MEDICAL TECHNOLOGY
Med & Lab
INTELLIGENT INFORMATION SYSTEMS

70th ESCVS
International congress of the European Society for Cardiovascular and Endovascular Surgery

7th IMAD meeting

A multidisciplinary approach for the stratification of patients with carotid artery disease

Risk Stratification Tool

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

Risk stratification Tool vision

Patient

Data Input

Circulating biomarkers

Lab-on-chip pharmacogenomics

Clinical

Imaging

MRI

CT

Ultrasound

Diagnostic & Prognostic models

1st Level (Primary care)
Imaging or not?
Non-imaging based models

Ultrasound

2nd Level (Secondary Care)
High Risk patients for MRI/CT?
Imaging (US) based models

Ultrasound

MRI

CT

3rd Level (Tertiary Care)
High Risk patients for CEA/CAS vs BMT?
Imaging (US, MRI, CT) based models

Optimal Time for next US screening?
Plaque evolution models (progression, stabilization, regression)
Plaque rupture models (Biomechanical stresses)

Risk Stratification Tool

Diagnostic Support
Patient stratification
Prognostic Support
Risk prediction and treatment outcome
Therapeutic Support
Treatment planning and optimisation

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Risk stratification models in the 3 levels of care

1st LEVEL (PRIMARY CARE) - Use of Non-Imaging Data

Clinical Decision		Diagnostic or Prognostic model to assist clinical decision
Imaging or NOT?	√	**Diagnostic** prediction of < 50% or > 50% Stenosis **(ML model)**
	√	**Diagnostic** prediction of vulnerable plaque components **(ML model)**
	√	**Diagnostic** prediction of Silent Brain Lesions (SBL) **(ML model)**
	√	**Evolution of** Brain Structural Changes **(ML model)**
	√	**Prognosis** of Cerebral outcomes/events (SBL, Stroke, TIA, AF) **(ML model)**

Compare US vs MRA Risk prediction

2nd LEVEL (SECONDARY CARE) - Use of US Imaging Data

Clinical Decision		Diagnostic or Prognostic model to assist clinical decision
Identify ASYMPTOMATIC PATIENTS with higher risk for stroke in whom to recommend further screening with MRA and/or CTA for potential intervention CEA/CAS **(Full exploitation of Duplex US imaging)**	√	**3D Reconstruction & Plaque characterisation model** (Geometry & plaque composition)
	√ *	**Plaque growth model** (Plaque progression geometry & composition)
	√ *	**Blood flow & rupture model** (Computation of biomechanical forces/ stresses)
	√	**Diagnostic** prediction of Silent Brain Lesions (SBL) **(ML model)**
	√	**Evolution** of Brain Structural Changes (ML model)
	√	**Prognosis** of Cerebral outcomes/events (SBL, Stroke, TIA, AF) **(ML model)**
	√	**Prognosis** of CVD events (MI, Aneyrism Rupture) **(ML model)**
	√	**Prognosis** of Post-Surgery MACE **(ML model)**

3rd LEVEL (TERTIARY CARE) - Use of US plus MRA (and/or CTA) Data

Clinical Decision		Diagnostic or Prognostic model to assist clinical decision
Identify ASYMPTOMATIC PATIENTS with higher risk for stroke in whom to target intervention CEA/CAS versus BMT **(Full exploitation of Duplex US plus MRA and/or CTA)**	√	**3D Reconstruction & Plaque characterisation model** (Geometry & plaque composition)
	√ *	**Plaque growth model** (Plaque progression geometry & composition)
	√ *	**Blood flow & rupture model** (Computation of biomechanical forces/ stresses)
	√	**Diagnostic** prediction of Silent Brain Lesions (SBL) **(ML model)**
	√	**Evolution of Brain Structural Changes (ML model)**
	√	**Prognosis** of Cerebral outcomes/events (SBL, Stroke, TIA, AF) **(ML model)**
	√	**Prognosis** of CVD events (MI, Aneyrism Rupture) **(ML model)**
	√	**Prognosis** of Post-Surgery MACE **(ML model)**

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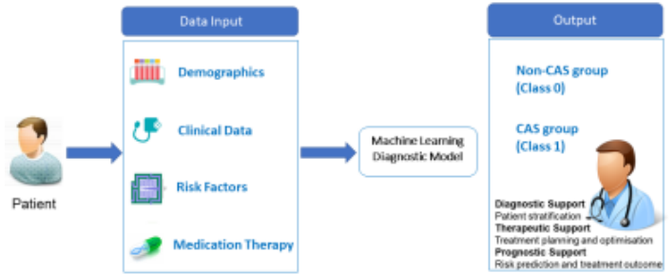
1st Level (Primary Care)

