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Stepwise Ablation of Permanent Atrial Fibrillation

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1. Introduction

The stepwise technique for ablation permanent atrial fibrillation (AF) is a combination and cumulative effect of several strategies (Calkins et al., 2009); pulmonary vein isolation (PVI), ablation of complex fractionated potentials, and linear lesions. This approach leads to termination of AF in 85% of cases without the need for pharmacological or electrical cardioversion and also produces unprecedented clinical outcomes in terms of maintaining sinus rhythm (SR) in the medium term, although more than 50% of patients require repeat procedures (Haissaguerre et al., 2005; O'Niell et al., 2006; Takahashi et al., 2007, Hocini et al., 2010). The cumulative effect of each step can be visualized as in figure 1. Termination of AF may occur at any point throughout the stepwise approach. The endpoint of ablation is termination of AF directly to SR (15%) or through intermediate atrial tachycardias (AT) with a mean of 2.6 atrial ATs per patient (Haissaguerre et al., 2005). With sinus rhythm successfully restored, the PVI and integrity of any linear ablation should be confirmed and if incomplete finished by further ablation as necessary, now in sinus rhythm.

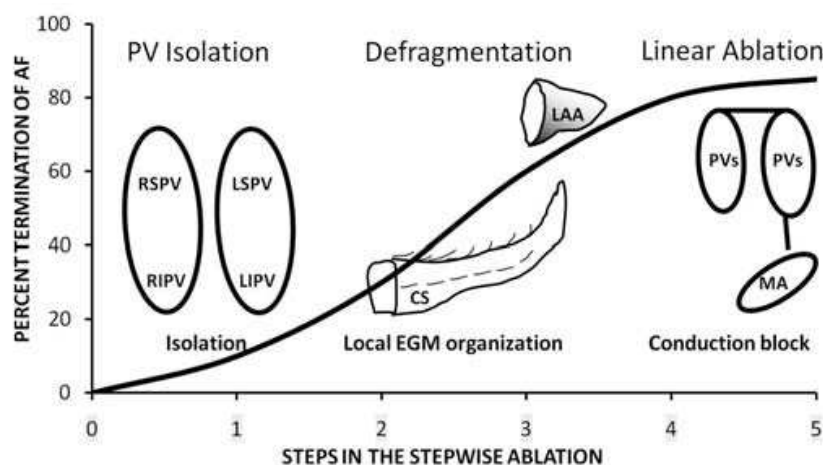


Fig. 1. Shows the cumulative effect of the stepwise ablation: with each next step, more termination of AF. The incremental benefit of each next step has a progressively smaller effect, until a ceiling of about 85% after which more ablation will not result in a higher success rate for AF termination (Hocini et al., 2010). PV Pulmonary Veins, RSPV and RIPV right superior and right inferior pulmonary veins respectively. LSPV and LIPV left superior and left inferior pulmonary veins respectively. MA mitral annulus. CS coronary sinus.

This chapter will go through in detail each step of this ablation approach. In addition, patient selection and preparation as well as post procedural care and complications will be described. Atrial tachycardia mapping and ablation will be described although it is not in the scope of this chapter to give a full description of this large topic. Finally, procedural outcomes and predictors of success will be discussed.

It should be emphasized that this chapter will describe the way the authors carry out their ablation procedures, there are many variations between centers, but generally the similarities in approach far outweigh any differences.

2. Patient selection and pre-procedural preparation

Persistent AF is defined as AF which that is sustained beyond seven days, or lasting less than seven days but necessitating pharmacologic or electrical cardioversion to restore sinus rhythm. Included in the category of persistent AF is "longstanding persistent AF" which is defined as continuous AF of greater than one year duration. Patients with symptomatic persistent AF who are refractory to antiarrhythmic drug therapy are candidates for the procedure if they accept the benefits and risks, as well as a >50% chance of requiring a second procedure. Catheter ablation of AF is a demanding procedure that may result in severe complications, a fact that should be explained to the patient prior to signing any consent form. Patients are not excluded on the basis of LA size or the presence of concomitant structural heart disease. On the contrary, selected patients with heart failure and/or reduced ejection fraction especially seem to benefit from restoration of SR.

2.1 Patient preparation

All patients undergo cardiac evaluation with imaging pre-procedure. A standard two-dimensional echocardiogram is most commonly used. Besides standard parameters such as atrial dimensions and ventricular function, other abnormalities such as an interatrial septal aneurysm or a persistent foramen ovale are actively sought for by the echocardiographer.

A transesophageal echocardiogram (TEE) is performed in all patients prior to the procedure to exclude LA thrombus, which is present in approximately 1% of cases despite appropriate anticoagulation and irrespective of the patients' CHADS₂ score (Scherr et al., 2009). The TEE is usually performed the day before to the procedure.

All antiarrhythmic drugs are stopped for at least 5 half lives prior to ablation except in the case of amiodarone, which is continued.

2.2 Pre-procedural advanced cardiac imaging

Computed tomography (CT) and magnetic resonance imaging (MRI) are increasingly used pre-procedure in order to gain more detailed atrial anatomical knowledge as well as for possible merging with 3-D electroanatomical mapping systems (see below). In addition, MRI can assess for areas of delayed enhancement (suggesting fibrosis/scar areas) but for now this additional information is usually part of research. However, neither current evidence nor personal experience has convinced us to routinely use pre-procedural 3D imaging and/or 3D electroanatomic mapping for every AF ablation procedure.

2.3 Anticoagulation

Patients are treated with oral anticoagulants to maintain an international normalized ratio (INR) between 2 and 3 for at least four weeks leading up to the ablation, with cessation 48 hours prior to the procedure. Patients with a contraindication to warfarin or who refuse oral anticoagulation are treated at the physician's discretion. Patients do not routinely receive bridging therapy with low molecular weight heparin between the cessation of warfarin and the procedure. However, in selected patients with major risk factors, e.g. prior embolic event or an enlarged LA with spontaneous contrast, low molecular weight heparin is administered as a bridging therapy.

3. Patient preparation and ablation set-up

The vast majority of our patients undergo the AF ablation procedure under conscious sedation and not under general anaesthesia, aiming to prevent and monitor for any complications such as cerebrovascular embolic events. Sedation is with midazolam and morphine, if any deeper sedation needed, this should be anaesthetist-guided. Arterial lines, urinary catheters or esophageal temperature probes are not routinely used.

One 6 French sheath and two 8 French sheaths (one of which is later replaced with the transseptal sheath) are placed in the right common femoral vein and a decapolar steerable catheter is placed in the CS such that its tip is at the 3 o'clock position in the 30° LAO view.

3.1 Rotational atriography and pulmonary vein angiography

Prior to the transseptal puncture 3D rotational atriography of the LA and pulmonary veins is usually performed (using a Philips Xper FD 10 system (Philips Medical Systems, Best, The Netherlands)). This is done by placing a 6 Fr pigtail catheter in the upper end of the inferior caval vein, with the C-arm carefully isocentered over the LA, and then injecting contrast. After a standard delay, usually 14 seconds (pulmonary transit time), the fluoroscopy is initiated and the C-arm rotates over a 240° arc with an X-ray acquisition speed of 30 frames/sec. The 3D data are automatically transferred and merged onto the workstation to enable on-line 3D reconstruction and as such catheter visualisation in 3D on-line. Details of rotational atriography are described elsewhere (Knecht et al., 2010). This gives very useful acute and precise anatomical definition of the ostia and hence help guide the ablation and minimises complications such as pulmonary vein stenosis, which can occur if ablating too distal into the vein.

A (less ideal) alternative to 3D atriography is selective angiography of the pulmonary veins. This is done by selectively engaging each of the four PV ostia with a multipurpose angiography catheter and injecting contrast media into each vein under fluoroscopy.

3.2 Transseptal puncture

Several different techniques are used to obtain a safe transseptal puncture. Centers should probably continue what they are experienced with and feel competent with. Here we suggest one way of proceeding: an antero-posterior X-ray position is used for the pull-down (usually started with a 4- to 5 o'clock needle position) and, once the jump onto the foramen ovale is seen, for the transseptal puncture. Before puncturing and crossing the needle into the left atrium, the monoplaner fluoroscopy system is briefly positioned in a left-lateral position to check for needle position in the sagittal plane (ideally between 12 and 1 o'clock).

Single transseptal puncture is performed with pressure monitoring and using contrast injection through the needle tip to confirm LA access prior to advancing the dilator and sheath assembly. A guidewire is advanced through the dilator and sheath assembly into a left PV and the dilator and sheath are pulled back into the RA to allow passage of the ablation catheter through the same puncture site into the LA (hence a single puncture technique). The dilator and sheath are then advanced over the guidewire into the LA alongside the ablation catheter, the sheath is aspirated and initially flushed with a bolus and subsequently continuously with heparinized saline at 200 ml/hr. Immediately after LA access, a bolus of heparin (50U/kg) is given intravenously. The ACT is checked every 30 to 60 minutes during the procedure and repeat boluses of heparin is administered to achieve a constant activated clotting time (ACT) between 250-300 seconds.

