
# BRNO UNIVERSITY OF TECHNOLOGY
VYSOKÉ UČENÍ TECHNICKÉ V BRNĚ

## FACULTY OF MECHANICAL ENGINEERING
FAKULTA STROJNÍHO INŽENÝRSTVÍ

## INSTITUTE OF SOLID MECHANICS, BIOMECHANICS AND MECHATRONICS
ÚSTAV MECHANIKY TĚLES, BIOMECHANIKY A MECHATRONIKY


# STRESS-STRAIN ANALYSIS OF CAROTID ARTERIES WITH ATHEROMA
DEFORMAČNĚ-NAPĚŤOVÁ ANALÝZA KAROTICKÝCH TEPEN S ATEROMEM

**SHORT PH.D. THESIS**
ZKRÁCENÁ VERZE PH.D. THESIS

| | |
|---|---|
| **BRANCH**<br>OBOR | **Inženýrská mechanika** |
| **AUTHOR**<br>AUTOR PRÁCE | **Ing. Ondřej Lisický** |
| **OPONENTS**<br>OPONENTI | |
| **SUPERVISOR**<br>VEDOUCÍ PRÁCE | **prof. Ing. Jiří Burša, Ph.D.** |
| **DATE OF DEFENCE**<br>DATUM OBHAJOBY | |

**BRNO 2022**

## Klíčová slova

Ateroskleróza, karotida, konstitutivní modely, mechanické vlastnosti, výpočetní modelování, zbytková deformace, zbytkové napětí.

## Keywords

Atherosclerosis, carotid artery, constitutive models, mechanical properties, computational modelling, residual deformation, residual stress

## Místo uložení práce

Vysoké učení technické v Brně
Fakulta strojního inženýrství
Ústav mechaniky těles, mechatroniky a biomechaniky
Technická 2896/2
616 69 Brno


ISBN 80-214-
ISSN 1213-4198

# Contents

# 1. Introduction

Contemporary lifestyles with unhealthy eating and predispositions often result in health problems like cardiovascular diseases, leading causes of death in many countries. The global trend seems to decrease, which can be attributed partially to increasing causes of malignant neoplasms (cancer), but more accurate diagnostics may help significantly. For asymptomatic patients, it is under coincidence whether problems are detected. Atherosclerosis affects most of arteries all along the body, e.g., coronary, carotid. Advanced plaques may rupture, resulting in clot formation with serious health problems. Early detection via imaging (computed tomography, magnetic resonance, ultrasound) provides a visual control where a level of stenosis (restriction in a blood flow) can be determined. Stenosis severity is still a primary factor for treatment guidance as it is easy to analyse its level and progression by frequent screening. Subsequently, the patient is advised to undergo carotid endarterectomy or stenting to prevent complete artery blockage or even plaque rupture, which might otherwise lead to fatal consequences. A closer examination of recent clinical trials indicates that current risk prediction is imprecise.

Consequently, patients (often +70 years) are exposed to risk during intervention even though they would not have gone on to have a stroke. Of course, it is unclear what risk would weight more, promoting and active research in this field. In order to enable early prediction of acute events, more accurate screening methods are necessary, introducing a variety of biomarkers. The role of mechanical forces is generally agreed in plaque progression and plaque rupture, although biomechanical stress-based indicators were not confirmed yet clinically to predict possible rupture. Our knowledge is based chiefly on ruptured plaques, which inspire geometry models and factors, but whether these models can help us predict future events is still far from being answered.

Nevertheless, we are still learning about new mechanisms inspiring experimental investigations. Moreover, the progression in imaging methods enables reconstruction of more complex computational models from *in vivo* data where we can benefit from the already gained knowledge, e.g., based on *ex vivo* inspired models. It would be ridiculous to believe that such a complex problem is solvable with a simple model. However, one should believe that every contribution could lead to a better understanding of disease plaguing us for a long time. As accurate predictive methods have not been established yet, the clinician has to decide about the treatment based on information from available technologies. We have to face this challenge and do our best to improve our methods and technologies.

## 1.1. Motivation

The motivation for this study is to thoroughly investigate the up-to-date biomechanical problems related to atherosclerosis of the carotid artery and to contribute as much as possible to the project from Czech Science Foundation no. 18-13663S solved in the Institute of Solid Mechanics, Mechatronics and Biomechanics in cooperation with the St. Ann's Faculty Hospital in Brno. Endarterectomy, an invasive treatment performed daily in this hospital, emerges typically from acute (symptomatic) cases and may also be indicated during preventive imaging, where only stenoses satisfying current criteria are taken into consideration for intervention. Computational modelling may contribute to decision making and bring another insight into the problem. However, modelling is related to many factors such as geometry model or mechanical behaviour and the related constitutive description, which should be considered for an appropriate description of stress-strain states in arteries. Even though this problem is still related to the primary research, the practical impact on clinical practice is not negligible. It may extend the clinicians' expertise in further intervention or pre-operative detection.

## 1.2. Goals of the thesis

1. To perform a thorough literature search on up to date problems solved within the biomechanics of atherosclerotic plaque.
2. To develop a methodology for plaque reconstruction from medical images.
3. To perform a sensitivity study of factors influencing stress in computational modelling of atherosclerotic plaques.
4. Experimental investigation of mechanical behaviour of carotid plaque and wall components and its appropriate constitutive representation.
5. Experimental investigation of layer-specific residual deformation of carotid arteries.

# 2. Atherosclerosis - clinical view

## 2.1. Pathogenesis of atherosclerosis

The name atheroma was firstly used in $18^{th}$ century, describing a thickened area in the vessel wall exuding yellow lipids. Despite the complexity of the plaques in histological sections, most of the lesions contained lipids, primarily cholesterol ester. Goldstein and Brown published multiple studies with a low-density lipoprotein pathway as a possible description of atherogenesis where human cells, including smooth muscle cells (SMC), are protected from the cumulation of sterols (Brown et al., 1976; Brown et al., 1975; Goldstein et al., 1977). Severe lesions may grow under conditions of violation of this regulatory mechanism (e.g., patients with genetic disorders such as diabetes). The response-to-injury hypothesis firstly mentioned by Ross et al. (1976) and then modified in Ross (1986) suggests that the primary event causing the growth of the plaque is endothelium damage. Early and advanced lesions consist of SMCs and macrophages. Macrophages predominate in fatty streaks while proliferated SMCs, macrophages, and leukocytes are present in advanced lesions, indicating possible defensive responses that have progressed to a pathological response. A thorough investigation in Ross (1993) brought more descriptions of early, intermediate and advanced atherosclerotic lesions where a presence of monocyte-derived macrophages, SMCs, and T-lymphocytes (Gown et al., 1986; Libby et al., 1991) was confirmed, pointing out the fundamental role of inflammation in atherogenesis. Cathcart et al. (1985) and later Rosenfeld et al. (1990) showed a primary role of oxygenized low-density-lipoproteins(oxLDL); their formation may cause migration of monocytes and T-lymphocytes into the sub-endothelial space. In Ross (1999) the atherosclerosis was accepted as an inflammatory disease. Moreover, the author suggested that an advance in molecular genetics will help determine the role of various genes with possible success in further prevention or healing. Atherosclerosis does not result simply from the accumulation of lipids. In contrast, other factors need to be taken into account.

## 2.2. Plaque vulnerability

The knowledge of the pathogenesis of atherosclerosis is fundamental for further treatment or prevention. However, this is a problem to be solved mainly by genetic engineers. The process of plaque formation is a long-term problem. Foam cells form at a juvenile age (Napoli et al., 1997) and gradually grow. Until the prevention is available, detection of advanced plaques suspected of health troubles is required. The interest in plaque ruptures ran together with pathogenesis research in the last decades. The first rupture of the plaque as a cause of the death was mentioned in 1844 (Falk, 1992). The rupture itself was then neglected for an extended period until an explosion of research about plaque

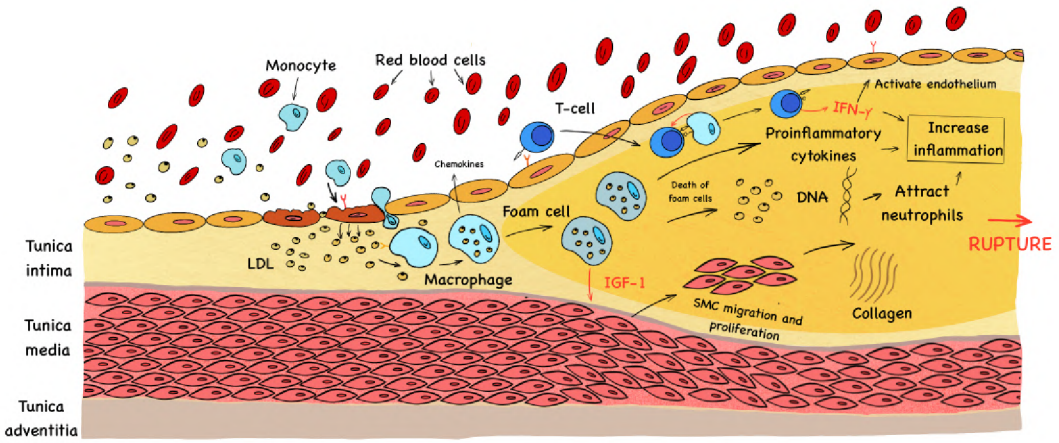


Figure 2.1: Stages in the development of atherosclerosis. Disruption of endothelial cells leads to a lipid migration into the tunica intima layer, starting the inflammatory reaction. Cell migration, proliferation and subsequent apoptosis form a plaque that may advance up to its rupture.

