Opportunities and challenges of current electrophysiology research: a plea to establish ‘translational electrophysiology’ curricula

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Cardiac electrophysiology has evolved into an important subspecialty in cardiovascular medicine. This is in part due to the significant advances made in our understanding and treatment of heart rhythm disorders following more than a century of scientific discoveries and research. More recently, the rapid development of technology in cellular electrophysiology, molecular biology, genetics, computer modelling, and imaging have led to the exponential growth of knowledge in basic cardiac electrophysiology. The paradigm of evidence-based medicine has led to a more comprehensive decision-making process and most likely to improved outcomes in many patients. However, implementing relevant basic research knowledge in a system of evidence-based medicine appears to be challenging. Furthermore, the current economic climate and the restricted nature of research funding call for improved efficiency of translation from basic discoveries to healthcare delivery. Here, we aim to (i) appraise the broad challenges of translational research in cardiac electrophysiology, (ii) highlight the need for improved strategies in the training of translational electrophysiologists, and (iii) discuss steps towards building a favourable translational research environment and culture.

Keywords
Translational research • Electrophysiology • Training • Arrhythmia • Cellular electrophysiology • Biological models • Curriculum

Introduction

The global landscape of biomedical research has witnessed substantial interest in translational science.¹ The primary motivation of this interest is to facilitate translation of basic science discoveries into improved clinical medicine. Although substantial progress has been made in our understanding of basic pathophysiological concepts of rhythm disorders and their integration into the management of arrhythmia patients over the last century, numerous challenges remain in many areas of basic cardiac electrophysiology research. This importance of fundamental scientific discovery and translational work in arrhythmia research has also been highlighted in a recent report from the Heart Rhythm Society.²

The authors believe that it is timely to appraise the role of translational research in the field of cardiac electrophysiology. First, we aim to explore the broad definitions of translational research. Secondly, we aim to briefly evaluate selected examples of translational research in major fields of cardiac electrophysiology. Thirdly, we aim to identify the trends and hurdles in translational electrophysiology research and to highlight strategies that can maximize success in such research programmes. Naturally, the education of translational electrophysiologists is an aspect of particular interest in any attempt to strengthen the integration of basic research and patient care.

The continuum of translational research

It is tempting to view translational medicine only as the application of basic science to improve prevention, diagnosis, and/or treatment of disease. However, ‘reverse’ translation is just as important, whereby clinically derived insight can lead to new hypotheses for validation in the basic research laboratory. Also, the concept of translational medicine should not be confined to this bi-directional paradigm of ‘bench-to-bedside’ and ‘bedside-to-bench’ flow of information and insight. The translational continuum also includes extension of basic research to the improvement of clinical medicine at the population level and in the public health domain. However, significant concerns have been raised regarding the efficiency of translation of basic discoveries to improved healthcare delivery, and several transitional ‘blocks’ have been highlighted, including infrastructure, database functionality and accessibility, regulatory, funding, etc.

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and personnel related issues. These factors may equally impact on basic bench research, particularly those of ‘blue-skies’ nature, whereby short-term returns or practical applications are not immediately apparent. Also, implementing basic research insights into individual patient care appears to be challenging in a culture aiming to adhere to evidence-based medicine in which the standard assessment of relatively large patient groups determines the recommended therapeutic strategy. Further development of clinical care and individualized electrophysiological therapy therefore requires clinician scientists with combined expertise, well trained in both ‘bench’ and ‘bedside’ research skills.

Translational research in cardiac electrophysiology—lessons from the past

This section highlights the selected examples of translational electrophysiology research that shaped the current practice of electrophysiology. Visible manifestation of the success of translational research often takes considerable time. Usually, it involves dedicated basic ‘blue-skies’ research, technological advances, patient or clinically oriented research, often guided by ‘reverse’ translation. Translating the discoveries from basic work into clinical practice is not straightforward and often requires a high organizational level for close collaborative efforts from many investigators and institutions.

Mapping and clinical electrophysiology

More than a century after the initial recognition of ‘animal electricity’ by Luigi Galvani, physiologist Augustus Waller recorded the first human electrocardiogram (ECG) using a Lippmann capillary electrometer in the late 1800s. However, the capillary electrometer was difficult to operate, and had slow response times and poor accuracy, limiting its clinical applicability. In 1903, Willem Einthoven presented his invention of a string galvanometer which was capable of highly sensitive and reliable ECG recordings. However, the clinical significance of this invention was not immediately appreciated until Sir Thomas Lewis used it in the first clinical studies of arrhythmias, which propelled the ECG into subsequent clinical practice. In this example, it is evident that basic research played a significant role in the very beginning of the investigation of the electrical activity of the heart. Successful translation of the ECG to the bedside involved technological breakthrough and dedicated clinical studies.