3.3 Sheaths and catheters

A 10-pole, 20 mm circular decapolar catheter is advanced via a transseptal sheath (SL-0, St. Jude Medical, St. Paul, Minnesota) and positioned just distal to the PV ostia to map the PV perimeter during PVI. An externally irrigated tip ablation catheter (eg Thermocool 3.5 mm-tip catheter, Biosense Webster Inc, Diamond Bar, CA) is used, usually with an F-curve, however, the size of the curve used should depend on the size of the atrium.

3.4 Radiofrequency delivery

Radiofrequency energy is delivered using a Stockert generator (Biosense Webster) with the power settings shown in Table 1. These power settings have been determined empirically to provide effective lesions while also minimizing the risks of PV stenosis, steam pops, cardiac tamponade and collateral damage to the phrenic nerve, esophagus and circumflex coronary artery. Target temperatures of 40-42°C are achieved (maximum temperature 45°C) by manual titration of irrigation rates from 5-60 ml/minute (0.9% saline via CoolFlow pump, Biosense Webster).

Ablation site	Power (Watts)	Usual total duration of radiofrequency delivery (mins)
Coronary Sinus	15 -25	4-8
Posterior wall LA	25 - 30	3-6
Anterior wall LA	30 - 35	3-6
Inferior LA	30 - 40	5-10
Roof LA	25 - 30	10-15
PVs	30	25-40
Septum LA	30	3-6
Right atrium	20 - 35	0-20
Mitral Isthmus	30 - 35	10-20

Table 1. The power settings and usual RF delivery time at each anatomic region.

3.5 Signal processing

During AF ablation procedures, 12 lead surface electrocardiograms and bipolar endocardial electrocardiograms are continuously monitored and stored using a digital amplifier and

computer recording system (LabSystem Pro, Bard Electrophysiology, Lowell, MA, USA). All signals are sampled at 1Khz with filter settings from 30 to 250Hz for intracardiac signals and 0.1 to 50Hz for surface electrocardiograms. Intracardiac signals are displayed at an amplification of 0.1mV/cm and with a gain of x16 for the mapping/ablation catheter, and 0.2mV/cm with a gain of x8 for the Lasso catheter and coronary sinus catheter.

3.6 Three dimensional mapping

While not routinely required, various 3-D electroanatomic mapping technologies may be used for assessment of anatomy, electrogram analysis, and quantification of the impact of ablation on LA and RA voltages. Occasionally, these technologies are useful for mapping ATs that may arise after AF termination or during subsequent procedures. Any electroanatomic mapping system may be used (EnSite NavX Navigation & Visualization Technology, St. Jude Medical, St. Paul, MN; CARTO3 System, Biosense Webster, Diamond Bar, CA), which allow real-time display of any cardiac catheter during ablation. The ability to display a lasso catheter allows for very rapid creation of a left atrial map and direction of the ablation catheter toward the desired poles on the lasso catheter.

3.7 Atrial Fibrillation cycle length

Assessment of the atrial fibrillation cycle length (AFCL) is an important tool in guiding the ablation procedure. Electrograms (EGMs) in persistent AF are complex and the cycle length cannot be reliably measured, except in the right and left appendages (Figure 2). Throughout the stepwise ablation the AFCL will gradually prolong and once a critical prolongation has been achieved, usually in the region of 180 to 200 ms, the atrium can no longer sustain the fibrillatory process and AF terminates to either SR or, as in the majority of cases, to an atrial tachycardia (AT) that can then be mapped and ablated conventionally.

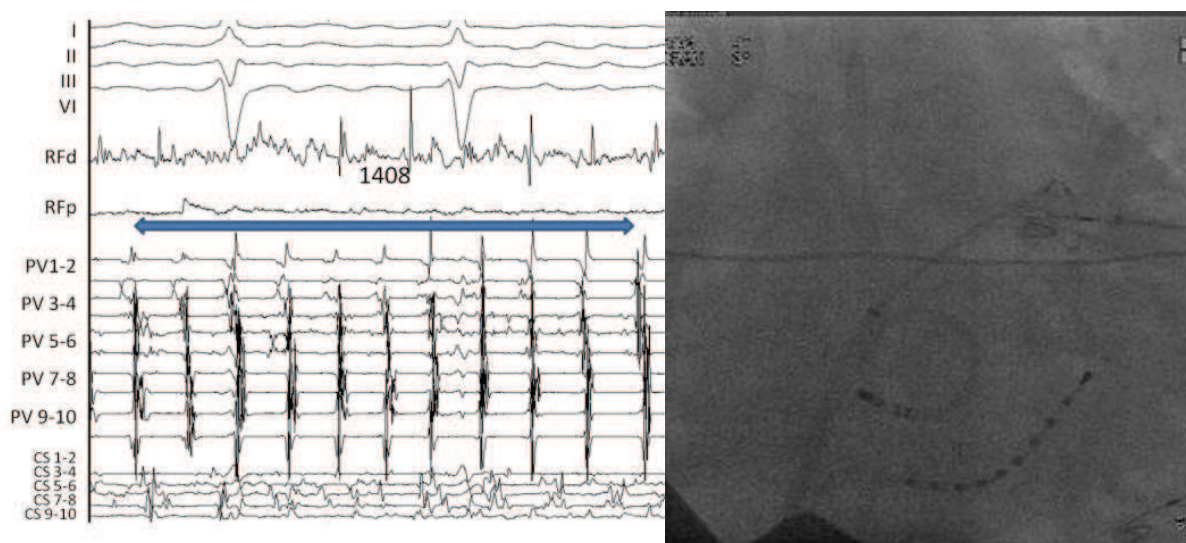


Fig. 2. Surface leads I, II, III and V1. Then the EGMs of the radiofrequency (RF) catheter, RFp (proximal) and RFd (distal), placed in the inferior LA. PV1-PV10 are the EGMs from a LASSO catheter placed in the left atrial appendage (LAA). CS 1-10 are the EGMs from a decapolar catheter in the coronary sinus. The AFCL cannot be measured on the surface ECG nor in the coronary sinus. However the LASSO catheter in the LAA enables measurement a more exact AFCL, here 10 cycle lengths are counted, giving an AFCL of 141ms.

4. Pulmonary vein isolation

Ablation strategies which target the isolation of the PVs are the cornerstone for most AF ablation procedures. The PVs can be isolated individually or as ipsilateral pairs, generally dependent on venous anatomy, catheter stability and operator preference. When the PVs are targeted, complete electrical isolation and elimination of all electrical near-field signals around the PVs is the goal. An example of isolation of the left superior pulmonary vein (LSPV) can be seen in Figure 3.

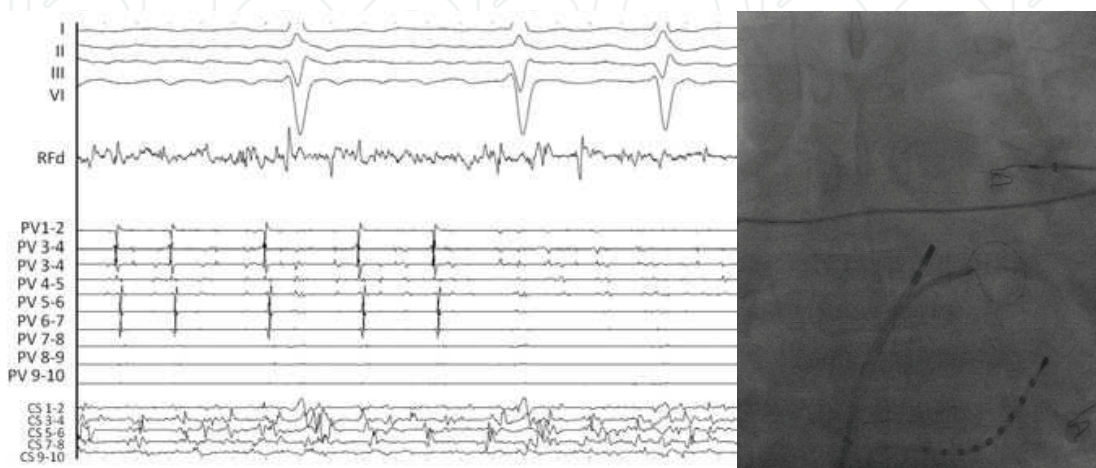


Fig. 3. Left panel shows surface ECG I, II, III and V1. Then, the RF ablation EGMs, followed by the poles 1-10 of the Lasso catheter and the lowest 5 EGMs are the bipoles of the decapolar catheter in the CS. The right panel shows fluoroscopy of the decapolar catheter in the coronary sinus, the Lasso catheter in the LSPV, and the RF catheter ablating just proximal to the ostium of the vein. There is 2:1 entry block into the vein prior to isolation.