pathogenesis in the 1980s (see Finn et al. (2010)). Researchers found that the instability of plaque often leads to rupture. In the 1990s, the concept of "vulnerable plaque," as an indicator of problematic lesions, started to be used, and it was terminologically unified in 2003 in the guide for clinicians dealing with patients with a higher risk of plaque rupture Schaar et al. (2003). The vulnerable plaque was defined by Grønholdt et al. (1998) as an advanced lesion with a large necrotic/lipid core (LC), thin fibrous cap (FC), and possible thrombosis. A presence of calcification should also be taken into consideration, as it may cause a discontinuity of FC as mentioned in Virmani et al. (2000). Burke et al. (1997) analyzed ruptured coronary plaques and identified the limit FC thickness $<65\ \mu m$ being critical in vulnerable plaques. Cumulation of information about atherosclerosis inspired Libby et al. (2015) to evaluate the concept of vulnerable plaque even though it served for years as a guide for identification and treatment. The post mortem analyses of ruptured plaques supported this paradigm despite the lack of information on non-ruptured plaques, which would suit the vulnerability definition. Monitoring of lesions with *in vivo* imaging methods (e.g., ultrasound Rioufol et al. (2002)) indicated that rupture occurs in lesions, though they should not be labelled as vulnerable. In the PROSPECT study, Stone et al. (2011) used the "virtual histology," which showed that only about five % of thin-capped plaques caused coronary events during 3.4 years. These exciting findings indicate that global interest based on plaque vulnerability could be inadequate. Its further refinement might decrease fatal cases. An extensive review of findings from several clinical studies on detection of high-risk or vulnerable plaques was proposed by Fleg et al. (2012). The study summarized available techniques, findings from patient follow-up studies, and, more importantly, proposed possible future directions. The grand challenge that arose is (i) finding more sensitive and predictive risk factors, (ii) developing new screening tools, (iii) identifying more vulnerable patients for plaque rupture and associated clinical events such as stroke and heart attack, and (iv) recommending a proper treatment plan to prevent a plaque rupture. From this perspective, biomechanics of atherosclerotic plaques may contribute to establishing the association of mechanical risk factors with biological/clinical events. Nevertheless, the level of stenosis is still the primary factor used as guidance for treatment decisions in practice.

# 3. Role of Biomechanics

It is fundamental to identify how the tissue structure behaves *in vivo* in order to prevent serious events. Correspondingly, *in silico* physiology may help by developing computational models that can predict a basic functionality. Computational modelling brings a powerful tool to integrate *ex vivo* (experimentally observed mechanical properties and tissue structure) and *in vivo* characteristics (model geometry, boundary conditions). The iterations between models and experiments provide an opportunity for numerical testing of hypotheses. Validated models have various applications in surgery, diagnostics, or bioengineering showing their importance.

Development in computing allows researchers to simulate complex non-linear boundary values in all engineering aspects in the last decades. It, therefore, enables a simulation of various problems in biomechanics related to hard tissue like bones and teeth and soft tissue like skin, muscle, blood vessel and lungs. All the fields mentioned above bring many possibilities for computational modelling but are rarely investigated by a single researcher. A general overview of biomechanics of soft tissue in the cardiovascular system is well described in the book Holzapfel et al. (2014a) describing the research directions up to the year 2014. A reader can see the complexity of the whole problem. Hence, it is common to follow one direction, as is atherosclerosis in a carotid artery in the case of this study.

From an engineering point of view, a plaque rupture occurs when a mechanical failure occurs, possibly due to stresses exceeding the FC strength. Therefore, one should be looking for maximal stresses within the cap, the so-called peak cap stress (PCS). Ideally, this value would be a simple indicator for plaque vulnerability for subsequent decision-making during a patient screening. Mechanical loading from a blood flow acting on an advanced plaque can be taken into account for vulnerable and stable lesions. Unfortunately, plaque stress cannot be measured directly, and hence another approach is needed. Modelling of underlying physics is one of the available possibilities. First computational studies began to appear in the late 80s and early 90s to investigate atherosclerotic plaque characteristics using 2D structure-only models. Richardson et al. (1989) analysed coronary plaques from 85 patients who died from a coronary thrombosis and investigated the plaques which had fissured. They found a correlation between high circumferential stresses with a site of intimal tears found at necropsy. Plain strain idealized section of the diseased artery was investigated by Loree et al. (1992) by using the finite element (FE) method. Reduced FC thickness increases circumferential stresses within the plaque, thus strengthening the paradigm of vulnerable plaque characterization. The following study Cheng et al. (1993) compared the lesions causing lethal myocardial infarction with the stable lesions. The use of patient-specific (PS) histology-based plane strain models pointed out an essential role of stress concentrations in plaque rupture. These initial studies showed the importance of computational modelling and inspired many researchers.

Artery narrowing affects blood flow and oxygen delivery. Therefore, computational fluid dynamics (CFD) or even fluid-structure interaction (FSI) analyses appear frequently when dealing with atherosclerosis. CFD is mainly used in terms of wall shear stress; their extremes may indicate the sites of artery more prone to plaque developments (Markl et al., 2010; Milner et al., 1998; Prosi et al., 2004; Yang et al., 2007). The use of CFD in advanced plaques is debatable when the lesion is already present and a possible invention is planned. However, it can be helpful in preliminary stages or assessments whether restenosis can occur. In the case of FSI, the benefits of solid and fluid states are exploited together, resulting in a more advanced investigation (Cilla et al., 2015; Tang et al., 2004, 2009; Yuan et al., 2015). However, a recent study Huang et al. (2014) showed that even though the FSI analysis may slightly differ from the solid only, it is very time-consuming and sometimes even not feasible with more sophisticated models as shown by Teng et al. (2015). Therefore, it is reasonable to focus on the FE method in rupture risk assessment when identifying essential factors for plaque rupture. The FE method is mainly used in biomechanics and is available in commercial software like ANSYS, ABAQUS, NASTRAN, EPYLISIS. Its fundamentals are well known, and home-made applications can also be seen, although they may lack validation. Nevertheless, it does not change that this method enables solving very complex three-dimensional non-linear problems in biomechanics.

Most computational studies aimed to investigate the stress distribution within the so-called vulnerable plaques. With information summarized in section Plaque vulnerability, the research should focus not only on those particular lesions but also on less severe cases. If it was possible to establish traceability of the most common principles leading to a higher rupture risk, further implementation into clinical practice would be more beneficial. The biomechanics may contribute to various problems that should be solved to understand the mechanism of plaque rupture. However, it is, unfortunately, impossible to fulfill all problems within this study. Therefore, specific problems defined by the author during a literature review will be further described in separate chapters. All parts such as model creation, acquiring mechanical properties, and residual deformations should contribute to computational modelling, which is of interest to help in research.

# 4. Consideration of stiffness of wall layers is decisive for patient-specific analysis of carotid artery with atheroma

Development in *in vivo* imaging methods enables to use of more accurate PS models based on high-quality medical images. There are several methods available, but their suitability might sometimes be questionable. One of the main disadvantages is a relatively tiny dimension of atherosclerotic tissue, which varies among arteries, e.g., carotid plaque is approximately 30 mm long with a diameter of 10 mm. A model reconstruction from medical images is done by a segmentation process where specific areas (often related to some level of image intensity) are assigned to components (see Figure 4.1).


Figure 4.1: 3D plaque model. Red: lipid core; grey: calcification region. (A) shows a non-smoothed model based on 1.5 mm slice thickness; (B) shows the MRI image of carotid plaque sample recorded ex vivo; (C) shows a smoothed model based on 0.25 mm slice thickness. Picture adapted from Lisickỳ et al. (2019).

Study Lisický et al. (2020) investigated 3D patient-specific FE models of the atherosclerotic carotid artery for two patients accounting for both media and adventitia layers in order to analyse maximal stresses on a plaque. These stresses are believed to be decisive for the plaque vulnerability, but most models from literature suffer from inaccuracy of input data, primarily when obtained *in vivo* only.

One hundred computational models based on *ex vivo* MRI are used to investigate the impact of wall thickness, MRI slice thickness, LC and fibrous tissue stiffness, and media anisotropy (see limit values in Figure 4.2) on the calculated peak plaque and PCS. The investigated factors are taken as continuous in the range based on published experimental results; only the impact of anisotropy is evaluated by comparison with a corresponding isotropic model. The Design of the Experiment concept is applied to assess the statistical significance of these investigated factors representing uncertainties in the model's input data. The results show that consideration of natural properties of the arterial wall in the model is decisive for the stress evaluation; assignment of properties of fibrous tissue even to media and adventitia layers as done in some studies may induce up to eightfold overestimation of peak stress see example in Figure 4.2. The impact of MRI slice thickness may play a key role when thin local FC is present. Anisotropy of the media layer is insignificant, and the stiffness of fibrous tissue and LC may become significant in some combinations.

