Radiofrequency catheter ablation in atrial arrhythmias : insight into pre-procedural evaluation and procedural guidance

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Chapter 1

General introduction and outline of the thesis

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Radiofrequency catheter ablation (RFCA) has become an important treatment option in the management of supraventricular arrhythmias such as atrioventricular (nodal) re-entry tachycardia, atrial tachycardia, atrial flutter and atrial fibrillation (AF). Particularly in the management of AF the number of RFCA procedures performed is growing rapidly.[1] Three-dimensional electroanatomical mapping combined with non-invasive imaging is currently a state of the art technique to guide RFCA for complex arrhythmias such as AF ablation, providing information on anatomical landmarks and arrhythmogenic substrate with higher accuracy and with less radiation exposure than fluoroscopy or conventional catheter based mapping. Importantly, accurate characterization of the arrhythmogenic substrate and the underlying mechanisms of the arrhythmia as well as visualization of anatomical landmarks are pivotal to optimize the results of RFCA.[2] Comprehensive pre-procedural evaluation may help to identify the appropriate substrate as well as to identify patients with a high likelihood to benefit from a RFCA procedure.

Pre-procedural Evaluation of Patients undergoing Radiofrequency Catheter Ablation for Atrial Fibrillation

Atrial fibrillation is the most common sustained cardiac arrhythmia in the developed world, with an estimated prevalence of 1-2 %.[3] Atrial fibrillation is associated with an increased risk for thromboembolic complications (e.g. stroke), congestive heart failure, hospitalisation and mortality.[3-5] As a result of the global population aging, the prevalence of AF is expected to at least double in the next 50 years. Consequentially, AF poses a major problem to society in terms of medical, social and economic expenses.

Management of AF is targeted at the prevention of AF related complications (e.g. stroke, tachycardiomyopathy) and at the reduction of AF related symptoms.[3] Prevention of complications is based on antithrombotic therapy, reduction of ventricular response rate and adequate treatment of concomitant cardiac disease. Although these therapies may already reduce symptoms, additional restoration of the sinus rhythm can result in further relief of symptoms. Sinus rhythm can be restored by cardioversion, antiarrhythmic medication and/or ablation therapy. Radiofrequency catheter ablation for AF is currently reserved for patients with symptomatic AF, refractory or intolerant to at least one Class 1 or 3 anti-arrhythmic drugs.[2]

The success of surgical treatment of AF in the early 1990s has led to an interest in the field of interventional cardiology to reproduce these results by creating a set of lesions similar to the surgical procedures using RFCA.[2] These approaches were based on the theoretical model by Moe et al. that a critical number of AF wavelets was needed to sustain AF.[6] The lesions set were designed to limit the number of circulating wavelets thereby avoiding the development and maintenance of AF. In the later 90s, Haïssaguerre et al. made the landmark observation that AF could be spontaneously initiated by ectopic beats originating from the pulmonary veins and that subsequent ablation of these ectopic foci could successfully cure patients.[7] These observations rapidly increased the increased interest in RFCA for AF and directed the attention to the pulmonary vein region. Currently, RFCA for AF is a rapidly evolving treatment modality that gains popularity.[1] A large variety of ablation strategies have evolved, however the pulmonary vein region remains the cornerstone of most RFCA procedures.[1,2] However, with a reported success rate of 66-89 %, not all patients benefit from RFCA for AF.[1,2] In addition, RFCA for AF is associated with a small but relevant risk for serious complications (e.g. tamponade, stroke, atrio-esophageal fistula).[1] To improve the outcome of RFCA for AF and avoid unnecessary procedure related risks a proper patient selection is mandatory.

The current Heart Rhythm Society/European Heart Rhythm Association/European Cardiac Arrhythmia Society expert consensus statement on catheter and surgical ablation of AF, recommends careful assessment of the risks and benefits of RFCA in each patient.[2] Ideally, the likelihood of sinus rhythm maintenance after RFCA should be estimated based on clinical characteristics, imaging studies and biochemical results. Risk factors for AF recurrence after RFCA are non-paroxysmal AF (persistent or longstanding), sleep apnea syndrome/obesity, left atrial enlargement, increased age, hypertension, concomitant structural heart disease and a high extent of left atrial fibrosis.[8-12] However, the evidence demonstrating the accuracy of these risk factors to properly identify patients with a high probability of maintaining sinus rhythm after RFCA is limited. Therefore additional markers, for example new markers derived from imaging technique or biochemical analyses, are needed to improve the patient selection.

