MAESTRIA

Deliverable 2.2

MAESTRIA AF Ablation 1st study subject approvals package

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HORIZON 2020 – RIA programme
Digital diagnostics – developing tools for supporting clinical decisions by integrating various diagnostic data

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Abstract

Atrial fibrillation (AF) and stroke are major health care problems in Europe. They are most often the clinical expression of atrial cardiomyopathy, which is under-recognised due to the lack of specific diagnostic tools. Multidisciplinary research and stratified approaches are urgently needed to prevent, diagnose, and treat AF and stroke and preempt the AF-related threat to healthy ageing in Europe. MAESTRIA is a European consortium of 18 clinicians, scientists and Pharma industrials who are at the forefront of research and medical care of AF and stroke patients. It will create multi-parametric digital tools based on a new generation of biomarkers that integrate artificial intelligence (AI) processing and big data from cutting edge imaging, electrocardiography and omics technologies. It will develop novel biomarkers, diagnostic tools and personalized therapies for atrial cardiomyopathy. Digital Twin technologies, a rich data integrator combining biophysics and AI will be used to generate virtual twins of the human atria using patient-specific data. Unique experimental large-animal models, ongoing patient cohorts and a prospective MAESTRIA cohort of patients will provide rigorous validation for new biomarkers and newly developed tools. A dedicated core lab will collect and homogenize clinical data. MAESTRIA will be organized as a user-centered platform, easily accessible via clinical parameters routinely used in European hospitals. A Scientific Advisory Board comprising potential clinician users will help MAESTRIA meet clinical and market needs. Dissemination and visibility of the MAESTRIA consortium mission will benefit from participation of the German Competence Network on Atrial Fibrillation (AFNET), and support from the European Society of Cardiology, clinicians, scientists, and other professional societies. MAESTRIA will be ready to tackle the major challenges of data integration and personalized medicine focused on atrial cardiomyopathy, AF and stroke.

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1. Introduction

The MAESTRIA (Machine learning and artificial intelligence for early detection of stroke and atrial fibrillation) project is an 18-partner Research and Innovation action (RIA) with the objective of developing and validating the first integrative diagnostic digital platform for atrial cardiomyopathy diagnosis. This platform will be designed to provide support for improved diagnostic accuracy that increases effectiveness and efficiency of treatments, as well as prevention of the complications of atrial cardiomyopathy, such as atrial fibrillation and stroke.

The main goals of WP2 is to use electrophysiological parameters as biomarkers to rigorously determine the complexity and progression of human atrial cardiomyopathy from early to advanced stages of atrial remodelling. Such parameters do not necessarily correlate with current simplistic classification in paroxysmal vs persistent atrial fibrillation but are likely to have important therapeutic implications. The WP will develop strategies to correlate various electrophysiological read-outs with genetic, molecular, cellular and organ-level mechanisms underlying AF.

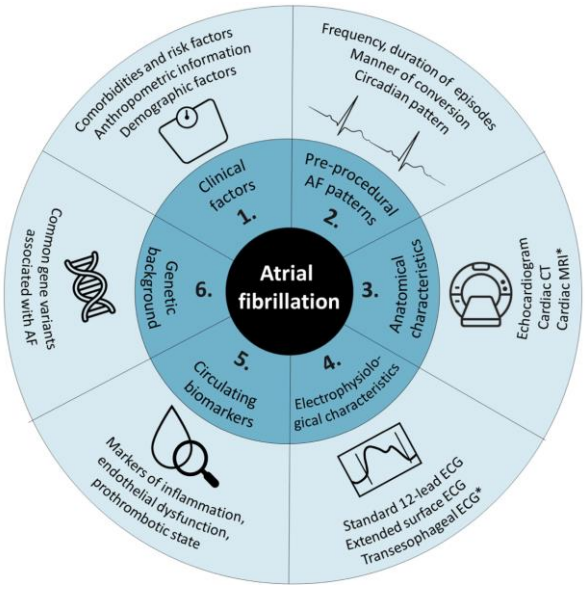
Deliverable 2.2 provides the legal basis, particularly the ethical approval for the collection of data in the AF ablation registry at Maastricht University. In the application this activity is referred to as ‘MAESTRIA AF ablation study’. Maastricht University is running a AF ablation registry called ‘ISOLATION’ since 2019. This registry will serve as source for both prospective and retrospective collection of the data to be used within MAESTRIA. In Feb 2023 ethical approval of an updated version of Isolation (called Isolation 2.0) was obtained with 1950 patients to be included in the next 5 years.