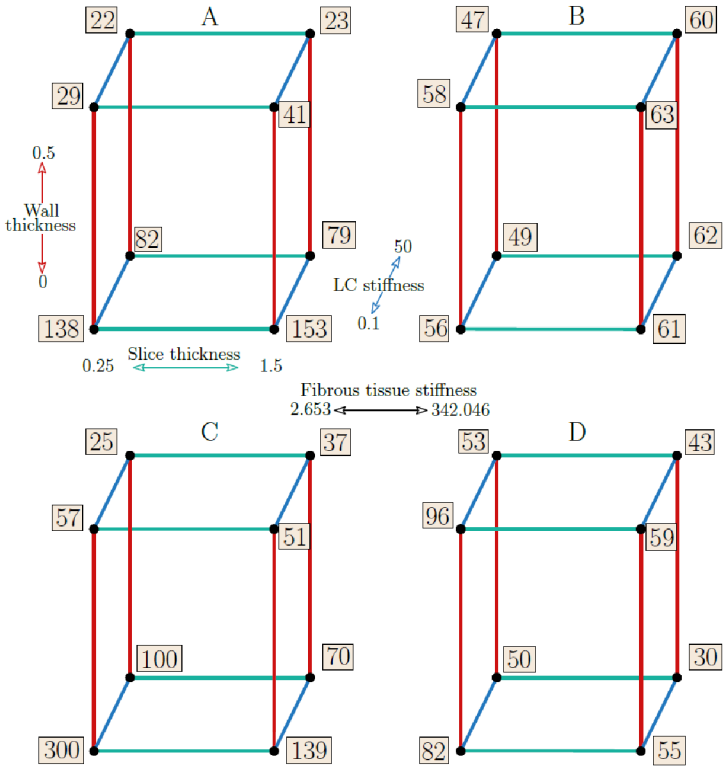


Figure 4.2: Cube plots of peak cap stress values [kPa]. Patient 1 (A-B) and patient 2 (C-D). Colours represent a specific factor; red – wall thickness, green – slice thickness, lipid core stiffness – blue. Cubes A and C represent low stiffness fibrous tissue while B and D high stiffness fibrous tissue.

Even though the presented models did not fully meet the vulnerable plaque definition, it is not clear whether such plaques are the only ones that should be investigated for high stresses by computational modelling in order to examine a mechanism of rupture. It appears that in FE modelling of the stress response in the FC, specifically of the PCS, which is believed to be decisive for plaque vulnerability, the following parameters play a crucial role: (i) stiffness of the fibrous tissue, (ii) stiffness of the LC, (iii) corresponding material properties of the media and adventitia layers of the arterial wall, especially their strain stiffening which is much more pronounced than at the fibrous tissue.

# 5. Constitutive models and failure properties of fibrous tissues of carotid artery atheroma based on their uniaxial testing

Computational modelling was presented to this point as an essential alternative for assessing plaque vulnerability, and approaches to obtain a model geometry were introduced. Knowledge of the underlying mechanical behaviour is therefore essential. The credibility of computational models is contingent on a realistic geometrical model also considering appropriate material models for the atherosclerotic plaque components. They are mostly modelled as isotropic (Akyildiz et al., 2011; Teng et al., 2015); this simplification may be caused by missing direction-dependent experimental results, as well as a lack of structural information on collagen fiber distribution. Comparison of plaque responses in the longitudinal and circumferential directions may help us better describe its behaviour and indicate the necessity of its more complex modelling and testing. Even though we know quite a lot about the mechanical behaviour of a healthy arterial wall (Holzapfel et al., 2014a; Humphrey et al., 2002) which comprises of three more or less homogenous layers (tunica adventitia, tunica media and tunica intima), the atherosclerotic tissue is a heterogeneous structure that influences its mechanical response.

More than 60 patients undergoing carotid endarterectomy provided samples for investigation with written consent during the author's studies. However, only 55 extracted samples were usable for uniaxial tension tests. Samples should be tested as fast as possible under an environment similar to the body. Accidentally, initial samples (n = 11) were collected and transported in the formaldehyde solution. Samples treated like this are fixed with a possible influence on mechanical responses. However, such a comparison was not performed till now; thus, it inspired the study Hrubanová et al. (2020) to take advantage of the mistake. The comparison was made with a comparable cohort of 16 samples; the total number of specimens was 26 in formaldehyde and 44 in a saline solution. Even though the testing of formaldehyde-fixed specimens was done within 24 h after the carotid endarterectomy, significant differences were found between the cohorts: the initial stiffness increases for formaldehyde specimens together with a reduction in variance.

A subsequent study Lisický et al. (2021b) was performed to obtain an experimental background for the description of mechanical properties of fibrous tissues of carotid atheroma. A cohort of 141 specimens harvested from 44 patients during endarterectomies was tested and reserved in saline solution only. Uniaxial stress-strain curves and ultimate stress and strain at rupture were recorded. With this cohort, the impact of the direction of

load, presence of calcifications, specimen location, patient's age, and sex were investigated and evaluated statistically using a linear mixed effect model.

A significant impact of sex was revealed for the stress-strain curves and ultimate strains. The response was significantly stiffer for females than for males, but the strength was not significantly different in contrast to ultimate strain. The differences in strength between calcified and non-calcified atheromas have reached statistical significance in the female group. At most of the analysed stress levels, the loading direction was found significant for the male cohort, which was also confirmed by significant differences in ultimate strains. The representative uniaxial stress-strain curves (given by median values of strains at chosen stress levels) were fitted with an isotropic hyperelastic model for different groups specified by the investigated factors. At the same time, the observed differences between circumferential and longitudinal direction were captured by an anisotropic hyperelastic model (see Figure 5.1).

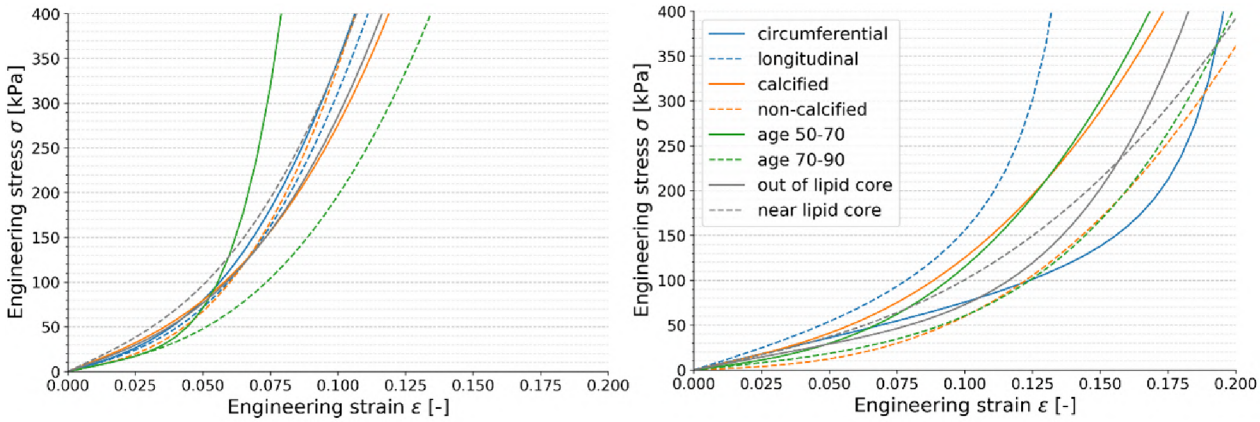


Figure 5.1: Stress-strain responses of the anisotropic model (blue) and isotropic model to medians of strains at each level of stress for all groups of females (left) and males (right). Reprinted from Lisický et al. (2021b).

To the best of the authors' knowledge, this is the first experimental study of the atherosclerotic fibrous tissue comparing ultimate stresses and strains with the non-linear stress-strain response of longitudinal and circumferential specimens. The obtained results should be valid also for the tissue of the FC Teng et al. (2014), the rupture of which is to be predicted in clinics using computational modelling because it may induce arterial thrombosis and consequently a brain stroke. Our results enable us to use these more specific constitutive models and limit values in the prediction of FC rupture with sex as simple *in vivo* predictors. Comparable responses in circumferential and longitudinal directions for females might support the application of isotropic models preferred commonly in computational modelling of atheromas, while the significant differences for males indicate the need for anisotropic modelling, followed by structure analysis.