Ablation is performed 1 to 2 cm proximal to the PV ostia. The ablation is typically started on the posterior wall towards the LSPV. Ablation can be done in a continuous manner, delivering energy at any given site for 30 – 60 seconds, until the local electrical signals have diminished, before moving on to the next site in a continuous fashion, slowly creating a posterior ablation line (vertical line from high to low) on the left side, followed by ablation within the first millimeters of the venous ostia to target the fascicles lying anteriorly until electrical PV isolation. Circumferential ablation is then repeated around the right PVs with a continuous circular lesion. It is unusual to achieve PV isolation after circumferential coalescent lesions without further ablation targeting the earliest PV activity or sites of reverse PV polarity as recorded on the circumferential mapping catheter indicating the residual anatomical connection. During ongoing AF, the sequence of PV activation is incessantly changing because (i) multiple breakthroughs are present in the most veins, (ii) changing incident wavefronts of activation at the PV ostia and (iii) rate-dependent conduction properties of the LA-PV connections. A consistent activation sequence usually means discrete sites of breakthrough, either spontaneous or following prior ablation. Delivery of RF narrows the width or number of LA-PV connections resulting in progressive consistency of the PV activation sequence. The endpoint of this step is complete electrical isolation of all pulmonary veins evident in the form of entrance block.

During AF, it can be difficult to distinguish far field potentials from local pulmonary vein potentials, both seen on the circular catheter at the PV ostium. Some guides to the differentiation are as follows:

- PV potentials represent local myocardial activation and therefore exhibit sharper electrograms with more rapid deflection than the far-field potentials.
- Activation sequence of PV potentials is constantly changing during ablation, while that of far-fields is relatively stable.
- Consistent prolongation of PV CL may be observed due to reduction of LA to PV connections with radiofrequency applications.
- If doubt remains, far-field potentials can be unmasked by putting a recording catheter in the suspected structure, in particular the LAA. Synchronous activity between LAA and PV potentials confirms an external origin of potentials recorded on the circumferential catheter.

As previously explained, long-standing persistent AF will terminate after PVI alone only in a small minority of patients although the global AFCL usually increase by 8ms (Haissaguerre et al., 2005a). Once sinus rhythm is restored, after the stepwise ablation approach, it is important to confirm complete PVI, this is best done by re-inserting the circumferential lasso catheter into each vein.

Figure 4 shows the AFCL prolongation achieved following pulmonary vein isolation. This tracing is from the same patient as who had an AFCL of 141ms in figure 2 and PVI in figure 3.

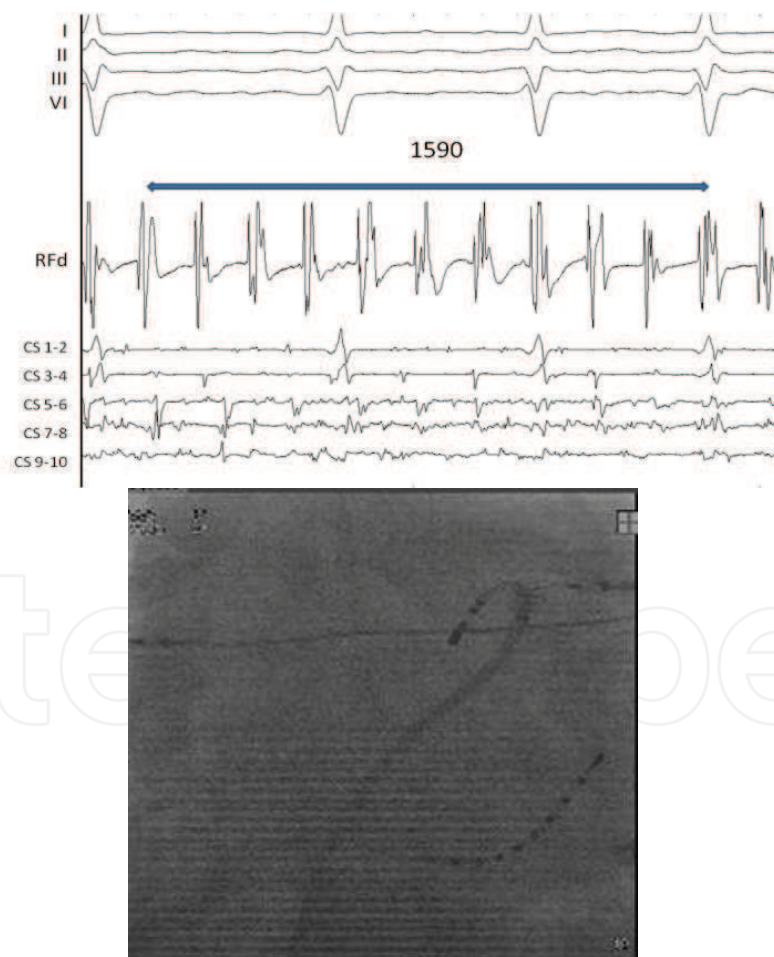


Fig. 4. Upper panel shows the surface leads I, II, III and V1. The EGMs from the RF catheter (placed at the base of the LAA) and lowest the EGMs from the 5 bipoles of the decapolar catheter in the CS. The AFCL is now 159ms. Lower panel shows the catheter placement on fluoroscopy.

5. Electrogram- based ablation during disorganized left atrial activity

The next step in the approach is electrogram based ablation, also colloquially called defragmentation. Following pulmonary vein isolation left atrial activity is usually chaotic with disorganized sites everywhere and the overall activity is too complex to map in terms of activation, morphology or local cycle length. The aim is to ablate favorable areas that would result in slowing and organization of global LA activity.

5.1 Targets for EGM-based ablation

Favorable areas in the left atrium for ablation are continuous electrograms with complex fractionated potentials that are noted at first sight, especially when the AFCL is around 140-150ms. When the AFCL prolongs significantly, we search for sites with a gradient of activation (significant electrogram offset between the distal and proximal recording bipoles on the map electrode), or regions with a cycle length that are shorter than the mean LAA cycle length (Haissaguerre et al., 2005). A recent study found that ablation of areas with continuous activity had the greater impact on AFCL prolongation and AF termination than ablation of areas with high fractionation index, EGM voltage and local cycle length (Takahashi et al., 2008).

The various zones of complex atrial electrograms may be explained by several different underlying etiologies. They may represent areas of colliding wave fronts, pivot points of moving wavelets or collision with barriers such as scars or existing structures for instance valves or appendages. Complex electrograms are seen in the periphery of sites of rapid activity, often with a frequency gradient to surrounding tissue. These sites are usually located at the base of the LAA, the PV ostial region and in the inferior LA along the CS. Figure 5 shows examples of complex electrograms.

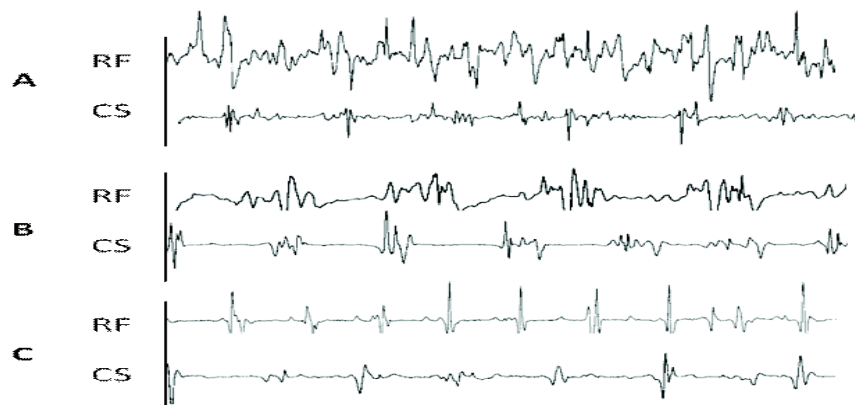


Fig. 5. Shows simultaneous recordings from the RF (in the LA) and CS catheters ; panel A is a recording of continuous activity on the RF catheter without a return to baseline, panel B shows a fractionated potentials on the RF catheter with an interposed isoelectric interval and panel C is an example of rapid activity recorded on the RF catheter with a frequency gradient to the CS.

5.2 Facilitating tools in localizing targets for ablation

Localizing and mapping areas for electrogram based ablation can be difficult. To facilitate this, various methods have been tried, including anatomical guided ablation, the use of multipolar catheters and the use of 3 dimensional mapping systems.

5.2.1 Anatomical guidance to defragmentation

Studies have been done to try determine anatomical areas within the left atrium where ablation has the greatest impact (rise in the LAA-AFCL by at least 5ms) on the AF process; in addition to the pulmonary vein isolation, the base of the left atrial appendage and the interface between inferior LA and the coronary sinus has the greatest impact (Haissaguerre et al., 2005). Figure 6 illustrates this concept. Figure 7 is an example of ablation of chaotic EGMs in the inferior left atrium.

