Review article

Current status and future catheter ablation strategies in atrial fibrillation

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A B S T R A C T

Catheter ablation of atrial fibrillation (AF) is a highly effective therapy to achieve freedom of recurrent arrhythmia and relief from symptomatic AF. Transmural ablation of atrial tissue is crucial for success. Thus steerable sheaths and catheter design with contact measurement as an additional feature have been developed to increase success rates. New 3 dimensional (3D) mapping technologies engage clinical routine to reduce fluoroscopy time and radiation dose for patients and medical staff to a minimum. To unmask dormant pulmonary vein reconduction and to avoid early pulmonary vein reconduction administration of adenosine is useful. Future approaches aim at individualized ablation strategies taking clinical and electrophysiologic characteristics of the individual patient into account. © 2013 The Czech Society of Cardiology. Published by Elsevier Urban & Partner Sp.z.o.o. All rights reserved.

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Abbreviations: AF, atrial fibrillation; CF, contact force; PVI, pulmonary vein isolation; TSP, transeptal puncture; CFAE, complex fractionated atrial electrogram; 3D, three dimensional

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Introduction

Atrial fibrillation (AF) is associated with an increased risk for thromboembolic events, hospitalization and mortality. The number of patients suffering from AF steadily increases, as patients get older and present with more comorbidities and structural heart diseases [1]. Treatment for AF has constantly evolved over the last decade. Catheter ablation has become a routine procedure, with excellent success rates accompanied by acceptable complication rates. Still careful patient selection is important for clinical success. Since superiority of catheter ablation against medical, antiarrhythmic treatment, avoiding recurrence of AF, is shown, ESC guidelines admit, that catheter ablation could be performed as a first line therapy for patients suffering from AF [2,3], which was consolidated by the MANTRA-PAF trial published in October 2012. This randomized comparison of first line catheter ablation in paroxysmal AF to antiarrhythmic drug therapy showed significantly more patients free from AF and symptomatic AF and better quality of life in the ablation group at the 24 month of follow up. AF burden though did not differ [4]. Therefore the 2012 expert consensus statement from the Heart Rhythm Society, European Heart Rhythm Association and European Cardiac Arrhythmia Society on catheter and surgical ablation of atrial fibrillation includes ablation, if performed by an electrophysiologist, who has received appropriate training in an experienced center, as a reasonable first-line therapy for preselected patients suffering from paroxysmal AF [5].

Mechanisms of AF

Mechanisms causing paroxysmal AF appear to be different from those causing persistent AF. Paroxysmal AF is defined by spontaneous termination and episodes shorter than 7 days. Persistent AF does not self-terminate and episodes last longer than 7 days. Haissaguerre first described focal triggers within the atrial muscular extensions of pulmonary veins [6]. High frequency electrical activity of these focal sources is crucial for initiating paroxysmal AF in 85–95% of patients. Knowing that has led to the development of effective ablation strategies to isolate pulmonary veins electrically. Circumferential, antral pulmonary vein isolation became a therapy of choice in patients suffering from paroxysmal AF [7]. Cumulative success rates, between 80% and 90%, after more than one procedure, are reported in the literature [3]. Main cause of recurrent arrhythmias in these cases is attributed to electrical reconnection of former isolated pulmonary veins [8]. In persistent AF mechanisms are multiple and therefore ablation strategies to ablate suffer from imperfection. Structural and electrical alterations in the atrial myocardium are accused of perpetuating AF. Coexisting hypertension, valvular disease and heart failure lead to abnormal atrial pressure, causing wall stress and regional fibrosis, which provides substrate for persistent AF [9]. Atrial rotors, focal driver and wandering wave fronts seem to play a decisive role in perpetuation of AF [10]. Patients with persistent AF have distinctively reduced success-rates. Up to 30% of this population develops recurrent AF over time [11]. During the long-term follow-up (5 years) only 29% of patients stayed free of any arrhythmia after a single procedure. Most recurrences occurred within the first 6 months after initial procedure. Additional procedures can raise long-term success to 63% at 5 years [12]. Another significant mechanism for recurrence, as a result of post-ablation modulation, is macro-reentry tachycardia, which accounts for about a third of recurrences after atrial defragmentation [13]. Creation of trans mural scars therefore represents a crucial endpoint in ablation of atrial fibrillation and bears a challenge for operator and technical equipment. Thus there is a constant development of procedure strategies and technical support to reach these endpoints.

