Atrial fibrillation (AF) is a growing indication for catheter ablation and is increasingly being performed in many EP centers. Although acceptable short and long term results have been reported for both paroxysmal and chronic atrial fibrillation, these are typically from high-volume centers with considerable institutional and operator experience. Currently there is a huge unmet need, comprising patients who are unable to have an ablation due to the lack of centers, and the lack of operators able to perform an ablation. This is in part due to the complex anatomy of the left atrium and the long learning curve necessary to perform safe and effective ablation. Complications, while rare, can be devastating. These include cardiac perforation, diaphragmatic paralysis and stroke. Additionally, even in experienced centers, recurrence of AF or atrial tachycardia (AT) is common, due in part to reconnection of the pulmonary veins.

Several studies have previously demonstrated that outcomes are better when procedures are performed in high-volume centers by high-volume operators, yet this does not answer the question as to how to perform more procedures. One potential solution is to make the procedure easier, reducing the time required to perform the ablation itself, and shortening the learning curve. To this effect a number of different technologies are being developed, from balloon-based catheters to advanced imaging and mapping solutions.

Ablation strategies

Catheter ablation of AF is dependent upon the substrate. Several studies have demonstrated that isolation of the pulmonary veins alone results in long-term freedom of AF for the majority of patients with paroxysmal AF [1-5]. However, this usually requires more than one procedure, due to recurrence of pulmonary venous (PV) conduction. The mechanisms underlying PV reconduction are unknown, but it is likely due to ineffective lesion delivery during the initial procedure. This may be due to poor catheter stability, inability to achieve transmural lesions, and acute tissue edema causing both temporary isolation and limited power delivery to underlying tissue [6].

Paroxysmal AF: pulmonary vein isolation
Isolation of the pulmonary veins is usually sufficient to treat the majority of patients with paroxysmal AF. Electrical isolation of the pulmonary veins requires ablation of the muscular sleeves that extend from the pulmonary veins into the left atrium. This can be performed in a targeted manner, at the ostium of the pulmonary vein and utilizing a circular mapping catheter to help localize the location of these electrically conducting sleeves.

An alternative method is to isolate the veins using a circumferential lesion either around both veins (typically on the right side) or single veins (typically for the left veins, due to the left anterior appendage being superior to the left superior pulmonary vein), at a more proximal location, the so-called antrum [7-12]. The endpoint of either technique is complete electrical isolation of the pulmonary veins [13]. Antral ablation has the benefit of destroying more atrial tissue, thus including non pulmonary vein sources, which tend to be clustered in this region, which is especially important in patients with chronic AF, but it is more difficult to achieve pulmonary vein isolation than with an ostial segmental approach.

One of the difficulties in achieving PV isolation is the variable anatomy of the pulmonary veins. The normal left atrium has four pulmonary veins draining into it (right and left superior and inferior veins). However, common variants include an additional right middle vein (seen in 23% of cases), common ostia (for example a left common ostia is seen in 35% of cases). Less
common are pulmonary veins that connect to the left atrium by its roof, yet isolation of such veins is required for a successful outcome [14-16].

**Persistent atrial fibrillation**

For patients with persistent and long-lasting persistent AF, isolation of the pulmonary veins alone is insufficient to achieve long-term freedom from AF. Different strategies have been tried with varying degrees of success, all of which aim to alter the atrial substrate.

Initially linear lesions were tried, typically a line connecting the left and right superior pulmonary veins, and a line connecting the mitral annulus to the left inferior pulmonary vein. However, the success rates of this procedure were unsatisfactory.

A different method targeted areas harboring complex fractionated atrial electrograms (CFAE), which was initially reported to result in acceptable rates of freedom from AF, but subsequent studies have not borne out these initially promising results [2, 17]. However, there are a number of studies that demonstrate that a combination of these techniques can provide good results. Pulmonary vein isolation in combination with ablation of CFAE, linear lesions with a procedural endpoint of AF termination and validation of all lesion sets performed, with additional ablation as required to achieve pulmonary vein isolation and conduction block across all linear lesions, has been shown to result in excellent medium to long term freedom from AF [18-20].

It should be noted that patients with persistent atrial fibrillation tend to require more than one procedure, predominantly due to recurrence of regular atrial tachycardias that can be effectively mapped and ablated. In two recent studies utilizing this combined approach for patients with persistent AF, sinus rhythm was maintained in 81% of patients at 20 months in one study [20] and in a different study 88% of patients were in sinus rhythm with a median of 34 months follow up [18].