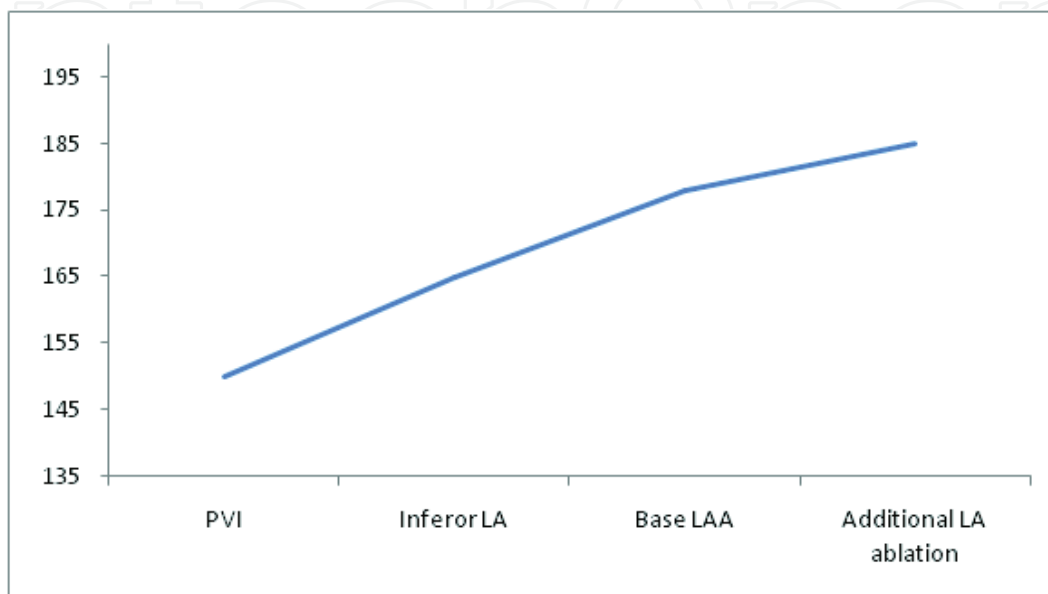


Fig. 6. With ablation of each anatomical area the AFCL gradually prolongs – a cumulative effect.



Fig. 7. Surface leads I,II III and VI. The EGMs on the RF catheter are of a complex nature. The decapolar catheter in the CS confirms AF. Ablating in the inferior LA can be done by dragging the catheter along the floor of the atrium, either from left to right (upper insert) or from right to left (lower insert).

5.2.2 Multipolar catheters

Another aid in determining left atrial areas/zones for ablation is the use of multipolar catheters, such as the LASSO catheter or the PENTA-RAY catheter (Biosense Webster, Inc, Diamond Bar, CA, USA), with 10 and 20 poles respectively (figure 8). The advantage, apart from the high density of electrograms, is the temporal and directional information such closely organized catheter poles can provide. These catheters are particularly useful in organized atrial fibrillation, as well as in mapping focal and localized re-entrant tachycardias (an example described below).

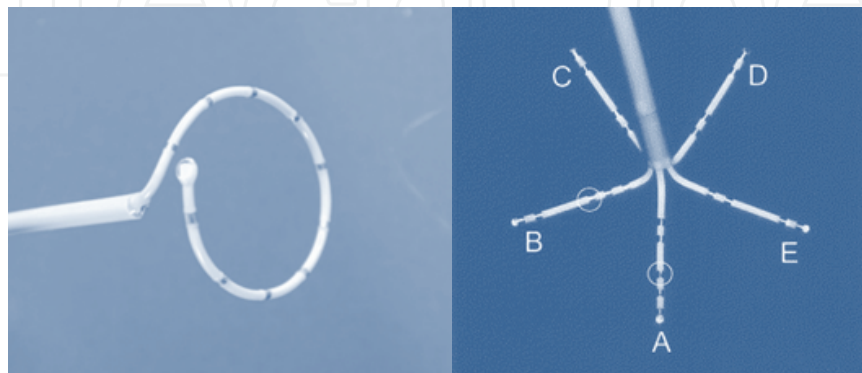


Fig. 8. Examples of multipolar catheters that can be used for mapping, to the left a spiral catheter, to the right a penta-ray catheter.

5.2.3 Three dimensional mapping systems

Finally, an aid can be 3 dimensional mapping systems that have algorithms to compute (on-line) areas of very short cycle lengths and fragmentation. Figure 9 shows an example of a NAVx (St Jude Medical, Inc., MN, USA) electroanatomic fractionation map of the left atrium during atrial fibrillation. The most fractionated (fastest cycle length) areas are represented by red, the least represented by blue, and grey represents scar or inactive areas.



Fig. 9. Shows a NAVx electroanatomic fractionation map of the left atrium (postero-anterior view). Circumferential PVI can be seen represented by brown ablation points.

5.3 Cycle length prolongation

Throughout the defragmentation the AFCL is prolonging and it useful to assess the AFCL after each step of ablation. Figure 10 illustrates the prolongation during defragmentation in the same patient as earlier. He had an initial AFCL of 141ms (figure 2) which prolonged to 159ms after PVI (figure 4). During defragmentation in the inferior LA, base of LAA and septum the AFCL prolonged to 183ms and during roof ablation converted to an AT (figure 10).

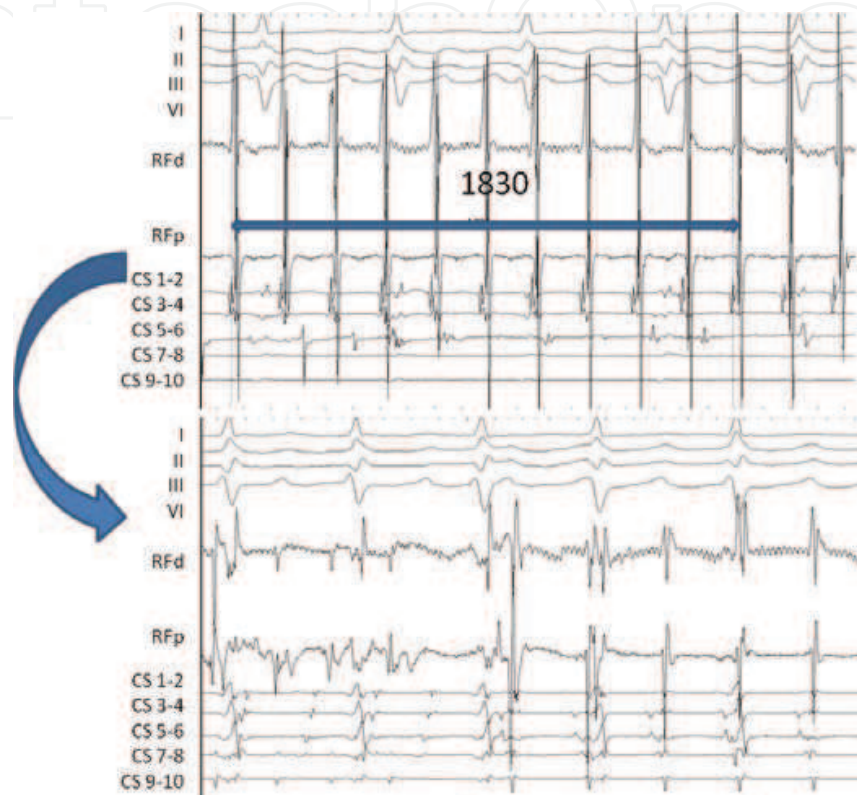


Fig. 10. Both panels show surface leads I, II, III, VI and a decapolar catheter in the CS. In the upper panel the RF catheter is in the LAA and the AFCL is measured over 10 cycles to be 183ms. With further ablation the AF converts to an AT (lower panel).

6. Linear ablation

If the patient is still in AF after the previous steps, the next stride in the stepwise ablation procedure is linear ablation. Linear ablation is an important tool in the step wise ablation procedure (Knecht et al., 2008). The efficacy of linear lesions may be related to interruption of wavelets and macro re-entries, ablation of autonomic innervations and atrial debulking. The left atrial roof and the lateral mitral isthmus are the most common sites for linear ablation. Linear ablation is often done during AF but proving bidirectional block can only be done in SR, usually towards the end of the procedure when SR has been reestablished. It is possible that that the previous steps have rendered the patient in an atrial tachycardia, in which case the lines are ablated (if appropriate) during the AT.

In general, linear ablation is the last step in the stepwise approach. This is because they can be very difficult, they may require not only a long time but also a large amount of radiofrequency to successfully achieve bidirectional block. This alone increases the risk for

complications such as perforation and tamponade. In addition incomplete lines are associated with arrhythmia recurrence and pro-arrhythmic effects (Gerstenfeld et al., 2004; Chugh et al., 2005). The 2 left atrial lines will be discussed separately.

6.1 Linear ablation at the left atrial roof

The left atrial roof line is relatively short, forming a continuous line between the already isolated left and right superior pulmonary veins. In the vast majority of patients this step is done during AF and the end point (during AF) is 85-90% diminution or complete abolition of local electrograms along the line. The line is performed as cranially as possible to avoid ablating the posterior LA, hence aiming to avoid complications such as damage to the esophagus.

The electrophysiological endpoint of roof ablation is the creation of a complete line of conduction block between the superior PVs. If the ablation is done during AF, supplementary ablation during sinus rhythm is usually required. Electrical block is confirmed in all patients following restoration of SR using a well described technique (Hocini et al., 2005).

6.1.1 The creation of the roof line

The ablation catheter is curved and dragged along the line with the tip of the irrigated catheter positioned parallel to the roof, either from right to left or left to right. A large loop in the LA is often helpful (figure 11). If the orientation of the catheter tip is perpendicular to the roof power settings should be reduced (to 25W) to lessen the possibility of steam pops and perforation.

