EURIZON FELLOWSHIP PROGRAMME
Remote Research Grants

Project report

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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: **Q2 (AGST-OCT)**

Content of the quarterly progress report for quarter Q2 PAGE

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Project report

1. Summary of progress

According to the Project time plan, it is stand that the 2nd stage (5 months) deals with the parallel development of all work packages (WP1-WP4) and assumes the development of the algorithms and models based on the initial results of the Q1 stage and some simplified benchmark solutions. In this report we have provided the information of Q2 (3 months) period that is a part of ongoing 2nd stage. Some key but intermediate results are followed bellow.

A symbolic regression (SR) method was further developed to model the viscoelastic nonlinear behavior of materials within WP1. An advanced benchmark problems is solved, focusing on the hyperelastic Ogden model and two viscoelastic models: standard linear solid (SLS) and the Maxwell model. Using symbolic regression, they developed a method for finding strain energy density functions, with the stress-stretch behavior synthetic data. The model achieved high accuracy, quantified by an inverse NRMSE score of 0.9373. The number of examined stress responses have been carried out under monotonic and harmonic strain functions at varying strain rates, revealing distinct responses at slow, normal, and fast rates. Key results include accurate stress-strain predictions and robust regression techniques adaptable to both hyperelastic and viscoelastic material models.

In WP2, some advancements in finite elements (FE) modeling of atherosclerotic plaques in blood vessels have been achieved, building on the initial schematic models developed in the project's first stage and informed by consultations with medical practitioners. Two key improvements have been introduced: a stochastic approach for randomizing plaque border distribution and an algorithm to simulate plaque growth over time.

The random plaque border distribution is achieved by generating a spline through randomly positioned keypoints, utilizing OCT image data processed through an algorithm from WP4. This enhancement allows for Monte Carlo simulations to analyze the stochastic nature of plaque development, providing a robust predictive model that accommodates plaque variability.

The second advancement models plaque growth as a linear progression, with plans for future integration of WP3 findings to enable non-linear growth modeling. Additionally, WP3's literature review has led to a cholesterol accumulation model correlating plaque growth with patient age, providing a foundation for incorporating age-dependent plaque behavior into WP2's model. These enhancements support more accurate simulations for medical prognosis and statistical analysis.

In WP4, progress focused on developing semi-automatic algorithms for processing medical images, particularly optical coherence tomography (OCT) scans, to support patient-specific prognosis models. A streamlined pipeline was developed for OCT image analysis, structured in four steps. The process begins with image calibration, ensuring accurate pixel-to-metric ratio alignment. This is followed by anomaly detection and inpainting using computer vision techniques like Hough line detection and thresholding to avoid interference in neural network training. Probe shadow detection and inpainting, and then eliminate further artifacts using template matching. Finally, vessel contours are annotated either manually with spline interpolation or automatically for certain areas using SAM2 segmentation.

Dissemination of results is also ongoing, with 1 conference-submitted presentation, ensuring broad visibility and early-stage scientific community feedback.

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. O. Larin and Ms. N. Fomenko studied the application of the symbolic regression model to determine such material models as the hyperelastic Ogden model and viscoelastic models: standard linear solid and Maxwell model. An approach for searching for strain density function by symbolic regression is developed.
The Ogden hyperelastic model is often used to model the behavior of rubber and soft biological tissues. We tested our symbolic regression model on it.
The strain energy density in this case has the following form:

$$W(\lambda_1, \lambda_2, \lambda_3) = \sum_{p=1}^{N} \frac{\mu_p}{\alpha_p} \left[\lambda_1^{\alpha_p} + \lambda_2^{\alpha_p} + \lambda_3^{\alpha_p} - 3\right] \tag{1}$$

where $\lambda_j, j = 1, 2, 3$ are the principal stretches.
The three stretches for uniaxial tension/compression are:

$$\lambda_1 = \lambda, \qquad \lambda_2 = \lambda_3 = \frac{1}{\lambda} \tag{2}$$

The uniaxial stress–stretch relation of the Ogden model

$$\sigma = \sum_{i=1}^{N} \mu_i \left[\lambda^{\alpha_i} - \lambda^{-\alpha_i/2}\right] \tag{3}$$

Having generated synthetic data, we divided it into a training (blue dots) and a testing (green dots) sample (fig.1). The error was calculated using the inverse NRMSE on the tested data (the symbolic regression model produced red points). The resulting calculation accuracy is 0.9373.