Diagnostic detection < 50% or > 50% Stenosis

Without Biomarkers

View #	Category	Features
View 1	Demographics	Age (years), Gender (male, female)
View 2	Clinical Data	Height (cm), Weight (kg), Body Mass Index (BMI) (kg/m^2)
View 3	Risk Factors	Smoking (Yes/No), Years of Smoking, Former Smoker (Yes/No), Alcohol Consumption (Yes/No),, Hyperlipoproteinemia (HLP) (Yes/No), Diabetes Mellitus (DM) (Yes/No), Hypertension (HTA) (Yes/No), Coronary Artery Disease (CAD) (Yes/No), Peripheral Arterial Occlusive Disease (PAOD) (Yes/No), PAOD Aortoiliac (Yes/No), Chronic Renal Disease (Yes/No), Aneurysm Disease (Yes/No),
View 4	Medication Therapy	Antiaggregant Therapy (Yes/No), Antihypertensive Therapy (Yes/No), Anticoagulant Therapy (Yes/No), Statin Therapy (Yes/No)

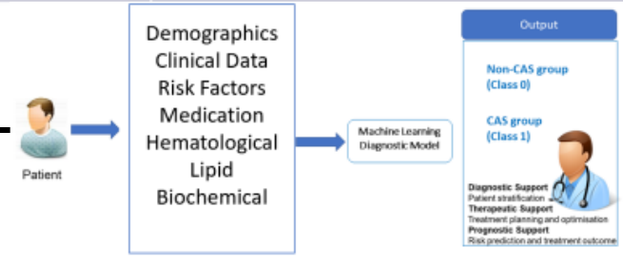


	Case 1		Case 2		Case 3		Case 4	
	Acc.	AUC	Acc.	AUC	Acc.	AUC	Acc.	AUC
J48	0.73	0.78	0.77	0.78	0.77	0.78	0.77	0.78
RF	0.75	0.81	0.8	0.88	**0.81**	**0.88**	0.81	0.88
NB	0.69	0.82	0.71	0.84	0.71	0.84	0.71	0.84
SVM	0.74	0.74	0.79	0.79	0.79	0.79	0.79	0.79
ANN	0.78	0.84	0.77	0.84	0.78	0.84	0.77	0.84
	Case 5		**Case 6**		**Case 7**		**Case 8**	
	Acc.	AUC	Acc.	AUC	Acc.	AUC	Acc.	AUC
J48	0.77	0.78	0.77	0.78	0.74	0.74	0.77	0.78
RF	0.8	0.88	0.81	0.88	0.8	0.87	0.82	0.9
NB	0.71	0.84	0.71	0.84	0.78	0.86	0.71	0.84
SVM	0.79	0.70	0.79	0.79	0.78	0.78	0.79	0.79
ANN	0.76	0.84	0.79	0.84	0.77	0.84	0.78	0.86

Kigka V. *et al.,* Detection of Asymptomatic Carotid Artery Stenosis through Machine Learning , EMBC 2022.

With Biomarkers

INPUT	
Clinical Characteristics & Risk Factors	Examination date, Gender, Age, Education, Height , Weight, BMI kg/m2 (19%), Asymptomatic , TIA, reversible ischemic neurological deficit (RIND), Chronic venous insufficiency (CVI) ,VB, HLP, Diabetes Mellitus (DM), HTA (2%), Smoking yes/no, Smoking years, Former smoker (12%), Alcohol consumption , Coronary disease, PAOD, PAOD Aortoiliac, Chronic renal disease, Aneurysm disease
Medication Therapy	Antagregant therapy, Antyhypertensive therapy, Anticoagulant therapy, Statin
Hematological Features	Hb g/L, WBC 109/ L, RBC 1012/ L, PLT 109/ L, HGB g/L PT S, PTT S, INR
Lipid Biomarkers	Glukoza_mmol/L, S-Holesterol mmol/L, S-HDL mmol/L, S-LDL mmol/L, S-Trigliceridi mol/L
Biochemic Features	Urea_mmol/L, Kreatinin_?mol/L, Mokracna kiselina_?mol/L, Uk.biliribin_?mol/L, S-Direktni Bilirubin/?mol/L, S-Totalni Proteini g/L, S-Albumin g/L, S-Hloridi mol/l, S-K mol/L, S-Na mol/L, S-LDH U/L, S-CRP mg/L, S-AST U/L, S-ALT U/L, P-Fibrinogen g/L I, Vrednost, P-D- dimer µg/L, P-Antitrombin III g/L



Classifiers	Accuracy	AUC	Sensitivity	Specificity	PPV	NPV
Random Forest	0.89	0.95	0.878378	0.886364	0.928571	0.8125
J48	0.88	0.92	0.888889	0.869565	0.914286	0.833333
Logistic model tree	0.89	0.96	0.952381	0.818182	0.857143	0.9375
Logistic regression	0.87	0.94	0.892857	0.807692	0.833333	0.875
SVM	0.89	0.9	0.925373	0.843137	0.885714	0.895833
ANN	0.89	0.95	0.913043	0.857143	0.9	0.875

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1st Level (Primary Care)

Diagnostic prediction of vulnerable plaque components

Input

View # 1	Demographics
View #2	Clinical characteristics
View #3	Medication therapy
View #4	Hematologic Features
View #5	Lipid Biomarkers
View #6	Inflammatory Biomarkers
View #7	Matrix degrading or proteolysis Biomarkers
View #8	Endothelial and cell adhesion Biomarkers
View #9	Metabolic Biomarkers