# 6. Interpretation of experimental data is substantial for constitutive characterization of arterial tissue

Regardless of the chosen experimental approach, the atherosclerotic tissue (the same applies for most soft tissue) often reveals high variation among tested samples/specimens. It is expectable as each person is unique, which applies to the tissue. Nevertheless, it is essential to experimentally investigate the behaviour of multiple samples to reveal some patterns in the behaviour. It is also crucial since the PS data are hard (or even impossible) to obtain, and thus some average response is needed. To specify a population-based model from multiple samples, averaging is often applied to specify a representative material response. However, methods used to analyse experimental data are often inadequate and may thus cause misinterpretation of the essential information. Average-mean together with a standard deviation is often used when describing the experimental data see, e.g., (Lawlor et al., 2011; Maher et al., 2009; Sommer et al., 2012) even though the data distribution was not investigated and showed high asymmetry. Ebenstein et al. (2009) characterised results of their mechanical study by box plots where highly asymmetric distribution is evident; in contradiction to this evident fact, however, they used average-mean value and standard deviation to show population behaviour, no matter that these values implicate negative initial modulus in a significant percentage of cases. Thus, this approach is not suitable for constitutive modelling such non-linear behaviour of materials. Another commonly used approach is to model each response by a constitutive model and to calculate average values of model constants. Here, isotropic (Maher et al., 2009; Schulze-Bauer et al., 2003), as well as anisotropic models (Holzapfel et al., 2005; Polzer et al., 2015; Sommer et al., 2012), were used without any analysis of data distribution and discussion on the appropriateness of this representation.

The study Lisický et al. (2021a) evaluated mechanical tests of soft tissues and the creation of their representative stress-strain responses and respective constitutive models. Interpretation of sets of experimental results depends highly on the approach to the data analysis. In this study, the published experimental data for atherosclerotic plaques (raw data of 7 studies consisting of 11 experimental data sets concerning the carotid wall and atheroma tissues) was digitised and then re-analysed comparing representative average responses. The sets of individual uniaxial stress-stretch curves are evaluated using three different protocols: stress-based, stretch-based, and constant-based and the population-representative response is created by their mean or median values.

The constant-based characterisation appears the least appropriate for population data description. It is due to its high sensitivity to ambiguous constitutive model parameters and the highest differences between the mean and median representations. The impact

of the approach to data processing was low only for nearly linear stress-strain curves, but also here, the mean constant-based characterization differs significantly from all the others, and the differences increase with higher non-linearity of the responses. Moreover, the resulting constants might also be influenced by the model's initial guess (starting points), which was not discussed in the papers the constants were taken. The stretch-based description showed very high skewness and flattened the responses, reducing thus their stiffening or even switching the tendency to softening with increasing stretch. Their mean responses show significant differences against the median characterizations, which preserve a higher strain stiffening typical for the individual responses. The stress-based data characterization includes most individual experimental curves and preserves their pronounced strain stiffening. Also, differences between the mean and median representations are the lowest, with only moderate skewness even negligible in some cases. The

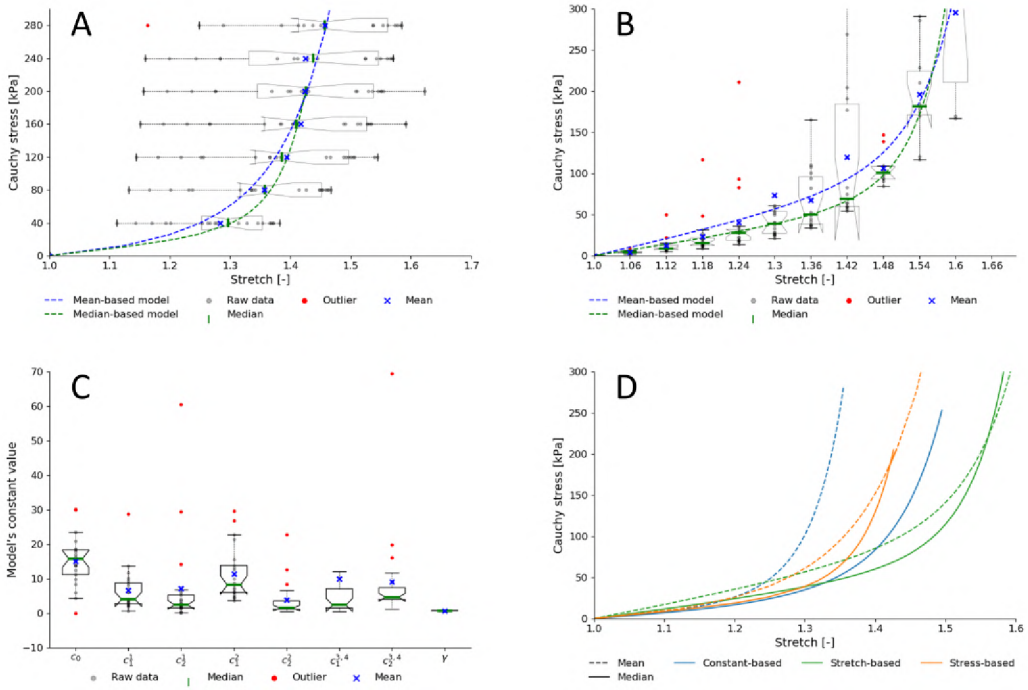


Figure 6.1: Stress-stretch curves based on stress-based analysis (A), stretch-based analysis (B), constant-based analysis (C), and their comparison are represented by box plots completed with mean (blue crosses) values for comparison. Mean and median values fitted with suitable constitutive models are compared in figures (D) for all the three approaches. Discretization of the curves for processing was denser, here only every fourth evaluated point is shown in graphs A and B for illustration. Reprinted from Lisický et al. (2021b).

present analyses show the importance of rigorous processing of experimental data to evaluate a population-representative mechanical response of soft tissue and its constitutive model. Biomechanical data seldom show symmetric Gaussian distribution; consequently, representation of the results through means ± standard deviation may be misleading and differ significantly from the more relevant representation based on the median. The authors recommend the stress-based evaluation represented by median stretch at each stress level as the most rigorous way for evaluating experimental data sets.

# 7. Evaluation of Image Registration for measuring deformation fields in soft tissue mechanics

Most of the experimental studies investigating the mechanical properties of atherosclerotic tissue assume a uniform response for the whole specimen. Therefore, the strains are analysed globally by tracking the displacement of, e.g., two markers resulting in average deformation in between. This approach is straightforward to translate into the stress-strain relationship, which can be approximated by a constitutive model. However, the assumption of homogeneous strain and thus stress fields in the analysed area might not be robust in biomechanics.

Moreover, this average response is then transferred into a computational model. This does not result from computational or theoretical limitations but rather from a lack of experimental quantification of possible local variations. The recent development of CCD cameras leads to their price decrease and thus in more frequent applications. The regional characterisation of strain can be addressed by a full-field method, namely digital image correlation (DIC), which is used frequently in many research fields but also the industry Zhao et al. (2019). Such an approach can be combined with an inverse analysis, possibly leading to more accurate results due to tissue heterogeneity.

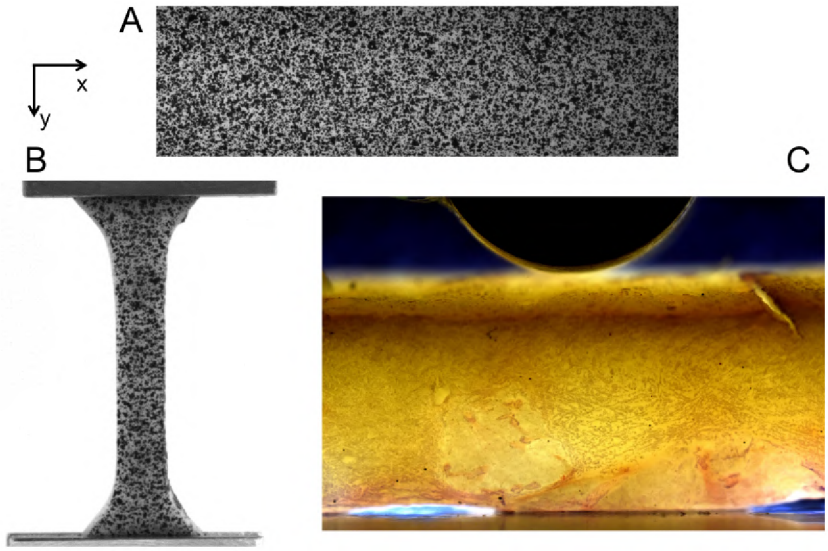


Figure 7.1: Three samples used in the study. A is reused from [39] where artificial heterogeneous displacement field was applied. B is an aorta sample in uniaxial tension and C is a skin sample under indentation test.

An alternative approach to DIC, based on image registration for full-field strain analysis, was evaluated as a part of the thesis, and a manuscript is currently under review in Strain journal. The approach was validated on a set of samples, including (i) complex heterogeneous deformations with sub-pixel displacements, (ii) a typical uniaxial tension test of the aorta, and (iii) indentation test of skin see Figure 7.1.

The results indicated advantages compared to DIC in extending the region of interest to the whole specimen when considering the natural pattern only. The possibility of extending the region of interest to the whole sample and exploiting a natural tissue pattern represents the main assets of the proposed method. In contrast, the results show similar accuracy as standard DIC when analysing sub-pixel deformations. This might be very important for limited specimen sizes from complex atherosclerotic plaques.

