

## **Brief note**

# **EX VIVO AND IN SILICO STUDY OF HUMAN COMMON CAROTID ARTERIES PRESSURE RESPONSE IN PHYSIOLOGICAL AND INVERTED STATE**

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Arterial walls are a multilayer structures with nonlinear material characteristics. Furthermore, residual stresses exist in unloaded state (zero-pressure condition) and they affect arterial behavior. To investigate these phenomena a number of theoretical and numerical studies were performed, however no experimental validation was proposed and realized yet. We cannot get rid of residual stresses without damaging the arterial segment. In this paper we propose a novel experiment to validate a numerical model of artery with residual stresses. The inspiration for our study originates from experiments made by Dobrin on dogs' arteries (1999). We applied the idea of turning the artery inside out. After such an operation the sequence of layer is reversed and the residual stresses are re-ordered. We performed several pressure-inflation tests on human Common Carotid Arteries (CCA) in normal and inverted configurations. The nonlinear responses of arterial behavior were obtained and compared to the numerical model. Computer simulations were carried out using the commercial software which applied the finite element method (FEM). Then, these results were discussed.

**Key words:** artery mechanics, residual stress, pressure-inflation test, common carotid artery.

## **1. Introduction**

Common carotid arteries consists of three main layers – tunica intima, tunica media and tunica adventitia, separated by elastin membranes – internal elastic lamina and external elastic lamina. The innermost layer - tunica intima, comprises mainly subendothelial connective tissue and lacks essential mechanical properties. Tunica media is mainly composed of elastin fibers scattered among smooth muscle cells and collagen fibers. The outer layer - tunica adventitia, is dominated by collagen fibers secreted by resident fibroblasts (Standring, 2008). Under load free condition the adventitial collagen fibers are arranged in loose and undulating manner (Gasser *et al.*, 2006; Wuyts *et al.*, 1995). Since the vessel wall presents the aforementioned complexity, arteries behave like composite structures with nonlinear stress-strain response (Sommer *et al.*, 2010; Holzapfel and Gasser, 2007). An additional intriguing phenomenon is the presence of residual stresses in the arterial wall. For the load free condition the wall strain and stress are not zero. Separation of the intact wall into adventitia and media-intima layers provides a partial release of the residual stresses. Subsequently, the longitudinal cut of separated layers determines nearly stress-free state and both

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layers of the artery form the shape of a horseshoe. The virtual procedure of removing residual stresses is presented in Fig.1.

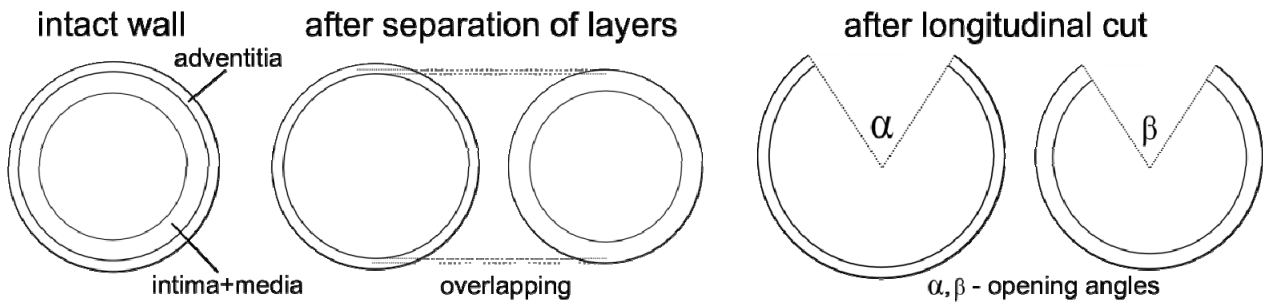


Fig.1. Scheme of removing the residual stresses. From the left: intact artery wall with residual stresses; separated layers – external diameter of media is larger than internal diameter of adventitia; longitudinally cut separated layers form the shape of a horseshoe, corresponding to the stress free state.

Since 1960' till now, studies on the origin and implications of the residual stresses have motivated a substantial body of research (Sommer and Holzapfel, 2012; Bergel, 1960; Chuong and Fung, 1986; Rachev and Greenwald, 2003; Fung, 1991). Choung and Fung in 1986 made a considerable contribution to the aforementioned biomechanical issue and determined the role of residual stresses as a mechanism which uniformes stress distribution among the arterial wall. Previous reports concerned only analytical or numerical analysis whether the residual stresses influence mechanical behavior of the artery. As experimental removal of these stresses without vessel wall damage is physically impossible, we proposed an *ex vivo* experiment accomplished on the inverted arterial segment which makes it possible to validate numerical simulations.

