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Mapping of atrial fibrillation – basic research and clinical applications

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Summary

Despite five decades of intensive research, mechanisms initiating and stabilising atrial fibrillation (AF) are still not fully understood. Nevertheless, mapping studies, next to clinical trials and research on cellular electrophysiology, have provided key information that has led to a much more profound understanding of the arrhythmia.

Contact mapping using multi-electrode arrays (MEAs) is the gold standard for high-resolution mapping in basic research and clinical trials, and continuously contributes to a better description of mechanisms perpetuating AF. It thereby provides information needed to target and test new pharmacological and interventional treatment options for AF therapy and to evaluate established ones, which were often implemented based on purely empirical assumptions.

In patients undergoing cardiac surgery high-resolution contact mapping studies are performed for basic research purposes to evaluate to which extent data derived from animal models of AF is comparable to data recorded in humans. The goal of these research projects is to develop algorithms that allow the identification and staging of the arrhythmogenic substrate. This information should then help to guide surgical therapy when applicable, or individualise treatment strategy involving catheter ablation, antiarrhythmic drug therapy or simply a rate control strategy.

Mapping techniques used in the catheter laboratory by interventional electrophysiologists represent a valuable tool for exact localisation of catheters and the points of interest for ablation. These techniques integrate data on individual anatomy (derived from CT scan or intracardiac ultrasound), local intracardiac electrograms (recorded point by point with a catheter) and the exact spatial position of the catheter.

While mapping techniques used with electrophysiological studies and ablations in patients are highly useful tools to optimise and document ablation results and significantly reduce fluoroscopy time, they fail to display the complexity of atrial activation during AF. This is mainly due to a limited number of simultaneously recorded electrograms and the low spatial resolution which is sufficient for its clinical use. At present, high-resolution mapping of AF in patients is only feasible during cardiac surgery. Endocardial catheter-based systems that have recently become available have to be further evaluated but might provide an option in this setting in the near future.

Key words: atrial fibrillation; mapping; contact mapping; endo-epicardial mapping; anatomical mapping; animal models; clinical mapping; MEAs

Introduction

Atrial fibrillation (AF) is a progressive disease frequently transforming from paroxysmal to persistent AF. The mechanisms underlying this process of increased stabilisation have been subject of extensive research. Major contributions to the understanding of the circumstances initiating and perpetuating the arrhythmia derive from mapping studies in patients and animal models of AF [1].

The term "mapping" is used for procedures recording local electrical signals at sites of interest in the endocardium or epicardium and then allocating them to a spatial matrix reflecting the mapping area. The following article will provide an overview of mapping techniques used for different purposes in basic research and as clinical tools.

Early mapping studies were performed using custom-made multi-electrode arrays (MEAs) recording between 64 and 256 simultaneous local epicardial electrograms. For electrogram acquisition MEAs were placed on the atria of patients

No conflict of interest.

undergoing cardiac surgery [2], animals in open chest experiments [3] or Langendorff-perfused hearts [1]. The signals were then allocated to a matrix reflecting the location of the corresponding electrode in the MEA. By interconnecting neighbouring points of simultaneous activation (isochronal lines) the activation sequence of the atrial surface reflecting propagation of fibrillation waves can be visualised more easily. Examples of activation patterns of the atrial free wall are shown in figure 1. The left panel displays a single wave propagating through the mapping area during sinus rhythm. Broad spaces between isochronal lines and the homogeneous orientated arrows (indicating local direction of propagation) can be interpreted as fast homogeneous conduction. The right panel shows a complex activation pattern observed during AF. Pronounced inhomogeneity of conduction resulting in local crowding of isochronal lines (= slowing of conduction) is present. Further, spots with radial spread of activation originating within the mapping area can be recognized. These events are likely to be caused either by a preceding endocardial wave, "surfacing" and then propagating in the epicardial plane ("breakthrough") or by true local automaticity.

This type of AF mapping (activation map) led to the description of different mechanisms that could be responsible individually or in combination for the property of AF to sustain itself.

The first hypothesis describing a potential mechanism leading to sustained AF without the need for a driving source was published by Moe and co-workers in 1959 [4]. They proposed the presence of multiple wavelets propagating through the atrium as a potential mechanism for the self-sustaining nature of AF. Twenty-six years later Allessie and co-workers using activation time maps of acetylcholine induced AF in isolated canine atria were able to demonstrate wavelets [1]. This was the first experimental demonstration of multiple wavelets propagating on the epicardial surface during AF. Konings et al. compared Allessie's findings in dogs to AF patterns in patients with Wolff-Parkinson-White syndrome undergoing cardiac surgery for accessory pathway interruption [2]. By mapping the right atrial free wall of these patients they could confirm the presence of multiple wavelets in pacing induced AF in humans. This was one of the first mapping studies to describe "breakthrough" events as a propagation pattern with radial spread of activation induced by either local automaticity or transmural activation of the epicardium from the endocardial bundle network during AF in patients. Since then breakthrough patterns (fig. 1, right panel) have been described in multiple studies and are still part of the ongoing discussion on mechanisms initiating and maintaining AF.