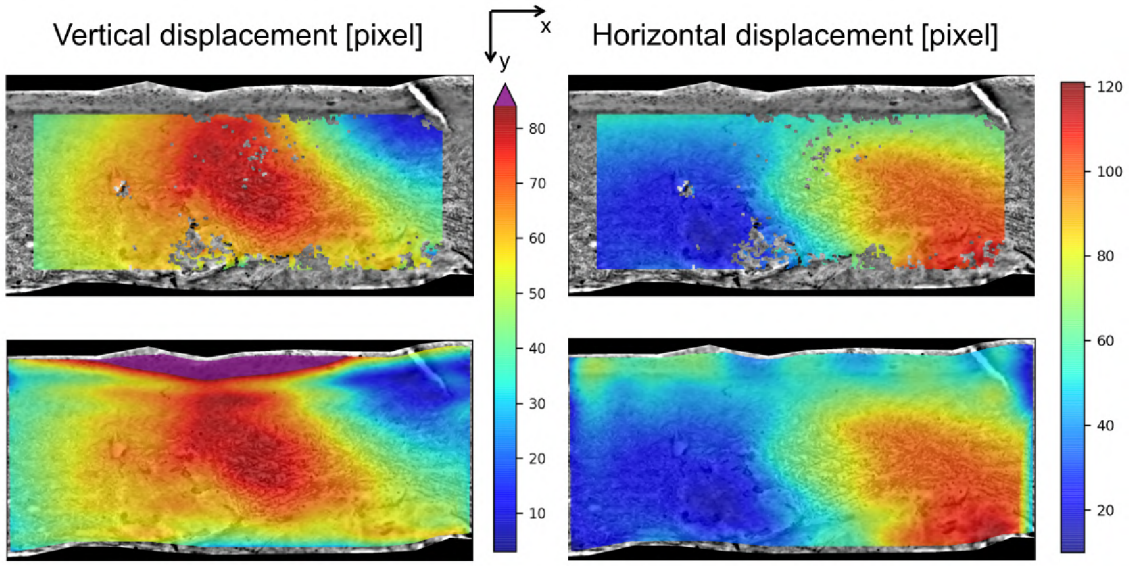


Figure 7.2: Comparison between vertical and horizontal displacement fields. DIC (top row) shows a lot of missing data due to a poor correlation coefficient while it was possible to analyse the whole sample with the IR approach (bottom row). To enable straight comparison, the colour bar scale is fixed based on DIC results. Therefore, the maximal vertical displacements in the left bottom figure are beyond the scale of DIC and depicted uniquely in purple.

Progression of atherosclerosis or formation of an aneurysm increases tissue heterogeneity, which contradicts the assumptions often used in mechanical testing and its subsequent evaluation. Additional information on tissue heterogeneity can help us to improve tissue characterization. This study shows possible advantages of the proposed image registration-based approach for mapping the deformation field in soft tissue mechanical testing. The approach provides an alternative to the well-established DIC, based on the open-source tool Elastix, and increases thus its potential exploitation. The incorporation is planned for a new set of samples in the following project, which is not a part of this thesis.

# 8. Residual deformation and stress

Residual stress (RS) and the related deformation are believed to represent the vital behaviour of arteries in adaptation to pathological changes in the wall structure during senescence. Even though the RS may be small compared to the stress existing in the loaded configuration *in vivo*, their impact on the stress distribution, which is then more uniform, cannot be neglected (Delfino et al., 1997; Holzapfel et al., 2007; Humphrey et al., 2002). The inclusion of the RS into computational modelling is necessary since the input model geometry should be stress-free (Cilla et al., 2012; Holzapfel et al., 2014b). Various studies focused on the simulation of the RS within a specific type of artery, which was modelled using previously published geometrical parameters (Alastrué et al., 2010; Cilla et al., 2012; Liu et al., 2019; Pierce et al., 2015; Raghavan et al., 2004; Schröder et al., 2016). However, the simulation was not always based on the experimental studies related to the simulated artery type. The conventional approach of the *opening angle* is the most general approach when investigating the RS (Chuong et al., 1986; Fung, 1983; Humphrey et al., 2002). The subsequent inverse models (i.e., closing an opened segment into a closed ring) define the RS. Most experimental evidence came from the whole wall without specific layer separation, and the complex multi-layered structure was neglected. Greenwald et al. (1997) investigated differences in the opening angle when the outer and inner ring were separated; this issue was also studied in Holzapfel et al. (2007) where the importance of 3D layer-specific residual deformations was investigated. The deformation of an axial strip should also be included. Sommer et al. (2010) were the first to provide an extensive investigation of the mechanical behaviour of separate carotid wall layers.

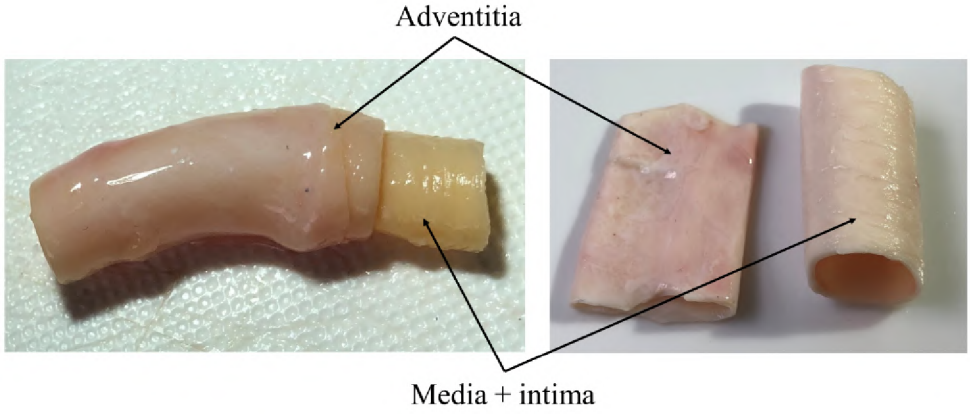


Figure 8.1: Outer layer (*tunica adventitia*) separation from the composite media. Colour differences and the boundary can be observed for all samples. The media holds its shape after the separation while adventitia keeps flat on the air (right figure).

Experimental investigation of layer-specific residual deformation of carotid arteries from a cadaver (provided from the Department of Anatomy of Masaryk University) was performed in the present thesis. The presence of atherosclerotic plaque was rare, and the experiment was thus focussing only on adventitia and media+intima layers. Two different protocols were compared: (i) layer separation after the RS is released following a protocol from Holzapfel et al. (2007) and (ii) in reverse order. The separation (see Figure 8.1) was done under supervision of an experienced surgeon from St. Ann's Hospital in Brno.

Results showed different openings for media and adventitia, where the latter remained almost closed while media opened considerably. Different residual deformation was confirmed for specific layers. High differences were found between two experimental setups with almost four times higher values for media+intima when the layer separation is done before the radial cut of circumferential sample see Figure 8.2. Moreover, the exciting behaviour of adventitia was detected as the circumferential ring was closing rather than opening, as expected from the literature. Similar discrepancies were also found for an axial strip of adventitia which mostly did not show any deformation and remains straight. These findings were attempted to explain by a correlation between opening angle and a ratio of the thickness of media+intima and adventitia. Statistically significant negative correlation (r = -0.72, p = 0.019) indicates that imperfect separation might influence the residual deformation and should be thus well addressed in future studies.

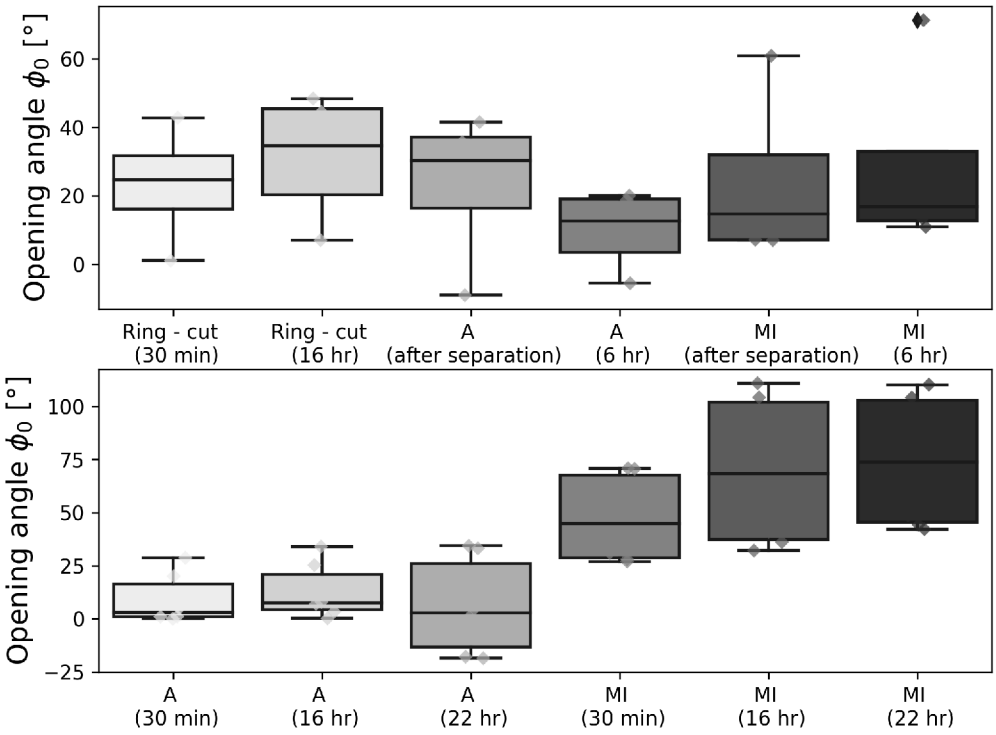


Figure 8.2: Average opening angles of specific segments. Experimental setup 1 - upper figure and experimental setup 2 - lower figure.