Echocardiography

Atrial fibrillation causes electrical and structural changes to the atria which play an important role in the perpetuation and progression of the arrhythmia.[13,14] This process is referred to as atrial remodeling. A large extent of atrial remodeling is associated with a limited efficacy of RFCA for AF.[11] Therefore, pre-procedural assessment of the extent of atrial remodeling could be used to identify patients with a high risk for AF recurrence after RFCA. Measurement of left atrial size is the most common used method to estimate the extent of atrial remodeling. Left atrial size is an independent predictor of AF in the general population as well as a well-recognized risk factor for AF recurrence after RFCA.[9,15-17] However as a selection criterion the clinical applicability of left atrial size is limited. Recently the use of contrast-enhanced magnetic resonance imaging to visualize, localize and measure atrial fibrosis in patients with AF was demonstrated.[18,19] However, despite the promising results, contrast-enhanced magnetic resonance imaging is not widely available in clinical practice and therefore alternative and better available methods to assess atrial remodeling are needed. In this regard, novel echocardiographic techniques provide information about atrial remodeling additional to left atrial dimensions, such as left atrial function (e.g. tissue Doppler imaging derived left atrial strain) and myocardial tissue properties (e.g. calibrated integrated backscatter derived left atrial fibrotic content and tissue Doppler imaging derived electromechanical delay [PA-TDI]).

Left atrial strain is an echocardiographic technique to assess the active contraction and relaxation of the atrial myocardium. In contrast to conventional methods to assess left atrial function (i.e. calculated from phasic volumes), left atrial strain is less dependent on loading conditions and provides information of the regional function of the myocardium. Kuppahally and coworkers demonstrated that left atrial strain and strain rate (assessed with speckle tracking echocardiography) correlated with the amount of left atrial fibrosis (assessed with contrast-enhanced magnetic resonance imaging) in patients with AF: patients with large areas of fibrosis had more impaired left atrial strain and strain rate.[20] In addition, these parameters have been associated with the burden of AF and with the outcomes of RFCA. In a recent study including 148 patients undergoing RFCA for AF, baseline left atrial strain was an independent determinant of favorable left atrial reverse remodeling at follow-up.[21]

Integrated backscatter is an echocardiographic technique that allows non-invasive characterization of cardiac tissue and may provide an alternative tool to estimate left atrial fibrosis and thereby atrial substrate remodeling.[22-24]

Calibrated integrated backscatter is based on the quantification of ultrasound energy reflected by scattering elements inside the myocardium. Integrated backscatter can be measured using two-dimensional echocardiographic gray-scale images and provides a global estimate of the fibrotic content of the left atrial wall.

The total atrial conduction time is determined by atrial size and conduction velocity and is thereby a marker of both electrical and structural remodeling of the atria. Echocardiographic assessment of the total atrial conduction time using tissue Doppler imaging (PA-TDI duration) may allow a more comprehensive estimation of the extent of atrial remodeling than left atrial size alone. The PA-TDI duration is measured as the time delay between the onset of the P-wave in lead II of the surface ECG and the peak A'-wave on the tissue Doppler tracing of the left atrial lateral wall (Figure 1).[25] The PA-TDI duration has been validated against P-wave duration on signal-averaged electrocardiography and has previously been used to identify patients with an atrial substrate vulnerable to develop AF.[26-28]

Multi-slice computed tomography

Multi-slice computed tomography (MSCT) is nowadays commonly acquired prior to RFCA for AF to plan and guide the ablation procedure.[2] MSCT contains information about pulmonary vein anatomy, pulmonary vein dimensions and the presence and extent of coronary artery disease. Potentially, pulmonary vein anatomy and dimensions could be of influence on the efficacy or RFCA lesion placement and the presence of coronary artery disease could have a negative impact on the efficacy of pulmonary vein isolation. Moreover, MSCT allows a more comprehensive evaluation of left atrial dimensions than two-dimensional echocardiography.[29] Potentially, this information could be used to improve the patient selection for RFCA for AF.