Present understanding of the Wolff–Parkinson–White (WPW) syndrome as a reentrant circuit arose from a series of bench and bedside studies. Early postulation of an accessory atrio-ventricular (AV) pathway in explaining the ECG features of pre-excitation was first demonstrated by an artificially created AV pathway in animal hearts, and subsequently confirmed in a human autopsy in 1943. However, it took another three decades before the arrhythmic mechanism of WPW was delineated by Durrer and Roos with mapping, programmed electrical stimulation, and successful termination of tachycardia through surgical ablation. Here, translational research involved basic research that first defined the anatomy of the normal conduction system and accessory AV connections, while subsequent technological advances in programmed electrical stimulation and invasive mapping studies allowed functional confirmation of the arrhythmic mechanism in WPW syndrome.

The pathophysiological mechanisms underlying atrial fibrillation (AF) remain incompletely understood despite increased translational research focus over the last few decades. Initial mapping studies had shown that AF was not electrophysiologically homogenous with evidence of intra-atrial reentrant circuits. This concept was affirmed by the highly effective surgical Maze procedure developed by Cox et al. for preventing the re-entry. However, through well-designed systematic clinical research and astute clinical observations, Haissaguerre et al. provided a seminal description of AF initiation by ectopic focal activity in the pulmonary veins in 1998, having first identified ‘unusual’ focal causes of AF in three patients 4 years earlier. This important discovery not only provided the basis for pulmonary vein isolation as the cornerstone of the catheter ablation strategy in AF patients, but also gave the impetus for basic research examining focal atrial discharges and cellular calcium handling. In this example, earlier pre-clinical findings regarding pulmonary veins harbouring independent electrical activations and the presence of muscular sleeves extending into both animal and human pulmonary veins did not seem to have played an important role. Nevertheless, this example shows reverse translation whereby clinical identification of an important electrophysiological mechanism for AF led to further basic research.

Cardiac pacing

In 1929, Mark Lidwill was the first to use electrical stimulation of the heart in stillborn infants. Wide application of cardiac pacing for bradycardia started in the early 1960s. Using the transvenous approach, the catheter electrode is usually placed in the right ventricle (RV). Of note, concurrent studies in animals with AV-block in the 1960s have demonstrated the crucial importance of pacing location, with superior cardiac pump function from most left ventricular (LV) over RV pacing sites. Importantly, a ‘bad’ RV pacing site was equally harmful to cardiac pump function as ‘bad’ AV-synchronization. Nevertheless, in the 1970s and 1980s, dual-chamber (DDD/R) pacemakers were developed to achieve AV synchronization, or ‘physiological pacing’. Subsequently, several large randomized clinical trials showed that physiological pacing did not reduce death compared with single-chamber ventricular pacing (VVI/R). In contrast, atrial pacing reduced the risk of heart failure and death when compared with any RV pacing. This led to the recognition that RV pacing-induced dyssynchrony increases the risk of developing heart failure.

The major effect of this new insight was an increased focus on dysynchrony and the development of cardiac resynchronization therapy in heart failure patients with left bundle branch block. Only during the past 10 years, clinical studies confirmed that LV pacing is superior to RV pacing, not only with the preservation of pump function but also with the reversal of cardiac function and dimensions in those with RV pacing-induced heart failure. With the evidence from large animal and human paediatric studies, the time is ripe for translational investigations into LV pacing for anti-bradycardic pacing in adults. Considerable advances in technology are being made that will facilitate single-lead LV pacing such as over-the-wire leads and leadless pacing. On the other hand,
a potential threat for applying LV pacing is the development of novel leadless devices consisting of a combined battery and electrode, implanted in the RV. The benefit of the lack of pacing wires should be weighed against the risk of worsening cardiac function. The latter increases with higher percentages of cumulative pacing and poorer pre-existing pump function. In summary, this example shows how electrophysiological therapy might benefit from improving translational education of electrophysiologists. It also shows that sometimes significant delays occur in the translation from basic science to clinical practice.