# 9. Conclusion

Atherosclerosis is an arterial wall disease in which a lesion forms continuously. The vessel lumen narrows, influencing a proper blood flow and thus the delivery of oxidized blood to essential organs. The lesion can be symptomatic or asymptomatic, which only becomes apparent when a problem occurs; this type is most important in clinics. Depending on the specific artery, the lesion increases the risk of severe health problems like myocardial infarction or stroke. Such events occur when the plaque ruptures, releasing its content into the blood flow and completely blocking the blood supply. These plaques are called unstable or vulnerable and their identification is essential to prevent critical events. Potential indicators of plaque vulnerability have been studied for decades. The idea is to recognize plaques of clinical interest during a control screening. The soft tissue biomechanics is trying to understand the rupture mechanics and to bring a potential tool for an early detection of unstable plaques.

The topic of the present study was very general, aiming at computational modelling of carotid arteries with atherosclerosis. An extensive literature review showed many potential directions for the research though only some were further elaborated in the original research. Even though many original studies were introduced, the main objectives can be separated into two general blocks. The first block of the study focuses on possible ways for geometry reconstruction from *in vivo* and *ex vivo* images using different modalities like computed tomography or magnetic resonance and subsequent use of the created models for plaque vulnerability assessment. The computational study showed potential shortcomings of the current way of modelling, which might be essential when peak stresses are evaluated. More specifically, the inability of a proper plaque component distinction during imaging often leads to unifications in geometry (carotid wall components), which is crucial when the blood pressure acts onto a plaque. This problem increases when additional factors are accounted for, such as considerable variation of mechanical properties. This factor was partially considered in the computational study Lisický et al. (2020) but mainly, it inspired a second block of the present study, which was experimental.

Atherosclerotic plaque samples from endarterectomy were collected during four years of the author's study in cooperation with St. Ann's hospital Brno. This enabled a thorough experimental study of the mechanical properties of plaque components, and thus improving our understanding of the diseased tissue. The included patients almost doubled the current maximum cohort size in the literature for the carotid plaques. Important *in vivo* factors were detected from the measured cohorts enabling a more targeted application in further computational studies. This, in combination with a proper representation of multiple experimental data, can be essential in plaque vulnerability assessment.

Last but not least, autopsy samples of carotid arteries from the Department of Anatomy of Masaryk University, primarily without atherosclerosis, were used to investigate the residual deformation of separated layers of arterial wall. Although the pandemic influenced the sample collection, exciting results showed that our current experimental

knowledge is very limited in this field. The residual stress release, requiring also layer separation, plays a crucial role in the resulting values used as inputs for subsequent computational modelling applications and deserves thus our thorough focus.

## 9.1. Future work

**Influence of calcifications**

Increasing interest in calcifications in computational modelling of atherosclerotic plaque can be seen, e.g., in recent studies Barrett et al. (2019) who summarizes current knowledge on calcifications within the atherosclerotic plaques and their possible impact on plaque's mechanical properties and subsequent applications and in Benitez et al. (2021) who investigated the impact of calcification on a plaque vulnerability in the carotid artery. Calcifications are often modelled as a single value which might be misleading as they are located instead as discontinuous micro-calcifications and should be considered particle composites.

**Residual stress modelling**

Layer-specific residual deformations were confirmed for the carotid artery. The extension to a complete artery with atherosclerotic plaque is of interest because the preliminary results indicated that the layer-specific RS might not be a critical factor. The present experimental investigation might be easy to adapt for the whole plaques from cadavers. Specific computational models could confirm the effect once evidence of the opening angles would be recorded.

**Collagen fibre distribution**

Determination of the collagen fiber distribution within the plaques remains a valid point. Minimal information can be found in the literature. Once this is properly investigated, a question about the necessity of anisotropic constitutive modelling will be closer to being answered.

**Stent deployment simulation**

Some crucial factors for computational modelling were revealed in this thesis. Their importance might be reflected during a simulation of stent deployment. The created complex geometry models can be used for this purpose with mechanical properties measured here.

**Machine learning in biomechanics**

Machine learning attracted attention rapidly in many fields, including very close topics like computer vision. Some discussion can also be found in a recent paper Holzapfel et al. (2021) where deep learning was used to predict a constitutive model of artery based on the sample microstructure. They showed a new potential direction where results of multiple different studies might be combined to increase the model validity. Sample size restricts the use in biomechanics, but some hybrid approaches might be an exciting way to combine computational modelling.

***In vivo* mechanical properties**

As it is possible to obtain a component-specific strain distribution during a cardiac cycle. It would also be interesting to find a connection between this characteristic and a whole non-linear function characterized by a constitutive model. Once this relation is found, a proper constitutive model can be used for computational modelling bringing the patient-specific models closer to their purpose. The identification can be further enhanced with above mentioned machine learning, taking into account also *in vivo* factors discussed in experimental investigations.

# References


Akyildiz, A. C. et al. (2011). "Effects of intima stiffness and plaque morphology on peak cap stress." In: *Biomedical engineering online* 10.1, p. 25.

Alastrué, V. et al. (2010). "Numerical framework for patient-specific computational modelling of vascular tissue." In: *International Journal for Numerical Methods in Biomedical Engineering* 26.1, pp. 35–51.

Barrett, H. E. et al. (2019). "Calcifications in atherosclerotic plaques and impact on plaque biomechanics." In: *Journal of Biomechanics* 87, pp. 1–12. ISSN: 18732380. DOI: 10.1016/j.jbiomech.2019.03.005.

Benitez, J. et al. (2021). "Evaluating the Impact of Calcification on Plaque Vulnerability from the Aspect of Mechanical Interaction Between Blood Flow and Artery Based on MRI." In: *Annals of Biomedical Engineering* 49.4, pp. 1169–1182. ISSN: 15739686. DOI: 10.1007/s10439-020-02655-1.

Brown, M. S. et al. (1976). "Receptor-mediated control of cholesterol metabolism." In: *Science* 191.4223, pp. 150–154.

Brown, M. et al. (1975). "Use of mutant fibroblasts in the analysis of the regulation of cholesterol metabolism in human cells." In: *Journal of cellular physiology* 85.S1, pp. 425–436.

Burke, A. P. et al. (1997). "Coronary risk factors and plaque morphology in men with coronary disease who died suddenly." In: *New England Journal of Medicine* 336.18, pp. 1276–1282.

Cathcart, M. K. et al. (1985). "Monocytes and neutrophils oxidize low density lipoprotein making it cytotoxic." In: *Journal of leukocyte biology* 38.2, pp. 341–350.

Cheng, G. C. et al. (1993). "Distribution of circumferential stress in ruptured and stable atherosclerotic lesions. A structural analysis with histopathological correlation." In: *Circulation* 87.4, pp. 1179–1187.

Chuong, C.-J. et al. (1986). "Residual stress in arteries." In: *Frontiers in biomechanics*. Springer, pp. 117–129.

Cilla, M. et al. (2012). "3D computational parametric analysis of eccentric atheroma plaque: influence of axial and circumferential residual stresses." In: *Biomechanics and modeling in mechanobiology* 11.7, pp. 1001–1013.

Cilla, M. et al. (2015). "A parametric model for analysing atherosclerotic arteries: On the FSI coupling." In: *International Communications in Heat and Mass Transfer* 67, pp. 29–38.

Delfino, A. et al. (1997). "Residual strain effects on the stress field in a thick wall finite element model of the human carotid bifurcation." In: *Journal of biomechanics* 30.8, pp. 777–786.

Ebenstein, D. M. et al. (2009). "Nanomechanical properties of calcification, fibrous tissue, and hematoma from atherosclerotic plaques." In: *Journal of Biomedical Materials Research - Part A* 91.4, pp. 1028–1037. ISSN: 15493296. DOI: 10.1002/jbm.a.32321.

