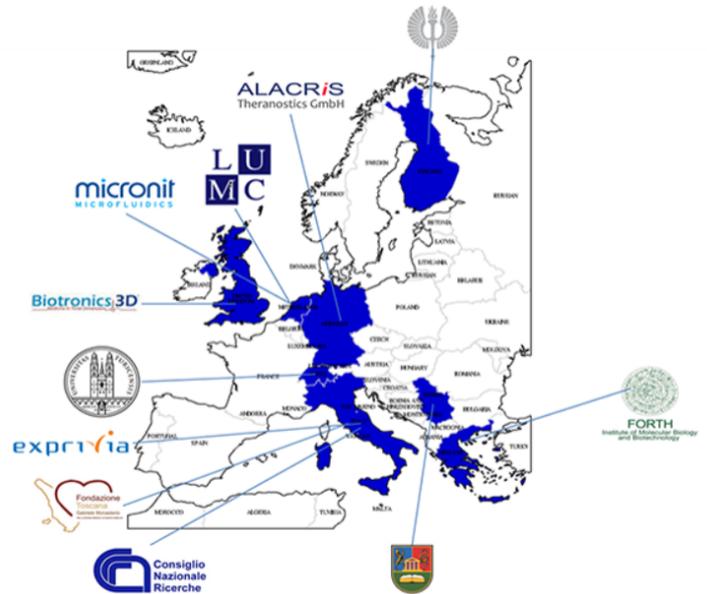


The best treatment of cardiovascular disease is to prevent the disease progression and predict future events

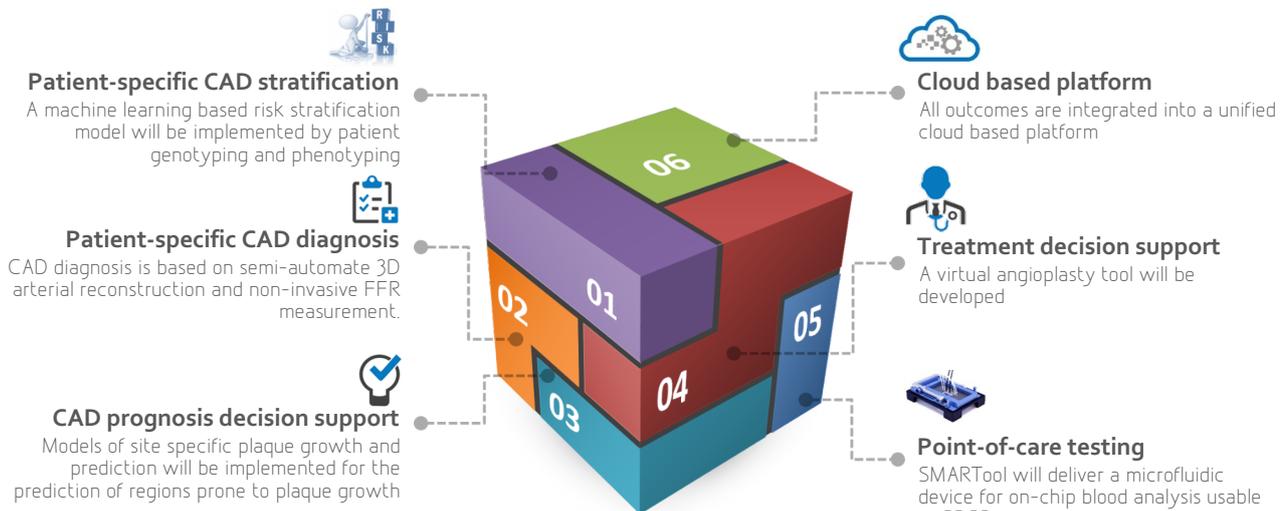
Number 4 - August 2018

SMART-er diagnostics in cardiology

The project "Simulation of coronary heart disease: a support tool for clinical decisions: SMARTool" (Grant Agreement No. 689068), funded by the European Commission under the Horizon 2020 Program and coordinated by the National Research Council - has just concluded. Institute of Clinical Physiology (CNR - IFC) of Pisa, developed a platform, based on artificial intelligence and cloud technology, for the management of patients with coronary heart disease by standardising and integrating heterogeneous clinical data. The platform includes a series of multiscale and multilevel models of coronary plaque characterisation and progression based on non-invasive coronary CT angiography (CCTA) [1-3] Integrated with data of various patient-specific nature (symptoms, risk factors, lifestyle, blood tests, genetic data, lipid profile) and processed by AI algorithms.



The project involved 10 public and private partners, specialised in clinical and scientific research from 9 European countries, and 4 clinical support centres for the collection of clinical data that worked closely for three and a half years, involving doctors, biologists, chemists, computer scientists and engineers.



Atherosclerosis is the pathology underlying coronary artery disease (CAD), a significant cause of morbidity and mortality, with a cost to the EU of almost 196 billion euros a year; its clinical and associated manifestations range from stable angina to acute events such as heart attacks and sudden coronary death. Local factors (high-risk plaques) and individual systemic biohumoral factors (inflammatory/thrombogenic/lipid profile and genetic profile) contribute to the development and progression of CAD.

The main reasons for the low efficacy of most of the strategies for preventing acute complications of CAD are linked both to the poor prognostic value of classic risk factors alone and to the difficulty of identifying the "high risk" plaques. The occlusive artery thrombosis and the onset of the acute ischemic coronary event could probably be triggered by the combination of local complications at plaque level (rupture, erosion, etc.) and systemic alterations with elevated blood levels of inflammatory molecules and/or thrombogenesis. The complexity of these processes and the number of factors involved explains why statistical risk models often fail in investigating and predicting the evolution of the disease.