**Ion channel electrophysiology and drug development**

Ion channels represent the fundamental components of the complex system underlying cardiac excitation. Understanding their function and dysfunction has been instrumental to the identification of therapeutic targets and optimization of drug therapy. Needless to mention, the discovery of ion channels as the main determinants of electrical activity in the heart together with the evolution of cellular electrophysiological techniques (patch clamp and fluorescent probes) have largely facilitated the development of many antiarrhythmic compounds.

In the early 90s, the detection of linkage between an arrhythmogenic syndrome and a gene variant opened the chapter of cardiac channelopathies. The advent of tools for large-scale genetic investigation has unveiled an unforeseen role of primary channel abnormalities in arrhythmic diseases. Furthermore, the combination of molecular and biophysical analysis of mutant channels has led to leap advancements in our understanding of channel structure and function. Such knowledge is at the basis of models of drug–channel interaction, a powerful tool in the design of new antiarrhythmic agents. Arrhythmias complicate a wide spectrum of myocardial conditions. Identification of a unique arrhythmogenic channel abnormality, shared by different conditions, may lead to the development of mechanism-directed therapy with broad applicability. An illustrative example of such an abnormality is enhancement of the ‘late Na+ current’, recently identified as maladaptive response to stress in many conditions and relevant to multiple aspects of cell dysfunction, including electrical instability and impaired cellular calcium handling. Hence, the late Na+ current represents a pleiotropic therapeutic target, potentially relevant to conditions covering almost the entire spectrum of common cardiac disease.

Because of system complexity, translation of knowledge on ion channel dysfunction into arrhythmogenesis is a daunting challenge. This has many untoward consequences, among them, our substantial inability to apply exponentially increasing information on genetic abnormalities to therapeutic management. Numerical models are of considerable help in integrating function of individual elements into system behaviour and novel hybrid computational—biological approaches, such as ‘dynamic clamp’ may prove to be of considerable value in translation. While the above considerations put the value of basic research in the advancement of cardiac electrophysiology beyond discussion, how much basic knowledge may be individually required for the practice of clinical arrhythmology is a so far unresolved question.

**Systems biology and individualised therapy—lessons for the future**

A significant hurdle for translation of basic (patho)-physiological concepts into function and malfunction of organisms is the complexity of the interaction of multiple mechanisms which as a whole shape the phenotype and behaviour of an individual. Systems biology aims at understanding the nature of these interactions. At present, there is no generally accepted concise definition of systems biology. The term is understood here as the *application of systems research principles to biological research*. This involves, from the outset, the combined application of reduction and integration, with the aim of understanding how a system maintains its existence via the mutual interaction of its parts, and how it supports and restricts the range of possible element interactions. Systems biology is by no means a new direction but the extent to which it receives attention today is presumably a response to the artificial division into ‘reductionism’ and ‘integrationism’ that arose in parallel with the molecular genetics revolution in our field. A ‘systems approach’ therefore can be regarded as the core of translation. Systems biology also serves as a suitable reminder of the need to consider the relevance of partial observations in the context of patho-physiological complexity and in particular if they involve projection between different species.

For biological modelling, in particular, were related to vascular, functional, murine models can offer excellent guidance, thanks to the vast existing tool box of genetically modified strains in general, and the further improved versatility of combinatorial tool boxes, such as the ingenuous Cre-loxP system. However, the translational value of biomedical research is, in part, a function of the model species used. For cardiac electro-mechanical research, murine models are not ideal, as they show different (at times opposite) responses compared with more slowly-beating mammalian hearts, which furthermore may change with genetic background strain differences. Thus, while the use of murine models offers a favourable cost–benefit ratio (funds, time, ethical considerations related to re-use of established models), a relatively low-risk/high-gain profile (tools already in place), and the potential for mechanistic insight (in particular if combined with quantitative modelling for cross-species comparisons), an alternative species is desirable for more clinically related aspects. The rabbit has arisen as an interesting alternative model system. It is the largest of the ‘small’ laboratory animals, and has been successfully used in transgenic research. Compared with mice, rabbits have heart rates (less than half of those in mice), action potential shapes (with a characteristic plateau phase), and relative cardiac dimensions that scale well to human. Their coronary architecture, response to ischaemia, and reaction to pharmacological interventions mimic the human heart more closely. It is of no surprise, therefore, that the rabbit has become an important reference model for pre-clinical evaluation of pharmacological agents and enhanced efforts into the generation and use of transgenic rabbit models of human disease may be of significant utility.

