Fluid-structure interactions in stenosed arteries

Lia-Aragnouet Marianne[1], Laperriere Antoine[1], Mescolini Giulia[2]
1) Section of Mechanics; 2) Section of Mathematics

***Abstract*—In this project, we studied the influence of the thickness of the atheromatous plaque's fibrous cap on the vulnerability of the plaque itself, by determining the limit thickness before fracture.**
We performed simulations with the software COMSOL® on a 2D axi-symmetric geometry, using a fine mesh (which passed the verification test of convergence) specially at the interface of interaction between fluid (blood) and structure (fibrous cap of the plaque).
We computed the Von Mises stress for varying thicknesses of the fibrous cap and obtained the attainment of the critical threshold value for rupture (370 kPa) only with thin fibrous cap (0.12 mm) and severe stenosis (83%).
The results have been validated with similar existing test cases in literature, and we obtained results in a comparable range; possible inaccuracies may be due to the fact that we restricted to laminar flows, and that several other factors affect the vulnerability of the plaque and should be considered together, but in any case our study proved that fibrous cap thickness has a non-negligible effect.

Keywords: stenosis, fluid-structure interaction, atheromatous plaque, COMSOL®.

I. Introduction

The mechanical properties of the **atheromatous plaque** in arteries affected by stenosis are a crucial subject of study in Biomechanics. Indeed, they play an important role in the framework of the atherosclerotic disease, which implies the reduction of artery lumen due to the creation of an obstacle in the vessels and can lead to severe consequences on the patient's health.
In particular way, stenosis with a reduction of more than 75% of the artery lumen are regarded as dangerous for health.

Atheromatous plaque is constitued mainly by macrophage cells, or debris, containing lipids, calcium and a variable amount of fibrous connective tissue. Two main parts could be identified:

- a **fibrous cap**: a layer of fibrous connective tissue containing macrophages and smooth muscle cells.
- a **lipid pool**, composed of clear, needle-shaped cholesterol clefts and/or clear, bubbly, granular, mostly anucleate necrotic debris of foam cells.

When plaque ruptures, the exposure to blood of collagen, lipids, and smooth muscle cells leads to the activation of platelets and the coagulation cascade system: so, coagulated blood forms a blockage in the vessel, which can have terrible consequences on the patient's health, including death.
To avoid this phenomenon, the doctors can opt for surgical removal of the plaque, and for taking this decision we should understand in the most complete way what are the main factors affecting plaque vulnerability.
The main criterion up to now is studying the severity of the stenosis (how much the lumen of the artery is restricted), but at the state of the art there is evidence for dependence on **morphology** and **constitution** of the plaque.

A. State of the Art

At the state of the art, several factors influencing the vulnerability of the plaque have been analyzed.
In [1], main reference for this work, it is highlighted how **steepness** of the stenosis or the **presence of bumps** can increase of more than 50% the mechanical stresses (which are used to characterize the fragility).
In another work by the same authors, [2], the effect of plaque consitution in terms of **deformability** has been analyzed. The conclusion is that the effects of pressure and shear loads applied by the blood are amplified if plaques are very deformable.
The paper [3] shows instead a more complex setting in which the subject of the research is how cap thickness and calcium distribution in lipids influence the biomechanical stress on the plaque.

B. Research Question

We chose to deepen into the effect of the **thickness** of the fibrous cap on the plaque deformation and evolution of stenosis.
The above starting point for reflection led to the research question examined in this project: **What is the limit thickness of the plaque's fibrous cap before its rupture?**

II. Methods

We now present the method adopted to answer the research question stated above.
After having chosen a suitable geometry and built a mesh (discussed in subsection II-A and subsection II-E), we defined the physical laws and boundary conditions and then we performed simulations with the software COMSOL®, where we varied plaque thickness in the range [0.02 mm - 0.05 mm] and plotted the **Von-Mises stress** (VM stress) distribution and the **fluid velocity**.
We chose the Von-Mises stress to describe fracture, because in literature this quantity is widely used to determine if a given material will yield or fracture, and in the reference paper we found critical values of this quantity to describe plaque rupture, hence we obtained results in term of this quantity to compare them with the reference value.

