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Project report

Principal Investigator**: Oleksiy LARIN**
ID# 3036
Project title **Computational Intelligence in Predictive Modelling of Mechanical Responses of Human Blood Vessels Affected by Atherosclerotic Plaque**
Project start date **01/05/2024**
Reporting period: **Q3 (NOV-JAN)**

Content of the quarterly progress report for quarter Q1 PAGE

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Project report

1. Summary of progress

The 3rd stage of the project focuses on the continued parallel development of all work packages (WP1-WP4), building upon the initial results from the Q1 stage and integrating advancements made during the Q2 period. Key intermediate results across the work packages are outlined below:

WP1: Symbolic Regression for Viscoelastic ModelingThe symbolic regression (SR) method was further refined to model the viscoelastic nonlinear behavior of materials. Advanced benchmark problems were solved by focusing on the hyperelastic and viscoelastic models. The SR approach was used for the derivation of strain energy density functions from synthetic stress-stretch data and real experimental data obtained for the rubber. Stress responses under monotonic and harmonic strain functions at varying strain rates were examined, revealing distinct behaviors. In a comparison of 1st and 2nd stages, we have proposed an approach that, in 2 steps, approximates a visco- hyper- elastic response with good quality. This development offers robust regression techniques adaptable to both hyperelastic and viscoelastic materials, and it has a good perspective for further modification of that approach considering its nonlinear and physically-informed peculiarities over the viscosity modelling as well as nonlinear elasticity modelling.

WP2: Parametric Modeling of Atherosclerotic PlaquesIn WP2, significant advancements were made in the finite element (FE) modeling of atherosclerotic plaques within blood vessels. The key improvement were introduced as statistical parametric modeling of plaque borders. A spline-based algorithm was enhanced to randomize plaque border distribution using key points derived from OCT image data processed via WP4 algorithms. This model supports Monte Carlo simulations, allowing for robust analysis of both the casual biases of the lipid plaque cover geometry and the stochastic nature of plaque development. Statistical modelling has been provided for the identification of the probability distribution of the strains in the lipid plaque's cover wall.

WP3: A comprehensive literature review informed the development of a cholesterol accumulation model that correlates with patient age. This foundational work supports WP2 by introducing age-dependent variables into the plaque growth model, enabling more precise simulations of atherosclerosis progression. A linear progression model was established to simulate plaque growth over time with its mean strand, with future plans to integrate for stochastic process model. That model was successfully integrated into the FE parametric modelling and provided us with a possibility to prognosis the trend line of the stain distribution over time and the lipid plaque cover wall zone.

WP4 focus was on the improvement a comprehensive approach to automate and improve the OCT image processing pipeline for heart vessel analysis. Developed a web-based application that combines classical computer vision techniques with modern deep-learning approaches to address the challenges of medical image processing. Our key contributions include a robust pipeline for OCT image preprocessing that eliminates common artefacts and a flexible annotation system that is easily accessible via the user-friendly web interface.

As part of our results dissemination strategy, we presented intermediate results at the international conference. The corresponding proceedings paper have been accepted and will be indexed in Scopus. Currently, 2 conference proceeding are accepted and 1 paper was successfully published and indexed in Scopus. The last has partially open access (green status) through Springer Publishing, with some minor restrictions.

The team also developed a project website featuring concise information about the project and its results. This site demonstrates our commitment to open science and promotes the project's findings and reports.

Website link: https://web.kpi.kharkov.ua/dpm/en/projects/cipm-v/

2. Current status of the project

The following specific task statements based on the Project Methodology are set for the current stage and within the scope of the following Work Packages (WP) :

WP1. Develop a symbolic regression method to identify a mathematical model for the non-linear material behavior description with hyper- and/or visco- elasticity (based on literature data). Develop an algorithm and Python code realization.

WP2. Develop a parametric form for the models as a set of macros-codes allowing their automatic creation based on the patient-specific or synthetically prognosis data

WP3. Development of a model and analysis for the prediction of the stochastic growth of atherosclerotic plaque

WP4. AI-based approach to blood vessel mech response prognosis.

Create an approach for the statistical estimation of the mechanical responses of human blood vessels with atherosclerosis.