Catheter tissue contact

Catheter tissue contact is crucial for radiofrequency lesion size and depth. Contact force (CF) >20 g applied to the atrial endocardium during AF ablation, correlates with better clinical outcome at the 12 month in AF ablation compared to less than 10 g [14]. Recently published data confirmed that there is significant difference in CF at different anatomical sites during pulmonary vein isolation (PVI) [15]. It could be shown, that the lowest contact force at the left pulmonary veins was applied to the carina anteriorly. At the right pulmonary veins lowest CF was to the carina. These segments correlate with usual regions of early electrical reconduction [16]. Knowledge about this may improve clinical outcomes during PVI. A notable improvement of stability and catheter contact to the atrium is provided by the use of steerable sheaths. Several clinical studies have proven the concept of better tissue contact achieved by steerable sheaths, that results in higher success rates without increasing complication rates. There is a significant reduction in fluoroscopy time, while procedure time is not prolonged due to the use of steerable sheaths [17–19]. As mentioned above, on the one hand sufficient catheter-tissue contact is crucial for pulmonary vein isolation, on the other hand data about amount and vector of force delivered to the tissue is important information in order to avoid thromboembolic events and perforation through the atrial wall. In general, it is difficult for operators to exclusively define a sufficient catheter-tissue contact by tactile feedback; up to now fluoroscopy and signal-quality have been additionally used to confirm proper touch to atrial surface, both of which are implicit variables defining adequate tissue contact. To generate reliable information about delivered pressure to atrial wall, ablation-catheters with different features of contact measurement or feedback have been developed and investigated in the past. Currently there are two different technologies to measure contact force via an ablation catheter. Specially designed catheters, with integrated force sensors in the tip have been developed. The Tacti-Cath™ (Endosense, Switzerland) System contains a pressure measurement based on a fiber-optic sensor technology with a sensitivity of less than 1 g. Another, quite similar system is represented by the SMART Touch™ Technology (Biosense Webster), which uses a mechanical catheter tip to provide valid data of pressure to the atrial endocardium, expressed in grams. Published data support the thesis that complications due to excessive
pressure could be reduced by the use of these technologies in ablation of atrial fibrillation [20]. Recently it has been shown that contact force correlates with better clinical outcome of patients after pulmonary vein isolation. Best results are achieved when ablation lesions are placed with an average contact force above 20 g. Complete clinical failure is reported when contact force during ablation does not exceed an average of 10 g [14]. Using contact force measurements can significantly reduce ablation and procedure time and can reduce acute pulmonary vein reconnection from 36% to 12% of patients [21]. A new method of impedance based contact measurement uses a very different approach to confirm tissue contact. The Ensite-Contact®-System (St. Jude medical, St. Paul MN), measures local impedance at the border between electrode and tissue and expresses a so-called electrical coupling index (ECI) [22]. ECI correlates to lesion-size and gives information about catheter–tissue contact. A decisive advantage of the Ensite-Contact®-System is that contact information is independent from catheter-orientation and tissue-type (smooth or trabecular atrial endocardium). Information about lesion formation, during ablation, is displayed by impedance drop. Discrimination of scar tissue from healthy atrial tissue is another advantage of this technology. As measurement of CF can improve outcome and safety it is important to mention that CF is still an indirect surrogate parameter of transmurality and quality of lesions. Visualization of lesion formation and extent would improve performance in ablation of AF. Maybe real time magnetic resonance imaging could be the answer to this question in the future.

**Validation of lesions**

Commonly circumferential antral PVI is performed using the electro-anatomical 3 dimensional (3D) mapping and double transseptal puncture (TSP) technique. Using this approach a decapolar circumferential catheter and an ablation catheter are advanced through the interatrial septum to the left atrium. By stimulating from the circumferential catheter, which is positioned in the pulmonary vein, exit block can be confirmed or excluded. By stimulation from the coronary sinus catheter entrance block can be proven or excluded. By stimulation from the coronary sinus catheter entrance block can be proven or excluded. While gating waiting time and adenosine-challenge in a cohort of 75 patients with paroxysmal AF, Yamane and colleagues demonstrated freedom of AF in 92% of patients during a mean follow-up of 370 days [29]. Therefore in general a waiting time of at least 30 min and testing with adenosine is an additional tool to ensure PVI in selected cases.