A last, but not least important, aspect is shared access to data and meta-data, from experiments, models, and clinics—where the lack of standardization of experimental models, protocols, and analysis procedures hamper comparability between studies. Also, privacy considerations and nationally differing legislation on use and re-use
of data continue to pose significant challenges for integration. We also need ways towards better representation of so-called ‘negative findings’, to prevent repeat work and to inform interpretation/planning of further studies. The combination of translationally more relevant biological study systems, and improved access to patient-related data should allow us to move on from evidence-based medicine to personalized medicine. Evidence-based medicine represented the attempt to apply (sub)-population statistics on an individual, thereby treating the individual as defined by the disease in the (sub)-population. In contrast, in a personalized approach the specific pathophysiological mechanisms of a single individual should be targeted which means to treat the patient instead of the disease. This would improve the safety and efficacy of interventions, and potentially expand the range of available pharmacological interventions.

Challenges in translational electrophysiology research

As explained in the previous sections, translational research in electrophysiology was tremendously helpful for developing better understanding of the general pathophysiology of many arrhythmias. Undoubtedly, this understanding has facilitated the development of numerous therapeutic strategies, such as ion channel blockers, cardiac pacing, or radiofrequency ablation of arrhythmias. The results of clinical trials in such groups of patients have generated a large amount of evidence-based knowledge on the efficacy of these treatments in these patient cohorts, which forms the basis for guidelines for the management of cardiac diseases.

However, the individual components of a disease although assessable by experimental research hardly have an impact on the choice of the therapeutic option. From experimental and genetic research, for example, we know that inflammation, fibrosis, reactive oxygen species activation, fatty infiltration, or the individual genetic background can increase the propensity of the heart to cardiac arrhythmias. However, these considerations are not integrated in the choice for an individual therapy. The reasons are manifold and include the presence of multiple mechanisms in parallel in an individual patient. Also the extent to which these mechanisms affect the specific patient’s phenotype may vary over time. This is also true for the individual genetic background, which with the exception of monogenetic cardiac diseases is not usually taken into full account in the decision on a therapeutic strategy. To overcome this ‘translational gap’ (Figure 1) is one of the most important challenges in modern medicine in general and also in cardiac electrophysiology. Techniques that can fill this translational gap include imaging, identification of biomarkers, complex genetics and pharmaco-genetics, computational and biological modelling. These techniques need

![Figure 1](image-url) Overcoming the ‘translational gap’ (see the text for explanation) by identification of individual disease mechanisms using validated imaging modalities, biomarkers, genetics, and individualized computer simulations may improve mechanism-based therapy of cardiac arrhythmias and outcome.
input from basic research on, for example, the potential role of structural alterations, specific biomarkers, or the impact of common gene variants on gene expression profiles. Basic research also delivers technology bringing this information together in, e.g. software for pathway identification, biomarker discovery, and individualized computer models. Clinical investigations will provide the platforms for screening the individual mechanisms and will link this knowledge to combinations of clinical signs and symptoms. The ultimate goal is to develop disease classifications which are based on clinical symptoms and signs, a hopefully short list of biomarkers and imaging tests to identify the leading mechanism of an arrhythmia in specific patients. This development is more than daydream. It is essential to the sustainability of our health care system. With the increasing restrictions of health care budgets future research will have to focus less on the development of again new and better therapeutic devices but much more on techniques that identify the right treatment for a specific patient.

Thus, patient-oriented research is vital, and the critical role of a scientific approach of physicians in translational research cannot be overemphasized. The necessity for a translational approach has an impact on the required expertise of electrophysiologists. Let us approach this from the standpoint of the physician with the ambition to implement basic research concepts in clinical care. This ‘physician-scientist’ faces significant challenges beyond the clinical skills required in the physician—patient interaction. Not only is there a need to delineate the biological role of various cellular, molecular, and genetic mechanisms of disease but also the extension of positive results into epidemiological and health-service research. Specifically, over the last few decades, significant advances in biotechnology have facilitated exponential growth of knowledge in basic cardiac electrophysiology derived from studies involving patch clamp, molecular biology, genetics, systems biology, and computer modelling/simulations. Indeed, the high-throughput capabilities of current biological research have ushered in an unprecedented ‘information explosion’. On the other hand, with increasing specialization in medicine and biomedical research, it has become harder for highly focussed investigators to extract the relevant information from the literature, and to communicate effectively with experts in other disciplines.