In a later mapping study Konings et al. described causes underlying fractionation of electrograms and thereby contributed to the background of those targets of catheter ablation therapy referred to as complex-fractionated atrial electrograms (CFAEs) [5–7].

It is probably due to technical reasons and to the fact that the atrial wall is considerably thinner than the ventricular wall, that the majority of mapping studies used a two-dimensional, predominantly epicardial, approach-resulting in the description of two-dimensional patterns such as spiral waves, wavelets [1], rotors [8, 9], multiple unstable reentrant circuits [10] or foci [11].

Although the third dimension of the atrial wall was frequently taken into account in the discussion on breakthroughs and foci, very few studies so far have provided data on simultaneous endo-epicardial high-resolution mapping [12]. Considering the complexity of the atrial structure and the irregular pattern of fibrillation waves, insight into the three-dimensional organisation of AF is needed in order to elucidate the origin of breakthrough activity and other possible mechanisms underlying the increasing stability of AF over time.

While high-density contact mapping using MEAs or optical mapping techniques are at present mainly used for basic research purposes in patients and animals, in recent years catheter-based mapping techniques have become established as valuable clinical tools for interventional electrophysiologists in order to facilitate complex electrophysiological procedures, increase anatomical accuracy and patient safety and reduce fluoroscopy times.

Electroanatomical mapping systems integrate local electrograms recorded by the mapping and ablation catheter and the three-dimensional anatomy of the mapped cardiac chamber.

The purpose of this article is to give an overview of the current basic research and clinical applications used for mapping of AF.

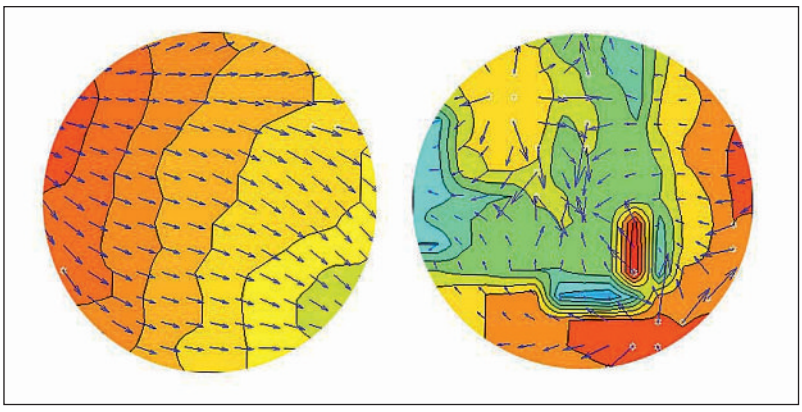

Figure 1

Activation time maps showing wave propagation over the atrial free wall. Isochronal lines indicate 5 ms time differences; earliest activation is in red, latest in blue. Arrows represent local direction of propagation. White stars mark sites of supra-normal local conduction velocities due to oblique activation. Diameter of the mapping area displayed is 48 mm.
Left: Homogeneous fast propagation of a single wave during sinus rhythm.
Right: Complex activation pattern during AF with a broad wave coming from the right and lower side, a second wave originating in the left upper quadrant leading to a "breakthrough" pattern with radial spread of activation and a number of smaller waves. The narrow spaces between some isochronal lines represent slow conduction, the wide spaces areas activated almost simultaneously.

Mapping sequence and parameters

All mapping techniques described in the basic research and the clinical application section are based on the acquisition of local electrograms. A significant difference between direct contact mapping using MEAs or optical mapping and catheter-based mapping techniques is the simultaneous versus the sequential fashion of recording the electrograms. Whilst simultaneous recording allows demonstration of continuous complex patterns of wave propagation, sequential recording "only" represents a number of single snapshots. Despite this in cases of more homogeneous and stable activation patterns such as those present in atrial tachycardia or atrial flutter, these snapshots can be connected to a sequence most likely representing the actual pattern of propagation.

This explains why sequential mapping fails to produce maps displaying the activation sequence (activation-map) of complex propagation patterns during AF. All the following parameters can be obtained from both approaches:

The local amplitude of electrograms (voltage-map) is a parameter used to identify areas of scaring and fibrosis (low voltage) caused by past interventions or degeneration due to intrinsic degenerative processes.

The local AF cycle length (frequency-map) provides information about sites possibly "driving" the arrhythmia (short cycle length) and bystanders (long cycle length).

The degree of fractionation of local electrograms (fractionation-map) is used to locate targets for ablation based on the hypothesis that sites with a high degree of fractionation (CFAEs) are responsible for the perpetuation on the fibrillatory process [6].

Mapping of atrial fibrillation – Present basic research

Several animal models ranging from mice to dogs and goats are used for mapping of AF and atrial arrhythmias. Even though caution is required when extrapolating data derived from animals studies to human pathologies key findings that have influenced AF research and therapy in humans have been derived from animal models of AF. Examples to be named are the demonstration of multiple fibrillation wavelets [1], electrical remodelling [13] and fractionation of fibrillation electrograms [5]. Although there are models presenting with spontaneous initiation AF we still lack an animal model to study the role of pulmonary vein (PV) triggers, which play a highly important role in the initiation of paroxysmal AF in humans [11]. Next to extensive studies aiming at a better understanding of the circumstances contributing to the progressive time course of AF, recent and ongoing studies evaluate the effects of established or newly developed drugs for prevention or conversion of AF. In this context mapping experiments permit to study the changes in AF morphology (AF cycle length, number of waves present, width of waves, conduction velocity, electrogram changes) preceding cardioversion or preventing it.