We looked for the areas in which they were more critical, and as threshold value for the Von-Mises stress gradient we adopted 370 kPa as done in reference [3].
Basing on this value, we determined the limit thickness for the fibrous plaque before the rupture of the plaque.
We now present more in detail each aspect of the methodology.

A. Geometry

The geometry chosen to model the arterial stenosis is an axisymetric 2D cylinder.
The geometry is composed of three different materials: a healthy arterial wall tissue, a fibrous cap and a lipid core. The arterial wall has an inner radius $R_i = 1$ mm and an outer radius $R_o = 1.3$ mm [1], the cylinder length is $L = 40$ mm and the plaque geometry (fibrous cap and lipid core) is defined by a polygon at 50% of the whole artery length as can be seen in Figure 1. This polygon was generated by random points that represent the overall plaque's geometry seen in the literature [2].

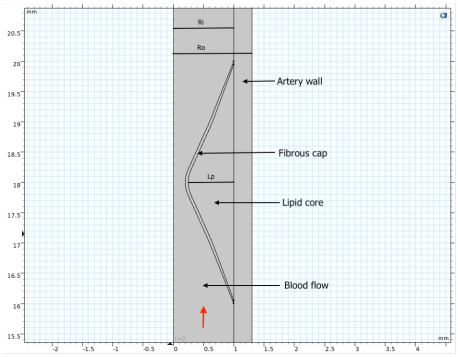

Fig. 1: Plaque's geometry on COMSOL®; Lp is the peak length of the plaque, Ri the inner radius of the artery, Ro the outer radius of the artery; the red arrow shows the direction of the blood flow.

As stated in the introduction, dangerous stenosis have a severity above 75%, hence the stenosis considered in this study will have a severity of 78%.
Therefore, the peak of the plaque will be situated at 78% of the inner artery radius, $\mathrm{L}_p = 0.56$ mm.
Again, the thickness of the fibrous cap will be varied between [0.02 mm - 0.05 mm]. It is important to note that the edges of the plaque were carefully generated in order to be smooth, therefore they will not cause a concentration of stress at that point nor a too complex mesh.

B. Physical Laws

In this section, we present the physical laws regulating the model, which involves fluid-structure interaction.

1) Flow model: the blood flow is modeled as an unsteady pulsatile and laminar flow. The fluid is Newtonian, incompressible and viscous and it follows the Navier-Stokes equations:

$$\begin{cases} \rho\frac{\partial \mathrm{u_{fluid}}}{\partial t} + \rho(\mathrm{u_{fluid}}\cdot\nabla)\mathrm{u_{fluid}} = \nabla\cdot[-p\mathrm{I}+\mathrm{K}]+\mathrm{F} \\ \rho(\nabla\cdot\mathrm{u_{fluid}}) = 0 \\ \mathrm{K} = \mu(\nabla\mathrm{u_{fluid}} + (\nabla\mathrm{u_{fluid}})^T) \end{cases} \tag{1}$$

where:

- ρ is the fluid density;
- $\mathrm{u_{fluid}}$ is the fluid velocity;
- p is the pressure;
- F is the body force;
- μ is fluid coefficient of friction.

The non-stationary system is solved with the initial conditions of [1]:

- $\mathrm{u_{r,0}} = 0$ [m/s];
- $\mathrm{u_{z,0}} = 0$ [m/s];
- $\mathrm{p_0} = 94$ [mmHg].

2) Solid properties: we considered that all components of the model (arterial wall, fibrous cap and lipid core) to be hyperelastic, incompressible and homogeneous (as done in [1] and [4]). For the solid displacements, the following equilibrium equation is solved:

$$\rho_s\frac{\partial^2\mathrm{u_{solid}}}{\partial t^2} = \nabla\cdot(\mathrm{FS})^T + \mathrm{F_v}, \mathrm{F} = I + \nabla\mathrm{u_{solid}} \tag{2}$$

- F is the deformation gradient;
- $\mathrm{F_v}$ is the volume force;
- $\mathrm{u_{solid}}$ is the solid displacement;
- S is the first Piola-Kirchoff tensor;
- ρ_s is the density of the solid.

