ATHEROMA CAP RUPTURE DUE TO MICRO-CALCIFICATIONS

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Introduction

The mechanical stability of an atheroma fibrous cap is a crucial factor for the risk of heart attack or stroke in asymptomatic vulnerable plaques. Common determinants of plaque vulnerability are the core size, cap thickness, and the presence of micro-calcifications (μCalcs). Higher local stresses have been linked to thin caps and thick necrotic cores. More recently, our lab demonstrated how μCalcs can potentially initiate cap rupture [1-3]. When combined, these factors can compromise to a greater extent the stability of the plaque. On this basis, we quantitatively analysed both individual and combined effects of key determinants of plaque rupture using a tissue damage model.

Methods

We performed 10 finite element simulations on three-dimensional multi-layered idealized atherosclerotic geometries presenting 70% stenosis and 1.6 remodelling index. We considered three values for the fibroatheroma (FA) cap thickness (200, 100 and 50μm), three relative core thicknesses in the case of the 100μm cap (25%, 50% and 75%), and two μCalc scenarios (no μCalc and one spherical μCalc, D=18μm). Each artery was expanded by a ramp pressure up to 120mmHg. To replicate the rupture of the fibrous cap, we implemented a custom-made user subroutine coded in FORTRAN based on the hyperelastic failure description proposed by Volokh et al. [4]. We considered a max. principal stress for rupture of 300kPa[5]. The arterial layers were described by the Ogden 3rd order constitutive model (**Table 1**). The lipid core and the μCalc were considered as elastic materials (E_{core} = 5kPa, ν_{core} = 0.49; $E_{\mu Calc}$= 18,000 kPa, $\nu_{\mu Calc}$=0.3).

	μ_1	μ_2	μ_3	α_1	α_2	α_3
Int	0.015	2e-5	0.042	4.9	19.2	-1.9
Med	0.002	1e-5	0.0011	6.3	15.3	0.5
Adv	0.0014	1e-6	0.015	8.5	25	-0.8

Table 1: Layer-specific values for the Ogden 3rd model.

Results

To obtain a detailed analysis of the cap stresses, a sub-modeling approach was implemented using ABAQUS (V. 2019 Simulia, Providence, RI) (**Fig. 1A**). The μCalc was introduced into the center of the cap in the third submodel. The stresses and strains reported for each model represent the average value of 200 nodes selected either along the central cap thickness (no μCalc) or around the μCalc tensile poles. Our results confirm that thinner caps and thicker cores induce higher cap stresses. However, no model without μCalc reached the threshold stress for rupture (**Fig. 1B**). On the other hand, when the μCalc was embedded into the tissue, the models with fibrous cap thickness of 50 and 100μm, and with a relative core thickness of 50 and 75% ruptured acutely. In the models with large cap thickness and small core size, the cap rupture didn't occur, although the stresses around the μCalc were significantly higher than the corresponding models without μCalcs. The stress concentration factor (SCF) - ratio between the maximum stress at the tensile poles of the μCalc and the background stress in the tissue - exhibited a SCF of about 2.2. - 2.5.

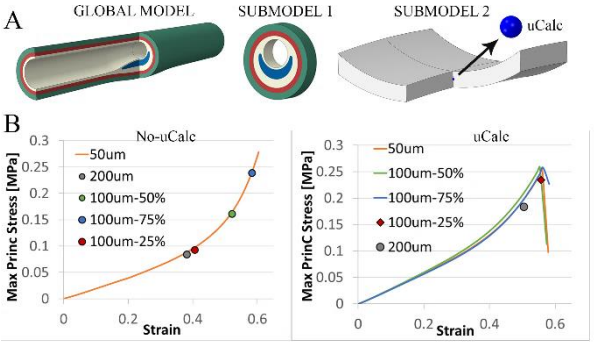

Figure1: (A) Illustration of the sub-modeling approach, from the global model to the portion of the cap. (B) Max Princ. Stress vs Strain for the models without μCalc (left) and with μCalc (right). Cap rupture only occurred when a μCalc was present in a cap ≤ 100μm thick and with a core ≥ 50% thick.

Discussion

Our results clearly show the multifactorial nature of plaque vulnerability and the significance of micro-calcifications on the cap mechanical stability. The presence of a μCalc strongly amplifies the stresses in the surrounding tissue, which when combined with other factors such as the cap and core thicknesses, it can exceed the ultimate strength of the material. The novel implementation of the tissue damage description that we are presenting allows one to quantitatively analyze the individual and combined contribution of key determinants of cap rupture, which precedes the formation of a thrombus, myocardial infarction and sudden death.

References

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