For **WP1**, Prof. Larin and Ms. N. Fomenko explored the application of the symbolic regression model to identify material models: hyper- and visco- elastic. After refining the symbolic regression model, they tested it on synthetic data, specifically a fictitious hysteresis loop in the form of an ellipse - representing the typical stress response to a harmonic strain process in a linear viscoelastic solid material. This was done in order to assess whether the resulting view of the elastic deformation potential is adequate from the point of view of mechanics. Having assessed the results as satisfactory (Fig. 1), we proceeded to test the model on experimental data for rubber.

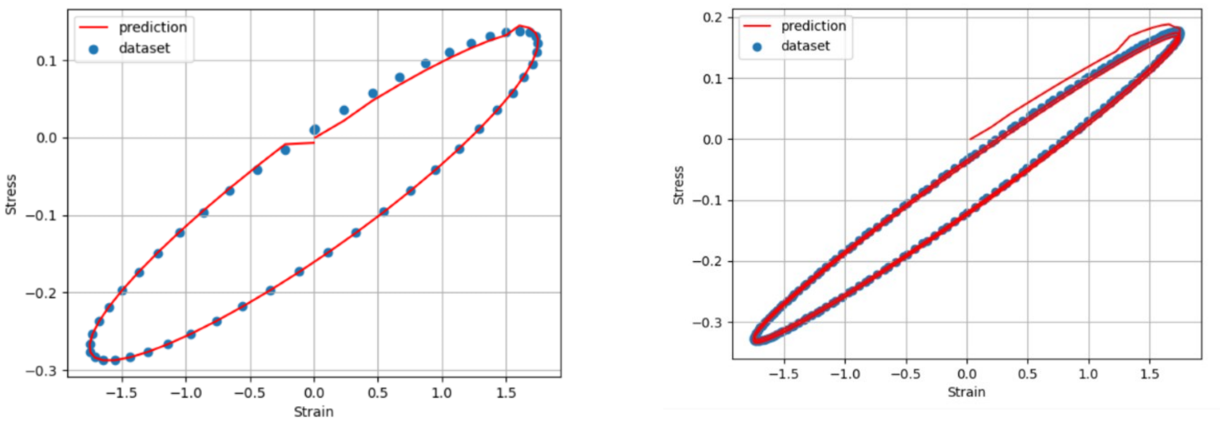


Fig. 1. Stress-strain dependency for standard linear solid harmonic case

Considering the next stress response (1) for standard linear solid model, we assume an expression for finding the relaxation function (2) as a linear combination of pure hyper-elastic nonlinear part and linear viscosity:

$$\sigma = \int_0^t G(t-\tau)\dot{\varepsilon}\,(\tau)d\tau \tag{1}$$

$$G(t) = \frac{\partial^2 W}{\partial \varepsilon^2} + E_1 e^{(-E1/\eta t)} \tag{2}$$

where σ – stress; ε – strain; E_1 – elasticity module; η – viscosity coefficient G – relaxation function; $\dot{\varepsilon}$ – strain rate, W – elastic deformation potential.

The expression for the relaxation function has been proposed to find out in 2 consequent steps:

- the first term is the second derivative of the elastic deformation potential, which could be identified without viscosity and based on the stress-strain response curve with constant monotonic deformation and quasi-static conditions
- the second - the negative exponent function that approximates the viscosity.

To describe the process of the program for finding the elastic deformation potential (W) that represents the first step, a symbolic regression (Model SR) is used. The same solver and software procedure are used for the second step, however the negative exponent function was manual hard-coded into the final formulation allowing in the second step just to identify the constants only. This was done just as a first estimation of physically-motivated relaxation function description. The results are compared with quality criteria to assess the model's performance. The flowchart (Fig. 2) captures the iterative process of finding a mathematical model for the elastic deformation potential based on input data using symbolic regression. Considering the above, we tested the model's performance on experimental data for rubber samples. The approximation of the experimental data (blue dots) by the expression obtained using symbolic regression (red line) can be seen in Fig. 3