The first Piola-Kirchoff tensor is given by:

$$\mathrm{S} = \mathrm{S_{inel}} + \frac{\partial W_s}{\partial \epsilon} \tag{3}$$

- $\mathrm{S_{inel}}$ is the first Piola-Kirchoff tensor for the inelastic part;
- W_s is the solid strain energy;
- ϵ is the infinitesimal strain tensor;
- σ is the Cauchy stress tensor:

$$\sigma = \mathrm{J}^{-1}\mathrm{FSF}^T, \quad \mathrm{J} = \det(\mathrm{F})$$

The infinitesimal strain tensor ϵ is defined as:

$$\epsilon = \frac{1}{2}(\mathrm{F}^T\mathrm{F} - \mathrm{I}) \tag{4}$$

We selected the *Mooney-Rivlin* hyperelastic model [4] with five parameters to describe the material properties of the arterial wall.
The corresponding strain energy function W_s is given by:

$$\begin{aligned} W_s =& C_{10}(I_1-3) + C_{01}(I_2-3) + C_{20}(I_1-3)^2 \\ &+ C_{02}(I_2-3^2 + C_{11}(I_1-3)(I_2-3) \end{aligned} \tag{5}$$

where I_1 and I_2 are the first and the second invariants of the right Cauchy–Green deformation tensor.

For the lipid core and fibrous cap, the nonlinear modified *Yeoh* hyperelastic model [4] was selected to describe the material properties:

$$W_s = \mathrm{c}_1(\mathrm{I}_1 - 3)^2 + \mathrm{c}_2(\mathrm{I}_1 - 3)^2 + \mathrm{c}_3(\mathrm{I}_1 - 3)^2 \tag{6}$$

The initial values for solid displacement and velocity are:

- $\mathrm{u}_{\mathrm{solid},R,0} = 0$ [m];
- $\mathrm{u}_{\mathrm{solid},Z,0} = 0$ [m];
- $\mathrm{v}_{\mathrm{solid},R,0} = 0$ [m/s];
- $\mathrm{v}_{\mathrm{solid},Z,0} = 0$ [m/s].

C. Boundary conditions

1) Blood Flow Inlet: at the inlet, the pulsatile blood flow velocity $\mathrm{u}_{\mathrm{fluid}}$ is given by a time-dependent function, with u_0 being the normal inflow velocity and n being the normal vector to the boundary of the solid. T is a parameter describing the period and BF is the pulsatile function (given by [4]):

$$\mathrm{T} = \frac{2\pi}{0.8} \tag{7}$$

$$\begin{aligned} BF(t) = {} & 0.1589 + 0.1007\cos(Tt) + 0.0764\sin(Tt) \\ & - 0.0034\cos(2Tt) - 0.0092\sin(2Tt) \\ & + 0.0294\cos(3Tt) + 0.0337\sin(3Tt) \\ & + 0.0195\cos(4Tt) - 0.0129\sin(4Tt) \end{aligned} \tag{8}$$

Then, it is needed to adapt this pulsatile function to the cardiac flow characteristics. Parameters have been added to ensure that the period is 0.8 s which corresponds to 75 pulsation per minute (average heart rate at rest) and that the velocity at T$= 0$ s is 0 m/s.

$$\mathrm{u}_{\mathrm{fluid}}(t) = -\mathrm{u}_0 \cdot \mathrm{n} \tag{9}$$

$$\mathrm{u}_0 = 500 \cdot \frac{BF(t + 0.4988)}{(60\pi \cdot 0.2^2)} \tag{10}$$

A plot of this function can be found in the Appendix (Figure 5).