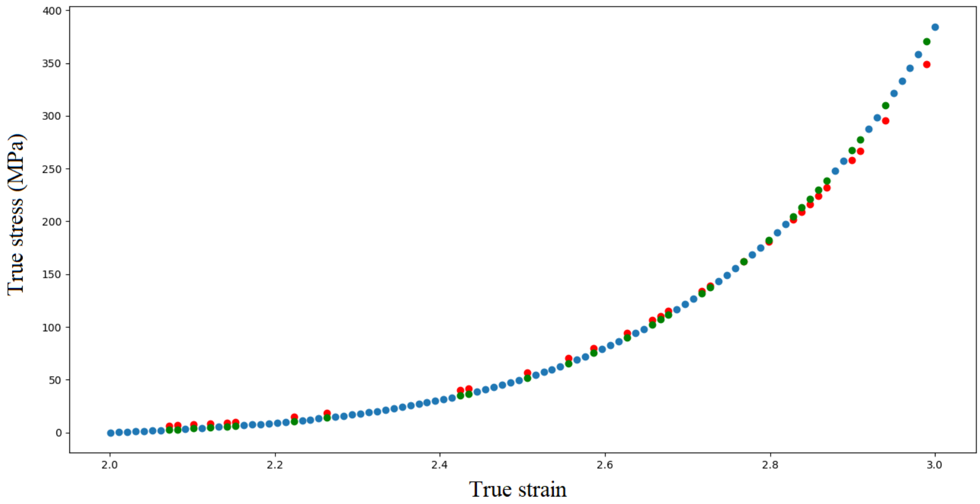
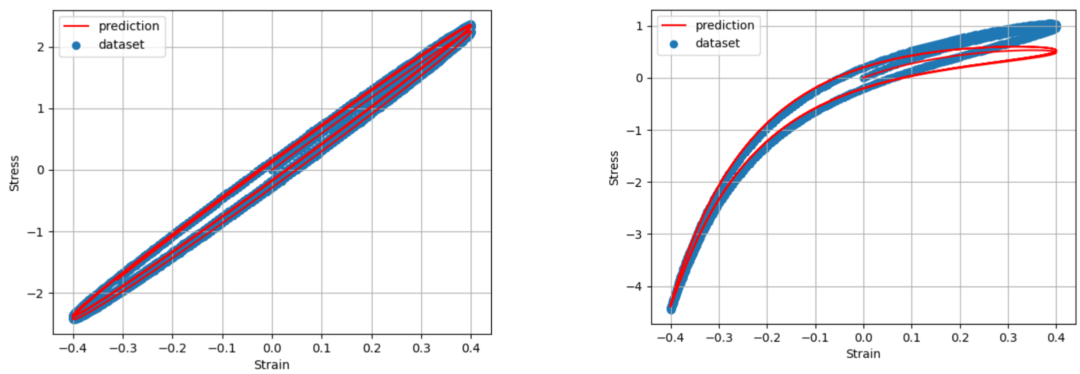


Fig.1 Stress-strain dependency for Ogden model, for $\mu = 3,\ \alpha = [7,\ 0.4]$.

In general, calculations were performed for fixed alphas ($\alpha = [7,\ 0.4]$) and different μ ($\mu = 1,\ 3,\ 5,\ 7$)
Using the previous approach of finding the Cauchy stresses from the strain energy density, a number of calculations were performed for relaxation function of such viscoelastic models as standard linear solid (SLS) and Maxwell model (fig. 2). As well as for two types of strain function:

- Monotonic $eps_0 \frac{t}{t[vectlen-1]}$
- Harmonic $eps_0 * \sin\left(\frac{3*2*\pi*t}{t[vectlen-1]}\right)$

We investigated 3 cases of strain rate (slow, normal, fast). In order to model this, we changed the time of strain application, 0.1, 1, 10, respectively.
Strain rate for monotonic case: “slow” - 4% per sec, “normal” - 40% per sec, “fast” - 400% per sec.
Strain rate for the case of harmonic deformations: “slow” - 24% per sec, “normal” - 240% per sec, “fast” - 2400% per sec.



a) b)

Fig. 2. Stress-strain dependency for: a) SLS at normal strain rate for harmonic case; b) non-linear elastic model at slow strain rate for harmonic case

For **WP2** Prof. O. Larin, Dr. K. Potopalska, Mr. I. Hovoruha and Mr. M. Mironenko are set as the responsible group. For this WP at the current stage of the project, two improvements in parametric modeling have been developed: the implementation of a methodology for modeling a random distribution of the atherosclerotic plaque border and the modeling of plaque growth over time.

