Multi-scale, patient-specific modelling approaches to predict neointimal hyperplasia growth in femoro-popliteal bypass grafts

Donadoni, F.[1], Bonfanti, M.[1], Pichardo-Almarza, C.[1], Homer-Vanniassinkam, S.[1], Dardik, A.[2], Diaz-Zuccarini, V.[1]

[1] University College London, UK

[2] Yale University School of Medicine, New Haven, USA

1. Introduction

Neointimal hyperplasia (NIH) is a major obstacle to the long-term patency of peripheral vascular grafts. The disease has a complex aetiology which is influenced, among other phenomena, by mechanical forces such as shear stresses acting on the arterial wall.

2. Objectives

The aim of this work is to use a multi-scale modelling approach to assess the impact of haemodynamic factors in NIH growth. We hypothesized that both low and oscillatory shear should be considered simultaneously when assessing the proclivity of a certain region in bypass grafts to develop NIH and we simulated NIH progression using a multi-scale computational framework that we previously developed, comparing our results to a patient-specific clinical dataset (obtained with the patients' informed consent for research and publication).

3. Methods

Simulations were performed on datasets from two femoro-popliteal and one femoro-distal bypass patients. Patient data (imaging and haemodynamics) was obtained from Yale University School of Medicine. In this work, smooth muscle cells and collagen in the vascular tissue were modelled using ordinary differential equations. These were linked to wall shear stress (computed using CFD) through its relationship with nitric oxide and growth factors. A moving boundary method [2] was also introduced to simulate the movement of the arterial wall.

4. Results

Results obtained by simulating the growth via the combined CFD and mathematical biology framework seems to outperform analyses performed with haemodynamic indices (obtained by CFD) alone. This indicates that the non-linear and complex interplay of factors affecting NIH can be better quantified through an integrative approach. At the same time, assessing different haemodynamic conditions enabled to pinpoint the locations of hyperplasia, and also to achieve better quantification of its growth. Our results highlight the impact of two different measures of

wall shear stress (TAWSS and HOLMES) [3], and the importance of the interaction between TAWSS and OSI in NIH progression. In all cases, the simulation model correctly predicted areas of NIH growth, with values that were similar to the stenoses observed in the CT scans when using the HOLMES index, with a maximum discrepancy (presented as % area) of 8% between stenosis values observed in patients 1-3 when compared to CT scans. When using TAWSS, not all NIH-stenotic regions are predicted and for those that are, the amount of luminal narrowing is consistently underestimated and sometimes by a significant amount - as in the case of patient 3 - with a reported difference in terms of NIH growth area of 41%.This suggests that TAWSS is an unreliable metric to estimate both plaque location and the degree of stenosis in vein-grafts.

5. Summary and Conclusion

The study presents a patient-specific, multiscale simulation framework to model NIH progression. While a previous version of the model [1] underestimated the occlusion of the lumen due to NIH, the results presented show an improvement in estimating occlusion by accounting for movement of the arterial wall, oscillatory behaviour of shear stress and non-Newtonian properties of blood viscosity and tests some of the current theoretical framework in the literature of vascular remodelling.

6. References

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