2) Blood Flow at outlet: the pressure p, with p_0 the outlet pressure is defined as follows where PR is a pulsatile function (given by [4]):

$$[-pI + K]n = -p_0\mathrm{n} \tag{11}$$

$$\begin{aligned} PR(t) = {} & 84.9722 - 3.3107\cos(Tt) - 2.2932\sin(Tt) \\ & - 9.8639\cos(2Tt) + 8.0487\sin(2Tt) \\ & + 3.0278\cos(3Tt) + 3.8009\sin(3Tt) \\ & + 2.2476\cos(4Tt) - 3.2564\sin(4Tt) \end{aligned} \tag{12}$$

The same time step as for the inlet velocity is applied on the pressure outlet:

$$p_0 = PR(t + 0.4988) \tag{13}$$

A plot of this function can be found in the Appendix (Figure 6).

3) Tissue wall: a no-slip boundary condition is applied on the fibrous cap wall and inner arterial wall, where u_{tr} is the wall translational velocity:

$$\mathrm{u}_{\mathrm{tr}} = \mathrm{u}_{\mathrm{fluid}} \tag{14}$$

4) Constraints: all the outer arterial walls are fixed thus the condition $\mathrm{u}_{\mathrm{solid}} = 0$ is applied on theses surfaces (the displacement is set to zero).

5) Fluid-structure interface: at the blood-tissue wall (artery-fibrous cap) interface, a fully coupled fluid-structure model with a fixed geometry is applied. The force F_A exerted by the fluid on the tissue wall is given by the following equation :

$$F_A = [-pI + K] \cdot \mathrm{n} \tag{15}$$

This load represents a sum of pressure and viscous forces.
The translational wall velocity is determined by the equation:

$$\mathrm{u}_{\mathrm{tr}} = \frac{\partial \mathrm{u}_{\mathrm{solid}}}{\partial t} \tag{16}$$

D. Material properties

The following material properties were set in the COMSOL® simulation (found in [4]):

Material	Model	Material parameters
Blood	Newtonian	$\rho = 1060$ kg/m^3, $\mu = 0.005$ Pa·s
Arterial wall	Mooney-Rivlin	ρ = 900 kg/cm^3 $\mathrm{C}_{10} = -8418$ kPa, $\mathrm{C}_{01} = 9189$ kPa $\mathrm{C}_{20} = 70,101$ kPa, $\mathrm{C}_{11} = -18,538$ kPa $\mathrm{C}_{02} = 12,834$ kPa
Fibrous cap	Yeoh	ρ = 900 kg/cm^3 $\mathrm{c}_1 = 135$ kPa, $\mathrm{c}_2 = -28.4$ kPa, $\mathrm{c}_3 = 4.9$ kPa
Lipid core	Yeoh	ρ = 900 kg/cm^3 $\mathrm{c}_1 = 49.8$ kPa, $\mathrm{c}_2 = -6.19$ kPa, $\mathrm{c}_3 = 0.898$ kPa

Table I: Material properties

E. Numerical Model

The simulations were performed using the software COMSOL®, version 6.0.

1) Mesh: we used an unstructured mesh with 89567 elements. To reduce computing time and improve the precision of the results, we used different mesh sizes upon the components of our geometry. There is a boundary layer inflation at the interface between the blood and the artery wall/fibrous cap. This inflation is composed of 30 layers with a first layer thickness of 100 nm and a stretching factor of 1.2. This finer mesh will model precisely the fluid forces applied on the fibrous cap.
For the fluid domain, fine fluid mesh has been chosen. For the solid part, the lipid core and the artery wall are defined with a fine solid mesh. For the fibrous cap a finer solid mesh was set: it will enable us to model in a better way the stress in this area, which is our point of interest in this study. Referring to COMSOL® quality indicators, the average quality is 0.9144.

2) Element Types: we used rectangular elements on boundary layer inflation, while triangular elements on the rest of the domain.

3) Solver: fully coupled and time dependent as the blood flow is pulsatile.

III. Results

The Von Mises stress and blood flow velocity profile were plotted for a firbous cap of 0.05 mm and an occlusion of 0.15 mm on Figure 2. The VM stress legend is on the right is in Pa and the fluid velocity is on the left in m/s.