**Avoiding early pulmonary vein reconnection**

Recurrence of AF in patients after successful PVI is still a major problem and often requiring more than one procedure to achieve suppression of AF [24]. Predominantly this recurrence is due to recovered electric conduction to the left atrium of primary isolated pulmonary veins [25,26]. Mostly this is the result of insufficient ablated (not trans mural ablated) tissue. About 30% of reconnection occurs within 30–60 min waiting time after complete isolation of pulmonary veins. Predominant regions in the left atrium are on the left side at the intravenous ridge and the ridge between upper pulmonary vein and left atrial appendage. On the right side usually the roof and the floor of the right pulmonary veins develop early reconnection [16,27]. That may be due to low catheter contact force to these anatomical regions. When entrance- and exit-block is achieved there is still the possibility of dormant pulmonary vein conduction, which can be unmasked by administration of adenosine. Positive adenosine response predicts spontaneous reconduction of dormant pulmonary veins after 30–60 min waiting time [28]. Investigating waiting time and adenosine-challenge in a cohort of 75 patients with paroxysmal AF, Yamane and colleagues demonstrated freedom of AF in 92% of patients during a mean follow-up of 370 days [29]. Therefore in general a waiting time of at least 30 min and testing with adenosine is an additional tool to ensure PVI in selected cases.

**3D-mapping**

In interventional cardiology, conventional fluoroscopy is still the leading imaging technology. The most significant advantage for the operator, using this technology, is that catheters are displayed in real time. Fluoroscopy in different angels is used to ensure correct positioning of catheter tips. While providing a two dimensional orientation, especially in AF procedures, fluoroscopy is associated with a significant amount of X-ray exposure to patient and physician [30,31]. For better orientation and reduction of X-ray exposure and fluoroscopy time 3D-mapping technologies have been implemented and are routinely used today [32]. Today two different electroanatomical mapping systems are widely used in clinical practice. The CARTO mapping system (CARTO-3), which relies both on a magnet-based visualization of ablation...
catheter and an impedance-based system that allows for both tip and catheter curve visualization and simultaneous visualization of multiple electrodes. The second electroanatomic mapping system is guided by electrical impedance mapping (NavX, St. Jude medical, St. Paul MN) using voltage and impedance for localization. Both of them have demonstrated reduction in fluoroscopy duration [32,33]. A small case series is published with 20 patients undergoing AF ablation using zero fluoroscopy with NAVX Ensite System (St. Jude medical, St. Paul MN) which speaks for the accuracy of electroanatomical mapping nowadays [34]. Another technique is intracardiac echocardiography (ICE), which significantly reduces fluoroscopy time and time spent in left atrium compared to preprocedural magnetic resonance imaging (MRI) [35]. There is also a safety advantage about using this technique to guide transeptal puncture and titrate energy delivery, to recognize complications like pericardial effusion, pulmonary vein stenosis at an early stage [36]. To keep the X-ray exposure low and still have the familiar view of fluoroscopy, a new 3D catheter mapping technology, which allows real time device tracking in prerecorded, conventional fluoroscopy cine loops, was recently implemented. The guided medical positioning system (St. Jude medical, St. Paul MN) is constructed from three components: (I) an electromagnetic reference sensor (patient reference sensor, PRS), which is placed at the patient’s upper end of the sternum like a conventional adhesive ECG electrode, (II) multiple transmitters, which generate a set of alternating low intensity electromagnetic fields (200 μT) and (III) passive single coil sensors (<1 mm²), which can be incorporated to different kinds of intracardiac devices, like electrophysiology-catheters, steering sheaths, pacemaker leads or coronary guidewires [37]. This system has a quantitative accuracy of less than 0.5 mm positional error and less than 1° orientation error, allowing precise navigation inside the heart. It continuously receives and processes information from signal sources and real time ECG. By that, cardiac and respiratory motion is compensated and the sensor-equipped devices can be displayed to prerecord, ECG-synchronized fluoroscopy cine loops (e.g. in left oblique and right oblique view), with a latency of 80 ms, which is due to capture and computation of signals. (Fig. 1) With this technology a reduction of 50% fluoroscopy time for AF ablation, from 31 min to 16 min, has been achieved [38]. By using a sensor equipped, irrigated tip ablation catheter, also displayed by the same technology, a further reduction in fluoroscopy time has been achieved to less than 2 min, in the primary experience of AF ablation [39].