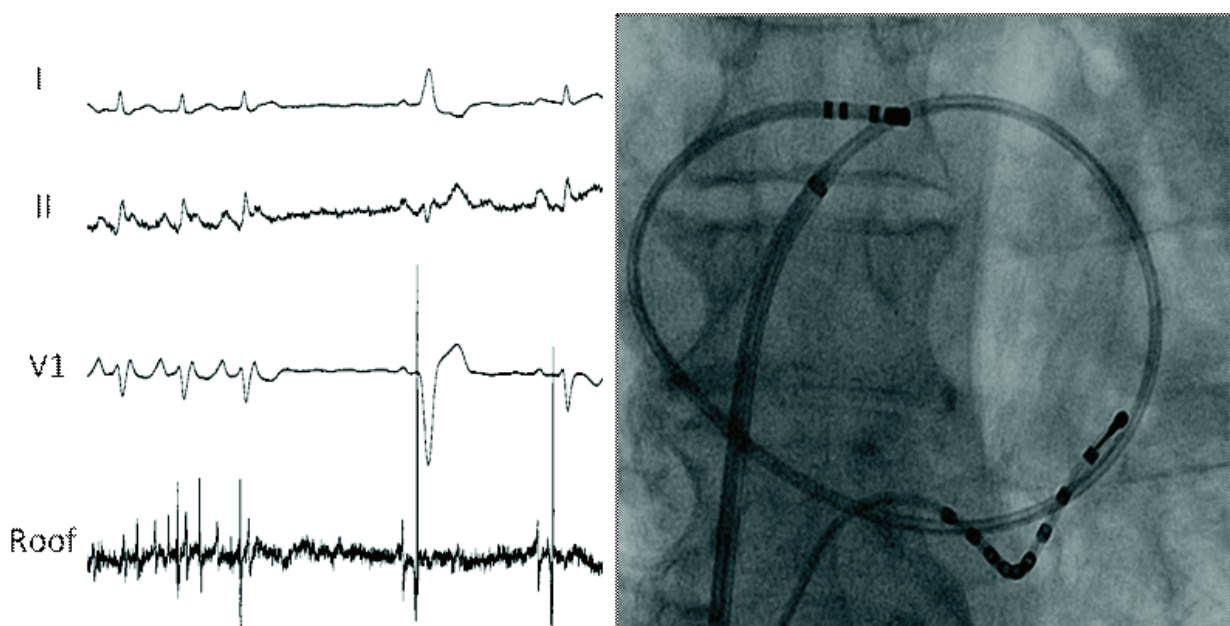


Fig. 11. Surface lead I, II and VI together with the EGMs from the RF. This roof line is carried out during roof dependent atrial tachycardia; fractionated EGMs can be seen on the RF catheter prior to completion of the line when the SR is restored.

6.2 Linear ablation at the mitral isthmus

Ablation of the mitral isthmus, achieving bidirectional conduction block further increases the success rate of catheter ablation in persistent AF (Jais et al., 2004). In general this ablation step is only carried out if deemed necessary; if the previous steps have not terminated the atrial fibrillation or if the patient is in a mitral isthmus dependent atrial tachycardia. If the line is carried out during AF, the endpoint is the same as that for the roof line; abolition of all local electrograms along the line, usually with the creation of double potentials all along the line. If carried out during atrial tachycardia (mitral isthmus dependent flutter) the goal is arrhythmia termination. Once in SR, the electrical block must be confirmed using bidirectional pacing and sensing from the CS catheter and the mapping catheter (see below). Again, it is likely that more ablation is needed once in sinus rhythm to achieve bidirectional block. It must be noted that even in the best pair of hands, block of the mitral isthmus cannot be achieved in about 10% of patients.

6.2.1 The creation of the mitral isthmus line

The mitral isthmus is short, 2-4cm, from the mitral annulus to the left inferior pulmonary vein ostium (or the left atrial appendage). It is often needed to extend the line from the ostium of the inferior pulmonary vein to the base of the LAA in order to achieve block as well as it is needed in up to 80 % to ablate within in coronary sinus to achieve block (Jais et al., 2004). The mitral isthmus line is begun at the ventricular aspect of the mitral annulus, see figure 12. With clockwise rotation on the sheath and catheter the lesion is extended to the left inferior PV and further to the base of the LAA if needed. If mitral isthmus block is not achieved by this, the ablation is extended to the epicardial aspect of the mitral isthmus, via the coronary sinus (Jais et al., 2004). The overall goal remain the same for all linear lesions, elimination of local EGMs along a line connecting 2 electrically inactive sites, e.g. the mitral valve annulus and the encircling lesion of the LIPV.

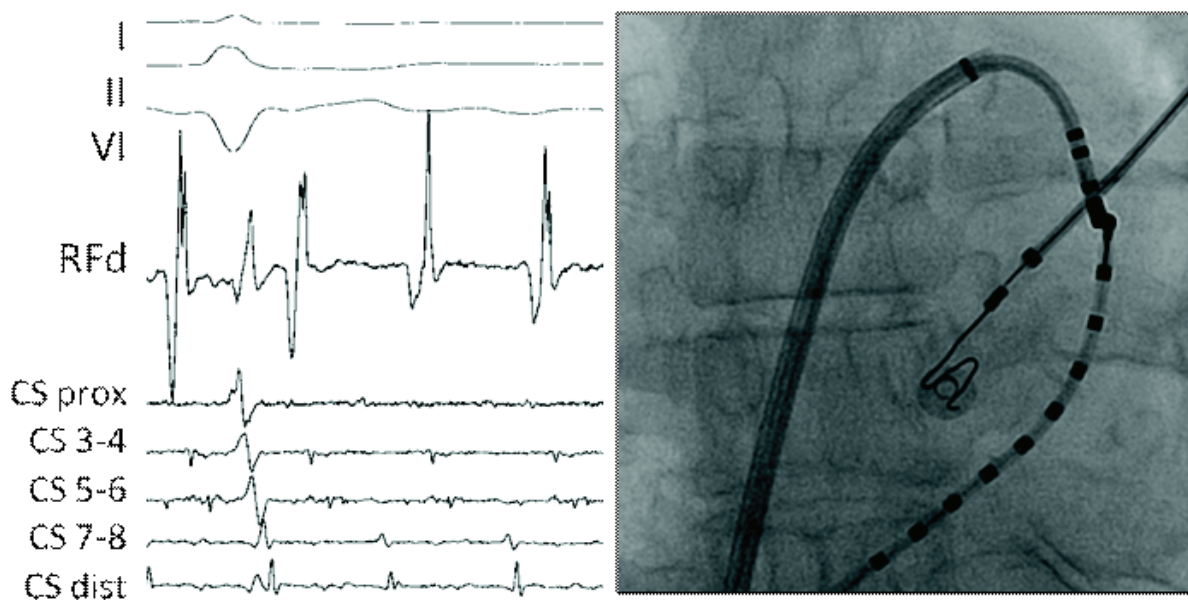


Fig. 12. Surface leads I, II and VI, the RF catheter and the bipolar EGMs of the decapolar catheter in the CS. The RF catheter is at the start of the linear ablation of the mitral isthmus. Often there are high amplitude EGMs at the mitral isthmus pre ablation.

7. Right atrial ablation

In 15% of patient with persistent AF, SR cannot be restored by ablation in the LA and the presence of perpetuators in the RA should be considered (Hocini et al., 2010). This state of affairs should be suspected when the AFCL in the RAA prolongs less than the AFCL in the LAA during ablation; a shorter AFCL in the RAA compared to LAA can be due to the drivers of AF originating in the RA (figure 13). Similarly, pauses in activity in the LA electrograms without corresponding pauses in the RA electrograms would suggest the RA as the driving chamber. The approach to mapping and the electrogram ablation within the RA is the same as for the LA. Preferential anatomical areas at which there is a higher incidence of AF termination during ablation of complex fractionated atrial electrograms are the right atrial appendage, the intercaval region, the SVC and the CS ostium.