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 689068



newsletter

The best treatment of cardiovascular disease is to prevent the disease progression and predict future events

Number 4 – August 2019

In a vision of e-Health 2.0, supported by advanced computer systems optimized on artificial intelligence (IA), a possible strategy is to create a predictive model of severity and progression of the plaque that integrates, in a single platform, all the local and systemic factors of the individual patient, from parameters with complex statistical models, valid in a population with different degrees of severity and progression of the disease and frequency of events. This platform could be used as a tool to support clinical decision-making for risk stratification, diagnosis, prognosis and treatment of patients with coronary artery disease.

The project confirmed that the concentration in the blood of inflammatory molecules such as Interleukin-6, equal to twice the value compared to healthy subjects, is associated with a higher risk of disease progression over time [4], while a low plasma concentration of leptin, a hormone involved in the regulation of the energy balance, with a reduction up to 50% of the value compared to the control group, is directly linked to the severity of the disease [5]. The advanced analysis of the lipid profile in the blood also revealed a series of lipid classes associated with the presence and severity of the disease.

References

- [1] Siogkas PK, Anagnostopoulos CD, Liga R, Exarchos TP, Sakellarios AI, Rigas G, Scholte AJHA, Papafaklis MI, Loggitsi D, Pelosi G, Parodi O, Maaniitty T, Michalis LK, Knuuti J, Neglia D, Fotiadis DI. Noninvasive CT-based hemodynamic assessment of coronary lesions derived from fast computational analysis: a comparison against fractional flow reserve. *Eur Radiol.* 2019 Apr;29(4):2117-2126.
- [2] Kigka VI, Rigas G, Sakellarios A, Siogkas P, Andrikos IO, Exarchos TP, Loggitsi D, Anagnostopoulos CD, Michalis LK, Neglia D, Pelosi G, Parodi O, Fotiadis DI. 3D reconstruction of coronary arteries and atherosclerotic plaques based on computed tomography angiography images. *Biomedical Signal Processing and Control* 2018 Feb;4(0):286–294.
- [3] Djukic T, Saveljic I, Pelosi G, Parodi O, Filipovic N. Numerical simulation of stent deployment within patient-specific artery and its validation against clinical data. *Comput Methods Programs Biomed.* 2019 Jul;175:121-127.
- [4] Caselli C, Rocchiccioli S, Rosendael A, Buechel R, Teresinska A, Pizzi MN, Smit JM, Magnacca M, Del Ry S, Vozzi F, Knuuti J, Pelosi G, Parodi O, Scholte A, Neglia D. Biohumoral predictors of coronary atherosclerosis progression in patients with suspected coronary artery disease from the SMARTool Study, Congress of European Society of Cardiology ESC 2018, Munich, Germany
- [5] Caselli C, Rocchiccioli S, Rosendael A, Buechel R, Teresinska A, Pizzi N, Smit JM, Poddighe R, Del Ry S, Vozzi F, Knuuti J, Pelosi G, Parodi O, Scholte A, Neglia D. Low leptin plasma levels are associated with progression of coronary atherosclerosis in patients with stable coronary artery disease from the SMARTool Study, Congress of European Society of Cardiology ESC 2019, Paris, France

The analysis of the expression of circulating RNAs is allowed to identify a series of genes, involved in the mechanisms of apoptosis, metabolism, immune response and hematopoiesis, associated with the presence / severity of CAD and is allowed to use an innovative diagnostic algorithm for the calculation of the risk score with an accuracy of 80% [5]. Moreover, thanks to the use of CCTA, it was possible to highlight how non-calcified plaques present a more significant progression of the volume over time compared to those calculations, demonstrating that hypertension is a risk factor for plaque progression and that finally statins, drug used to control cholesterol levels in the blood, stabilize the plaques, favouring their calcification [6].

"The ultimate goal of the project is to provide the cardiologist with a system capable of helping him in identifying as accurately as possible the subject really at risk of adverse clinical events such as heart attacks" [7] declares the project coordinator, Dr. Silvia Rocchiccioli, "favoring both a better treatment of the patient in terms of effective care, and making the diagnosis system more efficient with a significant reduction in costs for health systems in EU countries".

[6] Smit JM, Van Rosendael AR, Barbon F, Neglia D, Knuuti J, Buechel R, Teresinska A, Pizzi MN, Poddighe R, Caselli C, Rocchiccioli S, Parodi O, Pelosi G, Scholte AJ. Quantitative CTA analysis of coronary plaque progression in SMARTool clinical study: the association between baseline clinical parameters and plaque progression, Congress of European Society of Cardiology ESC 2018, Munich, Germany

[7] Sakellarios A, Siogkas P, Georga E, Tachos N, Kigka V, Tsompou P, Andrikos I, Karanasiou GS, Rocchiccioli S, Correia J, Pelosi G, Stofella P, Filipovic N, Parodi O, Fotiadis DI. A Clinical Decision Support Platform for the Risk Stratification, Diagnosis, and Prediction of Coronary Artery Disease Evolution. *Conf Proc IEEE Eng Med Biol Soc.* 2018 Jul;2018:4556-4559.

S(ocial)MARTool

To keep updated on SMARTool activities and progress, visit our website or follow our Facebook, Twitter and LinkedIn pages



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 689068