The majority of human high-density mapping studies for basic research purposes are performed in patients undergoing cardiac surgery. At present, this data is correlated with findings derived from animal models to develop algorithms for "staging" of human AF based on individual mapping data.

Three major fields of mapping in basic research will be discussed in the following section: Contact mapping using MEAs in animal models, contact mapping using MEAs in patients, and optical mapping in animal models.

Contact mapping using MEAs in animal models of AF

Direct contact of the MEA and the atrial tissue is the gold standard for high-resolution mapping of AF. Depending on the principal research question addressed and the technical possibilities, a standard mapping setup usually consists of an MEA (commonly 256 electrodes), a mapping amplifier and a computer for data acquisition and analysis. Although the required hardware is commercially available many systems are custom-made to address specific questions. Three examples of custom-made MEAs are given in figure 2. The left panel shows a "Spoon electrode" which is used in animals and humans, with a diameter of 48 mm, consisting of 256 single electrodes. This device allows the simultaneous recording of electrograms of the entire right or left atrial free wall during AF (as shown in fig. 1). The mid-panel shows a recently developed mapping tool ("Crocodile electrode") used for simultaneous high-resolution endo-epicardial mapping (as shown in fig. 3). First results using this technique in the goat model of AF have recently been published and provide new insight into the three-dimensional organisation of AF [14]. With this tool we could demonstrate that, while there is simultaneous activation of the endocardial bundle network and the subepicardial layer during sinus rhythm, there is considerable endo-epicardial dissociation of activation during AF (fig. 3). These findings were fully in line with data published by Schuessler et al. demonstrating for the first time that endo-epicardial dissociation of electric activity during acetylcholine-induced AF in perfused preparations of canine atria using high-density mapping [12]. In our goat model of long-term AF we were able to demonstrate that

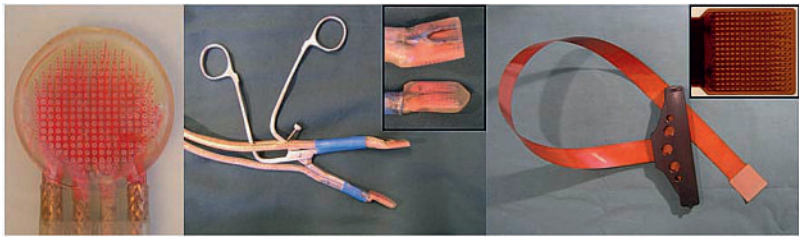

Figure 2

Custom-made multi-electrode mapping arrays (MEAs):
Left: "Spoon" 256 electrodes, spatial resolution 2.4 mm, used for mapping of the atrial free wall in animals and humans.
Middle: "Crocodile" 246 electrodes, spatial resolution 1.6 mm, used for simultaneous endo-epicardial mapping of the atrial free wall in animals. By inserting the lower part of the clamp into the atrial cavity, the atrial wall between the two MEAs can be mapped simultaneous endo- and epicardially.
Right: Single use Flex-MEA, 256 electrodes, spatial resolution 1.5 mm, used for high resolution epicardial contact mapping in patients during cardiac surgery.

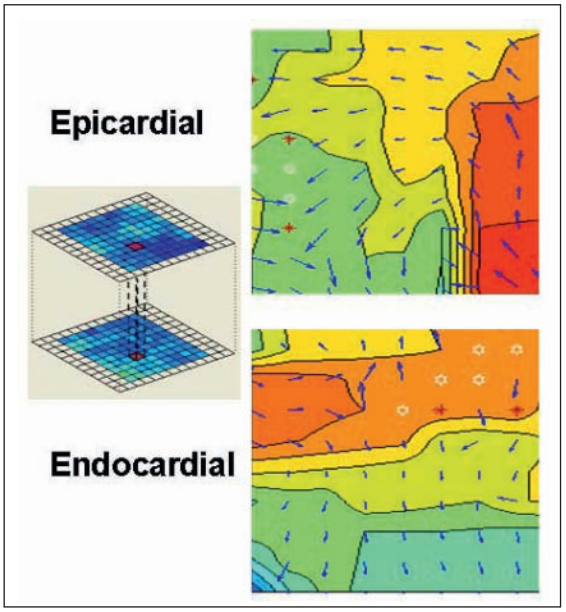

Figure 3

Isochronal map of an endo-epicardial recording of AF using the "crocodile" electrode in a goat. Both maps are recorded simultaneously at exactly opposing sites on the epicardial and the endocardial surface, respectively. Isochronal lines indicate 5 ms time differences, earliest activation is in red, latest in blue. Arrows represent local direction of propagation. White stars mark sites of supra-normal local conduction velocities due to oblique activation. Comparing the endocardial with the epicardial activation pattern reveals, that during AF electrical dissociation in time (delta activation time lower right corner = 35 ms) and direction of propagation (difference in direction of propagation upper left corner = 180°) between the subepicardial layer and the endocardial bundle network is present.

