

Wall shear stress as a stimulus for intra-plaque hemorrhage in carotid atherosclerotic plaque: An MRI-based CFD pilot study

G. Canton¹, H. Chen¹, M. Oikawa², H. R. Underhill¹, W. Yu³, T. S. Hatsukami⁴, C. Yuan¹, and W. S. Kerwin¹

¹Radiology, University of Washington, Seattle, Washington, United States, ²Cardiovascular Medicine, Tohoku University, Sendai, Japan, ³Radiology, Beijing Anzhen Hospital, Beijing, China, People's Republic of, ⁴Surgery, University of Washington, Seattle, Washington, United States

Motivation

Cells present in the arterial vessel wall respond to sustained altered values of hemodynamic forces modifying their structure and function at the cellular, molecular, and genetic levels to return these forces to their physiological values. However, under certain circumstances, this response may lead to pathologies, such as atherosclerosis. Recent studies have suggested that endothelial cells may modify the balance between cap-reinforcing extracellular matrix synthesis by smooth-muscle cells and extracellular matrix degradation by metalloproteinases secreted by infiltrating macrophages as a response to shear stress¹. These studies indicate that there might be a link between plaque distribution and composition and shear stress patterns.

Magnetic resonance imaging (MRI) has emerged as a powerful tool to characterize human carotid atherosclerotic plaque composition and morphology^{2,3}. Furthermore, MRI is able to identify plaque features that have been shown to be key determinants of plaque vulnerability^{4,5}; however, the pathophysiological mechanism responsible for the presence of those features still needs to be determined

Objective

The aim of this study was to explore the hypothesis that intra-plaque hemorrhage, a feature associated with adverse outcomes and plaque progression, is more likely to occur in plaques with elevated levels of wall shear stress.

Methods

Carotid Imaging: Vessel wall images were acquired from seven subjects with carotid atherosclerosis using a standardized protocol⁶ with a 1.5 T MRI scanner (Signa Horizon Echospeed; GE Healthcare). 3D time-of-flight (TOF), 2D T2- and PD-weighted FSE, and 2D T1-weighted pre- and post-contrast quadruple inversion-recovery FSE sequences were obtained. The protocol and consent forms were approved by the local Institutional Review Board. Informed consent was obtained prior to patient enrollment. Axial images were acquired covering the segment from 8 mm below the carotid bifurcation to 10 mm above it, so the entire carotid plaque was imaged. Custom designed analysis software (CASCADE) was used to register and segment the images⁷. Lumen and wall boundaries were outlined for each imaged slice, as well as, the lipid-rich necrotic core and hemorrhage boundaries, if present.

Computational Fluid Dynamics (CFD) Model: Unstructured tetrahedral meshes were constructed based on the geometrical information provided by the MRI luminal segmentation using a customized version of the MATLAB-based code (Matlab, R2007b, The Mathworks, Inc) developed by Persson and Strang⁸. Once the computational mesh was built, it was imported into a CFD software package (COMSOL Multiphysics, Stockholm, Sweden) to solve the Navier-Stokes equations that govern the flow using finite element analysis. Blood was treated as a Newtonian, viscous fluid with a density of 1045 kg/m³ and dynamic viscosity of 0.0035 Pa·s. Due to the lack of patient-specific flow information from the common, external, and internal carotid arteries, assumed flow conditions were defined at the inlet (common carotid artery) and outlets (internal and external carotid arteries) of the model: a fully-developed Womersley flow was assumed at the entrance with a peak Reynolds number of 609.63, and a normal stress of 1000 N/m² was imposed at the outlets. A no-slip boundary condition was applied along the luminal surface. The computational time step was set at 10 ms. Three cycles were computed to ensure a reproducible solution.