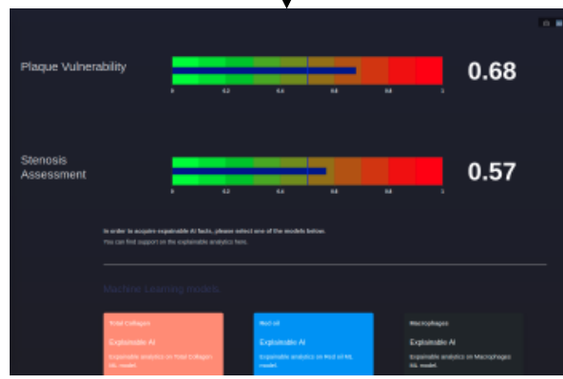
Output (histology based features)

Subproblem # 1	Lipid
Subproblem #2	Macrophages
Subproblem #3	Smooth Muscle Cells
Subproblem #4	Total Collagen
Subproblem #5	Collagen I
Subproblem#6	Neutrophils

Plaque vulnerability risk score

Low risk plaques | High risk plaques

Imaging or NOT?



Diagnostic prediction of silent brain lesions

Input

Ecrf dataset	
View # 1	Demographics
View #2	Clinical characteristics
View #3	Medical History
View #4	Medication therapy
View #5	Hematologic Features
View #6	Lipid Biomarkers
View #7	Inflammatory
View #8	Biochemics

Machine Learning based model

Output (based on Brain MRI analysis) **Silent Brain Lesion**

- No Silent Brain Lesions **84 cases**
- Silent Brain Lesions **33 cases**

- These types of lesions are not correlated with symptomatic patients (previous stroke, TIA)
- These lesions may be in a FU step as cerebral events
- Clinical doctors try to identify only the lesion caused by carotid territory

Kigka V. *et al.*, A Machine Learning Model for the Identification of High Risk Carotid Atherosclerotic Plaques, EMBC 2021.

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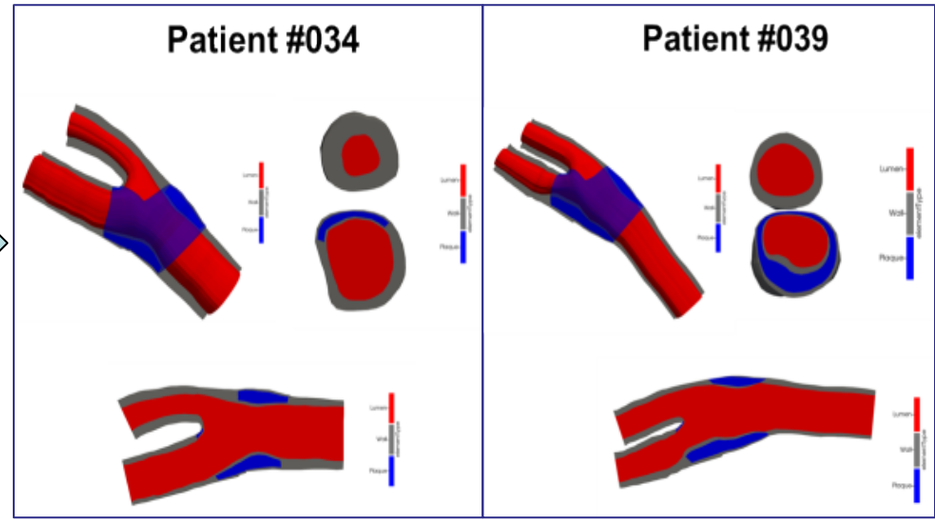
Risk Stratification Tool (Levels 2-3)

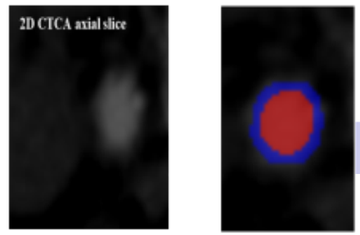
3D Reconstruction from US

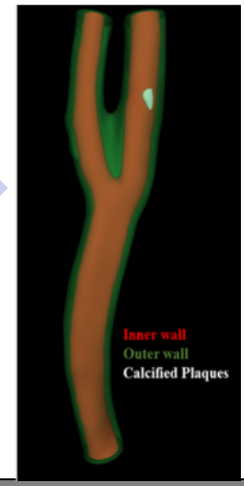


3D reconstruction of carotid artery and plaque using CT

Lumen & Outer Wall Segmentation

- Main Idea: Implementation of an extension of the active contour models[1] that incorporates a prior shape[2], aiming to segment an object whose shape is similar to the given prior shape (tubular mask for the lumen, segmented lumen for the outer wall)





1) Update of lumen intensities → 2)Approximation of an initial binary image → 3) Calculation of the speed function → 4)Implementation of Sparse Field Algorithm

