

Title: Metrology of automated data analysis for cardiac arrhythmia management

Abstract

Cardiovascular disease (CVD) is the most significant non-communicable disease in Europe, and electrocardiography (ECG) is essential for the initial evaluation and follow-up monitoring of patients with cardiac complaints. A more reliable and efficient diagnosis and treatment based on multi-parametric data analysis of ECG is necessary. For this to be possible, a novel digital reference database should be developed that allows assessment of uncertainty, different classification approaches for advanced data analysis should be assessed, and clinical applications of multi-parametric data analysis should be investigated.

Keywords

Multi-parametric medical measurements, personalised medicine, non-communicable disease (cardiology), data analysis, machine learning, cardiac arrhythmia, digital reference data

Background to the Metrological Challenges

ECG plays an important role as a non-invasive, cost-effective tool to evaluate arrhythmias and ischemic heart disease, and is the basis for the combination with other multi-parametric measurements, such as blood tests and multi-modality imaging. Continuous ECG-monitoring is recommended for the investigation of undiagnosed (so-called “silent”) arrhythmia resulting in large amounts of data that require automated analysis tools for detection and classification of arrhythmia. Medical diagnosis, treatment and prevention of cardiac diseases are based on multi-parametric data, but validated diagnosis of cardiac arrhythmia by automated analysis of multi-parametric electrocardiographic abnormalities is not yet possible.

Recently, computer assisted diagnosis techniques have been used for the analysis of large volumes of measurement data. In particular, machine learning techniques have been applied due to the advantages of being quick, cheap, and automatic as well as the for the ability to examine features not obvious to the human eye. However, a key challenge of computer assisted tools is the investigation of the influence of data uncertainty as well as the assessment of the technique’s uncertainty itself. In particular, machine learning algorithms rely on the “correctness” of training data and any wrongly classified data can result in wrong behaviour, which is highly unpredictable. Therefore, it is difficult to persuade health professionals and patients to trust in algorithms that are often so complex that their reasoning cannot be understood. From a regulatory point of view, there is a strong need for a metrological validation of algorithms using common reference data. However, since the uncertainty of current reference data is not known, its influence on the algorithm is unpredictable. Quantitative assessment of the uncertainty of modern data analysis approaches, such as machine learning, is essential for their acceptance in clinical practice.

Objectives

Proposers should address the objectives stated below, which are based on the PRT submissions. Proposers may identify amendments to the objectives or choose to address a subset of them in order to maximise the overall impact, or address budgetary or scientific / technical constraints, but the reasons for this should be clearly stated in the protocol.

The JRP shall focus on the traceable measurement and characterisation of multi-parametric electrocardiographic data.

The specific objectives are:

1. To investigate synthetic (electrocardiography) (ECG) reference data of a virtual population amenable to statistical evaluation. This should involve the use of existing multi-scale modelling frameworks to simulate electrophysiology for different cardiac anatomies, different types of conduction blocks and electrical conductivity alterations of cardiac tissue such as fibrosis and infarct necrosis. The ECG-database should be representative of a virtual population with a sufficiently large amount of ECG traces including healthy variations and pathologies.
2. To carry out the uncertainty analysis of the simulated ECG data. For this, the influence on the uncertainty of different parameters (e.g. anatomical variation, conduction blocks, tissue conductivity) that are inputs to models will be assessed for the multi-scale modelling.
3. To assess and compare the effect of different classification approaches for advanced data analysis. This should include the analysis of the uncertainty on a classification algorithm, which should be assessed by investigating i) the influence of uncertainty of ECG data on the classification algorithm, and ii) the influence of wrongly labelled training data on the classification. In addition, new approaches for machine learning should be developed, where the influence of uncertainty classification is not predictable.
4. To carry out a thorough investigation of selected clinical applications of multi-parametric data analysis. This should include i) the detection and classification of undiagnosed (“silent”) cardiac arrhythmia and ii) the monitoring of stroke and cardiac arrest patients in the intensive care unit (ICU).
5. To facilitate the take up of the technology and measurement infrastructure developed in the project by the measurement supply chain, standards developing organisations (e.g. CEN, ISO and IEEE) and end users (e.g. machine learning research, clinicians specialised on cardiology) This should include the publication of a guidance document on software validation to support the new EU medical device regulation (MDR 2017/745 and 2017/746) and clinical guidelines of the European Society of Cardiology (ESC).

These objectives will require large-scale approaches that are beyond the capabilities of single National Metrology Institutes and Designated Institutes, and it is expected that multidisciplinary teams will be required. To enhance the impact of the research, the involvement of the appropriate user community such as medical practitioners, hospitals and industry is strongly recommended, both prior to and during methodology development.

Proposers should establish the current state of the art, and explain how their proposed project goes beyond this. In particular, proposers should outline the achievements of the EMRP NEW04 Uncertainty and how their proposal will build on those.

EURAMET expects the average EU Contribution for the selected JRPs in this TP to be 1.8 M€, and has defined an upper limit of 2.1 M€ for this project.

EURAMET also expects the EU Contribution to the external funded partners to not exceed 35 % of the total EU Contribution across all selected projects in this TP.

Potential Impact

Proposals must demonstrate adequate and appropriate participation/links to the “end user” community, describing how the project partners will engage with relevant communities during the project to facilitate knowledge transfer and accelerate the uptake of project outputs. Evidence of support from the “end user” community (e.g. letters of support) is also encouraged.

You should detail how your JRP results are going to:

- Address the SRT objectives and deliver solutions to the documented needs,
- Feed into the development of urgent documentary standards through appropriate standards bodies,
- Transfer knowledge to the clinical sector.

You should detail other impacts of your proposed JRP as specified in the document “Guide 4: Writing Joint Research Projects (JRPs)”

You should also detail how your approach to realising the objectives will further the aim of EMPIR to develop a coherent approach at the European level in the field of metrology and include the best available contributions from across the metrology community. Specifically, the opportunities for:

- improvement of the efficiency of use of available resources to better meet metrological needs and to assure the traceability of national standards
- the metrology capacity of EURAMET Member States whose metrology programmes are at an early stage of development to be increased
- organisations other than NMIs and DIs to be involved in the work

Time-scale

The project should be of up to 3 years duration.