Results

A lipid-rich necrotic core was identified in five of the seven cases analyzed. Intra-plaque hemorrhage (IPH) was detected in three of these five cases (Figure 1). WSS data were extracted from the results of the CFD simulations to compare patterns between the cases with and without hemorrhage. We computed the mean value of the wall shear stress (for each time point of the cardiac cycle) at the region where hemorrhage and/or lipid-rich necrotic core (LRNC) was detected for the arteries where these features were identified (Figure 2). In the case of the two arteries where no necrotic core was detected, we computed the mean WSS for the section corresponding to the internal carotid artery. The value corresponding to the peak systole was then compared across the seven arteries (Figure 3) and showed that in 2 of 3 subjects with intra-plaque hemorrhage, the local wall shear stress was elevated.

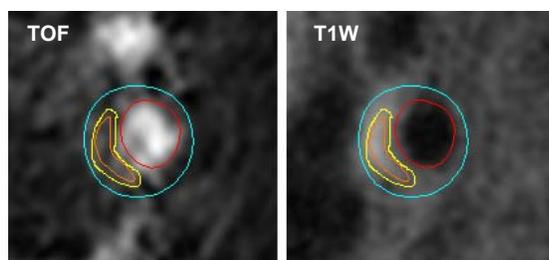


Figure 1. TOF and T1-weighted MR images showing hemorrhage (bright signal in both TOF and T1W delineated in orange) in an internal carotid plaque. Color-coded contours: blue, outer wall boundary; red, lumen boundary; yellow, lipid-rich necrotic core; orange, intra-plaque hemorrhage.

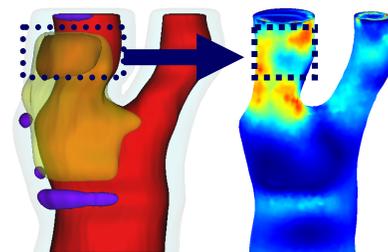


Figure 2. The 3D reconstruction of the arterial segmentation was used to identify the region where intra-plaque hemorrhage and/or necrotic core was detected in the CFD model. The WSS was averaged within this region.

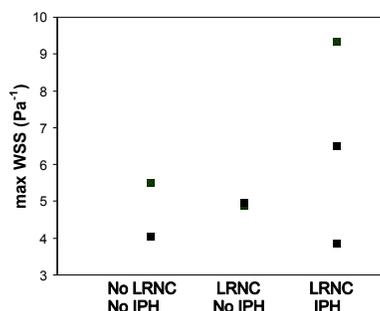


Figure 3. Peak systole WSS for the arteries without necrotic core (No LRNC/No IPH), with necrotic core but no intra-plaque hemorrhage (LRNC/No IPH), and with intra-plaque hemorrhage (LRNC/IPH).

Discussion

The results from this pilot study indicate a possible link between the presence of hemorrhage within a lipid-rich necrotic core in human carotid atherosclerotic plaques and the shear stress force acting on the luminal surface. Although different groups have successfully estimated wall shear stress patterns in carotid atherosclerotic plaques, there has not been any prior study that identifies shear stress patterns that may be responsible for the presence of a specific plaque component. If further studies bear out the association, wall shear stress might be used as a marker for the risk of intra-plaque hemorrhage and subsequent complications. An alternative view is that elevated wall shear stress may be the high risk feature and intra-plaque hemorrhage could be viewed as a marker for elevated shear forces on the plaque.

References:

1. Davies, P. F., *Nature Clinical Practice Cardiovascular Medicine* 2009, 6 (1), 16-26.
2. Cai, J. M., et al., *Circulation* 2005, 112 (22), 3437-3444.
3. Saam, T., et al., *Arteriosclerosis Thrombosis and Vascular Biology* 2005, 25 (1), 234-239.
4. Naghavi, M., et al., *Circulation* 2003, 108 (14), 1664-1672.
5. Naghavi, M., et al., *Circulation* 2003, 108 (15), 1772-8.
6. Yuan, C., et al., *NMR in Biomedicine* 2006, 19 (6), 636-654.
7. Kerwin, W., et al., *Topics in Magnetic Resonance Imaging* 2007, 18 (5), 371-378.
8. Persson, P. O.; Strang, G., *Siam Review* 2004, 46 (2), 329-345.