Computational model of abdominal aortic aneurysm inception and evolution

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Abstract

Incidence of abdominal aortic aneurysm (AAA) is increasing in the aging society of the western world. Development of AAA is mostly asymptomatic and is characterized by a bulge in the abdominal aorta. However, AAA may suddenly rupture, which results in an internal bleeding associated with a high mortality rate. Patients with AAA undergo regular screening until treatment indication. To date, statistical criteria are used to decide whether the risk of rupture exceeds the risk of intervention. Models of AAA development help to understand the disease progression and to yield patient-specific criterion for AAA rupture.

Up to date, sophisticated models of AAA development exist. These models assume the abdominal aorta as a thin-walled structure, which saves the computational effort. This thesis aims at investigating the importance of employing a thick-walled model of the aorta. The effects on AAA development that cannot be captured with a thin-walled model are of interest. In Paper A, the thick-walled model of growth and remodeling of one layer of a AAA slice has been extended to a two-layered model. The parameter study has been performed to investigate the influence of mechanical properties and growth and remodeling (G&R) parameters of two individual layers on the gross mechanical response and G&R of the artery. It was concluded that the adventitia acts to protect the arterial wall against rupture even in pathological state.

In Paper B, the model was extended to an organ level model of AAA development. Furthermore, the model was incorporated into a so-called Fluid-Solid-Growth (FSG) framework, where the AAA development is loosely coupled to the blood flow conditions such as wall shear stress. One patient-specific geometry of the abdominal aorta is used to illustrate the model capabilities. A transmurally non-uniform distribution of the strains of individual arterial constituents was observed. In addition, an increased aneurysm tortuosity was observed in comparison to a thin-walled approach. These findings signify the importance of a thick-walled approach to model the aneurysm development. Finally, the proposed methodology provides a realistic basis to further explore the growth and remodeling of AAA on a patient-specific basis.
Sammanfattning


List of appended papers

**Paper A:** Influence of differing material properties in media and adventitia on arterial adaptation – application to aneurysm formation and rupture.

H. Schmid, A. Grytsan, E. Poshtan, P.N. Watton and M. Itskov.


**Paper B:** A thick-walled fluid-solid-growth model of abdominal aortic aneurysm evolution: application to a patient-specific geometry.

A. Grytsan, P.N. Watton and G.A. Holzapfel.


In addition to the appended papers, the work has resulted in the following presentations:

A Thick-Walled Fluid-Solid-Growth Model of Abdominal Aortic Aneurysm Evolution.

Andrii Grytsan, Paul N. Watton, Gerhard A. Holzapfel.

Presented at European Solid Mechanics Conference, Graz, Austria, 2012.
Contribution to the papers

The author’s contributions to the appended papers are as follows:

**Paper A:** Designed and performed the numerical study. Interpreted the results together with Holger Schmid.

**Paper B:** Principal author, performed all simulation work, major active part in interpreting the results together with Paul N. Watton and Prof. Gerhard A. Holzapfel.
Contents

Abstract i
Sammanfattning iii
List of appended papers iv
Contribution to the papers v

Introduction 1
  Objective ........................................ 2
  Structure of arterial wall ......................... 2
  Structurally motivated material model .......... 2
  Model of arterial evolution ..................... 3
  Fluid-solid-growth framework ................... 4
  Numerical Results ................................ 4
  Outlook .......................................... 5
  Bibliography .................................... 6

Paper A

Paper B
Introduction

Arteries are blood vessels transporting blood from the heart towards different organs. Most arteries carry the oxygenated blood rich of nutrients. The pulmonary artery instead carries the carbondioxide-rich blood with carbon dioxide towards the lungs. Adaptation of the blood vessel system in response to change in lifestyle is of crucial importance. This aims at organizing the cardio-vascular system, a process that is usually very stable. However, adaptation may not lead to an optimal vessel but rather in developed vascular diseases, like abdominal aortic aneurysms (AAAs), which are among the most occurring and life threatening events in the western world.