Although this ablation strategy results in excellent results in terms of freedom from AF, the exact mechanism by which it is successful is not completely understood. Ablation of CFAE is relatively non-specific, as was shown in one study that extensively investigated which electrogram characteristics resulted in either termination of AF or a significant prolongation of AF cycle length [21]. This study demonstrated that only a gradient of activation (a difference inactivation from one bipolar to another of at least 70 ms, possibly representing a small circuit) and the duration of continuous fractionation were associated with a slowing or termination of AF. However, the positive and negative predictive value for continuous activity of >70% of the time window was 51% and 73% for favorable ablation regions. The presence of temporal gradient of activation was predictive of favorable ablation regions with positive and negative predictive values of 62% and 66% respectively.

There is obviously a long way to go before we fully understand the mechanisms underlying chronic AF, and although algorithms based on dominant frequency analysis have shown some promise [22] in the latter study this did not predict a favorable outcome from ablation [21].

**Advanced imaging solutions**

All of the above strategies require integration of an understanding of the anatomy of the left atrium and pulmonary veins with specific electrogram characteristics. The standard imaging technique in many laboratories is simple fluoroscopy. While this allows visualization of the ablation and mapping catheters, the operator has to have a high level of experience to understand the anatomy of the left atrium, as this is not directly visualized. This has led to different imaging modalities being used to help the operator.

Pre-procedural CT of the left atrium and pulmonary veins results in a high quality image that can be used at the time of the ablation [23] either by overlaying the three-dimensional shell on the live fluoroscopy screen or by integrating the shell into an electroanatomical mapping system (CARTOMERGE or NavX Fusion).

Although this technique results in a high quality 3D representation of the left atrium and other cardiac chambers, registration of the 3D shell is sometimes difficult due to changes that have occurred between the scan taking place and the ablation procedure. For example the patient’s rhythm may have changed from sinus to AF; the fluid status of the patient is likely to be different, and perhaps most importantly, the patient’s position on the operating table is different from that during the CT scan.

**Three-dimensional atrigraphy (3D ATG)**

To overcome the difficulties outlined above, and to reduce the radiation dose to the patient, a three-dimensional atrigraphy (3D ATG) procedure has been developed, based on three-dimensional rotational angiography (3D-RA) [24]. This uses the same C-arm system (Philips Allura Xper FD10) as that used
Figure 1. Three-dimensional atrigraphy (3D ATG).

Figure 1a. Preparation. The left atrium is isocentred; this is done by using the close relationship of the carina (red arrow) to the roof of the left atrium, and the coronary sinus catheter (white arrow) which defines the inferior margin of the left atrium. In a lateral view the upper margin of the spine (red line) is used to define the posterior border of the left atrium.

Figure 1b. Angiorotation. Radiopaque contrast has been injected into the right atrium, and after allowing for transit through the pulmonary vasculature, the C-arm rotates around the patient, acquiring images of the left atrium.

Figure 1c.d. Segmentation. The left atrium is autosegmented, but care is taken to check that it is correct and all the anatomical detail has been gained from the scan, such as the left atrial appendage.

Figure 1e. Registration. The 3D shell is automatically registered to the patient. However, this is always checked in case the patient has moved. Here the ablation catheter has been looped in the left atrium and excellent apposition to the wall of the left atrium of the overlaid shell is seen.

Figure 2. Mapping atrial tachycardia

Figure 2a. 12-lead ECG demonstrating atrial tachycardia (arrows point to the p waves).

Figure 2b,c,d. Taking points. Using EP, navigator points are taken within the left atrial shell. These images show the first point. The point is tagged in an AP view, and a line of sight shows where on the 3D shell this can be (anterior or posterior). The electrophysiologist can tell the operator where the catheter is, and this can be checked using orthogonal views.
Figure 2e. Checking the electrograms. The tagged point from the EP navigator is immediately associated with the electrical activity that is being recorded by the ablation catheter. On the BARD Labsystem Pro (C.R. Bard’s Electrophysiology Division), this electrical signal is then checked to ensure correct annotation with regard to the reference channel.

Figure 2f. Final activation map. When several points have been taken throughout the left atrium a color-coded map can help identify the mechanism of the atrial tachycardia. In this case the tachycardia was due to a small circuit localized on the anterior left atrium (orange) with later activation of the rest of the left atrium (purple). Ablation at this point resulted in tachycardia termination.
routinely for fluoroscopy in the EP lab. In this procedure, the left atrium is placed at the isocenter, and then contrast agent is injected into the heart, either from the inferior vena cava/right atrial junction, the pulmonary vein, or directly into the left atrium. The C-arm then rotates around the patient in a 240° scan lasting four seconds. This creates a three-dimensional data set similar to a CT scan that can be read by the EP navigator.