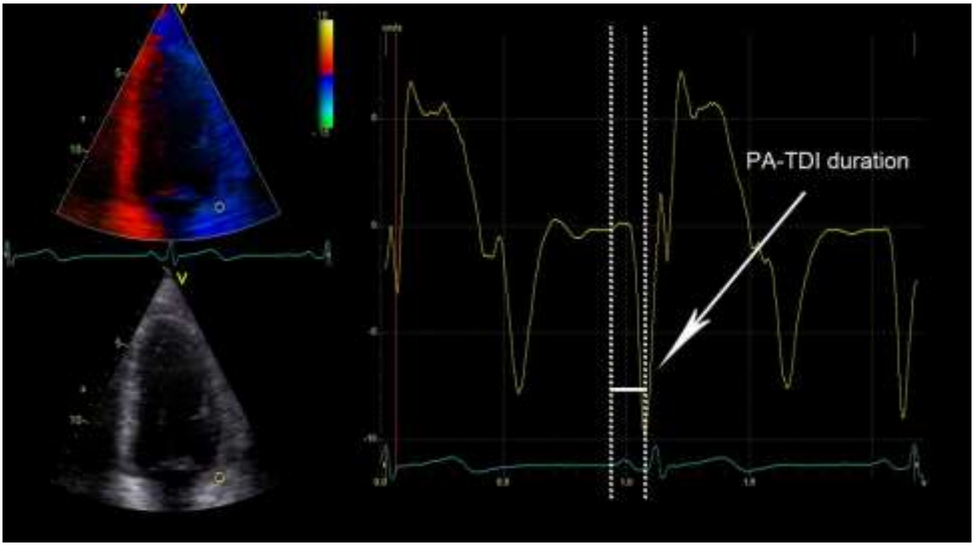

Figure 1. Measurement of the total atrial conduction time (PA-TDI duration). A fixed 9x9 pixel region of interest (yellow) was positioned in the left atrial lateral wall on a tissue Doppler recording to obtain a tracing of the mechanical activation in this area (yellow tracing). A simultaneously acquired registration of surface electrocardiogram lead II (blue tracing) was displayed underneath the tissue Doppler tracing. The PA-TDI duration (arrow) was assessed by measuring the time interval between the onset of the P-wave in lead II and the peak A′-wave on the tissue Doppler tracing.

Natriuretic peptides

Natriuretic peptides are hormones released from the atria and/or ventricles in response to volume or pressure overload and result in natriuresis.[30] Atrial natriuretic peptide is secreted primarily from the atria whereas B-type natriuretic peptide is primarily released from the ventricles.[30] It has been well recognized that in patients with AF, natriuretic peptide levels are elevated.[31,32] However it remain unclear whether this is solely caused by the presence of AF or reflects an underlying cardiac condition.[33] Elevated natriuretic peptides have been identified as a predictor of new-onset AF in the general population and have been related to a higher risk for AF recurrence after RFCA.[34-36] Potentially, natriuretic peptide levels can provide information about underlying cardiac conditions that limit the efficacy of RFCA for AF and could therefore be a valuable addition.

Imaging to facilitate Radiofrequency Catheter Ablation of complex Atrial Arrhythmias

As RFCA procedures become more complex, the need for adequate visualization of cardiac and surrounding structures increases.[2] Currently, most RFCA procedures are guided by fluoroscopy, allowing real-time visualization of intracardiac catheters. However, fluoroscopy does not allow visualization of anatomical structures such as the pulmonary veins and causes radiation exposure to both patient and operator. Alternatively, electroanatomical mapping systems have been developed that allow non-fluoroscopic navigation and can create a three-dimensional reconstruction of the cardiac anatomy using point-by-point contact mapping. Similar to fluoroscopy, electroanatomical mapping does not allow visualization of all cardiac structures and surrounding anatomy.

MSCT allows detailed visualization of the cardiac anatomy and can be integrated with an electroanatomical mapping system to facilitate RFCA procedures.[37] By performing a segmentation and registration process, a three-dimensional shell of the cardiac anatomy can be merged with the electroanatomical map of the heart thereby combining the advantages of non-fluoroscopic navigation with the anatomical information of MSCT. However, the validity of using this approach is highly dependent on the accuracy of the registration process.[38,39] Differences in fluid status, heart rhythm and heart rate between the time of MSCT acquisition and the RFCA procedure potentially compromise the quality of the registration process and thereby the accuracy of navigation.

Intracardiac echocardiography allows real-time visualization of important cardiac structures and can be used to guide lesion placement during RFCA.[40] In left-sided procedures (i.e. AF procedures or left atrial tachycardia), intracardiac echocardiography can be used to facilitate a safe transseptal puncture. Moreover, intracardiac echocardiography can be used to monitor and titrate energy delivery and allows for early detection of complications (e.g. thrombus formation on catheters or sheats, pericardial effusion).[40,41] However, intracardiac echocardiography provides two-dimensional images and lacks the 3-dimensional information that can be acquired using MSCT.

Ideally, RFCA procedures are guided by an imaging modality that provides real-time 3-dimensional visualization of the intracardiac catheters in relation to both cardiac and surrounding anatomy with low radiation exposure to patient and operator. In practice, such an imaging modality is not yet available. However, several mapping and fluoroscopy systems are being developed that allow integration of several imaging modalities.[42-44] An integrated approach using a combination of imaging modalities (e.g. fluoroscopy, electroanatomical mapping, MSCT and/or intracardiac anatomy) allows the operator to combine the advantages of these different techniques (Figure 2). The optimal combination has not yet been established but most likely depends on the type of patient, the operators experience and the availability of each imaging technique.

Outline of the Thesis

The objectives of this thesis were (1) to study the incremental value of new diagnostic markers on the pre-procedural evaluation of patients undergoing RFCA for AF and (2) to study the role of imaging to facilitate RFCA for complex atrial arrhythmias.