2. Progress of work and achievements

As stated above, the AF ablation registry 'ISOLATION' currently run at Maastricht University will serve as source of data on bothe the retrospective as well as prospective part of the 'MAESTRIA AF ablation study'. ISOLATION was initiated in 2019. Ethical approval for ISOLATION was already obtained in 2019, the respective documentation has been forwarded to the project coordinator and was included in the relevant reports on ethical aspects of MAESTRIA.

Design and Objectives of ISOLATION:

Continuous progress in atrial fibrillation (AF) ablation techniques has led to an increasing number of procedures with improved outcome. However, about 30–50% of patients still experience recurrences within 1 year after their ablation. Comprehensive translational research approaches integrated in clinical care pathways may improve our understanding of the complex pathophysiology of AF and improve patient selection for AF ablation. Within the "IntenSive mOlecular and eLectropathological chAracterization of patienTs undergoIng atrial fibrillatiOn ablatioN" (ISOLATION) study, we aim to identify predictors of successful AF ablation in the following domains: (1) clinical factors, (2) AF patterns, (3) anatomical characteristics, (4) electrophysiological characteristics, (5) circulating biomarkers, and (6) genetic background.



The 6 domains of interest in which predictors for successful atrial fibrillation ablation are sought: (1) clinical risk factors, (2) pre-procedural AF patterns, (3) anatomical characteristics, (4) electrophysiological characteristics, (5) circulating biomarkers, and (6) genetic background. AF, atrial fibrillation; CT, computed tomography; ECG, electrocardiogram; MRI, magnetic resonance imaging. Study procedures with an asterisk are conducted for a subset of patients.

ISOLATION (NCT04342312) is a prospective cohort study including 650 patients undergoing AF ablation. Clinical characteristics and routine clinical test results will be collected, as well as results from the following additional diagnostics: determination of body composition, pre-procedural rhythm monitoring, extended surface electrocardiogram, biomarker testing, genetic analysis, and questionnaires. A

multimodality model including a combination of established predictors and novel techniques will be developed to predict ablation success. In this study, several domains will be examined to identify predictors of successful AF ablation. The results may be used to improve patient selection for invasive AF management and to tailor treatment decisions to individual patients.

Current status of ISOLATION

As of September 2021 (first version of deliverable report D 2.2), 350 patients were included, with an inclusion rate of 15 to 20 patients per week. In January 2023, the maximal number of patients to be included of 650 was reached, a couple of months earlier than anticipated. In March (this update of the delioverable report), 321 out of 650 have reached one year follow-up. First crossectional studies on biomarkers and prediction models have been calculated and the respective abstracts will be presented at annual congresses of the European Heart Rhythm Association and the Heart Rhythm Society.

Continuation of the AF ablation programme through ISOLATION 2.0

In order to be able to continue patient enrolement a follow-up version of ISOLATION (called ISOLATION 2.0) was initiated. In Feb 2023 ethical approval for ISOLATION 2.0 was obtained. The approval is forwarded to the project coordinator together withis this updated deliverable report. The over-all design of ISOLATION 2.0 does not differ from ISOLATION. However, the power analysis has been reformulated so that 1950 patients can be enrolled during the next 5 years. Also, data transfer to other partners sites of MAESTRIA is now far easier because data sharing is included in the Patient Informed Consent Form.

D2.2 can be regarded as being finalized.