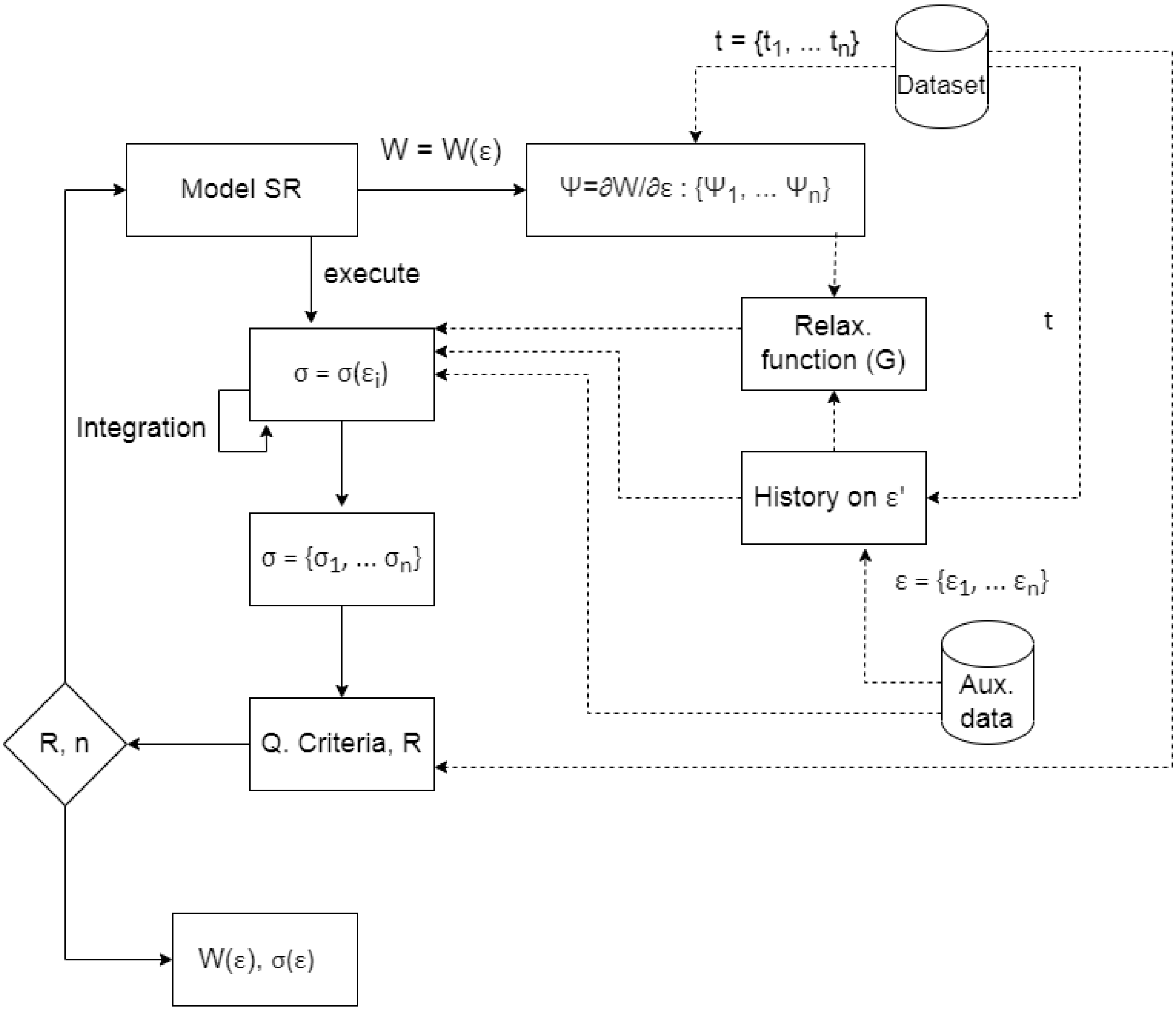


Fig. 2. Flowchart of the SR learning process

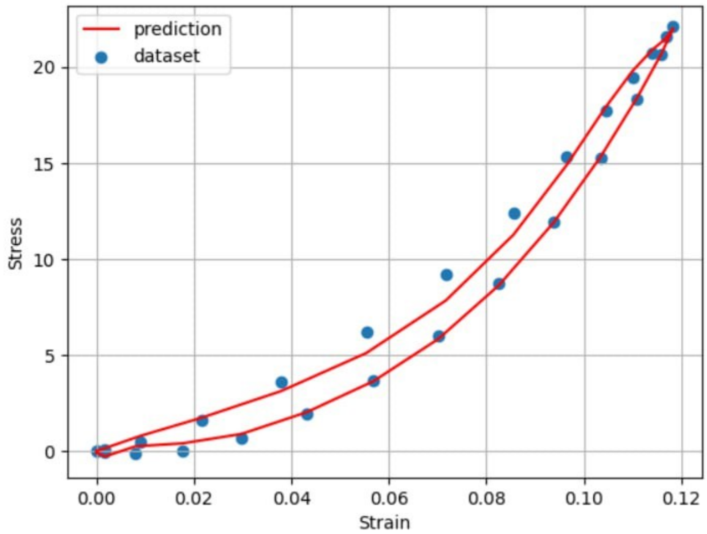


Fig. 3. Stress-strain dependency for experimental data and SR-proposed model for rubber

For **WP2** Prof. Larin, Dr. K. Potopalska, Mr. I. Hovoruha and Mr. M. Mironenko are set as the responsible group. At the current stage of this WP, two improvements in parametric modeling have been developed: the implementation of a methodology for modeling the random distribution of the atherosclerotic plaque border, including a Monte Carlo simulation, and the modeling of plaque growth over time (based on and using forward in WP3).

