

Distensibility measurements along carotid atherosclerotic plaques: how can we improve the mechanical modeling of atherosclerosis?

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Motivation

Biomechanical modeling of atherosclerotic plaques is emerging as a useful tool to provide markers of plaque vulnerability¹. However, the success of this modeling effort depends on the accurate estimation of local mechanical properties along the diseased vessel wall. Recent studies² in healthy carotid bifurcations reported differences in wall distensibility between common and internal carotid arteries, suggesting that current computational models of carotid atherosclerosis could be improved by accounting for these segmental differences in mechanical properties. Furthermore, the compositional variability among plaques may also have an effect on distensibility values; in this case, comprehensive characterization of the wall in terms of distensibility in addition to plaque burden and composition along the entire bifurcation may improve the performance of biomechanical models.

Objective

We sought to test the hypotheses that (1) in diseased arteries, distensibility changes as the carotid arteries bifurcate and (2) specific plaque components may alter the distensibility along the afflicted vessel wall. CINE magnetic resonance imaging (MRI) of human carotid atherosclerotic arteries was used to measure vessel wall distensibility, whereas a subsequent multi-contrast MRI protocol was used to characterize vessel wall morphology and composition.

Methods

Twenty five participants with a wide range of carotid stenosis were recruited. Informed consent was obtained prior to subject participation. The study protocol and consent forms were reviewed and approved by the institutional review board.

Morphology and Composition: The subjects' carotid bifurcations were imaged axially using a 3.0 T clinical whole-body scanner (Philips Achieva, R2.6.1, Best, The Netherlands) with a 8-channel custom-designed carotid coil. The imaging protocol included a standardized combination of black and bright blood sequences to characterize the vessel wall morphology and composition (Figure 1)^{3,4}. Custom designed analysis software (CASCADE⁵) was used to register and segment the images. Lumen and outer wall boundaries were outlined for each imaged slice. Lipid-rich necrotic core and calcification boundaries were also outlined if detected following histology-validated imaging criteria⁶. Plaque burden was characterized by the normalized wall index (NWI=wall area/total vessel area) and the maximum wall thickness (MWT). When lipid-rich necrotic core and calcification were detected, their percentage of the wall was computed (pNC and pCA, respectively).

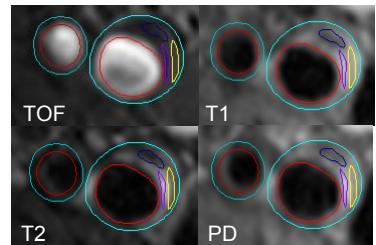


Figure 1. Characterization of plaque morphology and composition.

Distensibility: A CINE sequence was used to achieve multiphase (14-30 per heartbeat) imaging with retrospective ECG gating. Detailed imaging parameters are: TR/TE 16.5-7.1/9.4-4.3 ms, FA 30°, FOV 160x160, slice thickness 2 mm, 5 or 8 slices were acquired to include both common and internal carotid segments with 6 and 2 mm spacing, respectively. The luminal boundary was outlined on all phase images using CASCADE, which produced the corresponding luminal area. Systolic and diastolic areas were identified as the maximum and minimum measured areas, respectively (Figure 2). Brachial pulse pressure was measured before the images were acquired. Distensibility was calculated as $(\Delta A/A_s)/\Delta P$, where ΔA is the area change between systole and diastole, A_s is the diastolic area, and ΔP is the brachial pulse pressure ($P_s - P_d$).

Statistical Analysis: Statistical analysis was performed using SPSS (SPSS 12.0, Apache Software Foundation). Non-parametric methods were used for robustness. Differences in distensibility, plaque burden and plaque composition between the imaged common and internal carotid segments were evaluated using Wilcoxon signed rank tests. Spearman's correlation coefficient was used to identify associations between distensibility and plaque's burden and composition.

Results

Twenty five subjects were scanned in our facility. Gating failed for 3 subjects and blood pressure was not recorded in 4 cases, so these 7 patients were excluded. The mean age of the remaining 18 subjects (12 male) was 72±8 years (range 56-87). The mean systolic and diastolic pressures were 129±22 and 69±10 mmHg, respectively. Distensibility (10^{-5} Pa^{-1}) in the common (CCA) and internal (ICA) carotid arteries was found to be highly similar (3.70 ± 1.90 in the CCA versus 3.60 ± 1.80 in the ICA; $p=0.80$). Also, no significant association was found between distensibility and plaque's burden and composition.

Discussion

The ability of CINE MRI to reproducibly measure distensibility⁵ raised the possibility of combining the morphological and compositional assessment with mechanical parameters in a single non-invasive investigation. The significant difference in distensibility at the common and internal carotid arteries in healthy volunteers⁵ suggested that fluid-structure interaction (FSI) models of atherosclerotic carotid arteries could be further improved by incorporating the mechanical properties of the different segments of the modeled arterial wall. However, the similarities in distensibility found along diseased bifurcations indicate that the degenerative process of the vessel wall with age and atherosclerosis leads to a systemic, rather than local, decrease in wall distensibility. The contributions of plaque burden, calcification and lipid-rich necrotic core on wall distensibility have been found to be insignificant. The results from this cohort suggest that vascular stiffening in the carotid arteries might be less related to atherosclerotic plaque features than to other processes associated to age, such as elastic fiber fraying and fragmentation, supporting recent evidence demonstrating that plaque is not a major contributor to stiffness until the advanced stages of atherosclerotic disease⁷.

Conclusion

Distensibility was found to be similar along diseased bifurcations. Moreover, plaque burden and composition was not found to contribute to wall distensibility. This suggests that using a constant distensibility coefficient per subject in a diseased cohort would not represent a major discrepancy in biomechanical modeling.

References: [1] Makris GC, et al. *Brit J Radiol* 2010;83:729-735. [2] Canton G, et al. *Proc. Intl Soc Mag Reson Med* 2010;18:1350. [3] Li FY, et al. *J Magn Reson Imaging* 2010;31:168-176. [4] Yuan C, et al. *NMR in Biomed* 2006;19:636-654. [5] Kerwin W, et al. *Top Magn Reson Imag* 2007;18:371-378. [6] Saam T, et al. *Arterioscl Thromb Vas* 2005;25:234-239. [7] Santelices LC, et al *Clin Transl Sci* 2008; 1:62-66.

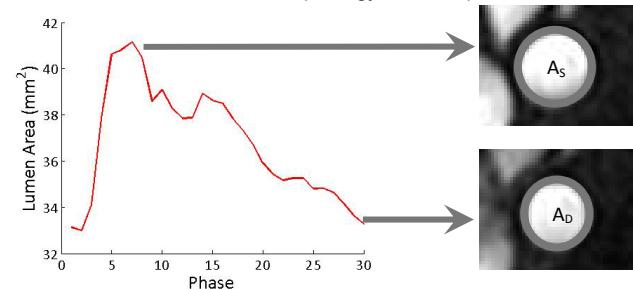


Figure 2. Luminal area change along the imaged cardiac phases. A_s and A_d are systolic and diastolic luminal areas, respectively.

Table 1. Correlation between distensibility and plaque burden and composition.

	Spearman's rho	p-value
Normalized wall index, NWI	0.08	0.74
Maximum wall thickness, MWT	-0.04	0.87
% Calcification, pCA	-0.05	0.84
% Lipid-rich necrotic core, pNC	-0.14	0.59