**Individualized ablation strategies**

Circumferential PVI has become a standard therapy for paroxysmal AF. Currently, patients with paroxysmal AF are approached by wide antral PVI to avoid pulmonary vein stenosis. Commonly irrigated radiofrequency ablation and point-by-point strategy is used nowadays. Three dimensional mapping systems are in clinical use to display anatomy of an imported computer tomography, to ease navigation and reduce X-ray dose. Satisfactory results are shown in a long-term 5-year follow-up of patients after AF ablation of paroxysmal AF. Sinus rhythm was present in 79% after one or more ablations. Also in this study 94% recurrent AF was due to recovered electrical reconnection of pulmonary veins [40].

For patients with persistent AF the optimal ablation approach remains uncertain. Success rates of AF ablation in patients with persistent AF are significantly lower than in paroxysmal AF; 20% single procedure success and 72% multiple procedure success during a 5-year follow-up were free of AF [41]. Ablation strategies therefore have become more extensive in patients with persistent AF, including ablation of complex fractionated atrial electrograms (CFAE), linear ablation (Fig. 2), ablation inside coronary sinus superior vena cava and autonomic ganglia. Willem and colleagues nicely demonstrated in a prospective randomized comparison that additional roof and mitral isthmus line significantly decreases AF recurrence in patients with persistent AF [42]. Creation of linear lesions across the left atrial roof or between the left inferior pulmonary vein and the mitral annulus is a common way to address left atrial substrate. To achieve complete block in linear lesions can be difficult, is time consuming and might promote left atrial macro-reentry tachycardia [43]. Recent data support the thesis, that additional lines and defragmentation in the left atrium does not improve success rate in persistent AF [44].

Another substrate for AF perpetuation could be represented by CFAEs. These rapid electrograms with multiple split components can be located both in the left and right atrium. Predominantly they are located at the interatrial septum (83%), around the pulmonary veins (67%), the left atrial roof (61%), the proximal CS (59%), the cavitricuspid isthmus (31%) and the mitral annulus (24%). Rarely, they are found at the infero-lateral aspect of the right atrium (7%) and the superior vena cava (4%). Ablation of CFAEs can terminate AF during ablation procedure without external cardioversion [45]. CFAEs may represent pivot points or rotors where excitation turns around and creates reentry to maintain AF.

**Fig. 1** – Left anterior oblique view of a prerecorded cine loop, showing the coronary sinus catheter (B, yellow tip) and a right ventricular apex catheter (A, blue tip). Decapolar ring catheter (C) is introduced through a long, steerable sheath and placed at the ostium of the left inferior pulmonary vein: brown. Left superior pulmonary vein: blue, right superior pulmonary vein: green, and right inferior pulmonary vein: red. Esophageal temperature-probe (D). Outer limits of the left atrium are marked with dotted lines.
Another prospective randomized trial, comparing linear ablation versus CFAE ablation in a cohort of patients with persistent AF, showed no difference in freedom of atrial tachyarrhythmias after one ablation. Though recurrence of persistent AF was more frequent in the linear lesion group, the group with ablation of CFAEs showed more recurrence due to atrial tachycardia. Freedom of any atrial tachyarrhythmia and re-ablation were almost the same in both groups [47]. Following the thesis of CFAE ablation has recently been investigated in the CONFIRM trial. Focal impulse and rotors modulation (FIRM) plus conventional ablation (FIRM-group) was tested against conventional ablation alone (FIRM-blinded-group). The primary endpoint (AF termination or consistent slowing) was achieved in 86% of FIRM guided procedures versus 20% of FIRM-blinded procedures. After a single procedure freedom of AF was achieved 82.4% in the FIRM-group versus 44.9% in the FIRM-blinded-group, which is statistically superior outcome for the FIRM group after a mean follow-up of 273 days [48]. Further studies are needed to investigate this new concept and to compare long-term follow-up with actual long-term results.