The plaque border is generated by constructing a spline through a set of randomly placed keypoints, which are created in a loop with a predefined level of discretization according to the implemented algorithm. The initial spline for the border is based on the results of image processing of the OCT file from the algorithm developed in WP4. These results enable the implementation of a Monte Carlo simulation to analyze the stochastic process of plaque development. An example of models created using this methodology is shown in Fig 3.

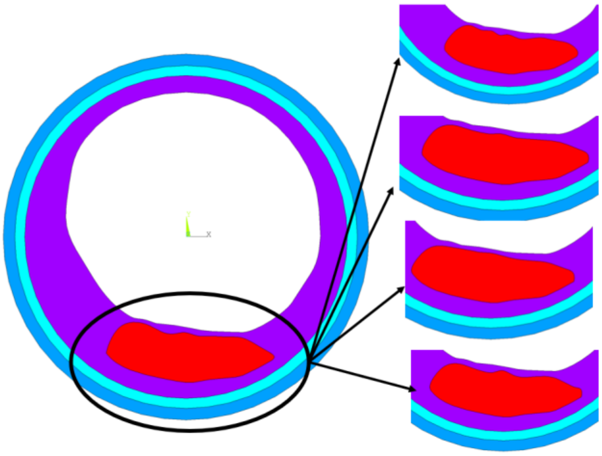


Fig.3 Example of model with random border of plaque

Another improvement to the algorithm provided in the previous report is the implementation of plaque growth over time. At this stage, the growth is modeled linearly, but in the next phase, the approach defined in WP3 will be incorporated into the algorithm. An example of plaque growth is shown in Figure 4.

For the current progress in **WP3**, Dr. Potopalska is engaged in an advanced literature review. An analysis of currently used approaches and investigations into the stochastic development of plaque in human vessels over time, as well as mathematical methods for estimating possible variations in plaque dimensions, has been conducted. Based on the current stage of the literature review, an approximation of cholesterol growth in the vessel's media-inner layer, dependent on human age, was developed. This result defines the percentage of area occupied by cholesterol in this layer. This outcome will be incorporated into the algorithm being developed in **WP2**.