Elastin degradation initializes AAA development, but it is not yet clear, how the elastin degradation starts. The AAA is a result of pathological remodeling of the extracellular matrix in the arterial wall. The AAA is a local enlargement of the aorta and is mostly asymptomatic. However, aneurysms may rupture suddenly with an overall mortality rate up to 90% [4]. Incidence of AAA increases with age. The AAA occurs in males about four times more often than in females [3]. Other risk factors for AAA are high cholesterol consumption, tobacco smoking, obesity and hypertension. Genetic disorders such as Marfan syndrome and Ehlers-Danlos syndrome correlate with AAA development. Diabetes is a negative risk factor for AAA [9]. Up to date, there is no effective medication available to prevent AAA growth or rupture. Open surgery or endovascular aneurysm repair (EVAR) are used to repair AAA. These methods are associated with 30-day mortality of 2% (EVAR) and 4% (open surgery). However, the long-term outcome is similar for both techniques [2]. Patients with aneurysms undergo regular screening until treatment indication, i.e. the risk of aneurysm rupture exceeds the risk of intervention. To this end, the maximum AAA diameter or the AAA expansion rate are used as an indication, as it is suggested from statistical data. Naturally, this cannot consider detailed patient specific information. Therefore, it is important to develop diagnostic methods that provide patient specific criteria of the rupture risk.

A realistic model of aneurysm evolution can improve our understanding of the pathology of the disease. The current models of the aneurysm evolution treat the artery as a thin membrane [12], [10]. However, the artery is a thick-walled structure and the effect of heterogeneities of the evolution of material properties throughout the arterial wall requires investigation.
Objective

This study extends a thick-walled model of growth and remodeling of a slice of medial layer of aorta [8] to a two-layered thick-walled model. The influence of different mechanical and adaptation parameters in two layers was investigated. Then, the model was extended to a full-length thick-walled model of aneurysm development and coupled to the blood flow following [11].

Structure of arterial wall

The artery wall is composed of three distinct layers, namely the intima, the media and the adventitia, see Fig. 1. The intima consists of a monolayer of vascular endothelial cells lining the luminal surface, a thin basal membrane and a subendothelial layer. It is often assumed that the intima does not contribute significantly to the load carrying capacity of the wall. However, sometimes normal and often pathological subendothelial layer has significant thickness and stiffness. The media is the middle arterial layer consisting of vascular smooth muscle cells (SMCs) interwoven with elastin and bundles of collagen fibers and form a complex three-dimensional structure. The media is separated from the intima and the adventitia by the internal and external elastic laminae, respectively. The adventitia is the outermost arterial layer that consists of mainly fibroblasts, histological ground substance and thick bundles of collagen fibers. The adventitia is surrounded by loose connective tissue and its outer boundary is not clearly defined.

The collagen fibers are very stiff and strong, serving as fiber reinforcements of the tissue. Fibers are wrapped around the lumen in double helical pitches. Fiber orientations are distributed around a mean direction. Individual fiber orientations deviate substantially from the mean. Mean direction of fiber orientation depends on the arterial layer and the location of the artery within the vascular system.

The artery in vivo is subjected to physiological loads, such as internal pressure and axial pre-stretch. Furthermore, the arterial tissue is a subject to 3-D residual stresses, which are thought to be caused by the arterial growth and adaptation [5].

Structurally motivated material model

For many applications the artery may be modeled as a thick-walled structure of two layers, the media-intima composite and the adventitia. The arterial tissue is often modeled as a nearly incompressible material. This is motivated by high amount of water in the tissue and low permeability of the arterial wall [6]. Roach and Burton [7] have shown that collagen-digested arterial tissue has isotropic mechanical properties, while elastin-digested tissue behaves anisotropically. Hence, the passive mechanical response of SMCs, elastin and ground substance is modeled with a simple neo-Hookean law [13]. The collagen fibers are then modeled with an exponential law based on the fiber stretch. The SMC-based active response is omitted in this work for simplicity.
Computational model of abdominal aortic aneurysm evolution

Figure 1: Idealization of arterial wall structure [1]. It consists of three layers: intima (I), media (M) and adventitia (A).