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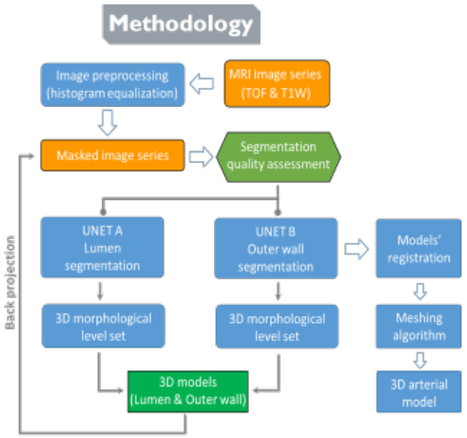
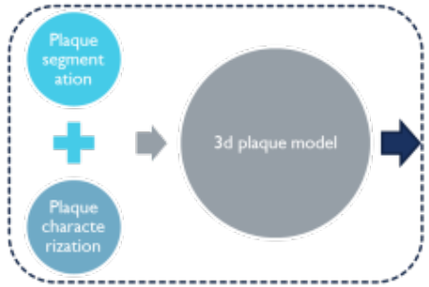
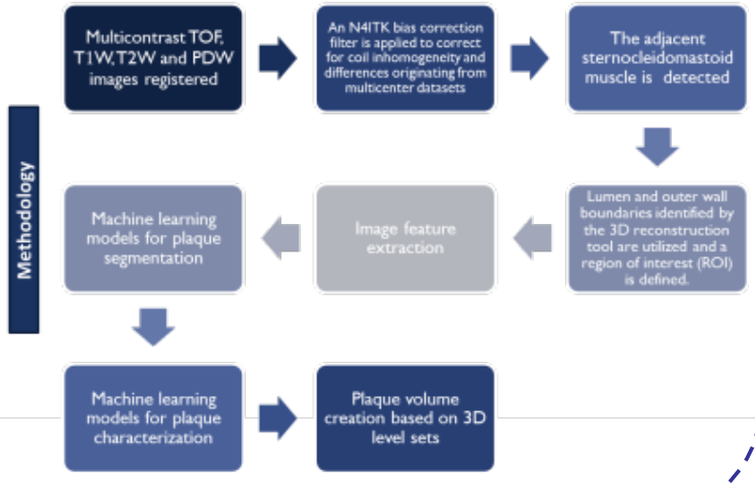
Risk Stratification Tool (Levels 2-3)