endo-epicardial dissociation is present in vivo and that it significantly increases if AF is maintained for up to six months duration. This circumstance is likely to contribute to the further increasing stability of AF after electric remodelling has occurred [15]. By demonstrating the presence of endo-epicardial dissociation during AF we further confirmed a prerequisite condition for the occurrence of breakthrough events. These events present as focal activity in conventional two-dimensional mapping and are an important subject in the ongoing discussion about the mechanisms initiating and perpetuating AF. One main question of this research focuses on the relevance of these events for perpetuation of AF and their actual origin, as this could be either truly local activity or part of a fibrillation wave propagating on the opposite layer of the atrial wall and emerging at this very site causing a "breakthrough" pattern. The differentiation of these two mechanisms appears to be important because it could contribute to the understanding of the time course underlying AF and help to tailor therapeutic interventions.

Contact mapping using MEAs in patients undergoing cardiac surgery

With new tools for surgical AF therapy becoming available and further refinement of established surgical approaches the option of contact mapping along with these surgical procedures provides a valuable tool to compare former findings from animal models to those in humans [16–18]. Along with this, mapping specific parameters are evaluated for their use in guiding ablation therapy and/or contributing to the decision making as to choice of an appropriate therapeutic approach based on individual mapping data.

An example of a newly developed single use high-density mapping MEA for intraoperative mapping in humans is displayed in the right panel of figure 2. This MEA is mounted on a positioning tool and placed at predefined locations of the epicardial atrial surface to simultaneously record up to 256 local electrograms. It is obvious that signals can only be obtained when the heart is still beating. Therefore mapping has to be performed before cardioplegia is started or during operations on the beating heart ("off pump"). With the establishment of minimally invasive procedures for surgical AF therapy, the use of Flex-MEAs in the context of this approach also appears to be feasible [18]. As the field of surgical interventions for AF therapy is expanding, direct access to the epicardial surface providing the option of high-density mapping might represent a relevant advantage of this approach in terms of identifying targets and direct evaluation of the ablation procedure [19].

Optical mapping in animal models of AF

Optical mapping represents an alternative mapping technique in basic research. It can be performed in isolated hearts or tissue preparations that are perfused with standard Tyrode solution. Together with the perfusate, a bolus of voltage sensitive dye (e.g., Di 4 ANEPPS) is applied that then integrates into the cellular membrane. The fluorescence of this dye is linearly proportional to the membrane potential. The emitted fluoroscopic signal thus reflects an ensemble action potential. Therefore, this signal can be interpreted in terms of measuring not only the activation time but also the action potential duration and the diastolic interval. By analysing sequential frames, which can be acquired as fast as 10 000/second, the spread of activation over the entire mapping area can be visualised as a movie (fig. 4). Spatial resolution of this technique is dependent on the optical hardware but can be as high as 100 µm. Despite superior spatial and temporal resolution, optical mapping involves a number of relevant disadvantages: firstly, the preparation has to be flattened out to provide equal distance of the mapped tissue to the optics. Secondly, only the upper 200 µm of the tissue contribute to the emitted signals and thirdly, an excitation con-

traction uncoupler (e.g., BDM, Cylochalase or Blebistatin) has to be infused to prevent movement artefacts due to contraction of the tissue.

Taking these factors into consideration, it is obvious that this method cannot be used for human mapping but nevertheless provides an attractive alternative method for experimental studies.

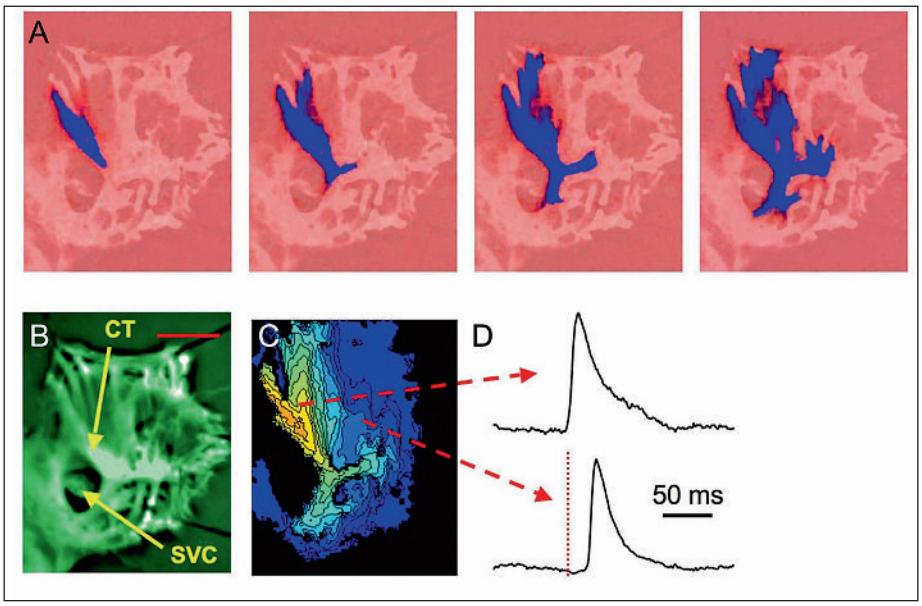

Figure 4

Endocardial optical mapping activation pattern during sinus rhythm in the right atrium of a rabbit.
A) Consecutive frames separated by 4 ms.
B) Endocardial bundle structure of the right atrium, CT = crista terminalis, SVC = superior vena cava.
C) Optical activation map in this preparation, red = early, blue = late.
D) Optical action potential in the CT (upper trace) and the thin layer between the trabeculae (lower trace).