## 2. Materials and methods

Numerical simulation were performed using the commercial software “ANSYS Mechanical” based on the Finite Element Method (FEM). The model definition and simulation procedure were similar to the one reported earlier (Piechna and Cieřlicki, 2013). In brief, the artery was treated as a two layer (media-intima and adventitia), thick, incompressible and elastic cylinder. This assumption is fully legitimate, as the Common Carotid Arteries on the long distance are straight and have no branches. Nonlinear material characteristics of both layers were modeled using isotropic strain energy function of the form

$$\Psi = C_{10}(\bar{I}_1 - 3) + C_{20}(\bar{I}_1 - 3)^2 + C_{30}(\bar{I}_1 - 3)^3, \quad (2.1)$$

with constants

for media	for adventitia
$C_{10} = 1.1788e5,$	$C_{10} = 1.7156e5,$
$C_{20} = -2.8472e5,$	$C_{20} = 1.4746e6,$
$C_{30} = 1.0301e7$	$C_{30} = 3.1155e8$

The computational domain was meshed using hexagonal elements SOLID186 and contact elements CONTA174 and TARGE170. Large deformation effects were compiled. Due to the axial symmetry of the artery model, the numerical mesh was restricted to a quarter of the cylinder. Mesh independence was checked. Finally, layers were meshed using 20 elements/90° in the circumferential direction and 40 elements in the radial direction. The computational procedure was divided into 3 steps. As the initial geometry a free stress configuration was taken. In the first step layers were bent to form two cylinders. In the second step both layers were pulled over and an intact wall with residual stresses configuration was obtained. Finally, in the third step an internal pressure was applied. A similar procedure was repeated to model an inverted artery. The difference was in the direction of bending layers in the first step. In the second step layers were pulled over in such a way that adventitia formed an internal layer and media formed an external layer.

An specially constructed apparatus was used to carry out pressure-inflation tests on arteries. The experimental procedure was similar to the one described by Ciszek *et al.* (2013). Shortly, just after extraction, the tissues were immersed in 0.9% physiological saline solution. An arterial segment of about 5 cm length was prepared. Afterwards, the specimen was mounted and sealed up on the catheter. The second end of the artery was closed by ligating clips. After preconditioning by a cyclic inflating using low pressure the smooth muscle tone was removed. Then, in a quasi-static condition, the artery was loaded by pressure to a value of about 0.5 atm (380 mmHg), which is slightly higher than the physiological value. Pressure values as well as the images of the arterial segments were registered and stored. In the second part of the experiment the arterial segment was carefully inverted, so the layers remained undamaged. Then, the pressure-inflation test was repeated, however this time the pressure value was increased until tightness loss.

Due to specific features of the ex vivo experiment, typical experiment planning could not be applied. Finally, six arterial segments extracted from 4 donors (2 women and 2 men, respectively 33, 51 and 50, 52 years old) were investigated.

### 3. Results

In this investigation we were interested only in arterial strains, as this is the actual measure which may be directly compared with the experimental results. Additionally, there is a number of studies concerning stress distribution in arteries (Rachev, 1997; Waffenschmidt and Menzel, 2014; Delfino *et al.*, 1997). In Fig.2 the pressure-strain relation obtained from the FEM simulation is shown. A dashed red line denotes an artery with residual stresses, whereas a blue solid line without. The inverted artery response is drawn with a black line. It should be added here that the compression of thin adventitia layer caused a numerical instability induced by buckling phenomena. One of the possible situations is displayed in Fig.2. The relevant, initial piece of the strain-pressure dependence is drawn with a dotted line, to mark its approximate character. Until now there was no research relating compression response of the adventitia, therefore the assumed material model should be treated with great caution, as a big simplification.

Images recorded during ex vivo experiments were analyzed using the home made software. The external diameter of the investigated arterial segment was extracted automatically by the modified flood fill algorithm. The radius values are correlated with the pressure values. Figure 3 presents pressure-strain relations obtained for 4 arterial segments. A solid line denotes the artery in normal configuration, a dotted line after inversion.

During the first phase of one experiment (CCA K51 (right)) transmural pressure was increased up to 1000 mmHg and caused minor tissue damage which was presented on images in Fig.3.