3D reconstruction of carotid artery using MRI



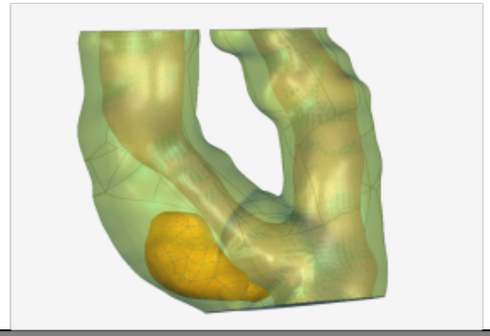


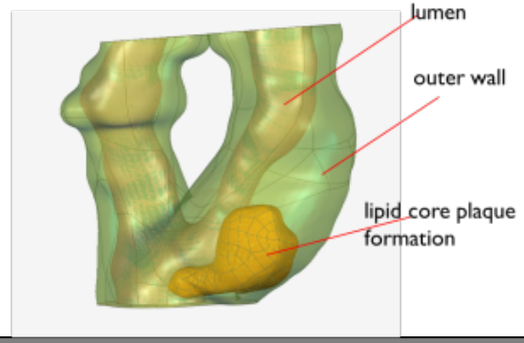
Plaque Characterization based on MRI

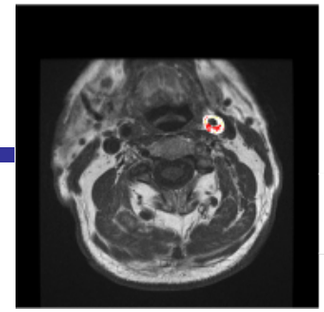


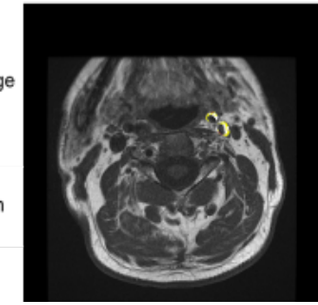
Plaque types

- lipid core
- fibrosis
- calcification
- hemorrhage
- fibrous cap









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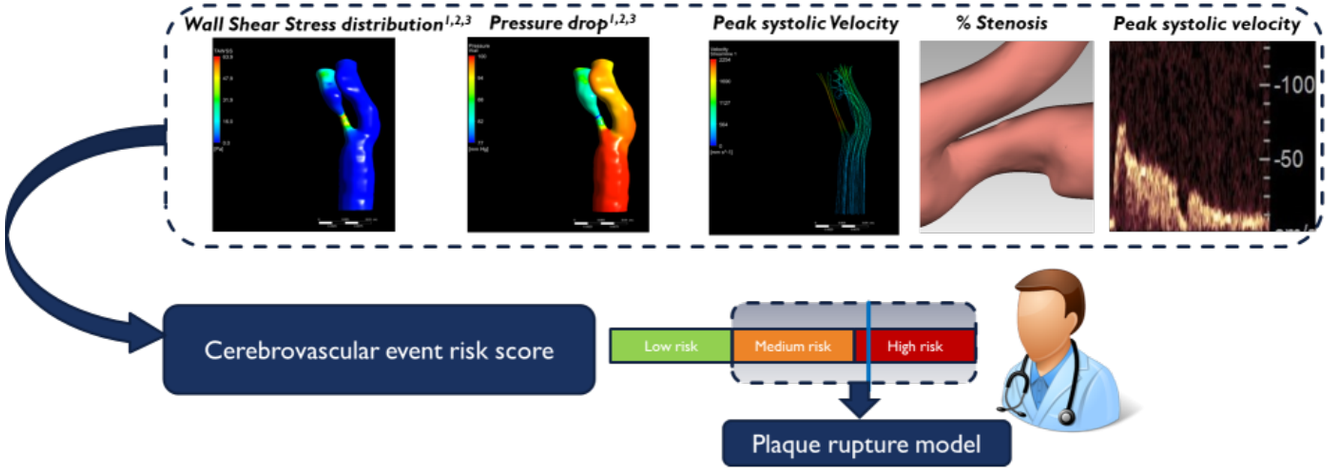
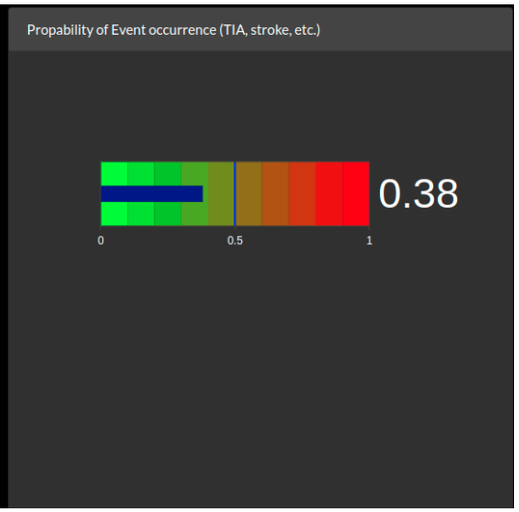
Risk Stratification Tool (Levels 2-3)

Blood flow modelling (model I)

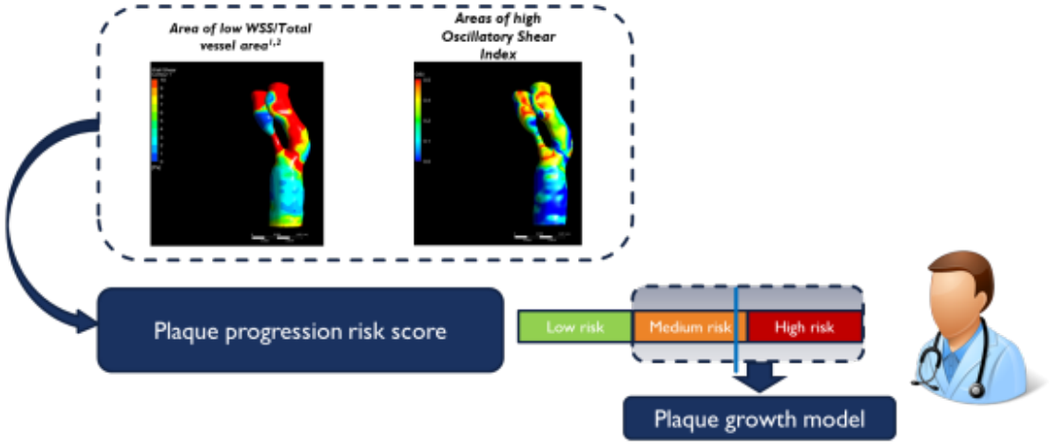


Blood flow metrics

parameter	value
peak TAWSS (Pa)	35
Pica/Pcca	0.98
Peca/Pcca	0.99
Vessel average TAWSS (Pa)	5.7
PSV (m/s)	0.125
ICA Stenosis (%)	50
ECA Stenosis (%)	10
Maximum Plaque Structural Stress (kPa)	74
Thin Fibrous Cap (0/1)	0
Plaque Burden (%)	45
Stenosis (%)	50

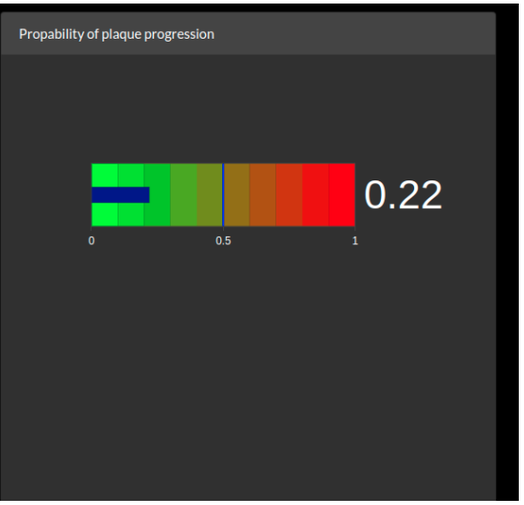


Blood flow modelling (model II)