At the previous stage, an algorithm for modeling the plaque border was developed. The border is generated by constructing a spline through a set of randomly placed key points, which are created in a loop with a predefined level of discretization according to the implemented algorithm. The initial spline for the border is derived from image processing of the OCT file using the algorithm developed in WP4. This parametric model was used to implement Monte Carlo simulations within both types of analysis: the first for probabilistic estimation of the possible variation (bias) of the strain concentration over the plaque cover and the second for the stochastic prognosis of the possible plaque (lipid pool) growth over time. The first model estimates some bias (causality of error) in identifying the border between the plaque (lipid pool) and its cover (the ply of the vessel that separate vessel wall, lipid pool and blood). This uncertainty of the initial data is proposed to be taken into account based on statistical estimation, considering the probability of strain amplitude values rather than exact data. The second is used for the stochastic prognosis of the ageing of the patient and atherosclerosis disease progression.

Some results presented in the Fig. 4 - Fig. 6.

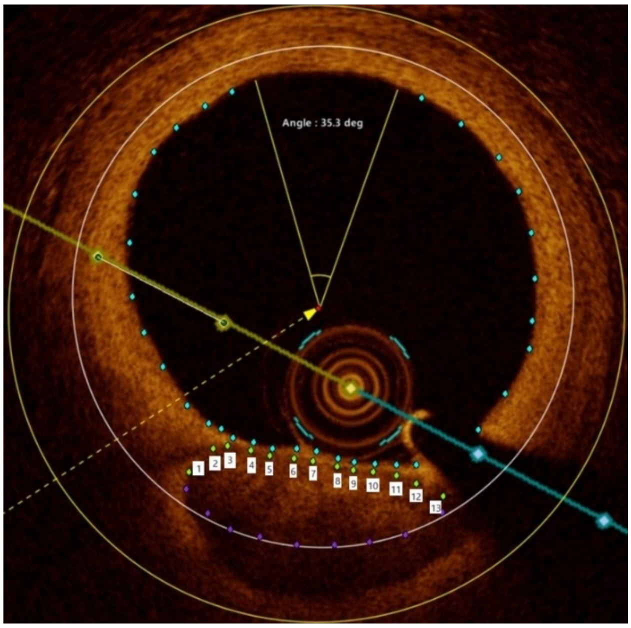


Fig.4 The location of nodes were used in model construction and for which the stain magnitude analyzed within a Monte Carlo simulations

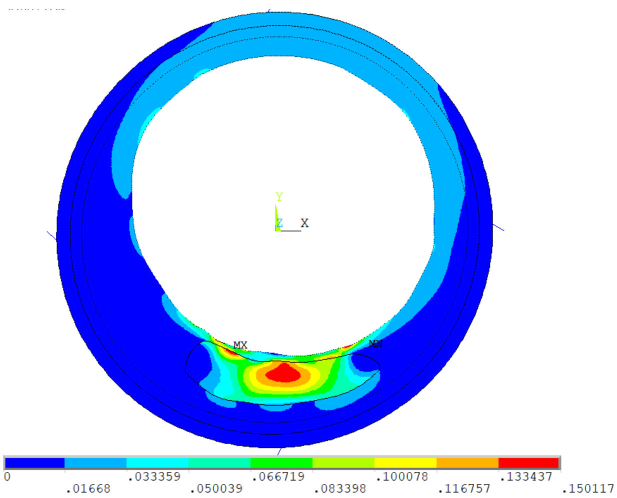


Fig. 5 the example of stain distribution

The histograms for the nodes located on the plaque, which exhibit the maximum strain values, are shown in Fig. 6.

