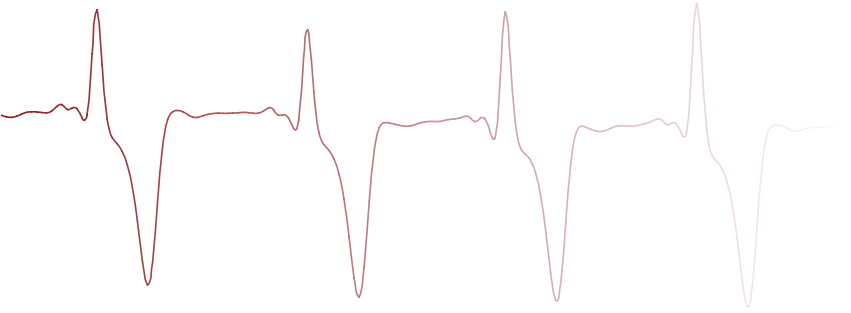
# Noninvasive reconstruction of cardiac electrical activity



# 10
# Valorisation

Cardiovascular disease remains a major cause of death and disability in western society. The results obtained in this thesis could bring improvements in screening, diagnosing and treatment of (the risk for) cardiac arrhythmias. Apart from a social burden, cardiac arrhythmias also create an economic burden on society. This chapter describes the valorization possibilities based on the knowledge obtained in this thesis. Knowledge valorization is "translating academic wisdom to societal benefit," and can be achieved by a broad range of activities and products. Examples includes patents, licenses, software, making models and systems available, co-publications with social or economic stakeholders, publications in journals and newspapers or other non-academic media, advice for organizations or companies, training programs, spin-offs and start-up companies. The results obtained in this thesis have a clear, direct clinical benefit, but could also be valorized in several indirect ways.

## 10.1 Screening for sudden cardiac death

In the United States of America (USA) alone, approximately 340,000 individuals per year die from sudden cardiac arrest. [186] Sudden cardiac death (SCD) is particularly important in young individuals, explaining two-thirds of the sudden deaths in individuals $\leq 40$ years [185]. Although it seems likely that (primary) cardiac arrhythmias are a major player in SCD in the general population, and especially in young individuals, it remains a challenge to assess the risk for SCD in apparently healthy individuals.

Electrocardiographic imaging (ECGI), the technique discussed in this thesis, might help to improve risk assessment for SCD in apparently healthy individuals, as it provides a detailed image of the electrical activity and recovery at the level of the heart surface. As discussed in Chapters 6 and 7, ECGI might detect arrhythmogenic substrate that is not apparent from screening tools such as the 12-lead electrocardiogram (ECG). More studies are needed to investigate whether ECGI indeed has a higher sensitivity and specificity to detect risk factors for SCD than the 12-lead ECG. Initial studies should focus on homogeneous groups of patients, e.g., with genetic mutations in cardiac ion channels for which the risk of SCD is not yet known. When the added benefit of ECGI is shown in these selective studies, risk factors for SCD could be studied in the general population.

ECGI's hypothesized improved sensitivity for SCD would help to treat and protect individuals in which risk factors for SCD are not detected with normal screening tools. This could prevent unnecessary death and disability, and the associated socio-economic costs. Improved specificity would help to reduce unnecessary treatment of healthy individuals, for example by reducing the number of implantations of implantable

cardioverter defibrillators (ICDs), thereby decreasing their psychological and economic burden.

Thus, the target groups for this application consist of patients and their family members, who receive more information about their risk for SCD; and cardiologists, who receive better tools to determine that risk and adjust treatment for their patients.

The socioeconomic effect of ECGI should be studied to determine its feasibility as a screening tool. The application of ECGI is time consuming and expensive, and studies are needed to investigate whether the cost (extensive screening) are outweighed by the benefits (reduction in SCD and unnecessary treatment).

## 10.2 Opportunities for personalized and translational medicine

ECGI allows to study mechanisms of arrhythmia, and the effect of treatment, in a personalized matter. An example of this is shown in Chapter 6, where the application of ECGI helped hypothesize possible mechanisms of induction of arrhythmia in a patient. Such insights can help to provide a better, more specific diagnosis for a patient's symptoms. Additionally, these data help to select the best treatment. Moreover, the effect of treatment could be assessed with ECGI.

Additionally, ECGI can help to bridge the gap between studies on cellular level and effects on organ level. For example, studies investigating the effect of genetic mutations on cellular level could provide hypotheses on organ level that can be investigated with noninvasive reconstructions of potentials at the heart surface with ECGI. This would allow to study the phenotypic results of genetic mutations in the intact organ in humans.

The target audience for this application again consists of patients and cardiologists, who are informed better of diagnosis and treatment options. Additionally, scientists can benefit from new opportunities to translate cellular findings to organ studies.

## 10.3 Improved ablation guidance

As discussed extensively in Chapter 7, premature ventricular contractions (PVCs) are arrhythmias that might require treatment, as they can impair the pumping function of the heart. Additionally, sick myocardial tissue can generate ventricular tachycardia (VT) that can be life threatening. However, the non-medicinal treatment of PVCs and VTs with invasive ablation therapy is still suboptimal. One of the reasons is the difficulty in localizing the culprit tissue during the ablation procedure, especially when the patient shows few or no PVCs or VTs during the procedure. ECGI can determine the origin of a PVC in a single beat, and can be performed pre-procedurally. This pre-procedural pre-

diction can be visualized during the ablation procedure and helps to guide the ablation, as discussed in Chapter 7. Previous studies have shown that this reduces the time needed for the procedure. However, the success rate of ECGI-guided PVC ablation appears to be similar to non-guided ablation in preliminary studies. Thus, more studies are needed to investigate whether there is a socioeconomic benefit of using ECGI during PVC ablation. Ultimately, improved treatment of PVC and VT would increase quality of life and might reduce the need for ICD implantation or repetition of unsuccessful ablation procedures.

A recent, preliminary study investigated completely noninvasively cardiac ablation by using radiotherapy. [176] For this application, catheter-based confirmation of the culprit tissue is unavailable, and ECGI provides a noninvasive alternative. The initial results should be confirmed in larger cohorts, and could initiate a new era to arrhythmia treatment by allowing for completely noninvasive diagnosis and treatment of cardiac arrhythmias. Clearly, this would allow for commercial exploitation of modalities that combine ECGI with radiotherapy.

## 10.4 Application outside the cardiac domain

Inverse problems are common outside the cardiac domain. For example, recordings of electrical signals on the scalp can be used to investigate the electrical activity of the brain. Other organs that exhibit electrical activity that could be noninvasively reconstructed include the stomach, intestines, uterus and skeletal muscles. The novel source models described in Chapters 4 and 5 could be applied to these inverse problems as well, especially when these problems can be expressed in a sparse way.

The spatiotemporal method introduced in Chapter 3, used to determine the moment of electrical events from reconstructed potentials, might be beneficial in those cases as well, especially when there is a clear natural relationship between neighboring signals on the organ's surface, for example, because they resemble an activation wave front.

## 10.5 Commercial benefits

The Maastricht implementation of ECGI is well investigated and validated, with a special (and novel) focus on recovery abnormalities. With the opportunities expressed in the previous paragraphs, commercial exploitation seems a logical prospect. An ideal ECGI system for clinical application is easy-to-use, allows a flexible attachment of electrodes on a variety of torso shapes, enables quick creation of a torso-heart geometry from CT scans, and provides a live visualization of inverse reconstruction during ablation procedures, electrophysiology studies, drug challenges and for screening purposes.