Blood flow mentrics

parameter	value
Area of low TAWSS (mm2)	53
Area of low TAWSS/Total vessel area (%)	8.1
Area of high OSI (mm2)	110
Area of high OSI/Total vessel area (%)	17



[1]L. Zouggari, "The Role of Biomechanics in the Assessment of Carotid Atherosclerosis Severity: A Numerical Approach OPEN ACCESS," vol. 1, 03/16 2018
[2]P. Xu et al., "Assessment of boundary conditions for CFD simulation in human carotid artery," Biomech Model Mechanobiol, vol. 17, no. 6, pp. 1581-1597, Dec 2018
[3]U. Morbiducci et al., "On the importance of blood rheology for bulk flow in hemodynamic models of the carotid bifurcation," Journal of biomechanics, vol. 44, pp. 2427-38, 09/02 2011.

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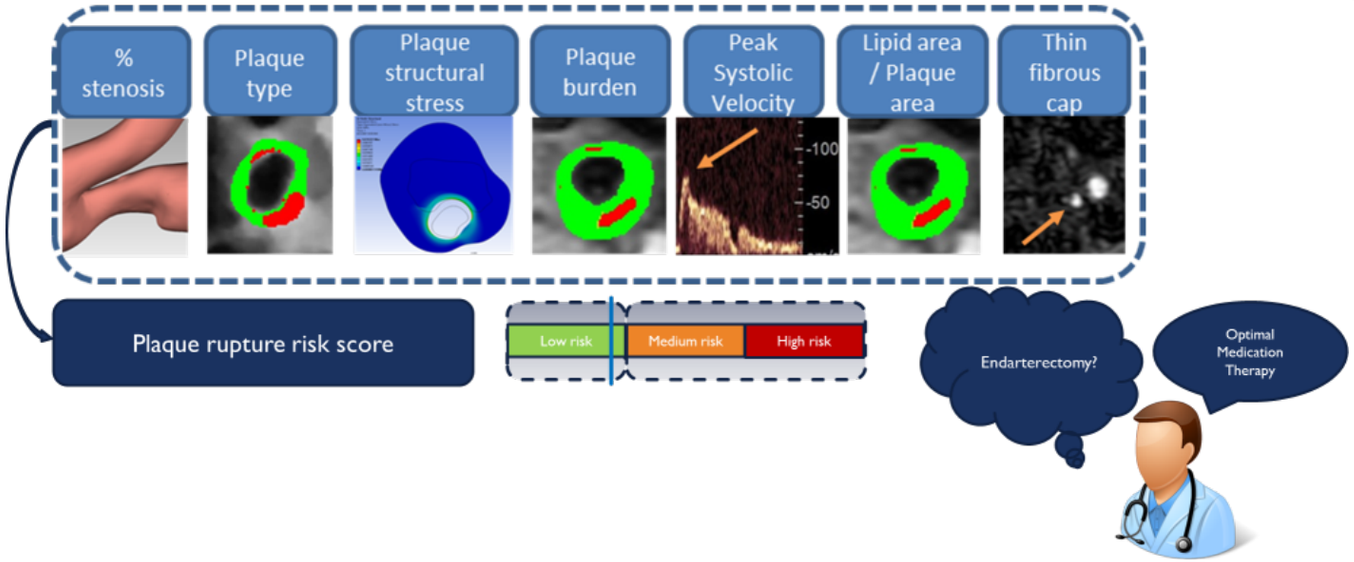
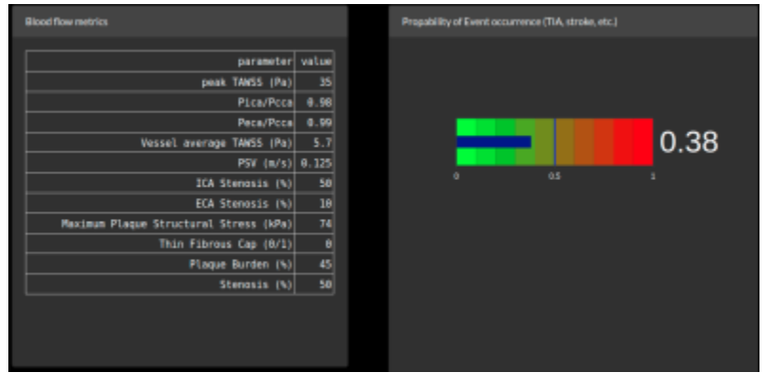
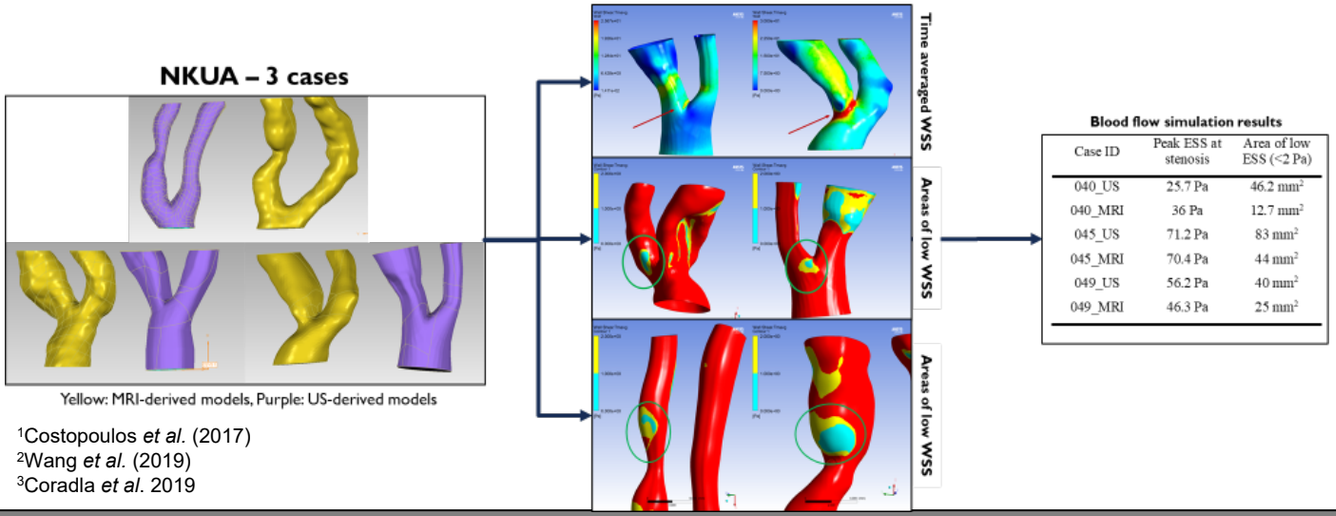
Risk Stratification Tool (Levels 2-3)

