

# TAXINOMISIS



Multidisciplinary approach → stratification of patients with carotid artery disease

**TAXINOMISIS plenary meeting**  
October 21-22, 2021 (virtual)

Extension of the project due to the Covid 19 outbreak up to June 30, 2023

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**TAXINOMISIS** is a European Commission funded research project which aims to develop a new approach for the stratification of carotid artery disease patients.

**TAXINOMISIS** takes bold step beyond the state of the art unwinding the pathobiology underlying symptomatic plaques, discriminating distinct disease mechanism-driven states and biomarkers, and developing a multiscale risk stratification model.

**TAXINOMISIS** will deliver, as a main outcome, a software platform, which can perform the risk stratification.



## Purpose

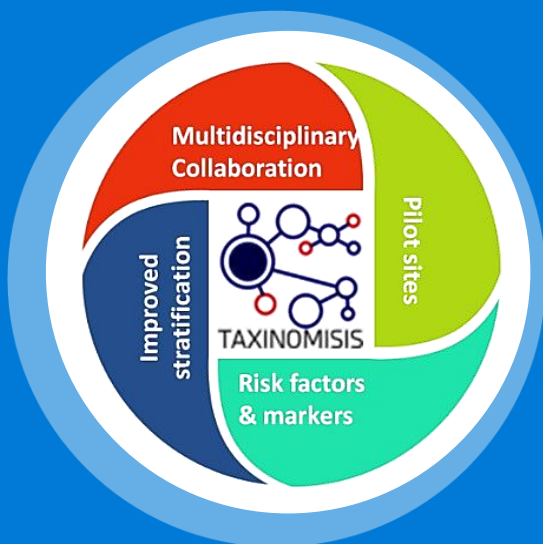
Provide novel disease mechanism-based stratification for carotid artery disease patients to address the need for stratified and personalised therapeutic interventions in the current era.



## Objectives


- Investigate the causal relationship of the major pathways and factors identified in symptomatic carotid artery disease
- Study disease phenotypes and disintegrate them into endotypes according to specific pathobiological mechanisms
- Integrate a computational model and an agent based model of plaque progression in the risk stratification tool
- Perform a test for determining the presence of single Nucleotide Polymorphisms and predicting drug response
- Evaluate the risk model of carotid artery disease stratification in an observational multicentre clinical study
- Present a cost-effectiveness analysis

## TAXINOMISIS innovation capacity



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 755320

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## Project challenges

- With exploring **longitudinal cohorts (WP1)** and **multi-omics data through mathematical models and systems medicine approaches (WP2)**, TAXINOMISIS disintegrates carotid artery **disease phenotypes into endotypes (WP2)**, **stratifies patients** according to the **underlying mechanism** driving the disease process rather than the level of stenosis (**WP3**) and provides more effective therapeutic interventions for carotid artery disease treatment. This takes into account common plaque and plasma **molecular phenotypes with individual's specific characteristics** in terms of transcriptomics, miRNAomics, proteomics, lipidomics and pharmacogenomics as well as imaging (MRI, CT and US) and clinical information.
- By developing **new risk stratification models (WP3)**, TAXINOMISIS will identify patients/patient groups in **high risk of cerebrovascular events** and assist clinical decision making. Finally, by providing a **lab-on-a-chip device (WP4)** for detecting multiple SNPs (pharmacogenomics markers) simultaneously, TAXINOMISIS will lead to the development of targeted therapies for carotid artery disease and **optimize medical treatment in a precise personalized manner**. This will **reduce unnecessary surgery** and hospitalizations, which are tormenting treatment of this highly prevalent disease, while opening up new avenues for the **development of disease mechanism based targeted interventions**.
- The novel TAXINOMISIS stratification concept is being evaluated in terms of accuracy and predictive ability in a real-time setting using information from an observational **clinical study during the project (WP5)**. The **cost-effectiveness** is also assessed (**WP6**). As the TAXINOMISIS is likely to significantly impact the current clinical practice, **regulatory analyses** on the implementation of the project's outputs constitutes an integral part of the project and involves key regulatory bodies and expert associations, such as the ESCVS (**WP6**). TAXINOMISIS has a strong translational focus and will therefore result in **strong research innovation opportunities**, which will be considered for commercialization and exploitation (**WP7**).