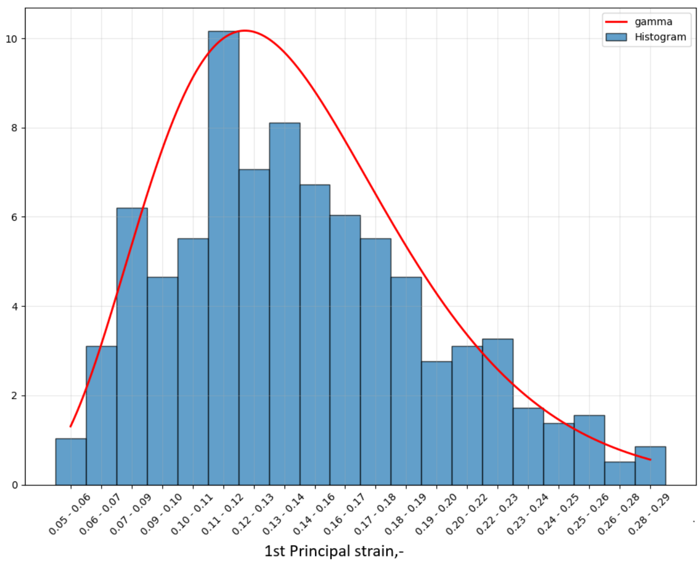


Fig.6 Histogram for most higher strain magnitude (point 10, see Fig. 4)

For the current progress in **WP3**, Dr. Potopalska provided an approximation of cholesterol growth in the vessel's media-inner layer based on human age, derived from a literature review. After analyzing and comparing various models, the exponential law was chosen as the best mean value curve (Fig. 7), which parameters was identified under regression procedure.

$$H(t) = H_0 e^{(-\gamma t)} \quad (2)$$

where H_0, γ – parameters of approximation (0.09 and 0.036 respectively).

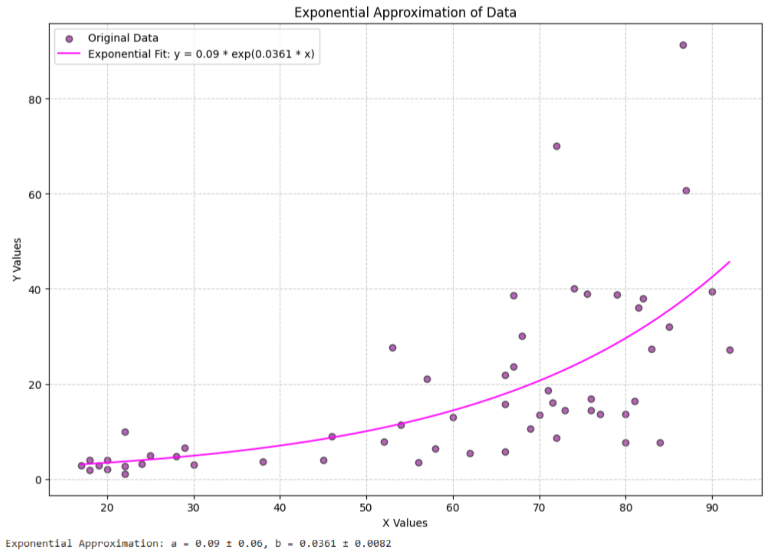
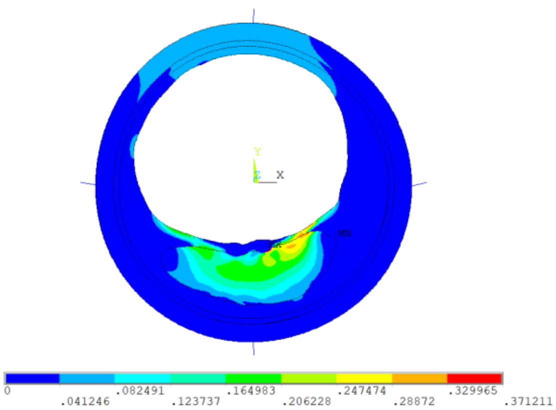
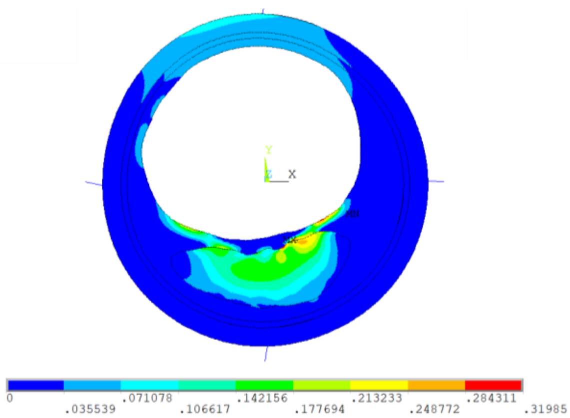