Plaque rupture modelling





MRI VS. Ultrasound modelling



[1]Costopoulos *et al.* (2017)
[2]Wang *et al.* (2019)
[3]Coradla *et al.* 2019

Blood flow simulation results

Case ID	Peak ESS at stenosis	Area of low ESS (<2 Pa)
040_US	25.7 Pa	46.2 mm^2
040_MRI	36 Pa	12.7 mm^2
045_US	71.2 Pa	83 mm^2
045_MRI	70.4 Pa	44 mm^2
049_US	56.2 Pa	40 mm^2
049_MRI	46.3 Pa	25 mm^2

- Proof-of-concept study which tries to provide a comparison between MRI-based and US-based 3D carotid arterial models for three patients with a >50% degree of stenosis.
- The areas of low WSS matched the two models in terms of location.
- The same trend was observed for the location of the peak WSS values, which were generally present either at the throat of the existing stenoses or at the bifurcation site.

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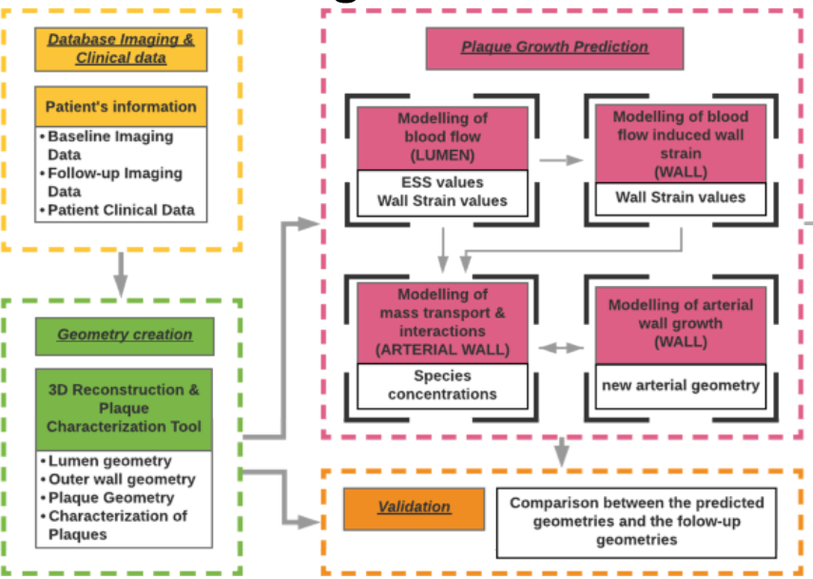
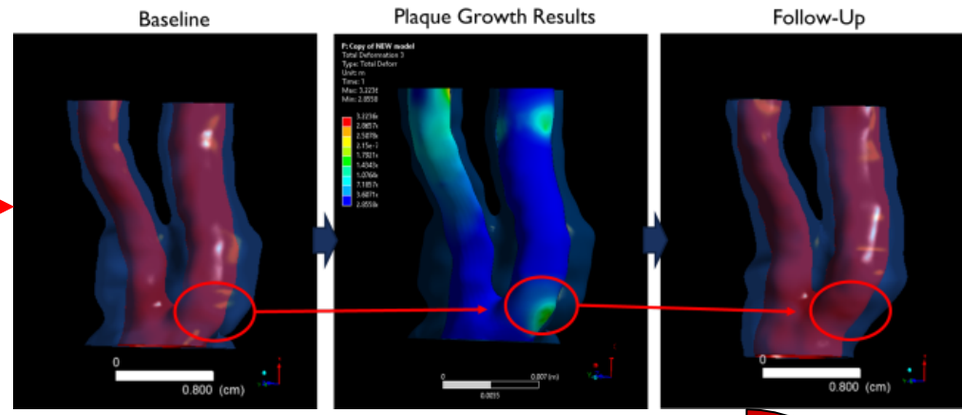
Risk Stratification Tool (Levels 2-3)

