of the core strongly influences the drug concentrations, due to the different density of binding sites in this region. The results suggest that lipid plaques give rise to higher drug concentrations than fibrotic plaques, while calcified plaques are drug-impenetrable, according to the assumptions assigned to the model. The impenetrability of calcified plaque has potentially important implications and, if large enough, may act as a significant barrier to drug from reaching arterial tissue where smooth muscle cells (SMCs) capable of proliferating and migrating to device-injured areas during implantation reside. The results also suggest that the presence of plaque, regardless of core composition, may slightly delay receptor saturation in the medial layer.
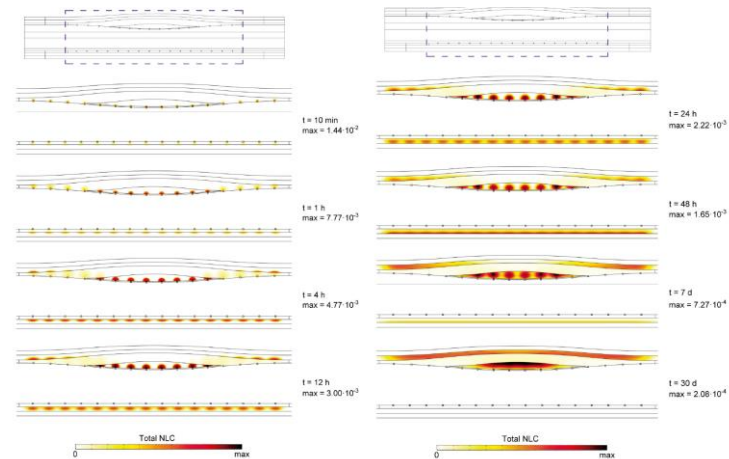

Figure 1. Spatial variation of sirolimus at five different time points (t=10 min, t= 1 h, t=4 h, t=24 h, t=48 h, t=7 days and t=30 days) for the baseline model.

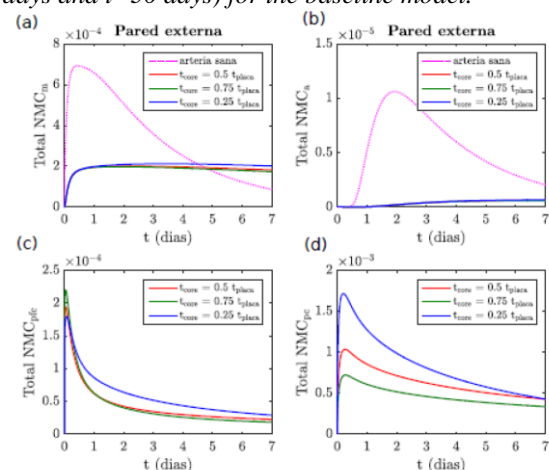*Figure 2. Spatial variation of sirolimus at five different time points (t=10 min, t= 1 h, t=4 h, t=24 h, t=48 h, t=7 days and t=30 days) after stent implantation for the baseline model*

References

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[2] Escuer J., Aznar I., McCormick C., Peña E., McGinty S., Martínez M. A. Influence of Vessel Curvature and Plaque Composition on Drug Transport in the Arterial Wall following Drug-eluting Stent Implantation. Biomech Model Mechanob.2021;20:767–78

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