Fig. 7 The approximation of cholesterol accumulation in vessel

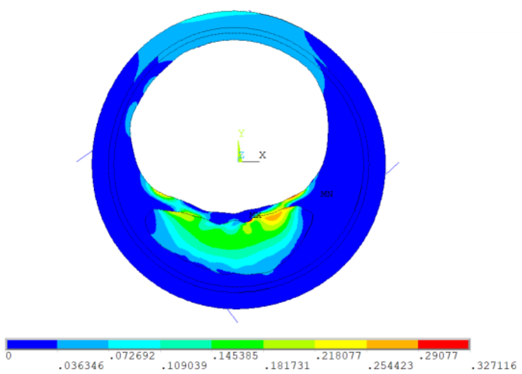
This result defines the percentage of the area occupied by cholesterol in this layer and has been incorporated into the algorithm being developed in **WP2**. As a result, we obtain a set of models that represented the different possible vessels damaged with lipid plaque and the strain distribution in the vessel over the time (Fig. 8).



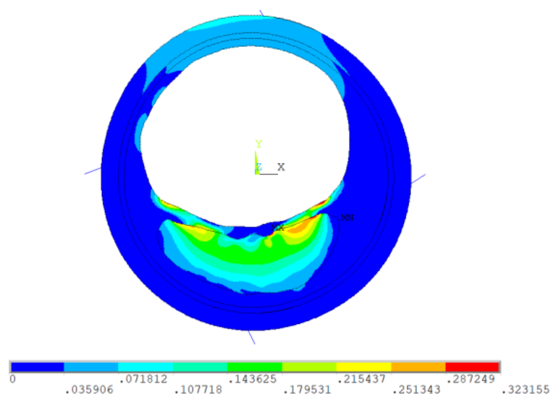
a) 43 years (initial)



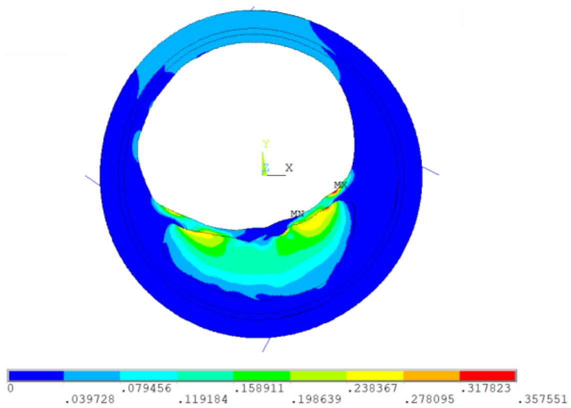
b) 44 year



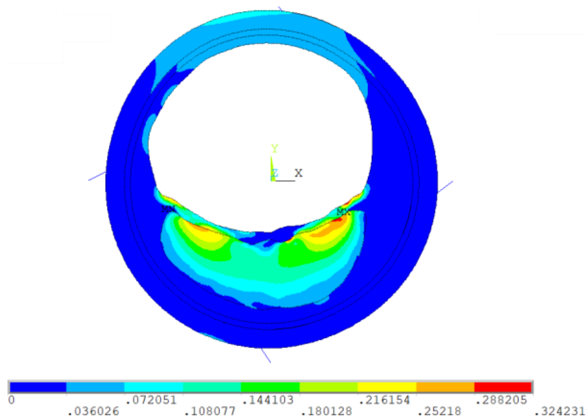
c) 45 years



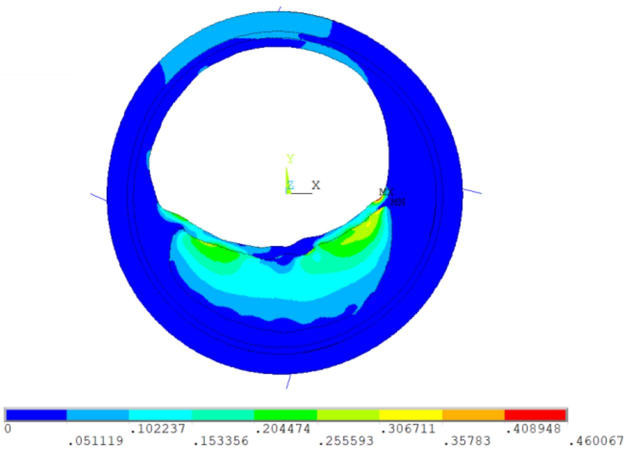
d) 46 years



e) 47 years



f) 48 years



g) 49 years

Fig.8 Strain distribution in vessel from 43 years (dedicated from OCT results) to 49 years according to proposed model of growth