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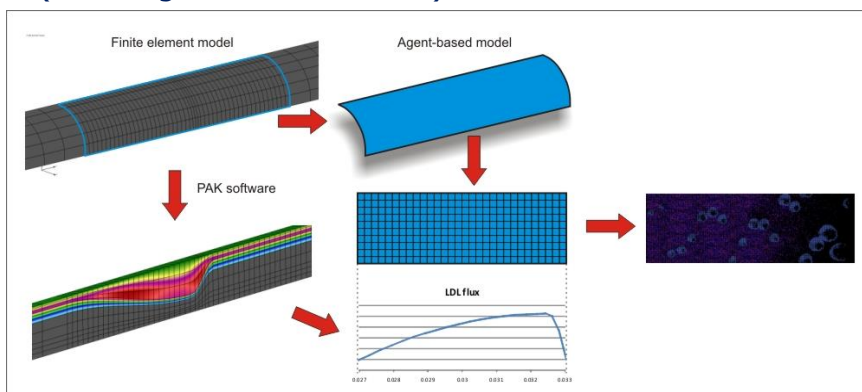


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## Project activities

- The conceptual framework of the TAXINOMISIS Risk Stratification Tool has been defined (WP3).
- Clinical and technical partners have worked together and four unresolved areas in the current standard of care have been selected in which TAXINOMISIS can contribute to improve risk stratification and management of carotid artery disease patients.
- The information flow of the Risk Stratification Tool has been defined and the overall system architecture and front-end mock-ups of the platform are being developed.
- Extensions of 3D carotid artery reconstruction and plaque characterization methodologies based on carotid MRI, CT and US imaging, have been developed and implemented in patients of the TAXINOMISIS prospective clinical study.
- Image quality control is being performed and a representative balanced sample of images capturing plaque tissue types is being created.
- Non-imaging based machine learning models are being developed and new progress has been made in blood flow and rupture modeling.
- Results from in-depth phenotypic analysis of carotid plaques performed during WP1 and WP2 provided important information, for cell populations and biological processes involved in plaque progression, which was incorporated in a new version of the computational plaque growth model.
- The Agent Based Model (ABM) of plaque progression includes modelling and simulations of changes in the geometry of the artery due to the cells' behaviors and plaque dynamics. A first version of the AMB of plaque progression has been developed. In addition, the integration of ABM with FEM will create a hybrid model more suitable to simulate the characteristic of the carotid artery disease dynamics governing the cells proliferations (including omics biomarkers).