On the other hand the Bordeaux group around Michel Haissaguerre and Pierre Jais recently challenged the concept of CFAE ablation. Using high density mapping (>400 points) in the left atrium, they elaborated that distribution of CFAEs is highly rhythm dependent [49]. Fractionated electrograms during sinus rhythm or coronary sinus pacing mostly result from wave collisions. Thus targeting these sites during sinus rhythm does not seem to be more specific to identify arrhythmogenic substrate. Therefore current strategies in CFAE ablation seem to target atrial myocardium with normal voltage and at least no scar tissue. Most of the sites with CFAEs seem to correspond to areas of wave-collision and these regions play a minor role in perpetuating atrial fibrillation. Quite commonly it is seen that patients suffering from persistent AF show normal voltage (>1.0 mV) in the left atrium during mapping in sinus rhythm and do not show any scar area. So the question is raised whether patients suffering from persistent AF show normal voltage (≥0.5 mV). Scar is depicted in gray (<0.2 mV). (B) AP view of a left atrium showing extensive septal substrate, which was defragmented by a lower septal line (black triangle), high septal line (white triangle) and a roof-line (white arrow). LSPV: left superior pulmonary vein; LIPV: left inferior pulmonary vein; RSPV: right superior pulmonary vein; RIPV: right superior pulmonary vein; LAA: left atrial appendage; and CS: coronary sinus.

Complications

Catheter ablation of atrial fibrillation is undoubtedly one of the most complex procedures in cardiac electrophysiology. The risk of suffering from any complication is therefore higher in atrial fibrillation than in ablation of any other arrhythmia. Necessity of transeptal approach, intracardiac catheter manipulation and ablation on delicate structures like left atrial wall, implicate about 4.54% major complications in total. Incidence of cardiac tamponade in a Worldwide Survey of AF ablation reports 1.31%. Cardiac tamponade is, with 25%, the most frequent cause of periprocedural death, which itself has an incidence of 0.15% [24,52]. The potential risk of delayed cardiac tamponade (>1 h post ablation) is always to be taken into account by taking care of these patients. Vascular complications, like pseudoaneurysms and arteriovenous fistulae occurring in about 1.5%, are due to size and number of venous sheaths and can lead to increased morbidity and additional therapy [24]. Stroke is another severe complication of AF ablation, which could either be caused by thrombo-embolism or air embolism. While the literature reports between 0% and 7% for thromboembolism,
in a worldwide survey stroke and TIA were present with about 1%; the incidence for silent microemboli is about 17% [24,53]. Up till now the impact on neurological and neurocognitive function of these microemboli is not clear and is a matter of ongoing research. Pulmonary vein stenosis became a rare complication (1.3%), because of wide area catheter ablation in AF and needs intervention in 0.3–0.6% of all cases [24,54]. Persistent phrenic nerve palsy occurs in 0.17% and can be avoided by high output pacing, especially when ablation is performed in the area around the right superior pulmonary vein and the vena cava superior [5]. Because of an extremely high mortality of 80% the left atrial esophageal fistula, which is occurring less than 0.1–0.25% of cases, is a complication which should be avoided by any means [5,24]. Patients should be informed about the delayed onset of symptoms (2–4 weeks) and should be cautious about taking proton-pump inhibitors for about 3 weeks following ablation.

So it is clear to say, that patient selection and inform consent are to be taken very seriously, because of the potential risk of severe complications, even if the incidence is acceptably low (Table 1).

### Table 1 – Major complications.

<table>
<thead>
<tr>
<th>Type of complication</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular complication</td>
<td>1.50</td>
</tr>
<tr>
<td>Cardiac tamponade</td>
<td>1.31</td>
</tr>
<tr>
<td>Stroke, TIA</td>
<td>1.00</td>
</tr>
<tr>
<td>PV-stenosis</td>
<td>0.3–0.6%</td>
</tr>
<tr>
<td>Atrium-esophageal fistula</td>
<td>0.04–0.25</td>
</tr>
<tr>
<td>Phrenic nerve palsy</td>
<td>0.17</td>
</tr>
<tr>
<td>Death</td>
<td>0.15</td>
</tr>
</tbody>
</table>

* PV-Stenosis, pulmonary vein stenosis, needed intervention.

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### Ethical statement

As this review article was written, no ethical statement is necessary.

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