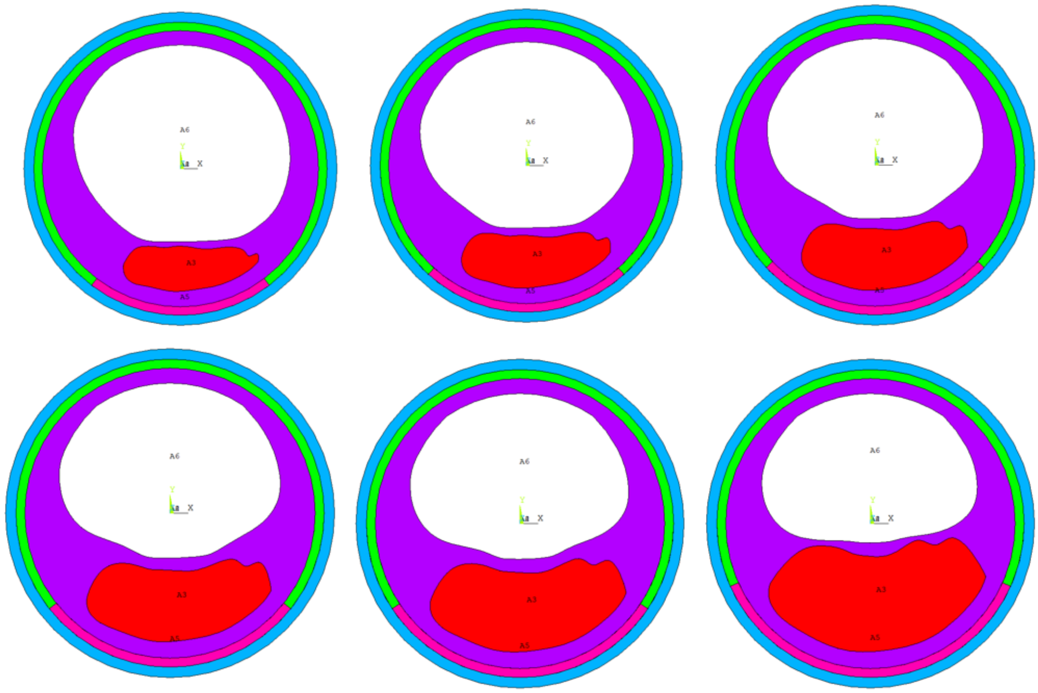


Fig.4 Example of plaque growth

For **WP4** (prof. Larin is responsible) focus was on the development of the physiologically realistic computational models based on the semiautomatic procedures that could provide practically oriented and objective patient-specific prognosis models. Within the Q2 period, We focused on the development of semi-automatic algorithms for medical image (based on optical coherence tomography procedure results) processing with computer vision (CV) tools. That might help strengthen the objectivities of the geometrical parameters of the model and get accurate patient-specific models.

OCT is a common procedure that helps to investigate the vessel's condition. Using a small probe a doctor scans a vessel from the inside and OCT frames are stored in a popular for the medical domain DICOM format. An example of frames can be found in Fig. 1:

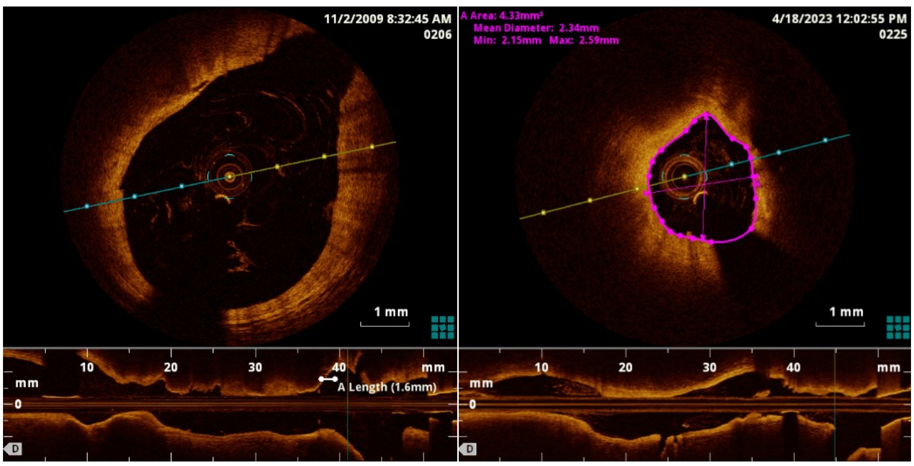


Fig. 5. Example frames of two patients.

Typical medical images that we could obtain from OCT have a lot of artificially motivated noise in the raw images and traditionally require some highly specific and experienced medical professionals engaging in manual labelling of different aspects of the data that are presented on the images. Raw files contain information about a patient and scans of the transverse section of a vessel on top and longitudinal on the bottom. Also, the images above show technical marks such as a ruler and doctor's notions, that, while helpful for human analysis, can harm the precision of the neural network, which is trained on such images.

Currently, the vessel reconstruction from obtained OCT scans is made by hand and requires validation by professionals to make sure that the final calculations are right. Considering that a single procedure results in 300+ frames, manual labeling is an extremely time-consuming process. Thus, automation using computer vision approaches is required.

Within the Q2 period of the WP4 we had proposed the pipeline of the algorithm of semi-automatic images processing that can be divided into 4 steps:

1. **Image calibration**. This is a crucial step where the pixel-metric ratio is set, so the obtained contours can be used for the reconstruction. This must be the first step, as the next step will remove the reference ruler.
2. **Anomalies detection and inpainting**. OCT scans contain built-in doctor's notions, a ruler to understand shown dimensions, and other technical marks that may harm further vessel analysis. The inpainting technique is a popular way to remove unwanted elements from the image. However, inpainting requires a mask - a grayscale image with black and white pixels, where white pixels denote the region to change and black pixels denote the immutable region. Such masks could be generated by hand or using a segmentation model. Considering the same nature of such anomalies, it's possible to omit training custom segmentation models and use a combination of lightweight computer vision approaches such as pixel intensity-based thresholding and Hough line detection.
3. **Probe shadow detection and inpainting**. Same as in the step above, it's possible to use the similarity of probes in different images and use a template matching algorithm to detect the shadow's mask for further inpainting.
4. **Image annotation**. This is the final step, where a trained human draws contours for each class that we need to reconstruct in a vessel.