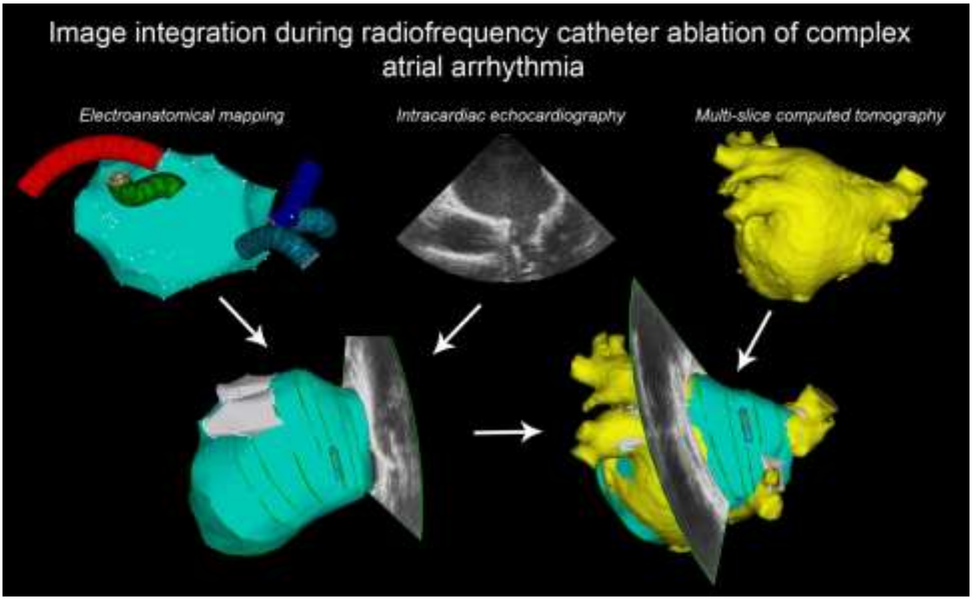

Figure 2. Example of integration of different imaging modalities to facilitate radiofrequency catheter ablation of complex atrial arrhythmia. The integration of electroanatomical mapping, intracardiac echocardiography and multi-slice computed tomography combines non-fluoroscopic navigation, real-time visualization of important cardiac structures and highly detailed three-dimensional anatomical information that can be used to guide the ablation procedure.

In part I, the impact of echocardiography, MSCT and biochemical markers on the efficacy of RFCA for AF is discussed. First, **Chapter 1** reviews the limitations of left atrial size as a criterion to select patients with a high likelihood to maintain sinus rhythm after RFCA for AF. Then **Chapter 2** focusses on the impact of left atrial fibrosis, assessed using echocardiography derived calibrated integrated backscatter, on the efficacy of RFCA for AF. Importantly, the interaction of left atrial size and atrial fibrosis on the efficacy of RFCA for AF is discussed. In **Chapter 3** the impact of the total atrial conduction time (PA-TDI duration) on the efficacy of RFCA for AF is studied. Similar to the chapter 2, a comparison with left atrial size was made and discrepancies between left atrial size and PA-TDI duration were highlighted. In **Chapter 4** the impact of coronary artery disease on MSCT on the efficacy of RFCA for AF is discussed. **Chapter 5** focusses on the impact of pulmonary vein anatomy and dimensions on the efficacy of RFCA for AF. Furthermore, this chapter evaluates the incremental value of 3-dimensional evaluation of left atrial dimensions on MSCT compared to left atrial size on echocardiography. Finally, **Chapter 6** evaluates the prognostic value of atrial natriuretic peptide and B-type natriuretic peptide to predict AF recurrence after RFCA. In addition, a comprehensive echocardiographic evaluation of atrial volumes, ventricular volumes and ventricular systolic and diastolic function was performed. The prognostic impact of serum natriuretic peptide levels was studied in relation to these echocardiographic parameters.

In part II, the use of intracardiac echocardiography, MSCT and electroanatomical mapping to facilitate RFCA for complex atrial arrhythmias is discussed. **Chapter 7** comprises a review of the use of intracardiac echocardiography during electrophysiological and other interventional procedures. **Chapter 8** further advances on the role of integration imaging to guide RFCA for AF and **Chapter 9** describes the integration of intracardiac echocardiography and electroanatomical mapping to successfully treat a patient with recurrent atrial tachycardia after a Senning operation for transposition of the great arteries. Finally, **Chapter 10** describes the use of electroanatomical mapping to facilitate RFCA of an atrioventricular nodal re-entry tachycardia in a patient who previously underwent a Mustard operation for transposition of the great arteries. In addition, the anatomical situation following the Mustard operation and its implications to perform RFCA are discussed.

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