COMPUTATIONAL MODEL OF NITRIC OXIDE TRANSPORT AND PRODUCTION IN FLOW CHAMBERS

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INTRODUCTION

Approximately 40% of deaths in developed countries are due to cardiovascular diseases. Atherosclerosis is an extremely common form of cardiovascular disease characterised by the formation of lipid rich plaques within the intima of the arterial wall. Such plaques can lead to the stenosis of arteries, and may eventually rupture causing a heart attack or stroke.

Areas prone to develop atherosclerosis are thought to be associated with complex blood flow environments, characterised by low and oscillatory Wall Shear Stress (WSS). Evidence suggests that Endothelial Nitric Oxide Synthase (eNOS) concentration and hence Nitric Oxide (NO) production, are related to WSS. As NO is a known atheroprotective agent, NO concentration may play an important role in the development of atherosclerosis.

Numerous experimental studies using parallel plate flow chambers have investigated the relationship between NO production in endothelial cells and WSS. The aim of this study is to develop a more detailed understanding of the NO distribution within such a flow chamber and to identify key parameters that regulate NO production and transport.

METHODS

Flow and NO distribution in the parallel plate chamber (17mm x 3.8mm x 400μm) are obtained using a Spectral/hp Element method solver (Nektar [1]). Transport of NO is modelled using the Advection-Diffusion-Reaction equation. NO reaction with the perfusion fluid is assumed to be second order. At the interface between endothelial cells and the flow a linear combination of Dirichlet and Neumann boundary conditions is applied in order to model the following phenomena: 1.) NO production rate depends on WSS magnitude, where the relationship between NO production rate and WSS is assumed to be sigmoidal [2,3] and 2.) NO production rate decreases with increasing endothelial NO concentration.

RESULTS AND DISCUSSION

It is found that a NO concentration boundary layer develops within the flow chamber (Figure 1). The structure of such a boundary layer depends on the reaction rate of NO with the media, the nature of the boundary condition applied at the endothelium, and the flow rate through the chamber.

The concentration of NO at the endothelial surface depends on WSS in a non-trivial fashion (Figures 2 and 3). An increase in WSS is associated with an increased NO production rate and increased NO convection from the chamber. Depending of the form of the endothelial response to WSS, the balance between these two phenomena may vary as WSS rises, resulting in a non-monotonic dependence of wall NO concentration on WSS.

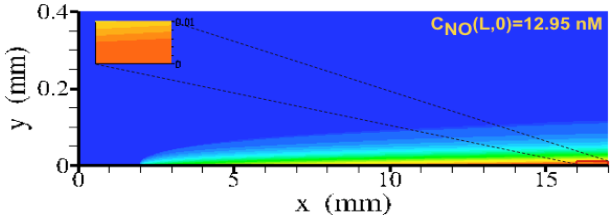

Figure 1: NO concentration (C_{NO}) within the flow chamber for WSS=3Pa.

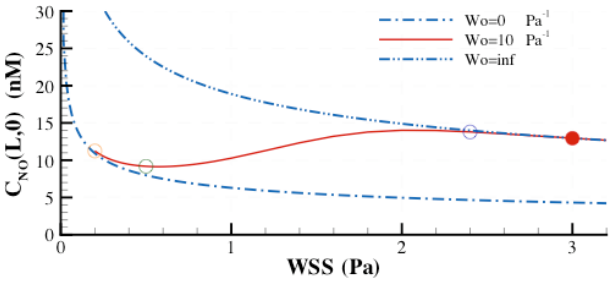

Figure 2: NO concentration at the exit of the flow chamber (L=17mm) for different WSS levels for a given endothelial response (solid line). The parameter W_o characterises the sensitivity of the endothelial response

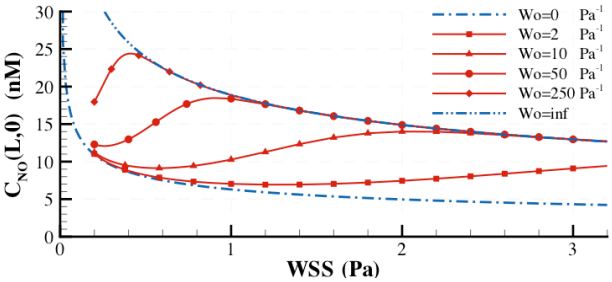

Figure 3: Variation of NO concentration at the exit of the flow chamber with WSS for different endothelial responses.

CONCLUSIONS

The relationship between NO production and WSS remains a point of contention. Experimental studies are scarce and often conflicting. Moreover they have repeatedly overlooked the importance of fluid-dynamical effects such as convection on the NO distribution within flow chambers.

This study has assessed the influence of mass transfer effects on endothelial NO concentration in flow chambers and determined the key parameters that regulate NO production and transport. Experimental determination of these parameters is necessary in order to model NO distribution in *in vivo* and *in vitro* environments.

REFERENCES

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