Falk, E. (1992). "Why do plaques rupture?" In: *Circulation* 86.6 Suppl, pp. III30–42.
Finn, A. V. et al. (2010). "Concept of vulnerable/unstable plaque." In: *Arteriosclerosis, thrombosis, and vascular biology* 30.7, pp. 1282–1292.
Fleg, J. L. et al. (2012). "Detection of high-risk atherosclerotic plaque: Report of the NHLBI Working Group on current status and future directions." In: *JACC: Cardiovascular Imaging* 5.9, pp. 941–955. ISSN: 1936878X. DOI: 10.1016/j.jcmg.2012.07.007. arXiv: NIHMS150003.
Fung, Y. (1983). "On the foundations of biomechanics." In:
Goldstein, L. et al. (1977). "The low-density lipoprotein pathway and its relation to atherosclerosis." In: *Annual review of biochemistry* 46.1, pp. 897–930.
Gown, A. M. et al. (1986). "Human atherosclerosis. II. Immunocytochemical analysis of the cellular composition of human atherosclerotic lesions." In: *The American journal of pathology* 125.1, p. 191.
Greenwald, S. et al. (1997). "Experimental investigation of the distribution of residual strains in the artery wall." In:
Grønholdt, M. et al. (1998). "Coronary atherosclerosis: determinants of plaque rupture." In: *European heart journal* 19, pp. C24–9.
Holzapfel, G. A. et al. (2007). "Layer-specific 3D residual deformations of human aortas with non-atherosclerotic intimal thickening." In: *Annals of biomedical engineering* 35.4, pp. 530–545.
Holzapfel, G. A. et al. (2014a). *Biomechanics of soft tissue in cardiovascular systems*. Vol. 441. Springer.
Holzapfel, G. A. et al. (2014b). "Computational approaches for analyzing the mechanics of atherosclerotic plaques: a review." In: *Journal of biomechanics* 47.4, pp. 859–869.
Holzapfel, G. A. et al. (2005). "Determination of layer-specific mechanical properties of human coronary arteries with nonatherosclerotic intimal thickening and related constitutive modeling." In: *J Physiol Heart Circ Physiol* 103.4, pp. 806–808. ISSN: 00221767. DOI: 10.1152/ajpheart.00934.2004..
Holzapfel, G. A. et al. (2021). "Predictive constitutive modelling of arteries by deep learning." In: *Journal of The Royal Society Interface* 18.182, p. 20210411. DOI: 10.1098/rsif.2021.0411.
Hrubanová, A. et al. (Nov. 2020). "IMPACT OF FORMALDEHYDE ON MECHANICAL PROPERTIES OF ATHEROSCLEROTIC CAROTID ARTERIES." In: *ENGINEERING MECHANICS 2020*. Chap. 166394, pp. 210–213. DOI: 10.21495/5896-3-210.
Huang, Y. et al. (2014). "The influence of computational strategy on prediction of mechanical stress in carotid atherosclerotic plaques: comparison of 2D structure-only, 3D structure-only, one-way and fully coupled fluid-structure interaction analyses." In: *Journal of biomechanics* 47.6, pp. 1465–1471.
Humphrey, J. et al. (2002). *Cells, tissues, and organs*.
Lawlor, M. G. et al. (2011). "Experimental determination of circumferential properties of fresh carotid artery plaques." In: *Journal of biomechanics* 44.9, pp. 1709–1715.
Libby, P. et al. (1991). "Involvement of the immune system in human atherogenesis: curent knowledge and unanswered questions." In: *Laboratory investigation* 64.1, pp. 5–15.
Libby, P. et al. (2015). "Requiem for the 'vulnerable plaque'." In: *European heart journal* 36.43, pp. 2984–2987.
Lisický, O. et al. (2021a). "Interpretation of Experimental Data is Substantial for Constitutive Characterization of Arterial Tissue." In: *Journal of Biomechanical Engineering*. ISSN: 0148-0731. DOI: 10.1115/1.4051120.

Lisický, O. et al. (Sept. 2020). "Consideration of stiffness of wall layers is decisive for patient-specific analysis of carotid artery with atheroma." In: *PLOS ONE* 15.9. Ed. by F.-B. Tian, e0239447. ISSN: 1932-6203. DOI: 10.1371/journal.pone.0239447.

Lisický, O. et al. (2021b). "Constitutive models and failure properties of fibrous tissues of carotid artery atheroma based on their uniaxial testing." In: *Journal of Biomechanics* 129, p. 110861. ISSN: 00219290. DOI: 10.1016/j.jbiomech.2021.110861.

Lisickỳ, O. et al. (2019). "Influence of Transversal Resolution on Reconstructing Atherosclerotic Plaque Components." In: *ECCOMAS Thematic Conference on Computational Vision and Medical Image Processing*. Springer, pp. 501–508.

Liu, H. et al. (2019). "Finite element simulation of three dimensional residual stress in the aortic wall using an anisotropic tissue growth model." In: *Journal of the mechanical behavior of biomedical materials* 92, pp. 188–196.

Loree, H. M. et al. (1992). "Effects of fibrous cap thickness on peak circumferential stress in model atherosclerotic vessels." In: *Circulation research* 71.4, pp. 850–858.

Maher, E. et al. (2009). "Tensile and compressive properties of fresh human carotid atherosclerotic plaques." In: *Journal of biomechanics* 42.16, pp. 2760–2767.

Markl, M. et al. (2010). "In vivo wall shear stress distribution in the carotid artery: effect of bifurcation geometry, internal carotid artery stenosis, and recanalization therapy." In: *Circulation: Cardiovascular Imaging* 3.6, pp. 647–655.

Milner, J. S. et al. (1998). "Hemodynamics of human carotid artery bifurcations: computational studies with models reconstructed from magnetic resonance imaging of normal subjects." In: *Journal of vascular surgery* 28.1, pp. 143–156.

Napoli, C. et al. (1997). "Fatty streak formation occurs in human fetal aortas and is greatly enhanced by maternal hypercholesterolemia. Intimal accumulation of low density lipoprotein and its oxidation precede monocyte recruitment into early atherosclerotic lesions." In: *The Journal of clinical investigation* 100.11, pp. 2680–2690.

Pierce, D. M. et al. (2015). "A method for incorporating three-dimensional residual stretches/stresses into patient-specific finite element simulations of arteries." In: *Journal of the mechanical behavior of biomedical materials* 47, pp. 147–164.

Polzer, S. et al. (2015). "Structure-based constitutive model can accurately predict planar biaxial properties of aortic wall tissue." In: *Acta Biomaterialia* 14, pp. 133–145. ISSN: 18787568. DOI: 10.1016/j.actbio.2014.11.043.

Prosi, M. et al. (2004). "Influence of curvature dynamics on pulsatile coronary artery flow in a realistic bifurcation model." In: *Journal of biomechanics* 37.11, pp. 1767–1775.

Raghavan, M. et al. (2004). "Three-dimensional finite element analysis of residual stress in arteries." In: *Annals of Biomedical Engineering* 32.2, pp. 257–263.

Richardson, P. et al. (1989). "Influence of plaque configuration and stress distribution on fissuring of coronary atherosclerotic plaques." In: *Lancet* 334.8669, pp. 941–944.

Rioufol, G. et al. (2002). "Multiple atherosclerotic plaque rupture in acute coronary syndrome: a three-vessel intravascular ultrasound study." In: *Circulation* 106.7, pp. 804–808.

Rosenfeld, M. E. et al. (1990). "Macrophages, endothelial cells, and lipoprotein oxidation in the pathogenesis of atherosclerosis." In: *Toxicologic Pathology* 18.4a, pp. 560–571.

Ross, R. (1986). "The pathogenesis of atherosclerosis—an update." In: *New England Journal of Medicine* 314.8, pp. 488–500.

Ross, R. (1993). "The pathogenesis of atherosclerosis: a perspective for the 1990s." In: *Nature* 362.6423, pp. 801–809.

Ross, R. (1999). "Atherosclerosis—an inflammatory disease." In: *New England journal of medicine* 340.2, pp. 115–126.

Ross, R. et al. (1976). "The pathogenesis of atherosclerosis." In: *New England journal of medicine* 295.7, pp. 369–377.

Schaar, J. A. et al. (2003). "Terminology for high-risk and vulnerable coronary artery plaques." In: *European heart journal* 25.12, pp. 1077–1082.

Schröder, J. et al. (2016). "An engineering tool to estimate eigenstresses in three-dimensional patient-specific arteries." In: *Computer Methods in Applied Mechanics and Engineering* 306, pp. 364–381.

Schulze-Bauer, C. A. et al. (2003). "Passive biaxial mechanical response of aged human iliac arteries." In: *J. Biomech. Eng.* 125.3, pp. 395–406.

Sommer, G. et al. (2010). "Biaxial mechanical properties of intact and layer-dissected human carotid arteries at physiological and supraphysiological loadings." In: *American Journal of Physiology-Heart and Circulatory Physiology* 298.3, H898–H912.

Sommer, G. et al. (2012). "3D constitutive modeling of the biaxial mechanical response of intact and layer-dissected human carotid arteries." In: *Journal of the mechanical behavior of biomedical materials* 5.1, pp. 116–128.

Stone, G. W. et al. (2011). "A prospective natural-history study of coronary atherosclerosis." In: *New England Journal of Medicine* 364.3, pp. 226–235.

Tang, D. et al. (2004). "Effect of a lipid pool on stress/strain distributions in stenotic arteries: 3-D fluid-structure interactions (FSI) models." In: *J. Biomech. Eng.* 126.3, pp. 363–370.

Tang, D. et al. (2009). "Sites of rupture in human atherosclerotic carotid plaques are associated with high structural stresses: an in vivo MRI-based 3D fluid-structure interaction study." In: *Stroke* 40.10, pp. 3258–3263.