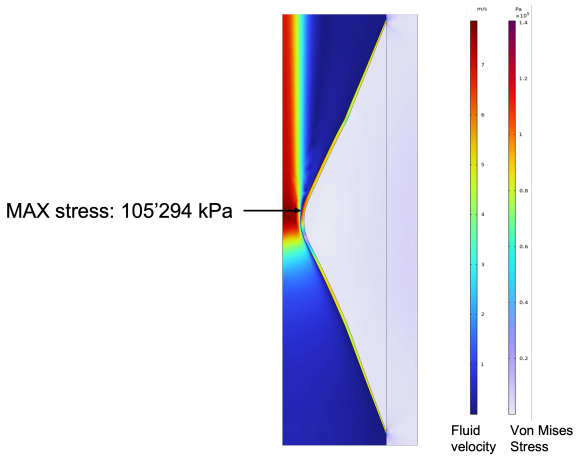

Fig. 2: Simulation with an occlusion of 0.15mm and a fibrous cap thickness of 0.05mm; maximum Von Mises stress location is showed.

We varied the thickness (i.e. [0.01 mm - 0.05 mm]) to see the different Maximal VM stress in the fibrous cap. The values are shown in Table II.

Fibrous cap thickness [mm]	Maximum Von Mises stress [kPa]
0.01	323,312
0.02	159,129
0.03	124,795
0.05	105,294

Table II: Maximum VM stress for different fibrous cap thickness in the range [0.01 mm-0.05mm]

No thickness in the range exceeds the rupture VM stress of 370 kPa. Between 0.05 mm and 0.02 mm the VM stress increases steadily, and at 0.01 mm, the increase is exponential.

IV. Discussion

As seen in the Tab II, even with a thin thickness of 0.01 mm, the stress on the fibrous cap does not reach the rupture value (370 kPa). However, in literature ([1],[4]), it is said that there is a high risk plaque's rupture at $\sigma_{VM} \geq 300$ kPa, especially if triggered by an increase of blood pressure. Therefore we can say that even though it does not reach the value, a fibrous cap at thickness th=0.01 mm is very likely to rupture if subjected to a sudden change in *external stimuli* (i.e. blood pressure). The location of the maximum Von Mises stress corresponds to the highest flow velocity location, therefore the result seems to be realistic.

A. Stenosis severity perentage - Sensitivity analysis

The effect of stenosis severity on the stress state of the fibrous cap was investigated and is shown in Figure 3. The initial value chosen was 78%; in the literature, values for stenosis that have a high risk of rupture range from $75\% - 99\%$ ([5]). Thus, we simulated for each thickness in the range ([0.02 mm - 0.05 mm]), the maximum VM stress values, in order to see the influence of the stenosis severity on the risk of rupture. To do so, we generated the results for 5 stenosis severity percentages $[78\%, 81\%, 83\%, 84\%, 85\%]$, which correspond to a width of the passage of blood of respectively 0.15 mm, 0.13 mm, 0.12 mm, 0.11 mm, 0.10 mm.

This time, the maximum VM stress exceeds 370 kPa (see Figure 3). In addition, the limit thickness this time is 0.02 mm for an blood passage width of 0.12 mm (equivalent to a 83% severity). Hence, the percentage of severity has a non-negligible influence on the VM stress magnitude, thus, on the risk of rupture.

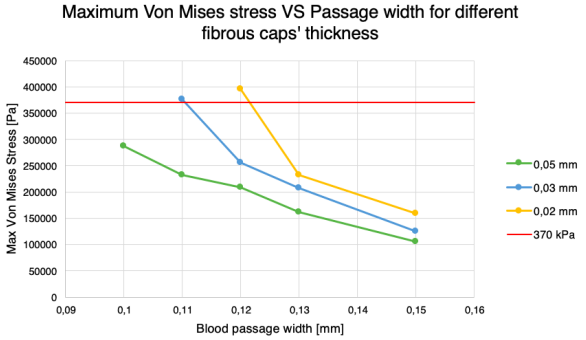

Fig. 3: Maximum Von Mises stress VS Passage width for different fibrous caps' thickness in the range [0.02 mm - 0.05 mm]

