Fibrous Cap Projection Length: A Better Biomarker of Plaque Vulnerability Than Lipid Core Size

D. Xu[1], N. Balu[1], H. R. Underhill[1], J. Cai[2], and C. Yuan[1]

[1]University of Washington, Seattle, WA, United States, [2]Chinese PLA General Hospital, Beijing, China, United States

Introduction

Atherosclerotic disease has become one of the leading causes of death and major disability in the United States. In the past years, with the rapid development of using high resolution magnetic resonance imaging (MRI) technology in assessing atherosclerotic components, more and more evidences have shown that plaque composition is the decisive factor determining plaque vulnerability. Cai et al[1] using gadolinium-based contrast enhanced MRI showed that post contrast T1-weighted images can provide accurate quantitative measurements of the intact fibrous cap (FC) in advanced carotid atherosclerotic plaques in vivo. Based on this observation, an automatic FC detection method was developed and validated in our previous research [2]. In this study, we further explore lesion index *Normalized Fibrous cap Projection Length Index* (***NFPLI***). Our preliminary trial result has shown its more predictive power in plaque vulnerability than other plaque measurements.

Methods

Study Protocol: Twenty four subjects scheduled for carotid endarterectomy were selected for CE-MRI in this study. Their symptomatic status was obtained from patients' clinical history and was defined as amaurosis fugax, transient ischemic attacks or overt stroke. Twelve subjects were symptomatic and twelve subjects were asymptomatic. The subjects were scanned in GE 3T Signa MR scanner with a head holder and 4 channel phased array carotid coils. 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 a 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 reviewed by a reviewer with CASCADE [4], blinded from symptomatic status. Vessel and plaque compositions were identified with multi-contrast weighting MRI (shown in Fig.1). In this study, FC is defined as the area between lumen and LR-NC. An automatic FC segmentation method was implemented by using a level set based active contour algorithm[2] to search curves that outline all LR-NC regions. The regions between the found curves and lumen were labeled as FC. The proposed lesion index (NFPLI)*** is defined as the ratio between FC projection length on lumen (*FCPL*) and lumen's circumference (as illustrated in Fig.2).

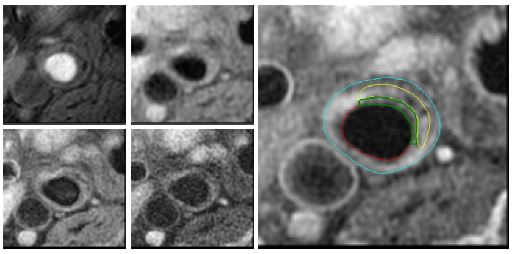

Fig.1 Example of plaque composition analysis.

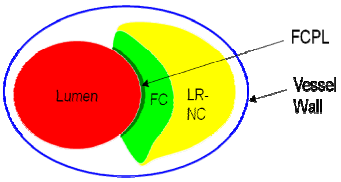

Fig.2 Definition of Fibrous Cap and FCPL

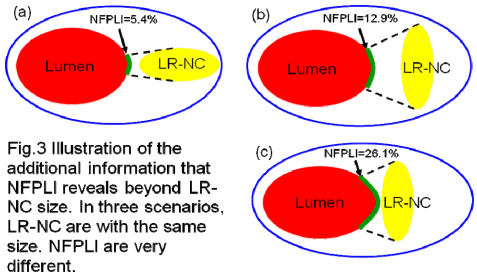

Fig.3 Illustration of the additional information that NFPLI reveals beyond LR-NC size. In three scenarios, LR-NC are with the same size. NFPLI are very different.

Evaluation of Lesion Index

Previous work has shown that increasing size and proximity to the lumen of the LR-NC [5] correlates to a higher incident of TIAs or stroke. In most studies, LN-RC's size is used as the biomarker to evaluate LN-RC's contribution to those clinical events. However, if LR-NC's progression does not change its distance to lumen, then the size increase may be less critical. Fig.3 shows some scenarios in which same LR-NC size has different impacts to lumen. Obviously, the design of *NFPLI* captures the combined contribution from the LR-NC's changes in size and distance to lumen during lesion progression.

In this study, four artery based parameters have been computed across all available subjects: maximum NFPLI, maximum LR-NC size, maximum wall area and minimum lumen area. Their differences between symptomatic and asymptomatic individuals are presented in Table 1. Logistic regression analysis including all metrics demonstrated that NFPLI (B = 17.8; $p = 0.03$) was the best predictor of patient symptom status and that no other variable contributed significantly to the model.

Table 1. Comparison of plaque metrics

	Asymptomatic (N = 12)	**Symptomatic** (N = 11)	***p-value****
Max. Wall Area, mm^2	61.8 ± 4.4	80.7 ± 3.8	0.004
Min. Lumen Area, mm^2	18.8 ± 3.4	20.9 ± 5.0	0.7
Max. NFPLI	0.38 ± 0.08	0.60 ± 0.05	0.001
Max. LRNC Area, mm^2	19.3 ± 2.2	31.5 ± 3.4	0.008

* Independent t-test between asymptomatic and symptomatic

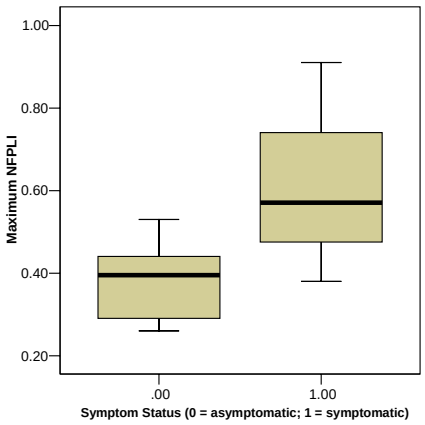

Fig.4 Boxplot of maximum NFPLI between individuals with and without neurological symptoms.

Summary

This study explores a new biomarker of plaque vulnerability - NFPLI. Statistical analysis has shown that it is a more reliable indicator than other plaque measurements that are widely used in atherosclerosis research, such as LR-NC size. This new biomarker can potentially be very significant to carotid artery disease evaluation and patient's symptom prediction.

Reference:

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4. Xu, et al, ISMRM 2004: 1195.
5. Takaya, et al, Stroke. 2006; 37: 818–823.