Mapping of atrial fibrillation – Present clinical applications

Present clinical mapping applications used by interventional electrophysiologists serve the purpose of finding goals for catheter ablation. This is achieved by analysis of local electrograms guided by conventional fluoroscopy and – when using an electroanatomic mapping system – by obtaining three-dimensional anatomical information and creating a reconstruction of a cardiac chamber (e.g., left atrium) to maximise anatomical accuracy (and patient safety) and to minimise radiation exposure.

Mapping in the clinical setting means to determine where an arrhythmia is originating from in case of a focal tachycardia (e.g., pulmonary vein tachycardia) or to identify the course of the circuit in case of a re-entry tachycardia (e.g., left atrial macro-re-entry tachycardia). In contrast to high-resolution contact mapping in research applications, clinical mapping tools used in conjunction with a standard focal mapping catheter result in a relatively low resolution and rely on sequential rather than simultaneous recordings of electrical activity. However, specific mapping catheters allowing simultaneous recordings of electrical activity from different poles are available for contact and noncontact mapping in interventional electrophysiology. An example of a multipolar ring catheter used for pulmonary vein recordings is shown in figure 5 and its use is further explained below.

The importance of the pulmonary veins as a source of ectopic beats and their role in triggering and maintaining atrial fibrillation was discovered more than ten years ago [11]. Based on these find-

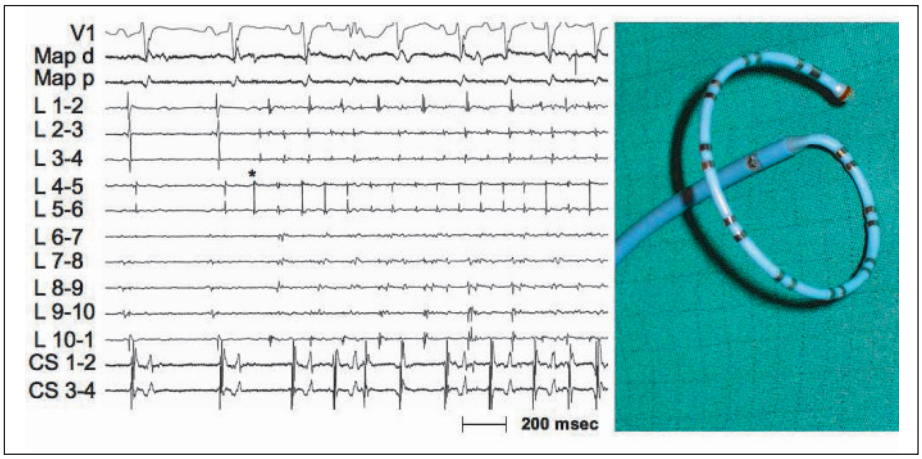

Figure 5

Left: Initiation of AF during Isuprel infusion (10 mcg/min). Shown are one surface lead (V1), and intracardiac electrograms recording the distal and proximal poles of the mapping and ablation catheter (Map d, Map p) positioned on the ventricular side of the mitral anulus, the multipolar ring catheter (L 1-2 [distal] to L 10-1 [proximal]) in the right superior pulmonary vein, and the coronary sinus catheter (CS 1,2 [distal] to CS 9,10 [proximal]). The first two beats are sinus beats with passive activation of the pulmonary vein. Then, rapid electrical activity (cycle length 100 ms) originating from the pulmonary vein with the earliest local endocardial activation recorded on L 4-5 (asterisk) initiates AF. Right: Example of a multipolar ring catheter with a variable diameter (LASSO 2515, Biosense Webster Inc. Diamond Bar, CA, USA) for mapping of the pulmonary veins.