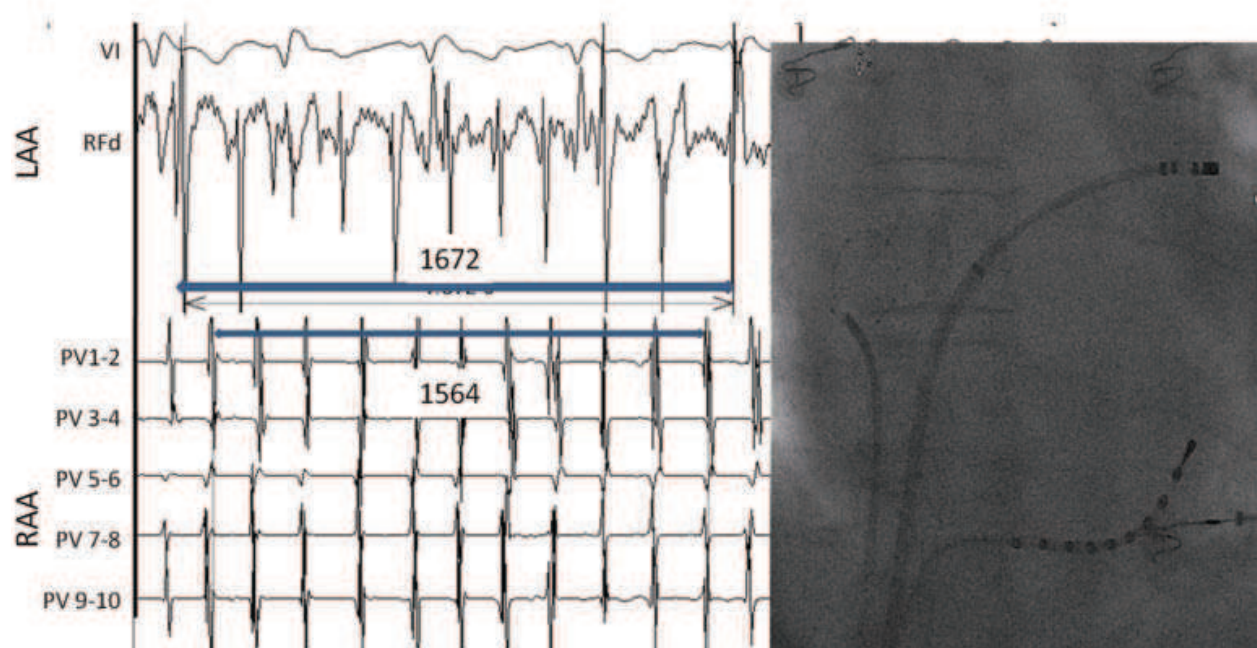


Fig. 13. Shows surface lead VI, EGM from the RF catheter placed in the LAA and the 5 bipolar EGMs from the LASSO catheter placed in the RAA as the lower 5 rows. The LAA AFCL is 167 and the RAA AFCL 156 suggestive of a driving source in the right atrium. The right hand panel is a fluoroscopy of the catheter placement.

8. Atrial tachycardia in the context of atrial fibrillation ablation

Atrial tachycardia may occur at any point throughout the stepwise ablation for atrial fibrillation; when the AFCL is so prolonged that the LA can no longer sustain the fibrillatory process. As described in the introduction, the endpoint of the stepwise ablation is restoration of sinus rhythm, and this re-establishment of sinus rhythm usually occurs via 1 or more ATs (Haissaguerre et al., 2005). In addition, AT is the dominant mode of arrhythmia recurrence in patients in whom AF was terminated during the index procedure (O'Neill et al., 2009).

Atrial tachycardia is characterized by a monomorphic P-wave and a consistent intracardiac activation sequence. In the context of AF ablation, we classify AT into three categories:

Macro re-entry is defined as a circuit involving 3 or more atrial segments, and where more than 75% of the circuit can be mapped.

Focal tachycardia is defined as centrifugal activation originating from a discrete site, and where <75% of the cycle length can be mapped. This tachycardia can be due to any of increased automaticity, triggered activity or re-entrant mechanisms.

Localized re-entry constitutes a circuit involving 1 or 2 adjacent segments, usually smaller than 2 cm in diameter and spanning more than 75% of the cycle length within the involved segments.

A recent series of 238 ATs occurring after ablation of persistent atrial fibrillation found that 46% were macroreentrant and 54% focal or microreentrant ATs. Of the macroreentrant tachycardias the commonest were perimitral circuits (56%), followed by roof dependent circuits (28%), and with a smaller proportion of tricuspid isthmus dependent circuits (16%) (Jais et al., 2009). More complex macro-reentrant circuits are less common e.g. double loop re-entry and circuits passing through gaps between the pulmonary veins and/or the LAA.

8.1 Mapping atrial tachycardias

An approach to mapping atrial tachycardias is shown in figure 14. The first step is to assess atrial tachycardia cycle length variation, if > 15% variable the AT is likely to be of focal or local re-entry aetiology, if < 15% the tachycardia can be of any of the 3 categories (Jais et al., 2009). Fig 15 is an example of a tachycardia with very little cycle length variation. If the cycle length variation is less than 15% the first aim is to deduct whether it is a macroreentrant tachycardia or of a focal source. This requires activation mapping and entrainment mapping. If the cycle length variation is more than 15% and the atrial tachycardia mechanism therefore most likely a focal or localized re-entry source, the aim then is to map the source.

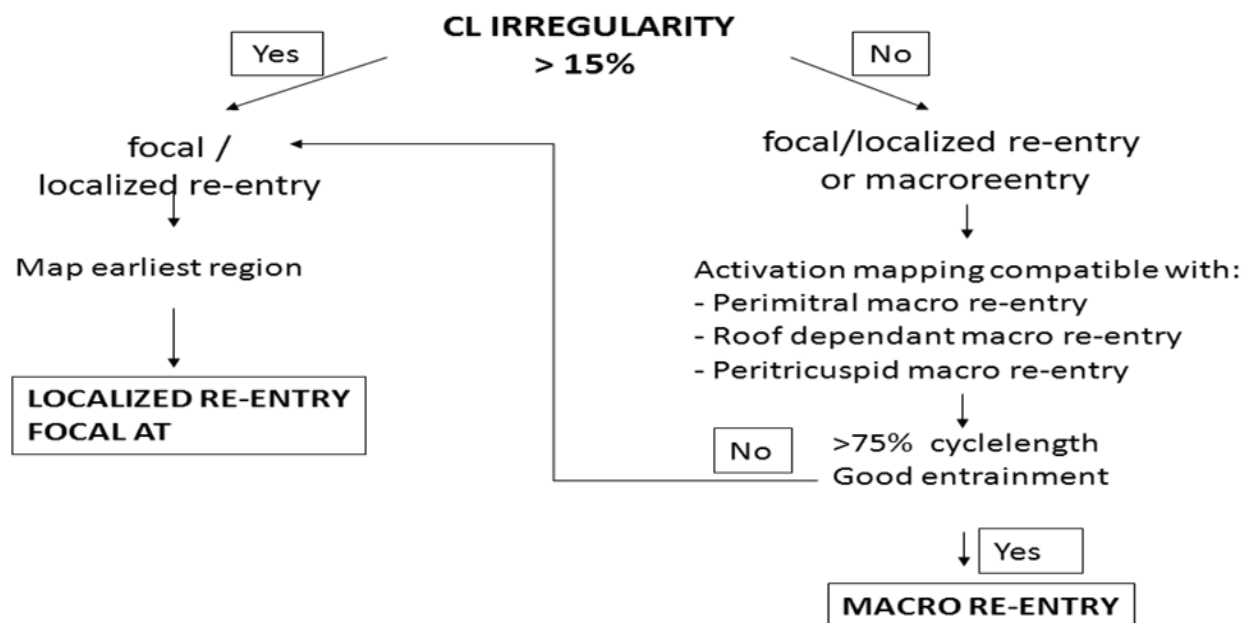


Fig. 14. Shows an algorithm for the diagnosis of atrial tachycardias.

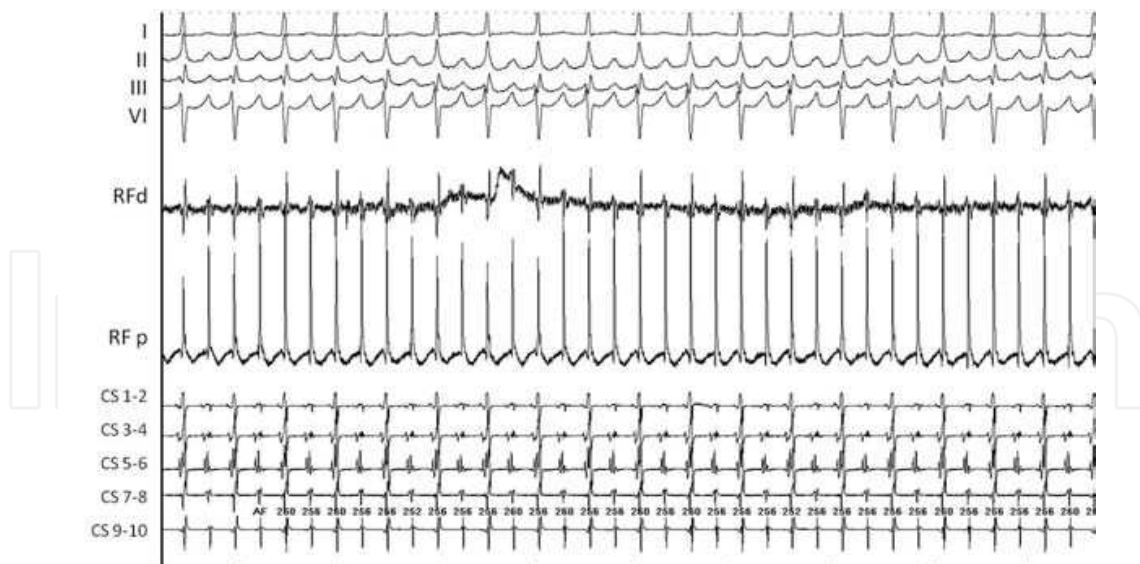


Fig. 15. Shows a tracing of an atrial tachycardia with very little cycle length variation, in this case 3%. The AT can therefore be either any of the 3 categories of AT: focal, localized re-entrant and macroreentrant. In such case, the first step is to rule in, or rule out, a macroreentrant tachycardia using activation mapping and entrainment. This tracing is from the same patient as in figures 2, 3, 4 and 10.