Automatic segmentation of the left atrium is performed, and this is checked and manually corrected as necessary. Following this the 3D shell is automatically overlaid on the real-time fluoroscopy image (Figure 1). A benefit of this system is that registration is not required, as long as the patient has not moved, given that the scan has been performed using the same equipment, under identical circumstances, and within a short period of time. Registration accuracy can be rapidly checked, normally by placing a catheter within the superior pulmonary veins and looking for the drop off between the pulmonary vein ostium and the left atrial body.

Following this step the ablation can then be performed with the operator being able to see the location of critical structures such as the ostia of the pulmonary veins, the ridge between the left atrial appendage and the left superior vein, and any anomalous pulmonary veins. The direct visualization of these structures obviously aids catheter placement, and helps avoid
potentially dangerous areas, such as the posterior wall with the underlying esophagus (which can be visualized and segmented with the 3D rotation), and helps to determine the level of isolation of the pulmonary veins (antral or ostial).

A recent two-center study comparing CARTO XP Electroanatomical Navigation System to 3D ATG with over 90 patients recruited has demonstrated equivalent results using both systems in terms of acute and short term procedural success, with equivalent fluoroscopy times whether using the fluoroscopy-based system or the CARTO system [25]. Although these images, whether CT, 3D ATG or electroanatomic systems, intrinsically make the operator feel more comfortable when ablating in the left atrium, it is less certain whether this translates into clinical benefit.

A retrospective study utilizing CARTOMERGE suggested that there was a clinical benefit to using the system [26]. However, in a later study by the same group no clinical benefit was seen, leading to the conclusion that a successful procedure is guided by electrical isolation of pulmonary veins rather than the technology used to achieve it [27].

While this could be seen as disappointing in terms of the benefit of imaging systems there are two important caveats. First, a learning curve was seen when using the CT overlay in the former study and, secondly, these studies are typically performed by experienced operators. As was discussed earlier there is a large population of patients who simply do not have access to a trained electrophysiologist who is capable of performing these difficult procedures, and any technology that lessens the learning curve has to be advantageous. Additionally, most complications occur when operators are learning a new technique, and as AF ablation will be increasingly performed throughout the world, these imaging techniques should help avoid unnecessary complications due to a lack of experience.

Integration with EP recording systems

Although 3D ATG has clear advantages over CT-based systems, one of its limitations is that it only provides anatomical information. Electrophysiology is the integration of discrete anatomical structures with discrete electrical properties. The integration of this information is what allows the electrophysiologist to successfully treat patients. For example, a common atrial tachycardia post AF ablation is peri-mitral re-entry, whereby electrical activation goes around the mitral annulus. To effectively terminate this arrhythmia a line of block between two electrically isolated areas has to be made to stop this circuit. Commonly this is between the electrically isolated left inferior pulmonary vein and the lateral mitral annulus.

In order to ablate this effectively the electrophysiologist has to perform several tasks: first, the activation wavefront needs to be mapped, then entrainment maneuvers need to be performed, in which pacing in or close to the circuit is able to capture and overdrive the circuit, and finally a line of block needs to be created, and any gaps identified.

This process thus requires integration of anatomy (the mitral annulus, the isthmus where the line of conduction block is going to be made) with electrophysiological data (wavefront of activation, the results of entrainment, and identification of conduction delay but not block).

We are currently working with C.R. Bard’s Electrophysiology Division and Philips Healthcare on a software prototype whereby the electrical data from the EP recording system is displayed in a color-coded format on the 3D overlay. This potentially allows rapid recognition of the direction of the wavefront for regular atrial tachycardias (Figure 2) and allows for color-coded entrainment mapping. This has been shown to be of benefit in a recent study, and easily demonstrates presence or absence of conduction block across linear lesions (Figure 3).

Additionally the software allows for dominant frequency mapping in atrial fibrillation, and wavelet analysis to try and localize areas that are critical to the AF process.

**Future improvements**

Although there have been huge technological advances in the EP laboratory over the last few years, the future holds even more promise.

Currently the overlaid 3D shell is static, whereas in practice the heart is moving, both due to cardiac contraction and to diaphragmatic movement. Real-time visualization of this movement will make catheter placement even more accurate, and possibly help to avoid inadvertent ablation within the pulmonary veins that can result in the complication of pulmonary vein stenosis.

Perhaps the most interesting possibility is the ability to integrate new information onto the 3D shell. For instance, areas of fibrosis could be...
References


Conclusion

Ablation of persistent AF is a difficult task, both to learn and to subsequently perform. The use of advanced imaging and mapping solutions will hopefully shorten the learning curve and make the procedure safer and more effective, leading to improved outcomes for patients and a greater number of patients being able to be treated for this debilitating condition."