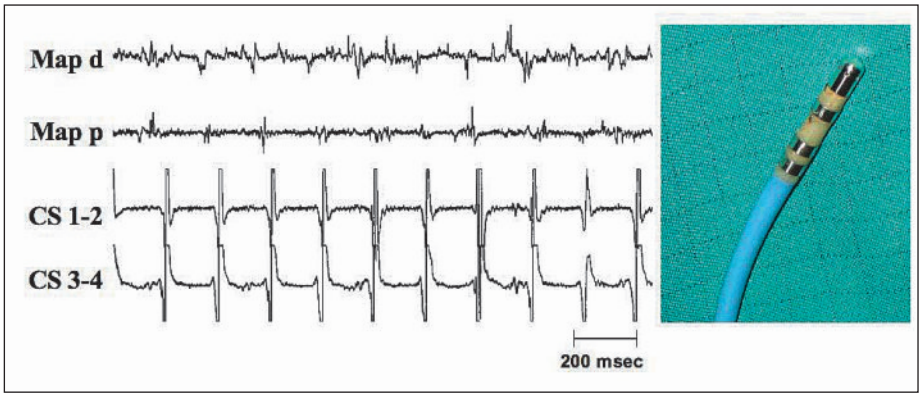

Figure 6

Left: Example of a complex fractionated atrial electrogram (CFAE) recorded with the distal pole of the mapping catheter (Map d) at a septal site in the left atrium. Note the high degree of fractionation and short cycle length of the electrogram on Map d. In contrast, the electrogram in the coronary sinus (CS) is well organised with a relatively stable cycle length of approximately 180 msec. Right: A 3.5-mm irrigated-tip catheter (Thermocool, Biosense Webster Inc. Diamond Bar, CA, USA) used for mapping (and ablation).

ings catheter ablation strategies were developed with the goal of electrically isolating the pulmonary veins from the left atrium [20, 21]. Further studies involving mapping techniques showed that not only is there a dynamic interplay between the pulmonary veins and the left atrium, but there are also mechanisms apart from the pulmonary veins in both atria that are relevant for the perpetuation of AF. This is particularly important in patients with the persistent and permanent form of the arrhythmia. These findings led to treatment strategies targeting sites in the left atrium displaying specific types of local electrograms (complex fractionated atrial electrograms = CFAEs, fig. 6), approaches including linear lesion sets in the left atrium with the goal of modifying the arrhythmogenic substrate and approaches targeting ganglionic plexi within the intrinsic cardiac autonomic system [6, 7, 22, 23]. The strategy of targeting CFAEs was based on findings of earlier mapping studies postulating that local electrograms are fractionated in case multiple waves are simultaneously present. CFAEs can occur due to complex fibrillatory conduction in areas with conduction disturbances and are considered to contribute to the maintenance of AF [5]. This hypothesis was supported by the work of Nademanee and co-workers who targeted sites of most extensive electrogram fractionation after creating electroanatomic maps of both atria [6]. Targeting these sites (plus additional ibutilide treatment in some patients) resulted in a high rate of conversion to sinus rhythm. However, a recent study showed that additional ablation of CFAEs after pulmonary vein isolation did not improve clinical outcomes in patients with long-lasting persistent AF [24].

Mapping and ablation procedures in patients with AF require accurate navigation in the left atrium. This can be accomplished using standard fluoroscopy or an electroanatomic mapping system, which combines the anatomical and electrical information that is gained during point-by-point mapping with the catheter and allows the construction of a three-dimensional shell of the left atrium or any cardiac chamber.

Anatomic mapping

An integral part of an electroanatomic mapping system is the functionality of localisation of a catheter in three dimensions without the need for fluoroscopy. There are two different electroanatomic mapping systems that are widely used in clinical practice. One is an electrical impedance mapping system (NavX, St Jude Medical Inc., Minneapolis, MN, USA) using voltage and impedance for localisation, the second one is a magnetic mapping system (CARTO, Biosense Webster Inc. Diamond Bar, CA, USA) using magnetic fields. The two systems are briefly explained in the following two paragraphs.

When using a magnetic electroanatomic mapping system (CARTO), the localisation is based on the principle that a coil in a magnetic field generates an electrical current [25]. The current is dependent on the strength of the magnetic field and the orientation of the coil. The magnetic field (three fields, 5×10^{-6} Tesla) is produced by a location pad which is placed on the patient's back. The tip of the mapping catheter contains a sensor with three coils oriented perpendicular to each other. The sensor measures the magnetic field based on the electrical current that is induced. Based on the fact that the strength of the magnetic field decays with increasing distance from the source, the distance from the three magnetic fields generated by the location pad can be measured. This allows accurate localisation of the catheter in space. Each location of the mapping catheter can then be registered on a three-dimensional map and a shell of the anatomical structure that is mapped (e.g., left atrium) can be constructed. Catheter positions and contact with the endocardium can occasionally be verified by fluoroscopy, local electrograms and in some laboratories intracardiac ultrasound. Anatomical landmarks (e.g., pulmonary vein ostium, oesophagus) can be tagged on the map. The accuracy of the map depends on the number of sampled points and the distance between them. Patient movement during the mapping procedure and respiration and cardiac motion are limitations to the accuracy of the map.