For **WP4** (prof. Larin is responsible) the focus was on the improvement a comprehensive approach to automate and improve the OCT image processing pipeline for heart vessel analysis Developed a web-based application that combines classical computer vision techniques with modern deep-learning approaches to address the challenges of medical image processing. Our key contributions include a robust pipeline for OCT image preprocessing that eliminates common artifacts and a flexible annotation system that is easily accessible via the user-friendly web interface.

Next Improvements were made during current stage:

1. Added the masks intersection limitation to handle complex cases when only a small part of layers is visible.

2. Added adjustable media layer width to better match human anatomy.

3. Minor technical improvements

- Improved the vessel layers masks visualization.

- Assigned fixed colors to each layer for easier masks interpretation.

- Optimized the code to speed-up the annotation process.

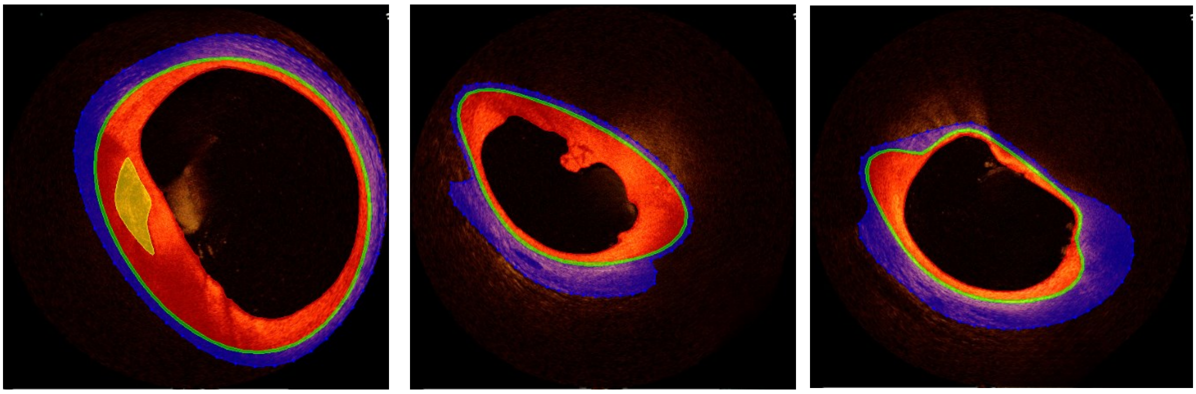


Fig. 9 Example of OCT image preprocessing

3. Summary of personnel commitment

Oleksiy LARIN - **WP1**: Integration of machine learning methods into the modeling the nonlinear behavior of soft biological tissues, for which, in particular, hyperelastic models, **WP2**: Improving an algorithm for random modeling of atherosclerotic plaque border. **WP4** Developing and enhancing a web-based application that integrates traditional computer vision techniques with advanced deep-learning methods to tackle challenges in medical image processing.

Preparing a conference paper *for* "ICTM-2024: Integrated Computer Technologies in Mechanical Engineering". (Application of computer vision approaches in optical coherence tomography image processing)

Nataliia FOMENKO – **WP1**: Investigation of the application of symbolic regression (SR) for modeling hyperplastic material behavior. Performing the calculation for the different metrics. **WP2**: Computer modeling of the process involves the development of a geometric model of a vessel with an atherosclerotic plaque. Development of APDL macros of parametric geometrical model. Taken part of algorithm development for image processing of vessel with an atherosclerotic plaque based on real patient diagnostic.

Kseniia POTOPOLSKA –**WP3:** Development of a model for the growth rate of atherosclerotic plaque in human vessels, approximation of plaque growth data from existing literature, and implementation of a well-defined mathematical model to predict the stochastic progression of atherosclerotic plaque.

Ilia HOVORUKHA – **WP2**: The development and enhancement of a Python algorithm for modeling the random border of vessel plaque. Conducting FEA calculations to determine the deformed state of a human artery with atherosclerotic plaque for statistical analysis. Establishing a method for approximating the random distribution of strain concentration nodes.