The flowchart in Fig. 6 shows the described steps and the selected approaches to complete those steps.

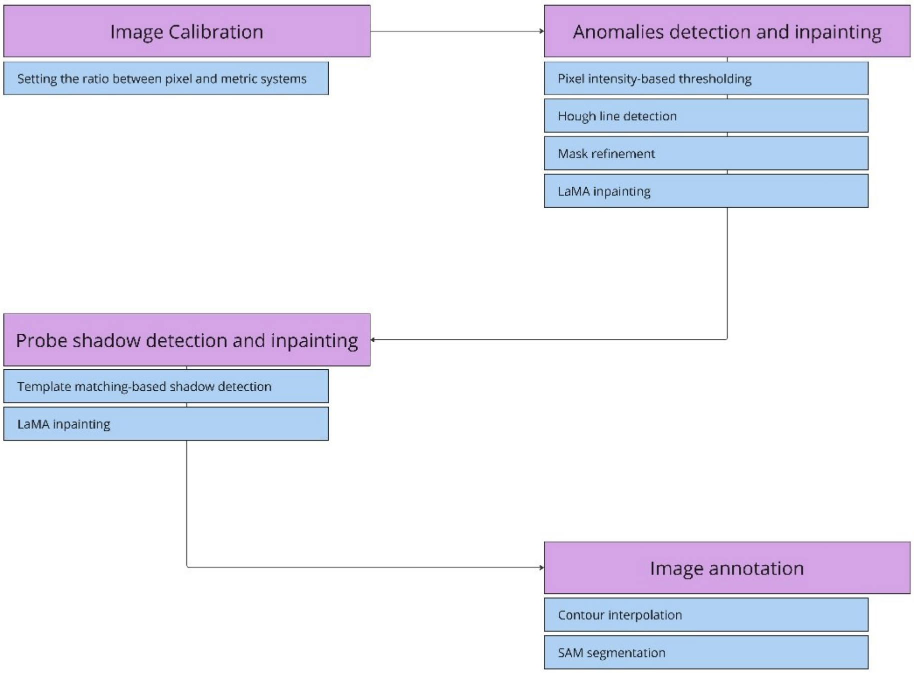


Fig. 6. Application flowchart.

The annotation tab currently contains two types of annotation:

1. Manual with available spline interpolation with different orders and smoothing tuning to create additional points in the mask.

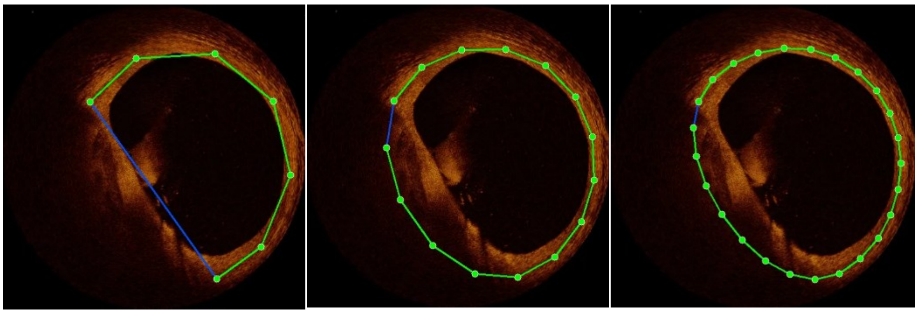


Fig. 1. Manual mask drawing results.

We can create a complete mask with several clicks, vary its smoothness, and extrapolate on uncertain regions.

2. Automatic using SAM2. It's suitable only for segmenting the hole because SAM was trained for general purposes and it's not able to distinguish between vessels' layers. Still, it creates an accurate mask with just a single click.

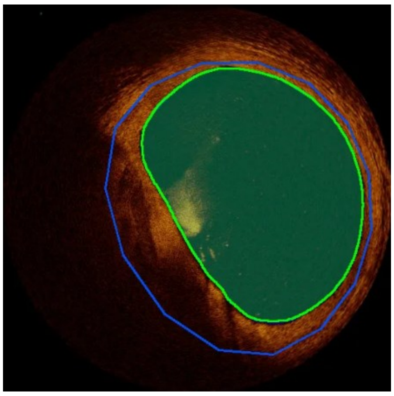


Fig. 2. SAM2 resulting mask painted in green.