Electrical impedance mapping systems (NavX) use three pairs of surface electrodes placed on the patient's chest in three axes (perpendicular to each other). Using these three electrode pairs, the chest is placed in an electrical field with a current of 350 μA at a frequency of

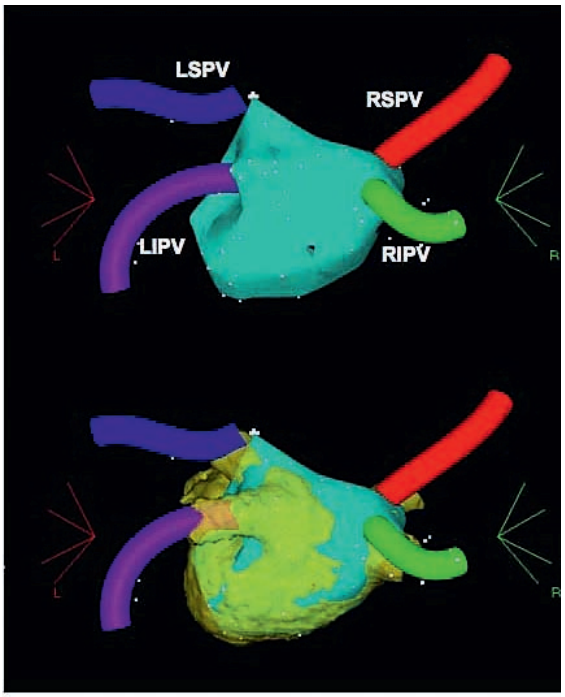

Figure 7

Top: Postero-anterior view of a three-dimensional reconstruction (CARTO map) of the left atrium (in green) acquired by catheter-based mapping. The pulmonary veins are tagged and drawn as isodiametric tubes (LSPV/LIPV = left superior/inferior pulmonary vein; RSPV/RIPV = right superior/inferior pulmonary vein). Bottom: Merging of the CARTO map with a three-dimensional reconstruction of the left atrium obtained by computed tomography (shown in yellow) by registration of landmark points at the pulmonary vein ostia.

5.7 kHz. This creates a transthoracic voltage gradient in the three axes. As a different frequency is used for each electrode pair, filtering recorded signals (from the electrodes of a catheter) for these frequencies allows the calculation of the three-dimensional position of the catheter and all its poles in case of a multipolar catheter. The calculation of the catheter position is based on the fact that the voltage and impedance changes measured by the catheter are proportional to the distance from the surface electrodes. An advantage of the electrical impedance mapping system is that more than one catheter and all poles of a catheter (in case of a multipolar catheter) can be visualised simultaneously and that all poles can be used to create the three-dimensional geometry of a cardiac chamber. However, changes in thoracic impedance may adversely affect the accuracy of the maps with this system.

With the aim of further improving the anatomical accuracy of the maps, integration of three-dimensional reconstructions of images obtained non-invasively by computed tomography (CT), magnetic resonance imaging (MRI) and of images acquired with intracardiac ultrasound during the procedure (before transseptal puncture) has become available. Image integration is performed by defining landmark points on the CT or MRI reconstruction of the left atrium followed by merging the CT or MRI image with the anatomical map that has been constructed using the mapping catheter (fig. 7). A limitation of this technique is that the CT or MRI image is not acquired real-time, but usually on the day before the procedure, and differences in volume status (open irrigated-tip catheter, anaesthesia) can result in significant differences in left atrial volume. Currently available image integration with intracardiac echo is based on two-dimensional ultrasound requiring "slice-by-slice" image acquisition for reconstruction of the left atrial shell, but has the advantage of real-time visualisation of the cardiac structures and the position of the catheter. Applications using three-dimensional intracardiac echocardiography are under development.

Electrical mapping

In order to achieve complete electrical isolation of the pulmonary veins during AF ablation procedures the operator needs a reliable tool to identify the electrical connections between the pulmonary veins and the left atrium. These electrical connections are preferably demonstrated with a multipolar circular mapping catheter with the shape of a Lasso (fig. 5). The electrical information gained by electrogram recordings from the circular mapping catheter not only shows the presence and the exact anatomical site of an electrical connection between the pulmonary vein and the left atrium, but also provides information on the electrical activity of the pulmonary vein with regard to triggering or driving AF. Furthermore, the recordings from the circular mapping catheter are the basis for demonstration of complete pulmonary vein isolation after ablation. If complete conduction block between the pulmonary vein and the atrium is present (= isolation), the electrical activity of the left atrium will no longer conduct into the pulmonary vein and therefore a circular mapping catheter placed distal to the line of block should no longer record local electrical signals (unless they originate in the pulmonary veins).

The pulmonary veins certainly play a pivotal role in paroxysmal AF, but treatment strategies exclusively focusing on pulmonary vein isolation appear to have significant shortcomings especially in patients with persistent AF. This is due to the fact that AF and especially maintenance of AF is not only dependent on the pulmonary veins, but also on the (arrhythmogenic) substrate, which is predominantly located in the remodelled left atrium. As mentioned earlier, specific types of local electrograms recorded with the mapping catheter (complex fractionated atrial electrograms = CFAEs) have been identified as targets for ablation (fig. 6). CFAEs are low-voltage electrograms that are fractionated and rapid (cycle length <120 ms) and catheter ablation at sites with CFAEs has resulted in successful treatment of AF in a number of patients [6].