B. Influence of shape irregularities

Another important parameter that can affect the VM stress result is the geometry. On Figure 4, the maximum VM stress point location is showed for a 83% severity stenosis with a fibrous cap's thickness of 0.02 mm. In this case, the point is located after the peak of the plaque. We notice that this point corresponds to one of the points that was used to create the polygon (see subsection II-A). Therefore, this point represents a slight irregularity in the geometry, which, at low stress, did not show any influence. However, now that the stress is higher, this points affects the VM stress distribution, creating a stress accumulation but also a considerable deformation of the plaque at this location. *Belzaq et al.*[1] have studied the effect of plaque morphology and shape irregularities on the vulnerability of atheromatous plaques. In their research they have concluded that bumps or increased steepness of the plaque can increase by 50% the mechanical stresses and greatly influence the rupture location.

C. Verification

The objective of this section is to ensure that the problem's resolution is correct. Therefore, we will proceed to a mesh

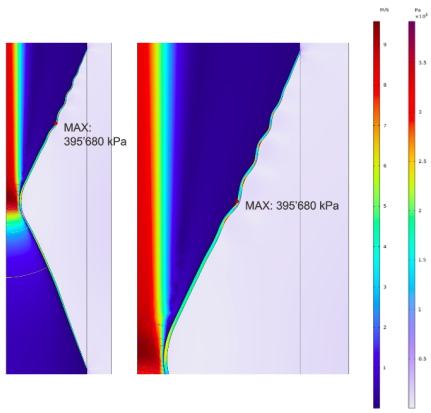

Fig. 4: Velocity and Von-Mises stress profiles at blood passage width of 0.12 mm and fibrous cap's thickness of 0.02 mm; the peak VM value is marked by "MAX"; on the right, there is the VM stress color bar legend in Pa and on the left the Fluid velocity color legend in m/s.

convergence analysis by computing the variables of interest in our project for various numbers of mesh elements. By doing so, we will check the number of elements that are needed for the convergence of the variables with our mesh choice (see subsection II-E). The study is performed on a fully coupled and stationary solver with the blood flow boundary conditions assumed to be constant (pressure at outlet and velocity at inlet), to get sustainable computational time. For the fluid domain, the chosen variables of interest are the blood pressure and the blood flow velocity and for the solid domain we took the maximum value of the VM stress.
For the pressure and the velocity of the fluid, both values have an error with the final stable value smaller than 2% with a number of elements corresponding to a fine mesh (86 902 mesh elements). Concerning the solid domain, the VM stress values converge and have a error $\leq$ 2% for a finer mesh, corresponding to a higher number of mesh elements (124 222 elements). Therefore, we chose a fine mesh for the fluid domain and a finer mesh for the fibrous cap domain. As the artery wall and lipid core are not the point of interest for the stress study, a fine mesh is applied. The model is thus supported by these arguments.
We conclude that the problem has been mathematically solved correctly.

D. Validation

The validation of our model will be done by comparing our results to analogue cases in the existing literature.
The critical thickness value of the fibrous cap for rupture was found at around 0.02/0.03 mm depending on the percentage of stenosis severity (83% and 84% respectively). *Kolodgie et al.* [5] have found that the thickness of the fibrous cap near the rupture site is approximately 0.023$\pm$0.019 mm with 95% of the caps measuring less than 0.065 mm. Therefore, the value found in this project can be validated as it is around the value in literature. However in their research, *Kolodgie et al.* [5] observe rupture at the thickness value mentioned ($<$ 0.065 mm) for lower stenosis severity (around 75%). This can probably be explained by the fact that they observe rupture mainly in patients that have necrotic lipid core, reducing the stiffness of the latter, thus increasing the vulnerability of the plaque. We then could still validate our result.
In the paper of *Wong et al.*[3], they modeled the VM stress distribution for a 90% stenosis with a fibrous cap of 0.05 mm thickness. They found a maximum VM stress at 350 kPa. Our results show that for a 85% stenosis at 0.05 mm fibrous cap, the max VM stress is at 300 kPa. Noticing that for this particular thickness, the stress increases almost linearly, at 90%, the stress will probably match the value of 350 kPa. Hence, our results are in line with the literature[3] stress, validating our answers.