8.1.1 Mapping macro reentrant tachycardias

If the AT CL variation is more than 15%, the first aim is to rule in or rule out a macro re-entrant tachycardia. Given that the majority of macroreentrant AT are one of the following three: 1) Mitral isthmus dependent flutter (Perimitral AT), 2) Roof dependent flutter and 3) Cavotricuspid isthmus dependent flutter (Peritricuspid AT); activation mapping around the mitral annulus, anterior and posterior LA, the roof and the tricuspid annulus are mapped to look for the presence of activity all through the period of one tachycardia cycle length. Each of the 2 left atrial circuits has their own distinct activation sequence of the LA (figure 16):

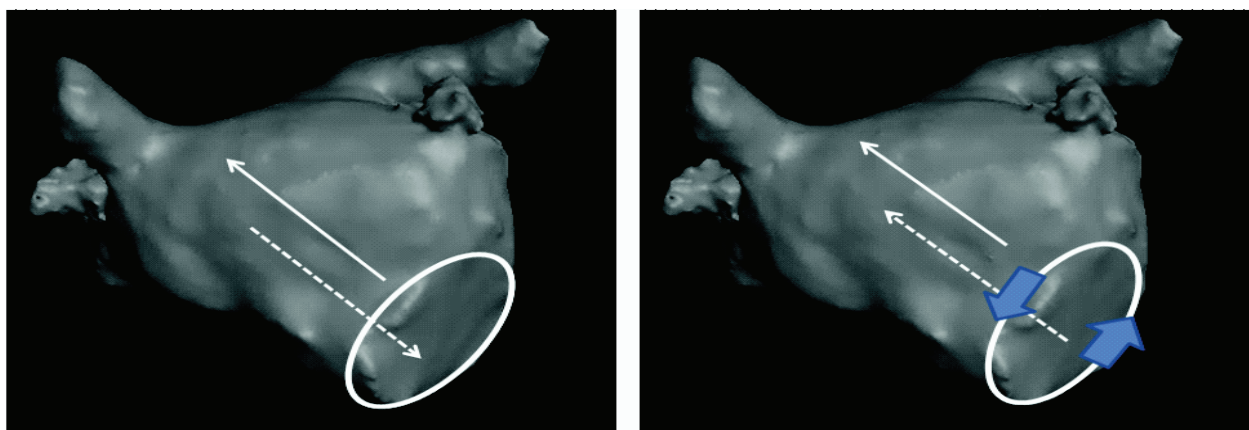


Fig. 16. Depicts the left atrial activation pattern of the macro reentry circuits: counterclockwise peri-mitral (A) and roof dependant (B)

Once the activation pattern of the macro-reentrant tachycardia has been established, entrainment from at least 2 opposite segments should be done to confirm (or rule out) the

diagnosis. If macro re-entrant circuits are ruled out the algorithm leads back to the top of the arm for focal and localised re-entrant tachycardias.

8.1.2 Ablating macroreentrant tachycardias

The perimitral atrial tachycardia passes through the mitral isthmus between the mitral valve annulus and the left inferior pulmonary vein, and hence ablation with complete isthmus block abolishes this arrhythmia. The roof dependent flutter is dependent on the relatively narrow part between the 2 upper pulmonary veins and a complete ablation line would terminate roof dependent flutter. The ablation of these two lines is described above. It is not in the scope of the chapter to describe the ablation of the right atrial peritricuspid flutter.

8.1.3 Confirming bidirectional block following line ablation – roof line

This very important step is undertaken after the SR has been restored, either from the stepwise ablation, or from direct current cardioversion. Following a complete roof line, pacing of the LAA will result in the activation of the posterior LA from inferior to superior direction as the activation front cannot travel posteriorly over the blocked roof. Figure 17 illustrates this concept.

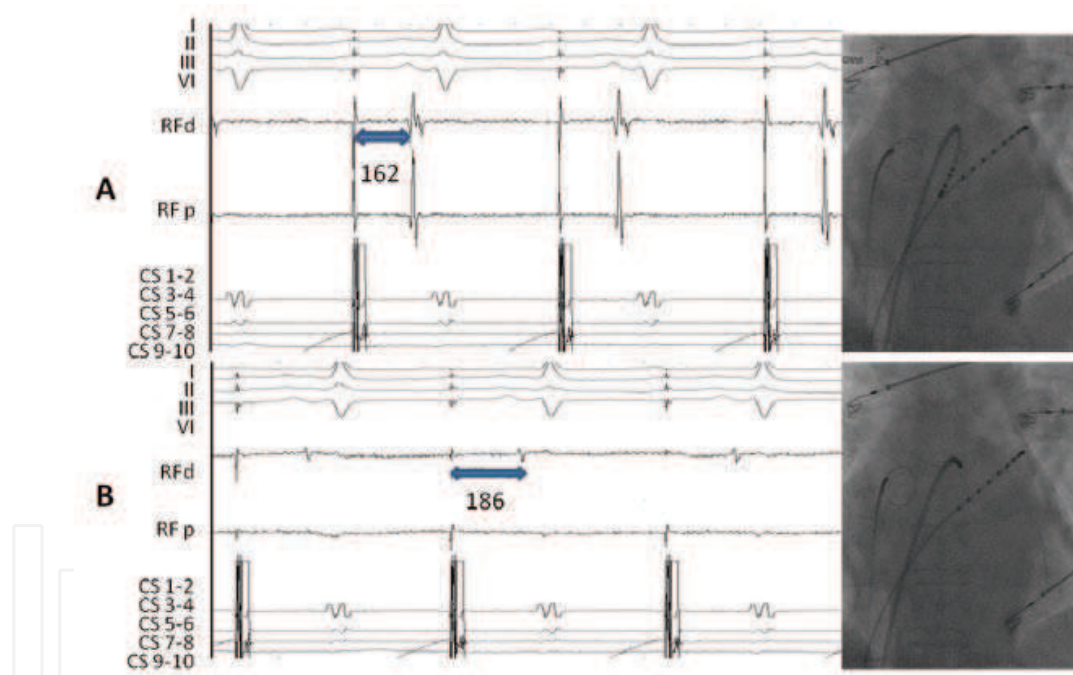


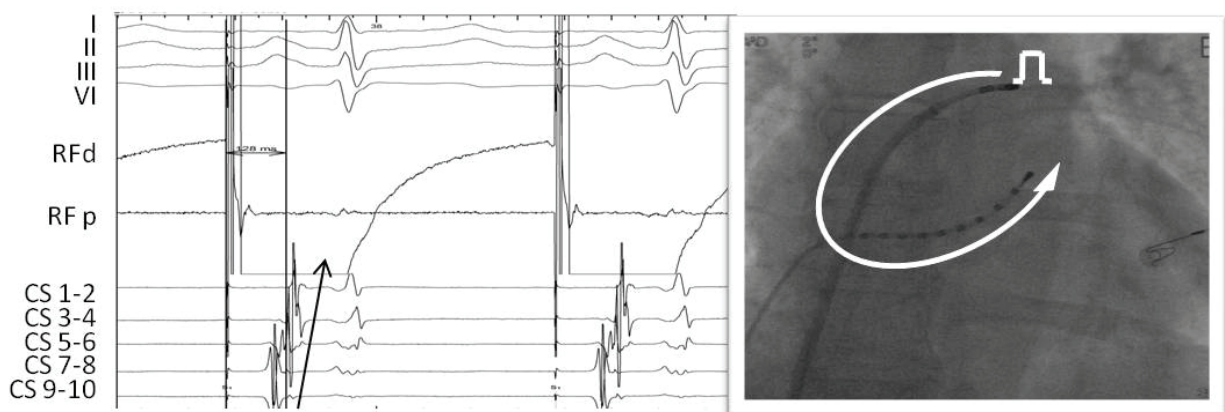
Fig. 17. The left panels show the surface leads I, II, III and VI. Then the EGMs of the RF catheter and lowest the 5 bipoles of the decapolar catheter – now placed though the transseptal puncture to the LAA. Pacing is done from the distal CS (LAA). In Panel A the RF catheter is placed low on the posterior wall and in panel B high on the posterior wall. During pacing from the LAA the time to low posterior wall is 162ms and to high posterior wall 184ms – thereby proving roof block.

8.1.4 Confirming bidirectional block following line ablation – mitral line

Following a mitral isthmus line, block is confirmed using differential CS pacing and pacing from the RF catheter at the lateral LA just anterior to the mitral line or in the LAA. In the

presence of block the activation front moves along the anterior wall to the septum and then along the posterior wall, septal to laterally, during LAA pacing. This gives a proximal to distal activation sequence of the CS. Figure 18A illustrates this. In the other direction, block is assessed by pacing the first the distal poles of the CS catheter, which is near the mitral line and measuring the delay to LAA. The pacing is then changed to a more proximal pole wherefrom the delay to the LAA should be shorter in the presence of blocked linear lesion. Figure 18B illustrates this.

