The influence of computational strategy on prediction of MRI-based mechanical stress in carotid atherosclerotic plaques: comparison of 2D structure-only, 3D structure-only, one-way and fully coupled FSI analyses

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Introduction: Currently, carotid luminal stenosis is the only validated diagnostic criterion for risk stratification, but this criterion becomes less reliable in patients with mild to moderate stenoses that underlie the majority of clinical events[1]. A 'vulnerable' carotid atherosclerotic plaque is characterized by the presence of plaque hemorrhage (PH), a large lipid-rich necrotic core, and fibrous cap (FC) rupture. However, although ~60% symptomatic patients exhibit PH or FC rupture at baseline[2,3], only about 15% will experience a recurrent event at one year[4]. It is thus clear that plaque composition detected by imaging alone cannot predict future cerebrovascular risk, and additional analyses or biomarkers are required. Under physiological conditions, carotid plaques are subjected to mechanical loading from pulsatile blood pressure. FC rupture may occur when this loading exceeds its material strength. As a consequence, many studies have tried to predict mechanical stress within the plaque structure[5-9], and to assess its clinical significance[10-12]. However, atherosclerotic plaques are multi-component structures with irregular geometries and highly non-linear material properties, and plaques undergo large deformations due to pulsatile blood pressure; it is therefore challenging to predict mechanical loading within the structure. Different computational strategies have been employed to examine plaque stress, including 2D structure-only[10,13,14], 3D structure-only[6,15], 3D one-way[16,17] and fully coupled fluid-structure interaction (FSI)[8,9,18] analysis. However, differences in assessing mechanical stress within carotid atherosclerotic plaques using different computational strategies have not been comprehensively analyzed.

Aim: To assess maximum principal stress obtained from 4 commonly used strategies in patient-specific modeling, namely 2D structure-only, 3D structure-only, 3D one-way and fully coupled FSI analysis.

Methods: ***(1) Imaging acquisition*** ECG-gated, high-resolution, multi-sequence *in vivo* MR (**Figure 1**) and CT images were obtained from 8 patients with symptomatic carotid atherosclerotic disease. Images were acquired at Addenbrooke's Hospital, Cambridge, UK. The following MR sequences were used: T1, PD, T2, and STIR. The field of view was 100x100 mm^2 and matrix size 256x256. Multi-detector CT angiography acquisition was performed either on a 16 or 64-section multi-detector CT scanner for the compensation of identifying calcium. Co-registration of CT and MR images was undertaken with reference to the carotid bifurcation, and considering the slice thickness and luminal shape. Plaque atherosclerotic components were manually segmented using CMRTools (London, UK). ***(2) Finite element analysis*** Under physiological conditions, the plaque is pressurized and axially stretched. In this study, a patient-specific shrinkage procedure was employed[19]. 2D slices were stacked together and axially interpolated using a cubic spline function to reconstruct the 3D plaque geometry. The arterial wall and all plaque components were assumed to be hyperelastic, isotropic, incompressible, and piecewise homogeneous. The modified Mooney–Rivlin formulation was used to describe the material property of each component. In 3D FSI simulations, the blood flow was assumed to be laminar, Newtonian, viscous, and incompressible. A non-slip condition between fluid and the vessel wall was applied. The incompressible Navier–Stokes equations with an arbitrary Lagrangian–Eulerian formulation were used as the governing equation. All analyses were performed in ADINA (ADINA R & D Inc).

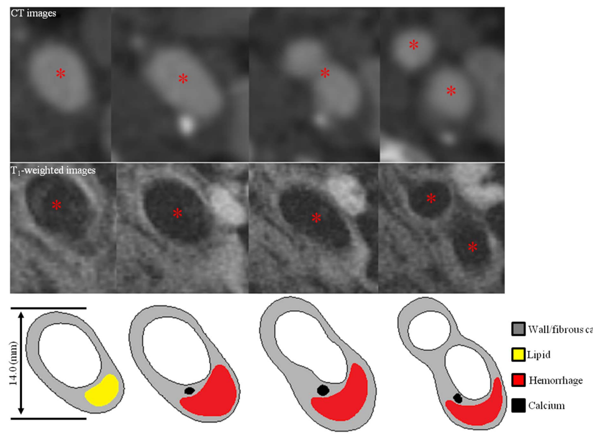

Figure 1. Carotid atherosclerotic plaque images (72-year old, female) CT, T1-weighted MR images and corresponding segmented contours (Red asterisk: lumen)

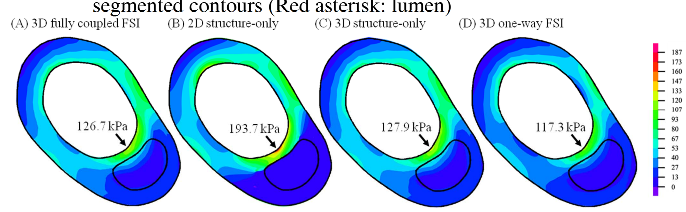

Figure 2. Maximal Stress-P1 predicted by 3D fully coupled FSI, 2D structure-only, 3D one-way FSI and 3D structure-only models

Results: Results obtained were assessed against 3D fully coupled FSI as the gold standard (**Figure 2**). 2D structure-only simulations resulted in a significant stress overestimation (94.1 kPa [65.2, 117.3] vs. 85.5 kPa [64.4, 113.6], $p=0.0004$) with wide scattering near the bifurcation region. The 3D models, including 3D structure-only, one-way FSI and fully coupled FSI analysis demonstrated a good qualitative agreement in predicting stress within the plaque structure. The 3D structure-only model produced a small yet statistically significant overestimation of stress levels (86.8 kPa [66.3, 115.8] vs. 85.5 kPa [64.4, 113.6], $p<0.0001$. In contrast, one-way FSI underestimated stress levels (78.8 kPa [61.1, 100.4] vs. 85.5 kPa [64.4, 113.7], $p<0.0001$**.**

Conclusions: Two-dimensional simulations yielded the poorest performance with a significant overestimation of plaque stress. Three-dimensional structural models showed good qualitative and quantitative agreement with the 3D fully coupled FSI, and are recommended as computationally inexpensive yet accurate approximations for plaques with moderate stenosis.

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