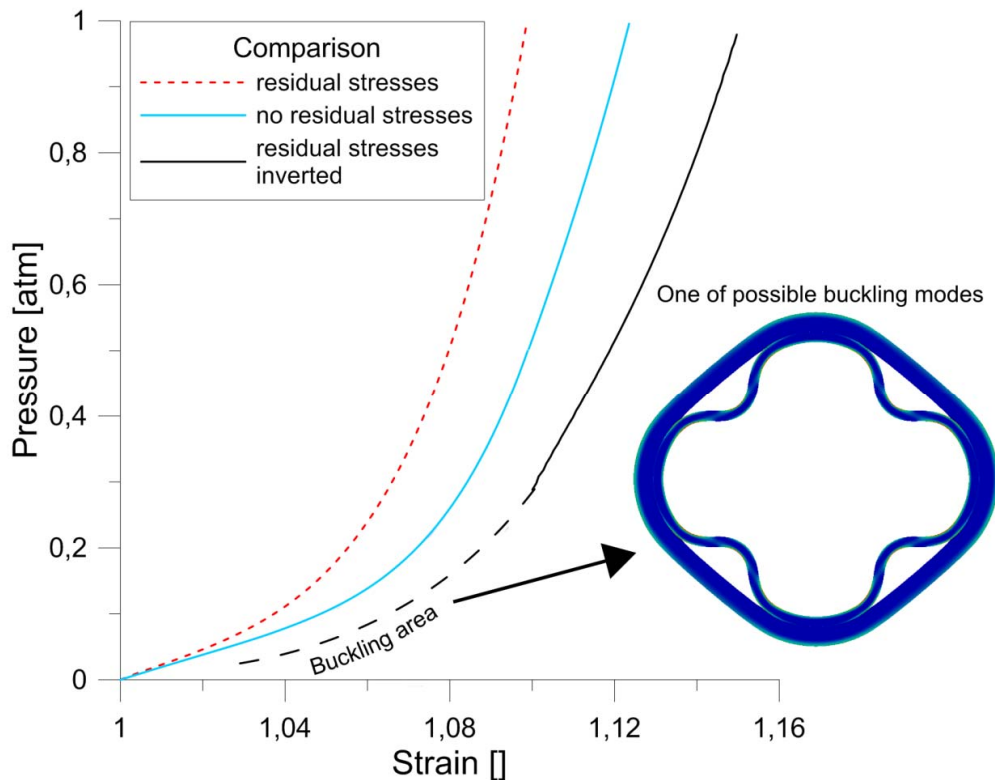
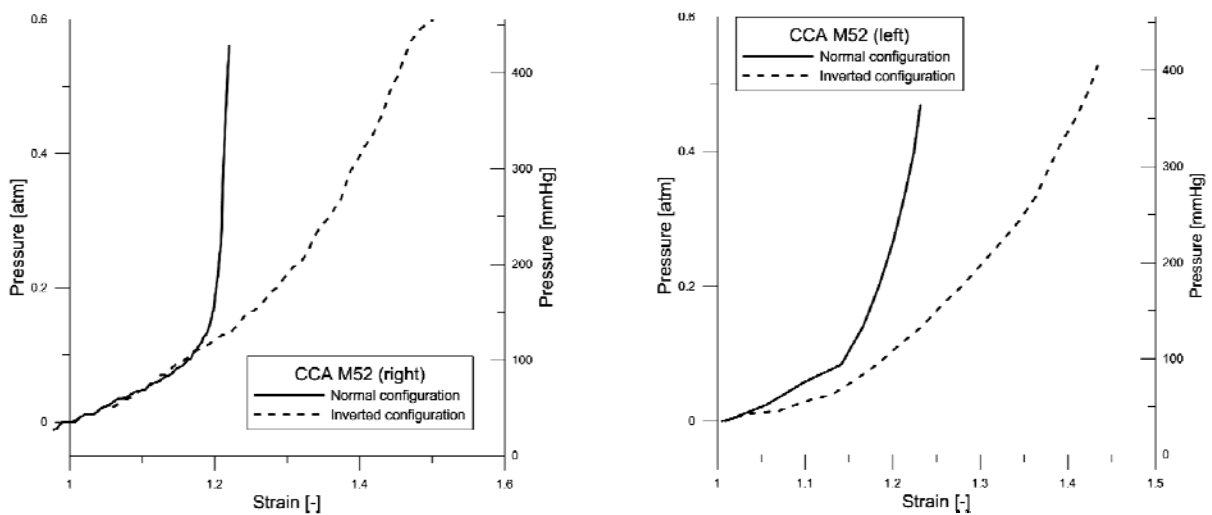


Fig.2. Pressure-strain characteristic obtained from FE simulation. Red dotted line represents artery with residual stress, blue solid line without. Black line denotes artery response after inversion. Black dashed line marks the region where adventitia buckling occurs. On the right one of possible buckling modes is presented.



