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PhD Thesis Review

Title: The noninvasive technique of determining local stiffness of human arteries

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1. Aim and Scope of the PhD Thesis

The PhD Thesis consists of eight chapters. Has 114 pages. The major objective of this PhD Thesis is to develop a noninvasive method for estimating the Young's modulus of the left common carotid artery (LCCA) using ultrasound measurements of arterial wall displacement and applanation tonometry for intra-arterial pressure measurement. The experimental setup, data analysis, and computations were conducted using the "ENTHRAL Non-invasive In Vivo Assessment of Stiffness of Human Artery Walls" system. This research was supported by funding from Norway Grants: UMO-2019/34/H/ST8/00624. The research was conducted within the cooperation between Silesian University of Technology and Norwegian University of Science and Technology.

To achieve the thesis objective, a testing rig was constructed, comprising an artery phantom, a pulsatile pump, and measurement devices to collect data on flow, pressure, and phantom wall displacement. A numerical model of the experiment was developed and validated comparing to the experimental data. This model was then applied to solve the inverse problem—estimating the stiffness, defined as the Young's modulus, of the material used as a substrate for the real artery. The selection of constitutive law was limited by the number of parameters to be estimated, leading to the consideration of only two models: linear elastic and Neo-Hookean. The model is solved using an open source software FEBio. Based on data from the experimental setup, the best-performing model was selected and paired with an extended Kalman filter to solve the inverse problem. This approach, along with the chosen constitutive law, was subsequently applied to patient data, what is very important for practical applications.

2. Content of the PhD Thesis

The thesis is organized into eight chapters.

Chapter 1 provides a literature review of existing techniques for noninvasive estimation methods and explores solutions to the inverse problem. The PhD candidate conducted a comprehensive review, identifying 18 papers relevant to the application of Kalman filters in artery research, sourced from ScienceDirect, Web of Science, and Scopus databases. The literature survey is thorough; however, it lacks a summary statement clarifying the novelty of this PhD thesis relative to the referenced papers. I recommend adding this novelty summary on page 17 of the monograph.

Chapter 2 introduces key concepts in continuum mechanics essential for understanding the formulation of constitutive models for linear elastic and hyperelastic materials. It also covers inverse problems, common techniques for solving them, and Kalman filtering algorithms. The chapter details the theory behind Linear and Extended Kalman Filters for state estimation, as well as parameter estimation techniques, including the Extended Kalman Filter and Simultaneous State and Parameter Estimation (Dual Extended Kalman Filter). However, in my opinion, this section would benefit from a summary of the advantages and limitations of the presented filtering algorithms.

Chapter 3 describes the experimental setup designed to collect data for developing and testing noninvasive assessment methods for the common carotid artery. It includes a detailed explanation of the measurement system, camera-based image processing, ultrasound image processing, and medical data sampling. While comprehensive, this chapter lacks information on the accuracy of the measurements (e.g., flow, pressure, and camera image processing), which I consider as important for the further validation of numerical algorithms.

Chapter 4 presents a mesh independency analysis comparing static and dynamic Finite Element Analysis (FEA). Two meshes, with 1,440 nodes and 3,696 nodes, were evaluated, showing only slight differences in displacement outcomes. The chapter details the geometry, mechanical properties, and the algorithm used for data processing. Differences between static and dynamic FEA for linear elastic and Neo-Hookean models were low. However, further discussion is needed on the rationale for selecting only two meshes for validation and the reasons behind the small differences between static and dynamic FEA results.

Chapter 5 focuses on model validation, comparing simulation results for linear elastic and Neo-Hookean materials against experimental data to select the most suitable model for subsequent analysis. The Neo-Hookean model was identified as the best fit, yielding the lowest root mean square error in three of four cases studied. However, the captions for Figures 5.4, 5.7, and 5.10 should include explanations of the legends (e.g., "febio_eng," "febio_true"). Additionally, a more detailed discussion of the results would enhance this section.

Chapter 6 provides a semi-empirical example to verify the extended Kalman filter code and procedure. The geometry and Young's modulus were assumed known, and the filter's convergence was tested against exact data. Results from the experimental rig and patient data are reported, with the dual extended Kalman filter (DEKF) demonstrating good agreement with laboratory experiments for pressure and displacement (Figures 6.2 and 6.3) and accurate predictions for patient data (Figures 6.4 and 6.5).

Chapter 7 offers a discussion and conclusions, suggesting potential improvements for real-world applications of the proposed approach. It examines a study on an LCCA phantom with varying thickness and mechanical properties, measured via X-ray, which revealed a bimodal thickness distribution in some cases. Validation in Chapter 5 showed good agreement with uniaxial testing data, despite challenges with ultrasound measurements caused by wave reflections in a water-filled glass container. Cameras provided higher precision in displacement measurements (error: 1e-4 mm) compared to ultrasound (error: 0.03 mm), with a mean difference of 0.0113 mm. The experimental setup, detailed in Sinek, Mesek et al. [77], used mixed effects to quantify measurement uncertainty.