An example of ABM and FEM coupling

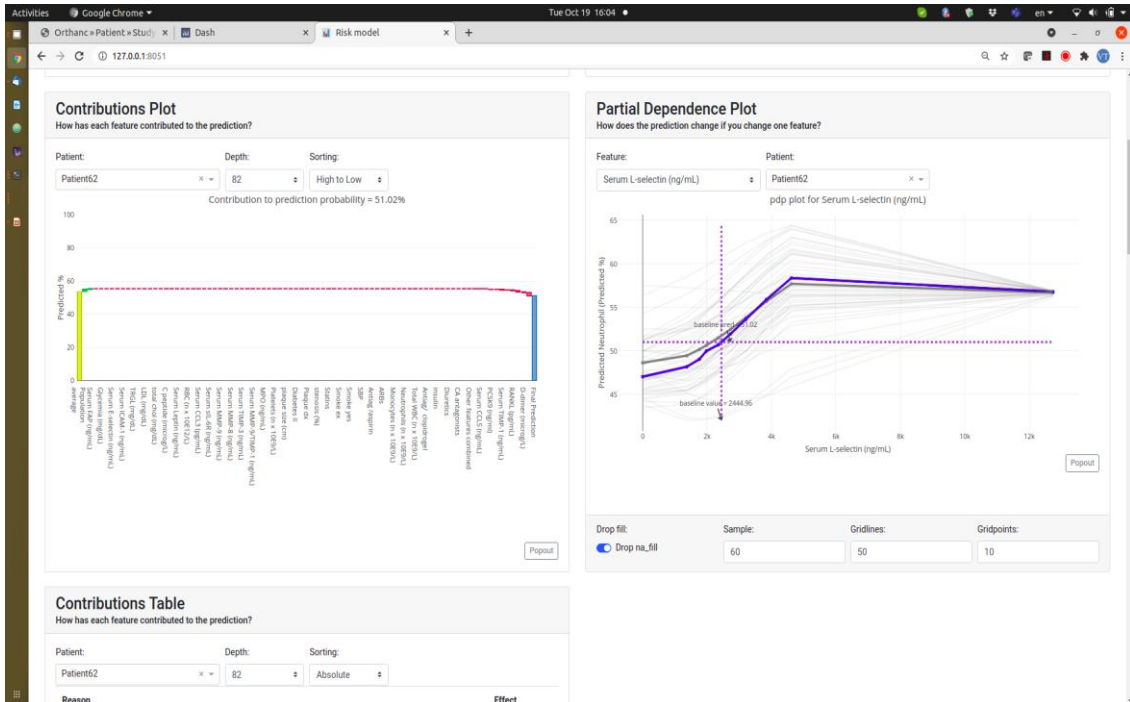
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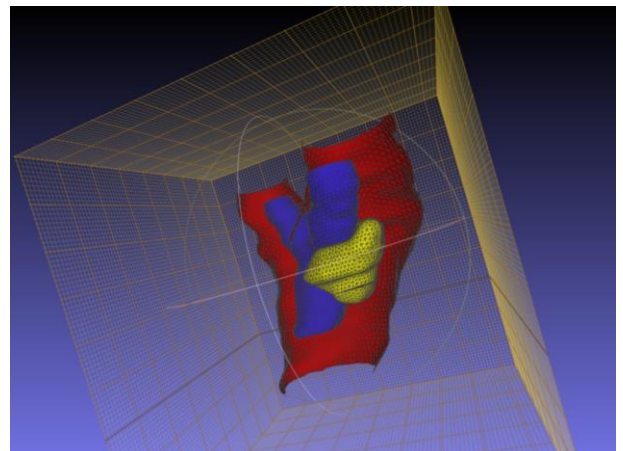
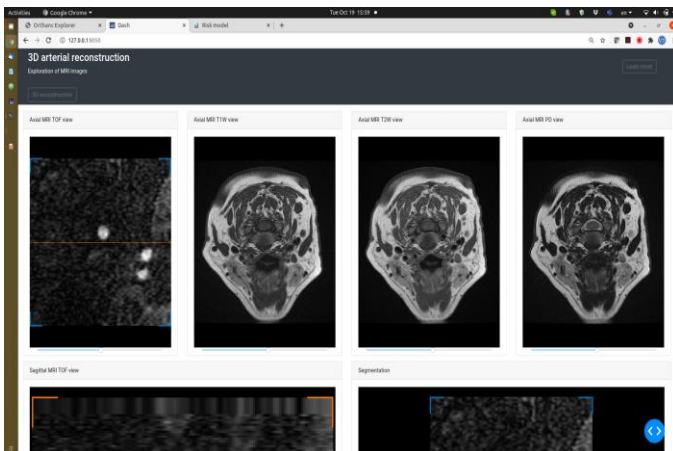
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## Project activities