E. Limitations

As we increased the severity of the stenosis, the blood passage width decreased, creating possible turbulence in blood flow. We assumed that the flow was laminar in our system. Therefore, maybe checking the Reynolds number of the flow in the artery would be good to assess if the laminar flow assumption is still valid. A turbulent flow may give rise to higher stresses on the fibrous cap.
Another relevant limitation is the solid material chosen model. Indeed, in our model the Moonley Rivlin hyperelastic model was chosen for the artery wall and the Yeoh hyperelastic model was chosen for the fibrous cap and lipid core. Many other hyperelastic models exist (i.e. Ogden, Neo Hookean, etc.) that could potentially influence the behaviour and vulnerability of the solid. Even within the model chosen, the influence of the model parameters are also to be observed: they were varied in COMSOL®, and showed some influence on the results. For example, in the Yeoh hyperelastic model (cf Table I), an increase in 50% of c_1 for the lip core showed a 20 % increase on the max VM stress in the fibrous cap. Therefore, these parameters need to be carefully selected.
Finally, as said in subsection IV-B, the plaque's geometry is an influential parameter in the model. Shape irregularities should be assessed and studied with particular attention.

V. Conclusion

The influence of the fibrous cap thickness on the maximum Von Mises stress was studied in this project. As the thickness decreased, the maximum Von Mises stress value increased. However, in our initial model, the peak stress value did not reach the rupture stress (370 kPa). By varying the stenosis severity a limit fibrous cap thickness was found for a 83% stenosis at thickness 0.12 mm.
The study of the fibrous cap thickness impact on the vulnerability of the plaque cannot be performed without the study of many other parameters: plaque shape and morphology, stenosis severity, flow type etc. That is why, in future studies, it would be interesting to improve the model by implementing a widely varying set of parameters and

determine their relation and influence on the Von Mises stress.

This study has validated that plaques with thin fibrous caps and a severe stenosis are at high risk of rupture. Fibrous cap thickness could be then considered as a useful indicator for plaque vulnerability and patient degree of risk in atheromatous stenosis disease.

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APPENDIX

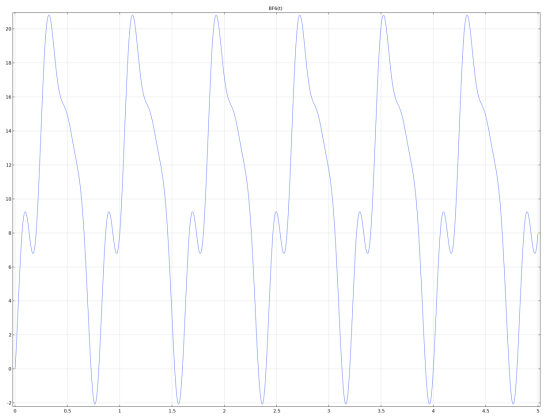

Fig. 5: Plot over time of the BF pulsatile function.

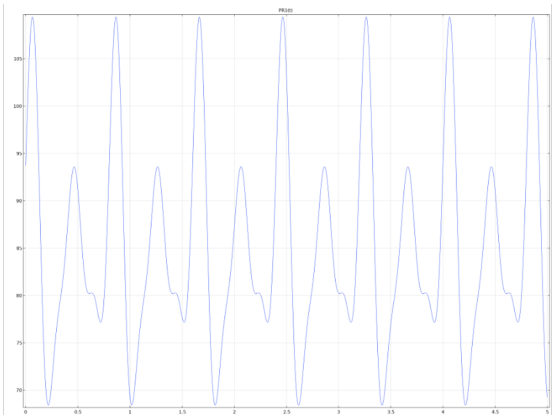

Fig. 6: Plot over time of the PR pulsatile function.