Electroanatomical activation mapping

When sampling points in the left atrium using a mapping catheter, not only anatomical (localisation) and electrical (voltage, impedance) information, but also data on the timing of electrical activation of a particular site can be gained. When combining the information on a three-dimensional electroanatomical map, the timing of the electrical activation of all sampled points can be colour-coded with early activation coded in red, later activation coded in green and very late

activation coded in blue and purple. In clinical practice without high-density mapping, this results in a demonstration of chaotic electrical activity of the left atrium in AF, but is particularly helpful for mapping of focal atrial tachycardias and macro-re-entrant atrial flutter. The latter arrhythmia is not infrequent after catheter ablation of atrial fibrillation and is usually mapped using activation mapping, entrainment mapping (measuring postpacing intervals), or both. An electroanatomical activation map in a patient with persistent atrial fibrillation and an activation map in a patient with a focal atrial tachycardia are shown in figure 8.

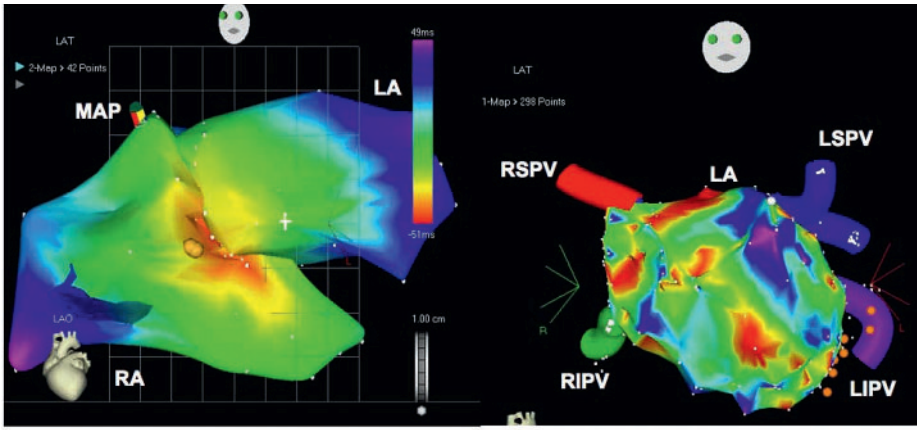

Figure 8

Left: Left anterior oblique view of a three-dimensional electroanatomical activation map of the right atrium (RA) and the left atrium (LA) in a patient with a focal ectopic atrial tachycardia arising from the interatrial septum. Electrical activation of the atria is colour-coded with early activation displayed in red and late activation displayed in blue/purple as shown in the colour bar. Early activation indicates the origin of the focal atrial tachycardia. Radiofrequency energy delivery at the site of early activation at the interatrial septum resulted in elimination of the tachycardia.
The yellow dot denotes the site of the His bundle recording. The position of the tip of the mapping and ablation catheter (MAP) is shown. Right: Antero-posterior view of a three-dimensional electroanatomical activation map of the left atrium (LA) in a patient with long-standing persistent AF showing the "chaotic" activation pattern of AF. The orange tags denote sites with CFAEs in the coronary sinus.

Mapping of atrial fibrillation – Future perspectives

As demonstrated in clinical mapping applications a combination of imaging and mapping techniques provides valuable additional information. While intracardiac ultrasound in combination with mapping and ablation procedures is already used, pilot studies evaluating the use of high resolution ultrasound to scan the epicardial mapping area are ongoing. Once available this technique might provide valuable additional information on the correlation between atrial electrophysiology and underlying tissue structure. It could further be used to define suitable anatomical landmarks for surgical ablation procedures.

The epicardial ablation approach performed either during open-heart surgery or a minimally invasive technique is developing rapidly and can be combined with intraoperative high-density contact mapping. The combination of these two techniques provides new opportunities to study the mechanisms underlying AF in patients and probably to individualise the therapeutic approach based on individual mapping parameters. Whilst trials including epicardial contact mapping in patients are ongoing, a safe technique for simultaneous endo-epicardial high-resolution mapping in patients has not yet been developed.

New perspectives for research and clinical applications will possibly evolve with the non-invasive technique of body surface mapping [26]. This technique acquires 224 body surface electrograms and calculates the epicardial isochrones by integrating the signal morphology and the three-dimensional position of each electrode using an individual MRI dataset of the patient studied. While there is already promising data for ventricular arrhythmias the contribution to mapping of AF is still open [19, 27].

With magnetic and robotic navigation and real-time acquisition of three-dimensional anatomical structures in the electrophysiology laboratory, the accuracy of mapping procedures is increasing further but still lacks the resolution required to display the complex patterns occurring during atrial fibrillation. Although preprocedure imaging with MRI or CT (or periprocedural imaging with rotational angiography [DynaCT]) or intracardiac ultrasound and image integration into the acquired maps are the standard of care in many electrophysiology laboratories, the cost-effectiveness of these tools needs to be shown.

New catheter-based technologies are still being evaluated as possible options for high-resolution endocardial mapping of AF in patients (En Site®, St Jude Medical, Inc. Minneapolis, USA) [28].

With the available mapping technologies from basic and clinical research and their implementation in clinical research we hopefully will be able to address crucial questions on the mechanisms underlying initiation and perpetuation of AF in patients and reach a more profound understanding of the disease in the near future. This should facilitate evaluation and refinement of established and new treatment strategies for AF and increase the efficacy and safety for our patients.

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