**Taxinomis platform - Risk model**



**3D arterial reconstruction based on MRI**



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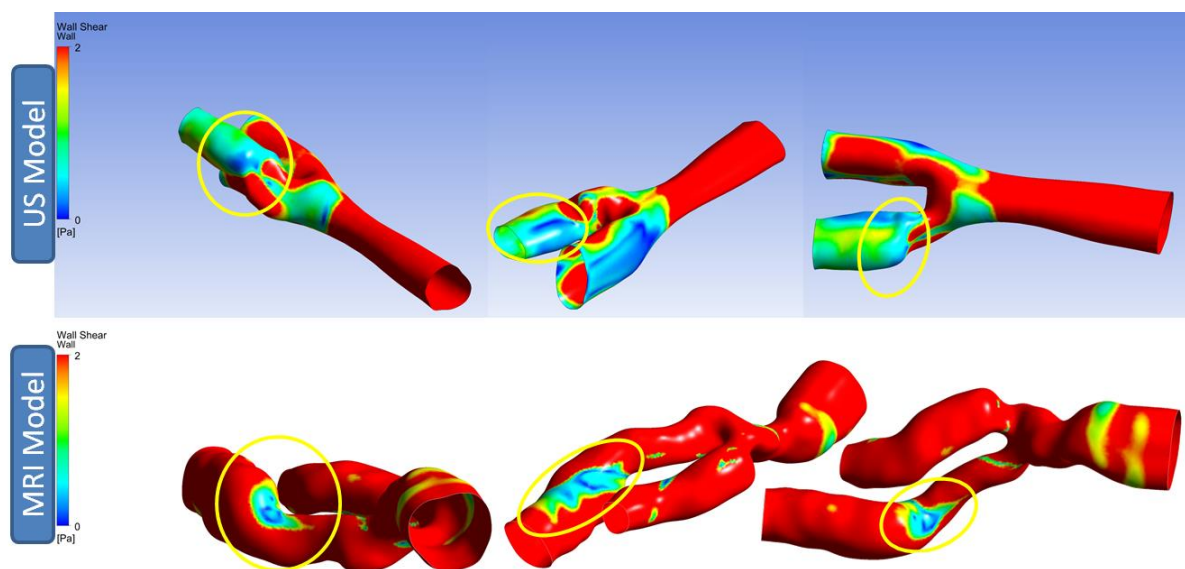
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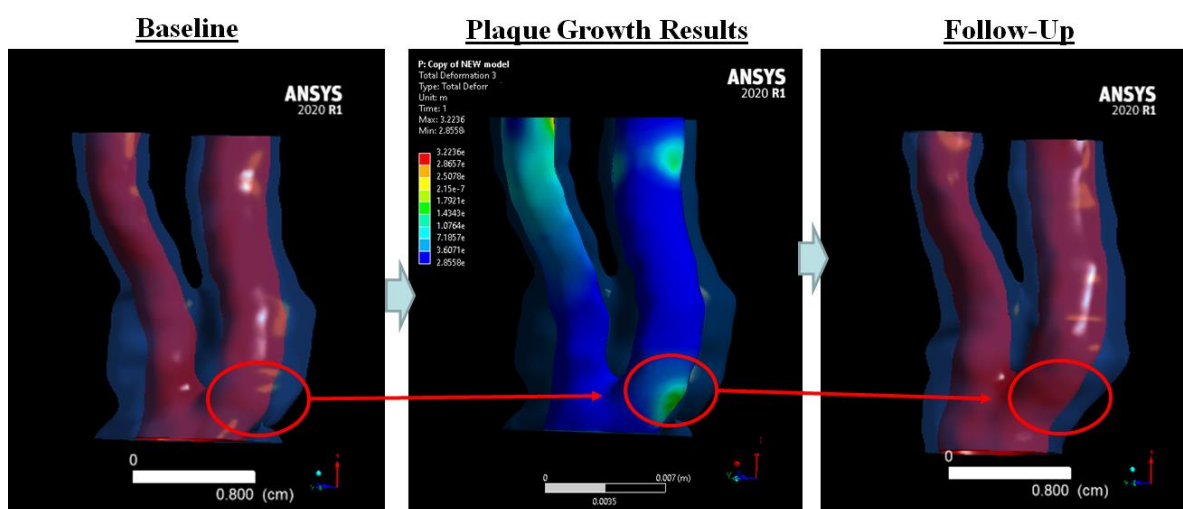
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## Project activities



## Comparative analysis of US and MRI models



## Computational simulation and analysis of plaque growth models



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## Consortium

TAXINOMISIS encompasses a highly multidisciplinary group of researchers with remarkable track record and complementarity from 12 world-leading institutions of clinical and research excellence, key medical and patients associations and 2 pioneering SMEs including:

- Medical experts
- Vascular surgeons
- Cardiologists
- Neurologists
- Biologists
- Software engineers
- Biomedical engineers
- Lab-on-a-chip experts
- Health research experts


TAXINOMISIS researchers are international leaders in their respective fields and have contributed to our current understanding of:

- the **clinical medicine surrounding carotid artery disease** (UMC, TUM, UBEO, USMI, FCRB, NKUA),
- the **molecular mechanisms** driving atherosclerosis in carotid and coronary arteries (UMC, TAUH, BRFAA, ZORA, USMI, UOXF),
- the **immuno-inflammatory processes involved** (UMC, BRFAA, USMI, UOXF, UBEO),
- the identification of **diagnostic markers and treatments** for cardiovascular disorders (TAUH, ZORA, IMEC, UMC, TUM, USMI, FCRB),
- the **development of new algorithms and simulation tools for atherosclerotic plaques and CVDs** (UOI, BIOIRC),
- the **development of risk prediction models** (UOI, BIOIRC),
- the design and production of **lab-on-a-chip devices** based on nanoelectronics (IMEC) and
- the provision of **retrospective data and cohorts** (NIVEL, TAUH, UMC).



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