Plaque growth modelling Workflow



Results

- Prediction of the arterial geometry over time
- Prediction of species concentrations over time
- Prediction of plaque generation and growth over time
- Prediction of any restenosis
- Prediction of plaque vulnerability



Plaque growth risk score

Low risk | Medium risk | High risk

Optimal time for next US screening

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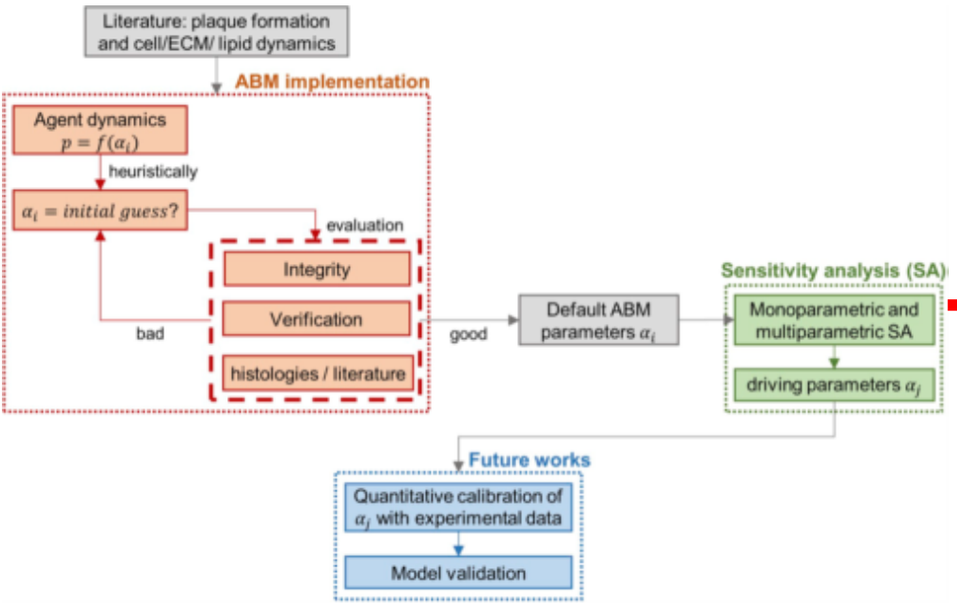
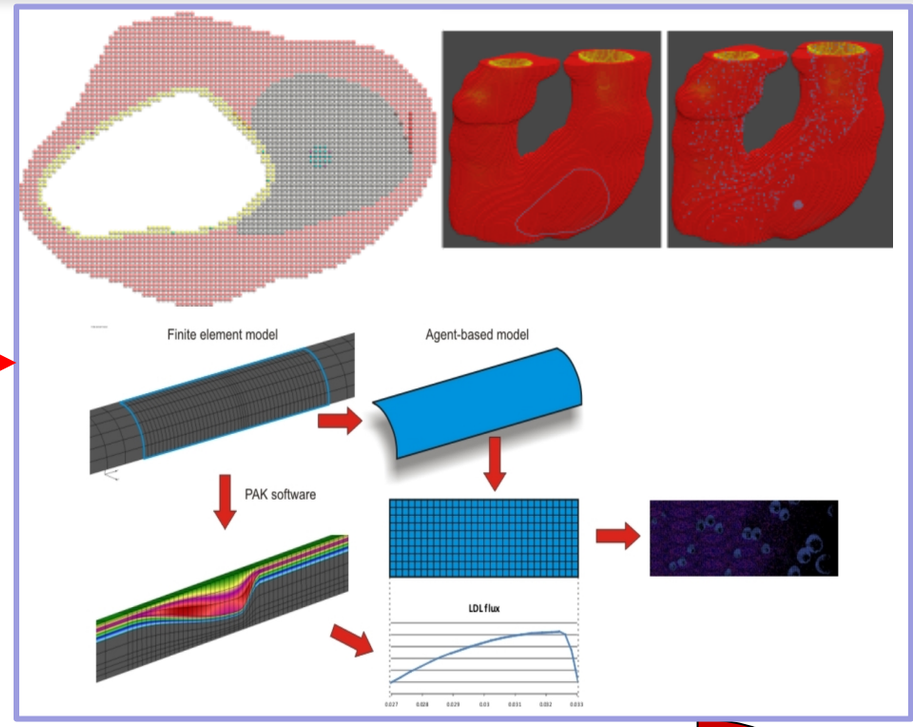
Risk Stratification Tool (Levels 2-3)

Plaque growth modelling via Agent Based Modelling Workflow





Plaque growth (ABM) risk score

Low risk | Medium risk | High risk

Optimal time for next US screening

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Thank you for your attention

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https://taxinomisis-project.eu/

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