In vivo MRI-based patient-specific simulation of fatigue process: a possible trigger for carotid atherosclerotic plaque rupture

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Background: Rupture of carotid atherosclerotic plaque with resulting thromboembolism is a predominant cause of ischemic cerebrovascular events. It has been widely hypothesized that plaque rupture occurs when the external loading due to blood pressure and flow exceeds the intrinsic material strength of fibrous cap (FC). However, experimental studies in animals and human subjects have reported pressures needed to produce plaque rupture, being 2-10 times higher than the maximum pressure which clinically results in plaque rupture. It seems that plaque rupture is not well characterized by considerations based on nominal strength or critical stress alone. Plaque is subjected to a repetitive deformation due to heart beat and damage may be accumulated causing FC fatigue. In this study, we explored the fatigue process in human carotid plaques using in vivo magnetic resonance (MR) imaging by assessing the initialization and propagation of fatigue cracks.

Method: Fourteen patients with atherosclerotic carotid artery disease were included in this study. Electrocardiograph-gated, multi-sequence, high-resolution MR imaging was performed to depict the plaque structure. MR slices with presence of FC rupture and ulceration were used for the fatigue study. Finite element simulations were performed using ADINA 8.6.1 to predict the stress condition within the plaque structure. The crack propagation was governed by modified Paris law and the propagation direction was perpendicular to the maximum principle stress at the integration node located at the vulnerable site.

Results: The predicted crack initiations in 14 patients all matched with the locations of the in vivo observed FC rupture and 12 out of 14 (85.7%) patients had the cracks propagate radially and eventually reached the enclosed atherosclerotic component (Fig.1). Further results showed that the crack length increased rapidly with numerical steps and it had an exponential relationship with the natural logarithm of the fatigue cycles. This indicated that once the fatigue crack was initiated, it developed exponentially during further loading cycles. The natural logarithm of fatigue life, which is the total number of loading cycles required for the crack to reach the enclosed component, decreased linearly with thinner local FC (R^2=0.675). Moreover, the Paris relation indicated that increased heart rate, mean blood pressure and pulse pressure would increase the risk of rupture by accelerating the crack propagation.

Conclusion: In contrast to the traditional hypothesis where plaque rupture is modeled as an acute syndrome, fatigue allows ruptures to occur at a seemingly low stress level after quiescent development. The study is helpful in understanding the mechanism of carotid plaque rupture. The results obtained may reiterate the importance of best medical therapy which is already used for patients with atherosclerotic plaque disease, such as the use of anti-hypertensives, cholesterol lowering agents and anticoagulants.

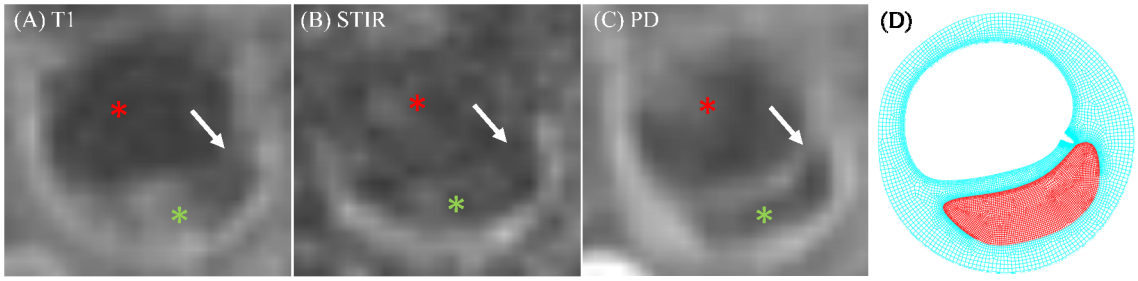

Figure.1 High resolution, multi-sequence MR image and corresponding finite element model. (A-C): MR images showing fibrous cap rupture (marked by white arrow) and ulceration (marked by green asterisk); (D): Simulated crack propagation showing a good accordance with the in vivo observation.

References:

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