Direction of Plaque Progression is a Significant Predictor in Plaque Vulnerability: An Evaluation by MRI

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Introduction

Vascular disease is the leading cause of death and disability in the United States. A great deal of evidence shows that atherosclerotic plaque components are a decisive factor determining plaque vulnerability. The rapid development of high resolution magnetic resonance imaging (MRI) technology has enabled the use of gadolinium-based contrast enhanced post contrast T1-weighted images to provide accurate quantitative measurements of the lipid-rich necrotic core (LRNC) and intact fibrous cap (FC) in advanced carotid atherosclerotic plaques in vivo [1]. Based on these measurements, we have previously developed a lesion index called *Normalized Fibrous Cap Projection Length* (***NFPL***) [2]. This measurement represents effective plaque coverage around the lumen and has a high correlation with symptomatic occurrences. Preliminary study results have demonstrated that NFPL is a potential imaging biomarker for carotid artery disease evaluation and a predictor of patient's symptoms. However, this conclusion is based on the projection length analysis in the axial dimension only. In reality, when plaque progresses, it may expand in all directions and it is possible that the projection length along other directions may be larger than the axial expansion. Do such progressions contribute to the symptomatic occurrence to the same degree as expansion in the axial direction that was analyzed before? In this study, we expand the coverage analysis from the axial direction to a 2D artery projection surface which includes both axial and longitudinal directions, and evaluate the impact of plaque's morphological change direction to vulnerability.

Methods

Study Protocol: Twenty-four subjects who had been scheduled for carotid endarterectomy were selected for Contrast Enhanced MRI (CE-MRI) before surgery. Their symptomatic status was defined as amaurosis fugax, transient ischemic attacks, or overt stroke. Half of the subjects were symptomatic and the other half were asymptomatic. MRI data was acquired on a GE 3T Signa MR scanner with a 4-channel phased array carotid coil. The imaging parameters were (TR/TE, ms): T1W(800/9), T2W(2400/20), PDW(2400/40) and TOF (23/3.8), FOV=16x12 cm, matrix=256x192. Scan coverage was 24mm with 2mm slice thickness. Pre-contrast and Post-contrast black-blood T1W images were obtained using quadruple inversion recovery (QIR)[3]. Post-contrast T1W images were captured 6-10 minutes after injection of a gadolinium DTPA (Omniscan, GE Healthcare, Milwaukee, USA), 0.1mmo/kg body weight.

***Data Analysis*:** The MRI images were analyzed by a reviewer blinded to symptomatic status with specialized plaque analysis software, CASCADE [4],.

Step 1: Plaque composition analysis: carotid artery lumen, wall and LRNC were outlined using information from multi-contrast weighting (MCW) MRI (shown in Fig.1).

Step 2: Plaque projection was determined in the cross-sectional direction $\boldsymbol{P_c}$: at each slice *k*, the region between LRNC and lumen is defined as FC and $\boldsymbol{P_{c\text{-}k}}$ ***is*** the ***NFPL***[2] measurement. $\boldsymbol{P_c}$ is the maximum of $\boldsymbol{P_{c\text{-}k}}$ across all slices.

Step 3: Plaque projection was determined in the longitudinal direction $\boldsymbol{P_l}$: this measurement is defined as the largest coverage of LRNC along the longitudinal direction of the artery.

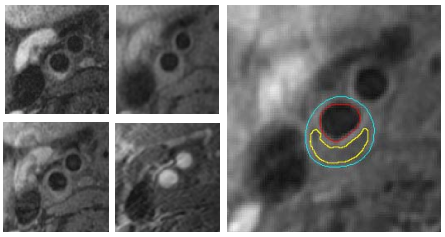

Fig.1 Example of plaque analysis with MCW MRI

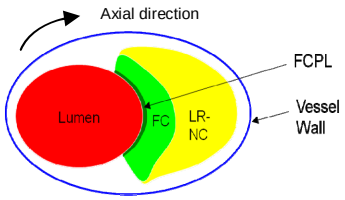

Fig.2 Illustration of Fibrous Cap Projection Length (FCPL) in cross-sectional slice.

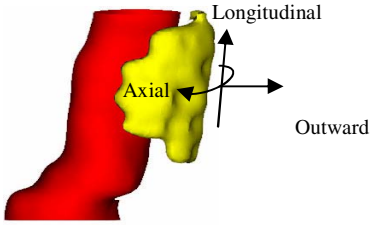

Fig.3 Plaque progression directions.

Evaluation of Plaque Progression and Results

Dr. Takaya's study [5] has shown that increased LRNC size and proximity to the lumen correlates to a higher incident of TIAs or stroke. LRNC size is used as a biomarker to evaluate LRNC contribution to clinical events in most studies. However, LRNC may not progress evenly in all directions. Fig.3 illustrates the possible directions that LRNC may expand. Obviously, when LRNC size increases outward/inward from the outer wall boundary, its coverage to lumen unchanged. Its impact to lumen is usually detected by other traditional measurements, such as minimum distance to lumen. When LRNC progresses along surface parallel to lumen, its direction can be split into the axial and longitudinal directions as illustrated in Fig.3, In such scenario, plaque's coverage to lumen will increase during lesion progression. This change can be measured by projection lengths in both directions. With the same change in LRNC size, will the progressions on different directions have the same degree of contribution to plaque vulnerability or occurrence of clinical events?

To evaluate the impacts to lumen caused by the progressions in each direction, the projection lengths along axial and longitudinal directions were computed for all available subjects and compared with corresponding patient symptom status. Differences between symptomatic and asymptomatic individuals are presented in Table 1. Logistic regression analysis was also conducted and its results demonstrate that Axial Progression ($B = 17.8$; $p = 0.03$) is a better predictor of patient symptom status than longitudinal progression and contributes significantly to the model.

Table 1. Comparison of LRNC progression metrics

	Asymptomatic (N = 12)	**Symptomatic** (N = 11)	***p-value****
Axial	0.38 ± 0.08	0.60 ± 0.05	0.001
Longitudina*,(mm)*	4.33 ± 1.8	5.48 ± 2.4	0.007

* Independent t-test between asymptomatic and symptomatic

Conclusion

This study explores the relationship between the direction of plaque progression and plaque vulnerability. Projection length along the axial and longitudinal directions were analyzed and correlated with subjects' symptom status. The statistical results show that plaque progression in the axial direction is a better predictor for patient's symptom than longitudinal progression. This means that the plaque's morphology change, in addition to plaque size which has been widely used in atherosclerosis research, can potentially be another significant factor to carotid artery disease evaluation and patient's symptom prediction.

Reference:

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2. Xu, et al, ISMRM 2008;5866.
3. Yarnykh et al, MRM 2002, 48:899-905.
4. Xu, et al, ISMRM 2004: 1195.
5. Takaya, et al, Stroke. 2006; 37: 818–823.