Teng, Z. et al. (2014). "Material properties of components in human carotid atherosclerotic plaques: A uniaxial extension study." In: *Acta Biomaterialia* 10.12, pp. 5055–5063. ISSN: 18787568. DOI: 10.1016/j.actbio.2014.09.001.

Teng, Z. et al. (2015). "The influence of constitutive law choice used to characterise atherosclerotic tissue material properties on computing stress values in human carotid plaques." In: *Journal of biomechanics* 48.14, pp. 3912–3921.

Virmani, R. et al. (2000). "Lessons from sudden coronary death: a comprehensive morphological classification scheme for atherosclerotic lesions." In: *Arteriosclerosis, thrombosis, and vascular biology* 20.5, pp. 1262–1275.

Yang, C. et al. (2007). "In vivo/ex vivo MRI-based 3D non-Newtonian FSI models for human atherosclerotic plaques compared with fluid/wall-only models." In: *Computer modeling in engineering & sciences: CMES* 19.3, p. 233.

Yuan, J. et al. (2015). "Influence of material property variability on the mechanical behaviour of carotid atherosclerotic plaques: A 3D fluid-structure interaction analysis." In: *International journal for numerical methods in biomedical engineering* 31.8, e02722.

Zhao, J. et al. (2019). "The state of the art of two-dimensional digital image correlation computational method." In: *Engineering Reports* 1.2, pp. 1–15. ISSN: 2577-8196. DOI: 10.1002/eng2.12038.

# ONDŘEJ LISICKÝ

## PERSONAL INFORMATION


*Born* *Czech Republic*, 5 November 1993

*Email* o.lisicky@seznam.cz

*Phone* (H) +420 605 292 174


## WORK EXPERIENCE

*2020–2021* **Part time**

*CEITEC CTlab*

Automatization of image registration process for dual-target nano-CT data in python.
Reference: Tomáš Zikmund +420 541 142 846 · tomas.zikmund@ceitec.vutbr.cz

*2018–presence* **Research assistant**

*Faculty of mechanical engineering*

Segmentation of medical images and subsequent reconstruction for a purpose of computational modelling. Inclusion of hyperelastic isotropic and anisotropic models into up to date research problems. Performing experimental studies focused on mechanical behaviour of soft tissue. Image analysis using python. Development of 3D printed mold for prostheses preparation. Manuscript preparation in English. Active participation on international conferences.
Reference: Jiří Burša +420 721 613 240 · bursa@fme.vutbr.cz

*2018–presence* **R&D Test engineer - part time**

*Resideo*

Participating on a new device development including test designs suiting device specification. Writing test protocols and presenting results in English. Daily cooperation with product quality engineer and participating on FMEA development. Design of measuring tools with support of Arduino controller.
Reference: Marek Kaňuch · +420 777 328 678 · marek.kanuch@resideo.com

*2015–2018* **R&D Technical support**

*Honeywell*

Technical support for mechanical department within R&D group. Mechanical testing of prototypes together with current products. Operating a 3D scanner COMET L3D (including model evaluation/comparison), uniaxial tension tester, MICRO-VU (optical measuring equipment). Designing testing tools.
Reference: Marek Kaňuch · +420 777 328 678 · marek.kanuch@resideo.com

*2010–2013* **Car mechanic**

*Auto Dědoch*

Part-time job during high school.
Reference: Pavel Dědoch · +420 777 161 515 · info@autodedoch.cz

## EDUCATION

*2018–presence* **Brno University of Technology, Brno**

*Ph.D.*

School: Faculty of mechanical engineering
Thesis: *Stress-strain analysis of diseased arteries*
Description: My thesis deals with modelling of atherosclerosis in a carotid artery and other related problems such as experimental evaluation of deformation field of arterial tissue.

*2016-2018* Brno University of Technology, Brno

*Master degree*

School: Faculty of mechanical engineering
Thesis: *Effect of spine on stresses in abdominal aortic aneurysm*

*2013-2016* Brno University of Technology, Brno

*Bachelor degree*

School: Faculty of mechanical engineering
Thesis: *Stress-strain analysis of the throttle valve components*

## AWARDS

*July 2018* SVS FEM

*Prof. Jaroslav Buchar award*

Award for thesis "Effect of spine on stresses in abdominal aortic aneurysm"

*December 2018* Společnost pro mechaniku

*Prof. Babuška award*

Award for thesis "Effect of spine on stresses in abdominal aortic aneurysm"

## PUBLICATIONS

Lisicky, O. et al. (2021) Constitutive models and failure properties of fibrous tissues of carotid artery atheroma based on their uniaxial testing, Journal of Biomechanics, 10.1016/j.jbiomech.2021.110861

Lisicky, O. et al. (2021) Interpretation of Experimental Data is Substantial for Constitutive Characterization of Arterial Tissue, Journal of Biomechanical Engineering, 10.1115/1.4051120

Lisicky, O. et al. (2020) Consideration of stiffness of wall layers is decisive for patient-specific analysis of carotid artery with atheroma, PLOS ONE, 10.1371/journal.pone.0239447

Lisicky, O., Mala, A., Bursa, J. (2019) Influence of Transversal Resolution on Reconstructing Atherosclerotic Plaque Components. *ECCOMAS Thematic Conference on Computational Vision and Medical Image Processing*. 10.1007/978-3-030-32040-9-51.

## COMPUTER SKILLS

*Basic* UNIX

*Intermediate* Python, MATLAB, Retomo, ANSA, Catia V5, Minitab, GOM Inspect, LaTeX, Microsoft Office

*Advanced* Ansys Workbench, Ansys APDL, ICEM, Creo Parametric

## OTHER INFORMATION

*Instrument operation experience*

3D scanner COMET L3D, MICRO-VU measuring device, biaxial tension testing machine for soft tissues

*Languages*

English · Advanced

German · Basic

*Interests*

Bicycles · Running · Science · Nature · Books · Animals

March 9, 2022

# Abstrakt

Ateroskleróza karotických tepen mnohdy vedoucí k mrtvici je součástí kardiovaskulárních příhod. Včasná a vhodně mířená diagnostika rizikových lézí může vést ke snížení kritických příhod, a tím potenciálně snížit počet úmrtí. Porušení nestabilního aterosklerotického plátu je ovlivněno působením sil od proudící krve. V biomechanice měkkých tkání je využíváno výpočtového modelování jakožto potenciálního ukazatele, díky němuž by bylo možné odhalit nestabilitu plátu u pacientů podstupujících pravidelná kontrolní měření. Komplexita a malé rozměry tkáně ovšem stále omezují možnosti tvorby výpočtových modelů a existuje tedy spousta faktorů, které je před možnou implementací do klinických postupů potřeba řádně vyšetřit. Studium problematiky naznačilo velké množství potenciálních směrů výzkumu, což by ovšem nebylo možné zahrnout do jediné práce. Řešená témata se dají rozdělit na: (i) ověření možnosti tvorby 3D výpočtového modelu ze snímků aterosklerotického plátu s následným rozšířením na výpočtovou studii zahrnující řadu faktorů pro ověření vlivu na napjatost, (ii) studium mechanických vlastností aterosklerotických plátů odebíraných z endarterektomie během celé doby řešení, (iii) možnosti analýzy deformačního pole u experimentů zahrnujících měkké tkáně a (iv) experimentální a výpočtovou studii zbytkové deformace, potažmo napětí v souvislosti s karotickými tepnami. Výsledky jednotlivých částí jednoznačně poukázaly na problémy spojené s výpočtovým modelováním jako například časté opomíjení přítomnosti komponent stěny tepny při modelování aterosklerotického plátu, nutnost správného pochopení mechanického chování, ale také na způsob vyhodnocení experimentů s vyšším počtem vzorků. V neposlední řadě bylo ukázáno, že zbytkové napětí nemusí být podstatným faktorem u aterosklerotických plátů karotických tepen.



# Abstract

Atherosclerosis in carotid arteries can cause a stroke and thus contributes significantly to health risks associated with cardiovascular diseases. Early detection of risky lesions is substantial to prevent an incident. The forces from the blood flow influence a rupture of a vulnerable plaque. The biomechanics of soft tissue is often incorporated with computational modelling as a potential tool to predict the plaque vulnerability for patients who underwent screening. However, the plaque complexity, together with a small size, influences a proper model creation leading to simplifications with an unknown effect on the mechanical characteristics. This is to be solved to incorporate computational modelling as a potential diagnostic tool. Many possible directions were discovered during the literature review, although their inclusion was possible only partly as it would require more than one thesis. The main topics of interest were: (i) creation of 3D models from imaging and their subsequent use in computational study augmented by other factors, (ii) study of mechanical properties of endarterectomy samples during the study period, (iii) study of full-field strain detection methods for soft biological tissue and (iv) experimental and computational study of residual deformations and stresses of carotid arteries. The results of each part indicated problems related to computational modelling of atherosclerotic tissue, like the omission of the arterial wall when the plaque stress-strain analysis is performed, the necessity of a proper understanding of mechanical responses, and its evaluation for more samples. Last but not least a negligible influence of layer-specific residual stresses for carotid plaques.