It is not a surprise that the training needed to become a physician-scientist in electrophysiology is lengthy. After years of medical education and clinical practice to gain a medical degree (e.g. MD), several more years of dedicated postgraduate scientific research training are needed that usually results in a doctorate degree (e.g. PhD), which is often followed by further subspecialization, postdoctoral positions, and training in the rapidly expanding field of invasive electrophysiological procedures. Although a combined MD/PhD track exists in some tertiary institutions, the training can be costly with the rising duration of education. In addition, research funding is becoming increasingly competitive, necessitating more time for the process of preparing grant applications. Grant support is crucial in allowing the physician-scientist to buy protected time for research while being in the clinic. Invariably, a translational investigator faces pressure in balancing the time dedicated to clinical responsibilities and research. No wonder there has been a decreasing trend in the number of physician-scientists involved in biomedical research. Many physician-scientists are exposed to a strong pressure caused by the combination of clinical care, increased competition for research grants, academic assessments, and necessity of administrative work. One cannot overstate the importance of a favourable environment for productive research both on the institutional and on the personnel levels such as dedicated administrative assistance and support for the electrophysiology physician-scientists.

**Strategies towards better translational electrophysiology research**

**Training ‘translational electrophysiologists’**

For the reasons explained above, we believe that there is a strong need for ‘translational electrophysiologists’, physicians trained in cardiology and clinical electrophysiology with awareness and scientific interest in arrhythmia mechanisms and their consequences for the therapeutic interventions or vice versa preclinical scientists with the intention to work on translation of pathophysiological concepts into clinical practice. The question ‘How can I become a translational electrophysiologist?’ is difficult to answer. There is no clear curriculum mapping a path into this field, while training of basic electrophysiology is generally limited in clinical electrophysiology programmes. We therefore suggest development of a ‘translational electrophysiology’ curriculum. Such a training format would give the trained translational electrophysiologist not only the ability to understand a broad range of clinical electrophysiology problems, but also foster faster application of basic research insight into patients. For the preclinical scientists, it could offer insights into basic principles of diagnostic tools, pacing and ablation therapies and use of antiarrhythmic drugs. With this, basic and clinical cardiac electrophysiology will no longer be on separate paths but translational electrophysiologists would be trained to bridge the gap between basic and clinical cardiac electrophysiology for fruitful and productive research.

Potential contents of a basic cardiac electrophysiology curriculum for training the translational electrophysiologist have recently been suggested. They have been reconsidered based on the analysis of the recent evolution of the discipline in cardiac electrophysiology. Table 1 shows the main learning objectives we believe should be integrated in a translational electrophysiology curriculum. Whether such curricula can be implemented as pre- or postgraduate course, as part of bachelor or master programmes, largely depends on the national education landscape. This question is therefore beyond the scope of this article. One option compatible with the Bologna-system might be an intercalated programme with for example, a 12-month training that could be integrated in Master programmes in many European countries. Alternatively, this training might become part of postgraduate sub-specialisation programmes (see below). Whatever format will be chosen for such curricula, the programmes need to undergo continuous evaluation and adaptation to account for the rapid evolution of cardiac electrophysiology.

The authors would like to stress that the ambition of such a curriculum cannot be to train all course participants up to the level of experts capable to perform unsupervised research in all these disciplines. Rather the aim is to provide a basic understanding of terminology and concepts enabling the successful course
participant to communicate with experts of these disciplines in a multidisciplinary team environment. Such team efforts are clearly required by the complexity and diversity of multidisciplinary translational electrophysiology.

**Embedding clinical care in a translational research environment**

Another aspect is the requirements which a training centre for translational electrophysiology should fulfil. Clearly, the combination of accredited clinical-electrophysiology training and established research education in basic electrophysiology within one institute provides a suitable environment for the education of translational electrophysiologists. However, the individual spectrum of the clinical and basic science programmes at any centre will depend on the economic situation, presence, and focus of medical centres in the region, and the ability of the centre to attract scientists in the field and funding. Clearly, the more aspects of translational science can be established in a specific centre the higher the chances are that this centre will be able to facilitate the implementation of new diagnostic or therapeutic strategies into the clinic, to improve the quality of clinical care at the institution, and finally to strengthen its economic competitiveness. Table 2 summarizes the main basic science facilities a translational electrophysiology centre should ideally provide.