As a result, for WP4 at the end of Q2 is a comprehensive approach to automate and improve the OCT image processing pipeline for heart vessel analysis. We have successfully developed a draft of web-based application that combines classical computer vision techniques with modern deep-learning approaches to address the challenges of medical image processing.

The current algorithm and developed software are prepared in the framework of cooperation and personal engagement with practical computer vision programmer Mr. Danylo Krasii.

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**: Creating an algorithm for random modeling of atherosclerotic plaque border. **WP4** Developing a web-based application that combines classical computer vision techniques with modern deep-learning approaches to address the challenges of medical image processing.

Preparing a conference paper *for* "ICTM-2024: Integrated Computer Technologies in Mechanical Engineering". (Application of computer vision approaches in arteriosclerotic human vessels semi-automatic 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.

Presented a paper at the conference IEEE 5th KhPI Week (The relevant topic can be found in the conference program https://khpiweek.ieee.org.ua/program/)

Kseniia POTOPOLSKA –**WP3:** Deep literature overview and development of modeling the growth rate of atherosclerotic plaque in human vessel, defining appreciable mathematical model of prognosis of the stochastic growth of the atherosclerotic plaque.

Ilia HOVORUKHA – **WP2**: The development and implementation of the algorithm in Python code for implementation of modeling random border of vessel plaque. Providing calculation for definition of human artery with atherosclerotic plaque deformed state for statistics.

Mikhail MIRONENKO – **WP2**: The development and implementation of the algorithm in Python code for determining geometrical parameters of vessel with plaque due to it growth in time in linear domain. Create an APDL macros for parametric model of vessel with plaque. Providing calculation for definition of human artery with atherosclerotic plaque deformed state.

4. Description of travels

No travels were provided during Q2 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.

Submitted conference papers:

1. D. Krasii, O. Larin, **”Application of computer vision approaches in arteriosclerotic human vessels semi-automatic optical coherence tomography image processing”**, (12 pages), 2024 (submitted for review and presentation)

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. The external consultations contributed to the improvement of the proposed algorithm for parametric models. However, the development of automatic and semiautomatic routing for the obtaining of the computational physically and physiologically realistic models has huge challenges that require many following consultations with practical medical surgeons as well as specific time-consuming data preparation issues.

8. Further elaborations, notes, etc.

In the next stage of the project, further developments will focus on advancing the methodologies established in WP1, WP2, and WP4.
For WP1, the next steps will focus on expanding the symbolic regression (SR) technique for application to experimental data from cyclic stress tests on rubber-like composite materials. This phase aims to refine the SR method to capture nonlinear viscoelastic responses, enhancing the model's utility in real-world scenarios. In particular, modifications to the SR procedure will be explored to handle the unique nonlinearity and hysteresis often observed in cyclically loaded viscoelastic materials. These developments are anticipated to improve the accuracy and predictive power of SR for viscoelastic and hyperelastic material responses, which is vital for modeling complex material behavior under varied loading conditions.
Additionally, a planned visit to RWTH Aachen by Ms. N. Fomenko will support this work through targeted traineeship activities and direct consultations with experts.

In WP2, under the supervision of Prof. Larin, efforts will be concentrated on integrating WP4's results, specifically developing an algorithm for generating high-accuracy finite element (FE) models of plaque-damaged vessels. These models will be based on semi-automatic OCT image processing (current results from WP4), ensuring precise patient-specific geometry. Furthermore, a computational approach to assess the probability of plaque rupture will be implemented, leveraging Monte Carlo simulations to account for variability in plaque structure. Some aspects of reliability analysis from WP2 and WP3 are near completion and will undergo testing and implementation after minor adjustments to existing models.
In WP4, further development of the computer vision (CV) approach is planned to create a semi-automatic technique for labeling the layers of blood vessels and identifying plaque geometry. Additionally, a novel generative graphical algorithm will be developed to address data loss or distortion in OCT images due to the in vivo experimental procedure, improving the quality and completeness of the image data for more accurate modeling.

PUBLICATIONS AND ACKNOWLEDGMENT

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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.**

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Acknowledgment of the EU funding

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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."**

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Signed by:

Oleksiy LARIN

Kharkiv, 08 Nov., 2024