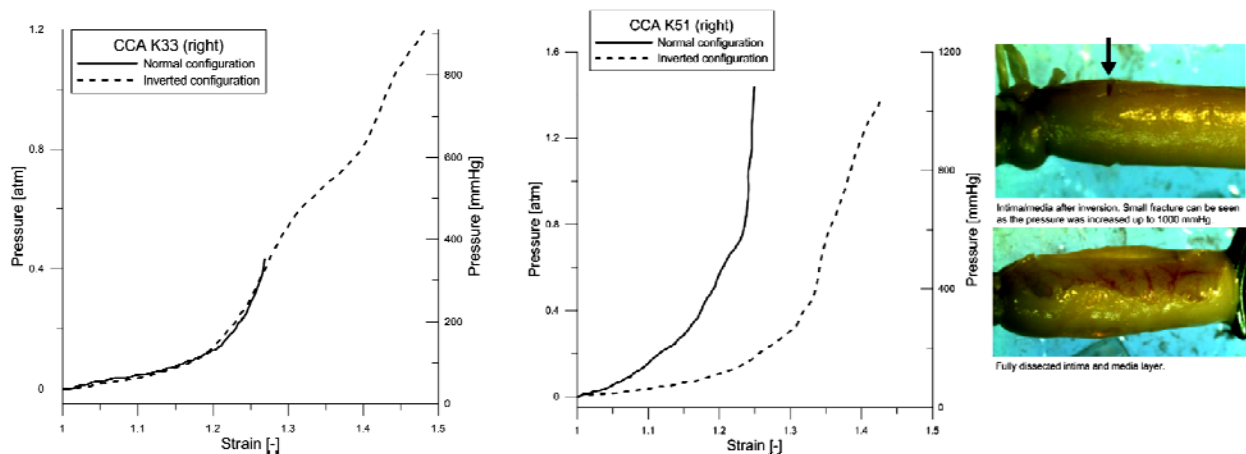


Fig.3. Pressure-strain characteristic obtained from *ex vivo* experiment. Solid line denotes normal configuration, dotted line denotes response after turning the artery inside out. For CCA K51 (right) images of the artery segment are also shown.

#### 4. Discussion

The numerical experiments indicate that the presence of residual stresses shifts the strain-pressure characteristic to the left in relation to the situation without them (blue line in Fig.2). In view of subtraction of the opposite oriented residual stresses and these coming from the pressure load in the media layer, such result seems quite intuitive. Because of residual strains, the artery is stiffer at the zero pressure state. It means that for the same pressure load, its outer diameter will be smaller, although, in the literature we found one contradictory opinion (Rachev and Greenwald, 2003).

In a normal state, overlapping of the layers makes the adventitia stretched. It results in straightening of collagen fibers reducing their waviness. In an inverted arterial configuration, layers interference is greater and has an opposite effect. The adventitia layer becomes compressed so the waviness of collagen fibers (at the zero pressure state) increases. Therefore, the straightening of collagen fibers takes place for higher strains. It explains why the strain-pressure relation is shifted to the right. Inversion has minor effect on residual stresses coming from bending. However, because the openings angles of CCA are lower than  $180^\circ$ , after inversion the bending stresses will be larger.

Three of four of our *ex vivo* experiments qualitatively support numerical prediction of shifting of the pressure-strain relation of the inverted segment to the right. Only in one experiment characteristics in normal and reversed configuration overlap. Possibly, the divergence of both relations would appear for higher strains. A similar slope of pressure-strain relation for low pressures remains in agreement with the assumption that elastin and smooth muscle cells are responsible for the artery behavior within this pressure range. During inversion there are no changes of elastin and muscle cell structure, so the addressed relation for low strains should be similar. It is also in agreement with CCA M52 (right) response, and partially with the CCA M52 (left) one. For the CCA K51 (right) case, the situation is different, because the internal layer was damaged in the first part of the experiment. To confirm that observations, due to differences in the obtained results, more experiments should be made.

#### 5. Conclusions

The main part of the research presented herein was an *ex vivo* experiment performed on the Common Carotid Arteries (CCA). Its purpose was to validate the numerical model of the artery with the residual stresses. Experimental characteristics were obtained and contrasted with numerical ones. To the authors' best

knowledge, an experimental validation of the residually stressed numerical model was presented for the first time. Although validation has a qualitative character it confirms the numerical trends. The research together with the discussion complements the actual state of the art of arterial mechanics. However, due to the specifics of the real tissue experiments (limited availability and species diversity) more experiments should be performed to formulate definite conclusions.

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