<table>
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<tr>
<th>Electrophysiological subspecialization</th>
<th>Objectives to be covered</th>
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| Molecular and cellular electrophysiology | - Biophysical properties of ion channels and transporters  
- Thermodynamics, voltage- and time-dependent gating of ion channels  
- Main determinants of the cardiac action potential at various locations  
- Excitation–contraction coupling, and cardiac Ca\(^{2+}\) homeostasis  
- Gap junctions and cell–cell coupling |
| General proarrhythmic mechanisms | - Automaticity, triggered activity, re-entry, multiple wavelet hypothesis  
- Conduction disturbances: regulation of the extracellular matrix, quantification of conduction disturbances by mapping, analysis of fibrillation electrograms  
- Conditions promoting proarrhythmic mechanisms |
| Arrhythmia substrate | - Developmental biology of the heart  
- Specific anatomy of the heart  
- Cardiac histology and extracellular matrix |
| Specific proarrhythmic mechanisms | - Heart failure  
- Ischaemia  
- Ventricular tachycardia and fibrillation  
- Atrial fibrillation |
| Channelopathies and genetically determined arrhythmias | - LQTS and Brugada syndromes  
- Acquired and inherited cardiomyopathies  
- Rare monogenetic diseases and genetic testing  
- Inheritability of cardiac arrhythmias, polygenetic arrhythmias, and GWAS (genome-wide association study). |
| Ablation | - Ablation technologies and basic principles  
- Ectopy  
- Supraventricular and ventricular arrhythmias  
- Atrial fibrillation |
| Cardiac Pacing | - Cardiac pacemaker technology  
- Indications and pacing modes  
- Pacing-induced remodelling and dyssynchronopathy  
- Biventricular and left ventricular pacing |
| Electropharmacology | - Antiarrhythmic drug actions  
- Classifications of antiarrhythmic compounds  
- Risks and limitations of antiarrhythmic therapy |
| Computational electrobiology | - Computer models of ion channels and action potentials  
- The translational axis in multi-scale models |
| System approaches | - Interaction between elements forming a system  
- Computational science for analysis and modelling of complex systems  
- Opportunities and hurdles of individualized therapy |
| The scientific environment | - Electrophysiological societies and associations  
- International funding structures  
- Perception of scientific content in a success-driven environment  
- Blinding techniques  
- Definition and importance of ‘positive’ and ‘negative’ results |
Take home messages

(i) Biomedical research experiences significant technological advances and information explosion.

(ii) Advances in mechanism-oriented therapeutic approaches in cardiac arrhythmias require reinforcement of multidisciplinary translational research.

(iii) More investigators engaged in both ‘bench’ and ‘bedside’ research are needed to implement basic research in clinical care and vice versa.

(iv) Training of these investigators in translational electrophysiology should be improved through a combination of dedicated translational electrophysiology curricula and dedicated research training programmes.

(v) The ambition of translational electrophysiology curricula should be to provide basic understanding of critical electrophysiological sub-disciplines enabling communication in multidisciplinary team efforts.

(vi) Medical schools, academic hospitals, scientific societies, and arrhythmia associations share responsibility for the implementation of such courses as well as for continuous promotion of a translational research culture.

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Incessant ventricular tachycardia and concomitant recurrent left ventricular thrombus: to ablate or not to ablate?

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We report the case of a 75-year-old man with ischaemic dilated cardiomyopathy complicated by a large apical aneurysm and previous left ventricular (LV) thrombosis presenting the first episode of sustained (>40 h at implantable cardioverter-defibrillator interrogation), haemodynamically tolerated, monomorphic ventricular tachycardia (VT) in September 2014 and a recurrence of incessant monomorphic VT in October 2014. He underwent both a cardiac computed tomography (CT) and a magnetic resonance imaging, for evaluation of a potential aneurysectomy, that showed recurrence of apical thrombus. As he refused the surgical option he was scheduled for radiofrequency (RF) ablation after 4–6 weeks of anticoagulation. In November 2014 he was hospitalized for incessant VT and, despite the persistence of a voluminous apical thrombus, we decided to perform RF ablation under intracardiac echocardiography (ICE) guidance to minimize the risk of potential fragmentation and dislodgement of the outer layers. CT images were available for integration with the electroanatomic mapping system and we obtained a detailed 3-D reconstruction of the LV anatomy with particular focus on the apical thrombus through ICE imaging (see Supplementary material online, Video S1) from the right ventricle before entering the LV chamber with the ablation catheter to perform substrate mapping and ablation of the region of interest at the border of the aneurysm (Figure and Supplementary material online, Video S2). The patient did not show any neurological complication.

Supplementary material is available at Europace online.

The full-length version of this report can be viewed at: http://www.escardio.org/communities/EHRA/publications/ep-case-reports/Documents/Incessant_ventricular_tachycardia.pdf.

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