Mikhail MIRONENKO – **WP2**: The development and enhancement of a Python algorithm for determining the geometrical parameters of a vessel with plaque over time based on approximated cholesterol accumulation data. Creating an APDL macro for a parametric model of a vessel with plaque. Conducting calculations to define the deformed state of a human artery with atherosclerotic plaque in the time domain.

4. Description of travels

No travels were done within the reported period

5. Dissemination

Dr. K. Potopalska and Ms. N. Fomenko are Executors of scientific project "Algorithms, models and artificial intelligence tools for two-level modeling of the behavior of complex materials for dual-purpose technology" 2023-2026 supported by Ministry of education and science of Ukraine.

Published papers:

> Fomenko, N.O., Larin, O.O. Investigating the Impact of Atherosclerotic Plaque Size on Human Arterial Wall Stress-Strain Hysteresis Loop and Deformed State Pattern. *Strength Mater* **56**, 999–1009 (2024). https://doi.org/10.1007/s11223-024-00718-5

The team also developed a project website featuring concise information about the project and its results. This site demonstrates our commitment to open science and promotes the project's findings and reports.

Website link: https://web.kpi.kharkov.ua/dpm/en/projects/cipm-v/

6. Delays and suggestions

The project process is proceeding according to the plan outlined in the proposal.

7. Issues or Challenges

The project process is proceeding according to the plan outlined in the proposal.

8. Further elaborations, notes, etc.

In the next project stage, WP1 will focus on upgrading the symbolic regression (SR) approach to approximate relaxation functions capturing both nonlinear viscosity and nonlinear elasticity. Planned activities include using experimental test data on rubber materials under varying strain amplitudes and harmonic frequencies. The SR method will also be applied to bio-material data from literature and project partners to enhance model robustness.

For WP2 and WP3, efforts will centre on integrating recent achievements to develop a procedure for predicting stochastic plaque growth over time in specific patients. A computational framework for estimating the reliability and probability of lipid plaque cap rupture will also be designed and discussed with medical practitioners to ensure clinical relevance.

WP4 will emphasize extensive discussions with medical experts regarding the accuracy and usability of the developed algorithms. Scientifically, the focus will be on integrating computer vision-based geometric identification from OCT images with finite element (FE) modeling to improve patient-specific simulations.

Dissemination will be prioritized, with plans to submit at least two research papers and one conference presentation. A short delegation visit to RWTH Aachen is also scheduled for in-person consultations, result dissemination, and collaborative discussions.

PUBLICATIONS AND ACKNOWLEDGMENT

Open Access to Peer-Reviewed Publications

These grants are funded by the European Union (through EURIZON H2020 project, grant agreement 871072) and, as mentioned in the Term of reference of the call, with this comes the obligation **to ensure open access (free, online access for any user) to all peer-reviewed publications relating to your research results.**

Peer reviewed publications refer to publications that have been evaluated by scholars (peers) in a given field of research. The predominant type of peer-reviewed scientific publication is the journal article, for which open access is mandatory. In addition, beneficiaries are also strongly encouraged to provide open access to other types of scientific publications, some of which may, in some cases, not be peer-reviewed, including monographs, books, conference proceedings, and grey literature (informally published written material not controlled by scientific publishers, e.g. reports).

Beneficiaries are free to deposit their peer-reviewed publications in those repositories most appropriate for their subject and publication (for instance a thematic or institutional repository). However, please note that **it is mandatory for them to continuously report all publications related to their project to the STCU and EURIZON Secretariat (dissemination template).**

Acknowledgment of the EU funding

As mentioned in the Term of reference of the EURIZON FELLOWSHIP PROGRAMME: "Remote Research Grants for Ukrainian Researchers" (Microsoft Word - EURIZON Remote Research Grants Terms of Reference for applicants draft.docx (desy.de)) :

For all communication relating to the Remote Research Grant and for any dissemination of results, such as through publications, posters, conference papers, etc. the selected Ukrainian teams (beneficiaries) and their European partners are required to ensure the visibility of the EU and EURIZON emblems, and to acknowledge the funding by including the following text, unless agreed otherwise: **"This project has received funding through the EURIZON project, which is funded by the European Union under grant agreement No.871072."**

For more information on publication and acknowledgment duties under European funded projects: https://ec.europa.eu/research/participants/docs/h2020-funding-guide/grants/grant-management/dissemination-of-results_en.htm

Signed by:

Oleksiy LARIN
08.02.2025, Kharkiv, UA