In the stress-free state of the vascular tissue, the collagen fibers are wavy and begin to carry load when the tissue is stretched by some amount. Consequently, the collagen fibers have a different reference (stress-free) configuration which can be modeled explicitly by a structural property called recruitment stretch. Hence, if the tissue stretch in the direction of the fiber is less or equal to the collagen recruitment stretch, its stress contribution is neglected. When the tissue stretch exceeds the recruitment stretch, ratio of the tissue stretch to the recruitment stretch defines the stretch of the collagen fiber.

Model of arterial adaptation

The collagen in the vessel wall is constantly degraded and synthesized by fibroblasts and other vascular cells. The collagen degradation and synthesis are balanced with a half-life time of human vascular collagen of about 60 days. Newly formed collagen fibers have to be deposited pre-stretched in order to maintain homeostasis. This amount of stretch is often called the deposition or the attachment stretch [11],[14].

Through the AAA evolution, the tissue constituents change their mass and/or volume. The normalized mass changes of the constituents are introduced to the material law to model the changes in tissue constitution. Collagen growth and remodeling is modeled by differential equation describing the evolution of the normalized mass change and the recruitment stretch of the collagen. These equations aim to minimize the difference between the actual collagen fiber stretch and the
collagen attachment stretch.

Elastin degradation is often prescribed by an exponential decay [12]. However, there is also evidence that the elastin degradation is linked to the blood flow and this thesis links it specifically to the wall shear stress (WSS) levels. Elastin normalized mass change is used to model the elastin degradation.

**Fluid-Solid-Growth framework**

It is assumed that the changes of the arterial tissue constitution is coupled with the blood flow. Due to clearly different time scales of the tissue remodeling (weeks) and the cardiac cycle (seconds), the two problems are loosely coupled, see Fig. 2. Firstly, the momentum equations are solved for the solid part of the aneurysm. Then, the blood flow is computed by solving the Navier-Stokes equations within the updated aortic lumen. More, up and downstream extensions are attached to obtain a fully developed flow in the aneurysm region. Next, the aneurysm growth and remodeling routines take in the information on the fluid and solid mechanical environment of the vascular cells and adapt the material properties accordingly. The new loop starts as the momentum equations are solved for the updated set of the material parameters.

**Numerical Results**

The patient-specific geometry of the abdominal aorta with the developed aneurysm has been obtained from computer tomography (CT) scans. The aneurysm region has been cut out and replaced by a conceptual model of a hypothetical normal aorta. A small initial bulging was generated by a local elastin degradation in order
to create the initial disturbance in blood flow, and hence in WSS. The evolution of the aneurysm is shown in Fig. 3. It can be seen that the aneurysm propagates upstream and the aneurysm evolution is asymmetric.

![Figure 3: The WSS distribution in the aneurysm domain and patient-specific up and downstream extensions is shown: before FSG (left), after 5 yrs of FSG (center), after 10 yrs of FSG (right).](image)

**Conclusions**

The novel thick-walled fluid-solid-growth model of aneurysm evolution has been developed. The model salient features of vascular wall adaptation. The results of the patient-specific application of the framework are able to predict typical AAA features observed in clinics, such as aneurysm propagation in the upstream direction and the asymmetry in aneurysm evolution. However, the framework is a subject to limitations. The conceptual geometrical model of a healthy abdominal aorta has been utilized as opposed to a patient-specific geometry of aorta with an aneurysm. There are restrictions on the boundary conditions: the contact with the spine has not been considered and the ends of the aorta have been fixed.

Naturally, also the constitutive model for the vascular wall has many limitations. For example, the remodeling of SMC-based active response and the volumetric growth have not been considered. Some of these limitations will be addressed in future work.
Bibliography