A major contribution of this thesis is the use of a dual extended Kalman filter (DEKF) to estimate state variables (pressure, displacement) and Young's modulus, yielding values (1.43–1.84 MPa) close to experimental results (1.38–1.99 Mpa). For medical data, Young's modulus ranged from 582–837 kPa, consistent with physiological norms (613–988 kPa). The method holds promise for real-time, noninvasive artery assessment, though challenges such as non-Gaussian noise in pressure transducers and blurred ultrasound images require further attention. A reduced-order model is recommended over external software for faster simulations, potentially enhanced to estimate wall thickness alongside stiffness.

Chapter 8 includes supplementary materials, such as visualizations of the Kalman filter's working principle and Python code for data processing and Kalman filter implementation.

3. Major achievements of the PhD Thesis

In my opinion the major achievements of the PhD Thesis are:

a) Development of a Noninvasive Method for Young's Modulus Estimation

The Dissertation successfully developed a noninvasive procedure to estimate the Young's modulus of the left common carotid artery (LCCA) by integrating ultrasound-based wall displacement measurements with applanation tonometry for intra-arterial pressure. This approach eliminates the need for invasive techniques, advancing clinical applicability.

b) Validation of the mathematical model on a specially designed test bench

A custom testing rig was used incorporating an artery phantom, a pulsatile pump, and precise measurement devices to capture flow, pressure, and wall displacement data. The experimental setup was rigorously validated, providing a reliable platform for both model development and testing. A numerical model was constructed and validated against experimental data from the testing rig. This model effectively supported the inverse problem of estimating arterial stiffness (Young's modulus), showing a good agreement with measured results. Through comparative analysis of linear elastic and Neo-Hookean models, the Neo-Hookean model was identified as the most suitable for describing arterial behavior, achieving the lowest root mean square error in three of four cases. This finding enhances the accuracy of stiffness estimation.

c) Application of the Dual Extended Kalman Filter (DEKF)

A significant contribution of the PhD thesis is the innovative use of a dual extended Kalman filter to simultaneously estimate state variables (pressure and displacement) and the Young's modulus. The DEKF yielded accurate results, with values of 1.43–1.84 MPa (compared to experimental 1.38–1.99 MPa) for the phantom and 582–837 kPa for patient data, aligning with physiological norms (613–988 kPa). This is in my opinion very good achievement. The PhD Thesis demonstrated the superior precision of camera-based displacement measurements (error: 1e-4 mm) over ultrasound (error: 0.03 mm), with a mean difference of 0.0113 mm. This improvement in measurement accuracy strengthens the reliability of the proposed method.

d) Real-World Applicability and Future Potential:

The proposed numerical method for Young's Modulus Estimation shows a relevance for real-time, noninvasive artery stiffness assessment in clinical settings. The thesis also identifies actionable improvements—such as addressing non-Gaussian noise and developing a reduced-order model for faster simulations—allowing for practical implementation. By applying advanced filtering techniques (DEKF) to artery research—a topic with limited prior exploration (with only 18 relevant papers identified based on the Scopus, Web of Science and Science Direct databases)—the thesis may fill an important research gap in the literature and can contribute to establish a novel framework for noninvasive biomechanical analysis.

4. Critical remarks

The following remarks should be addressed:

1. In my opinion the literature survey lacks a summary statement clarifying the novelty of this PhD thesis relative to the referenced papers. Therefore I would like to ask for adding the information about the major novelty of the PhD Thesis compared to the studied papers.
2. Please provide the major advantages and drawbacks (limitations) of the Dual Extended Kalman Filter Method

3. Please provide the information about measurements accuracy (for pressure, flow rate and displacement). In my opinion to compare with mathematical model it would be good to show the error bars of the measurements performed.
4. Why only two meshes were used for validation of FEM results ?
5. Why there exists a small difference between static and dynamic FEA results ?
6. The captions for Figures 5.4, 5.7, and 5.10 should include explanations of the legends (e.g., “febio_eng,” “febio_true”). Additionally, a more detailed discussion of the results is needed in Chapter 5.

5. Final conclusion

I highly recommend the evaluated PhD Thesis for a public defense, and request the Scientific Council of the discipline of biomedical engineering of Silesian University of Technology to admit the dissertation for public defense. In my opinion the PhD Candidate achieved all the objectives planned. A doctoral thesis also meets the requirements of the relevant laws (Act of July 20, 2018 - Law on Higher Education and Science, Journal of Laws of 2024, item 1571, as amended). The PhD Candidate developed a noninvasive Method for Young’s Modulus Estimation of the left common carotid artery (LCCA). The method was validated by extensive experimental measurements, and shows good accuracy, as well as a significant potential in a real word application. PhD Candidate has published one paper in Measurement journal (Elsevier, Q1), as well as 7 Chapters in Monographs. Based on the high value of the Thesis as well as good scientific achievements of the PhD Candidate I recommend the distinction of this Thesis.