18 A



18 B

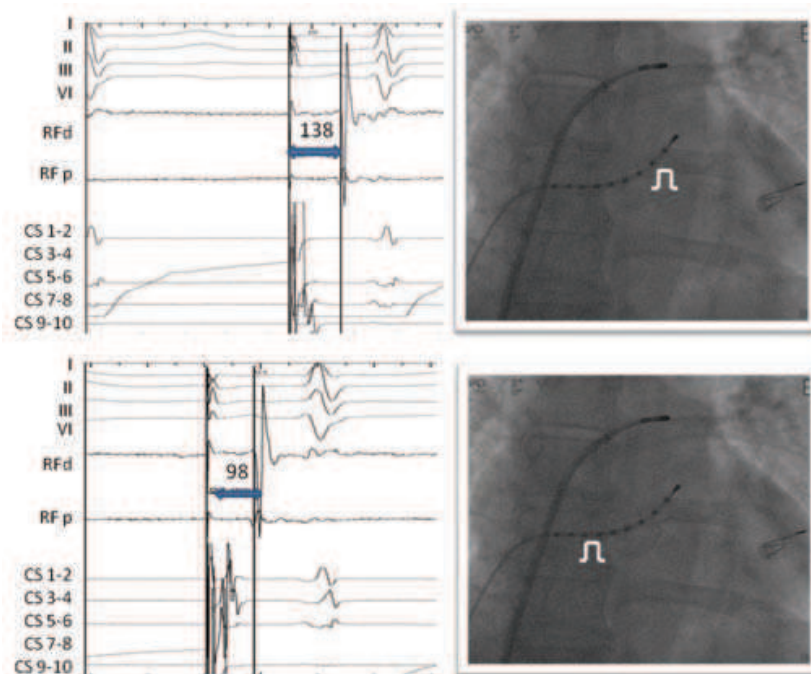


Fig. 18. A and B. The left panels show surface leads I, II, III and VI, then the RF catheter placed just anterior to the mitral line. Lowest is the EGMs of the bipoles of the decapolar catheter in the CS. In figure 18A pacing from the RF catheter confirms clockwise block over the mitral line by activating the CS catheter in a proximal to distal manner. Figure 18B confirms counterclockwise block by differential pacing, the pacing to RF is longer (138ms) when pacing the distal CS than when pacing the more proximal CS (98ms).

8.2 Focal and localized reentrant tachycardias

After macroreentrant tachycardias have been ruled out the next step is tracking the earliest potentials for a focal or localized re-entry AT. Once the suspected region of origin has been found, careful mapping will suggest whether it is a focal or localized reentrant tachycardia. Local activity spanning most of the AT CL suggest local re-entry whereas if only a limited part of the CL can be mapped, the likely etiology is a focal tachycardia. Overall, these 2 tachycardias are mapped and ablated in a similar manner.

8.2.1 Mapping focal and localized reentrant tachycardias

The aim is to gradually 'pinpoint' on the earliest spot. Often multipolar catheters can be helpful in localizing the earliest spot, simply by their ability to cover a larger area. Figure 15 was an example of an AT with a cycle length variation of 3% (same patient as in figure 2, 3, 4 and 10), where activation mapping and entrainment ruled out a macro reentrant circuit. The earliest region was found to be on the posterior wall and to aid localize the very earliest site of activation a LASSO catheter was used to map the posterior wall in detail. Figure 19 illustrates this:

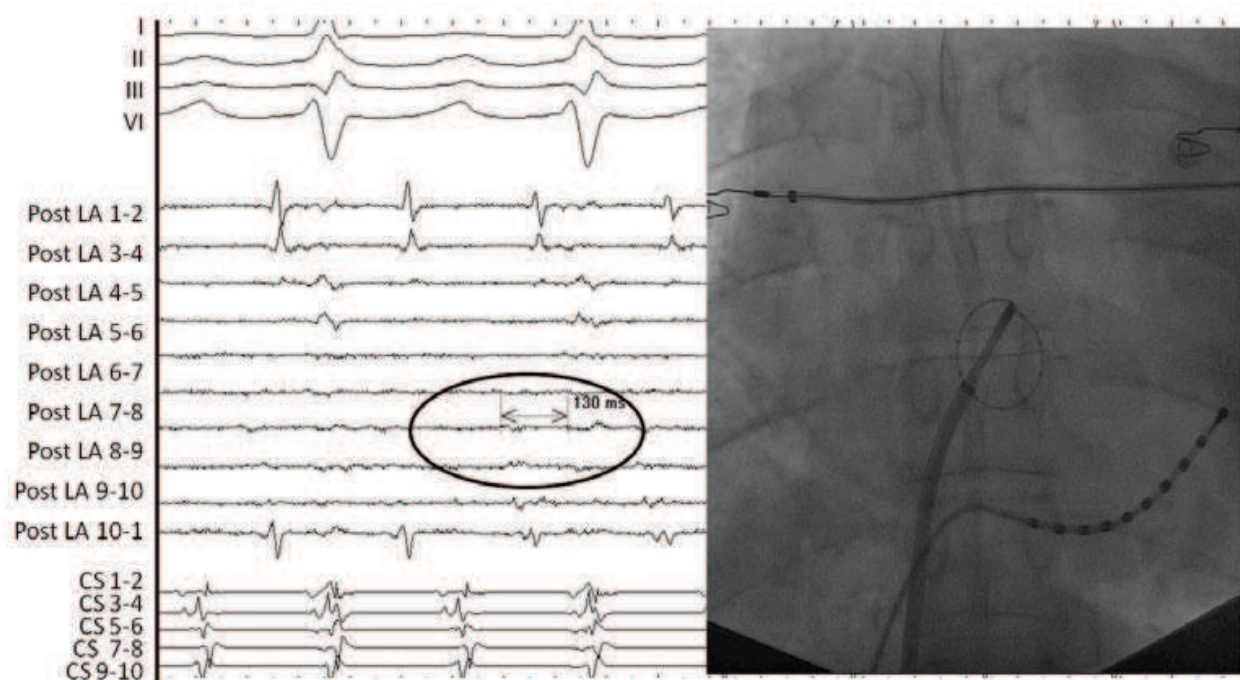


Fig. 19. Right panel shows the LASSO catheter on the posterior wall of the LA. The left panel shows surface leads I, II, III and VI at the top and the EGMs from a decapolar catheter in the CS at the bottom. The EGMs from the posterior wall shows the earliest potentials on the posterior wall to be near LASSO pole 7-8.

8.2.2 Ablating focal and micro reentrant tachycardias

Once the earliest potentials are located, be it a focal or localized reentrant tachycardia, ablation at the earliest point or at the site covering more than 90% of the tachycardia cycle length should eliminate the arrhythmia. Figure 20 shows the successful ablation of the tachycardia mapped in figure 19 with the lasso catheter to the posterior wall.

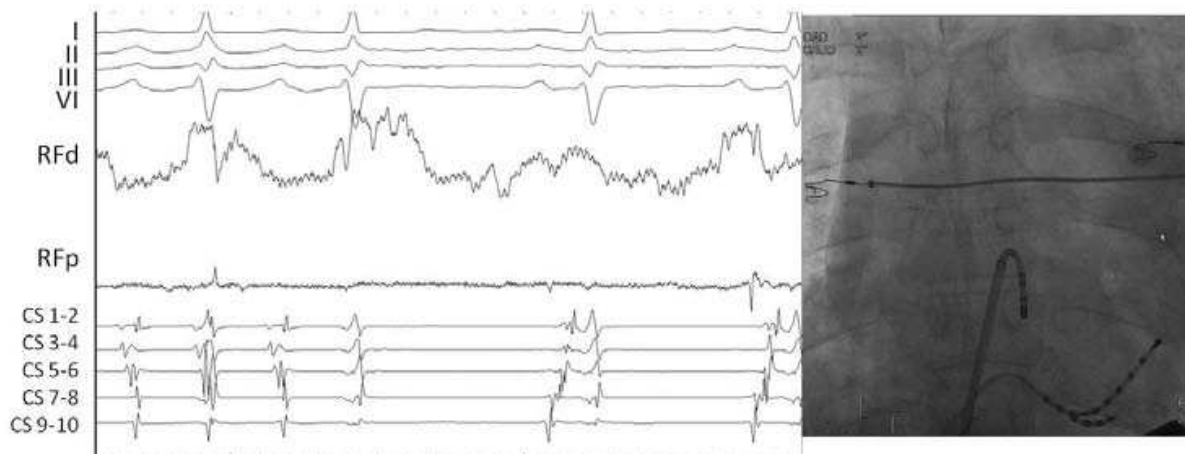


Fig. 20. Shows the successful ablation of the tachycardia mapped in figure 19. The LASSO catheter is replaced by an RF catheter and RF energy is applied to where the poles 7-8 were and the tachycardia converts to SR. This example is the same patient as in figures 2, 3, 4, 10 and 11, and he has now completed the stepwise ablation. However, before leaving the catheter laboratory it is paramount to ensure complete PVI and complete electrical block of any lines, now in the re-established SR.

9. Post procedural care

Following ablation, the guiding sheaths are pulled out of the left atrium and heparin is stopped. Patients will typically lie flat for 6 hours after sheaths are pulled due to the large sheaths used. All patients are treated with warfarin after ablation. Patients receive subcutaneous heparin injections beginning on the evening of the ablation and continuing until the INR is therapeutic. Patients are usually subjected to echocardiography and observed 48-72 hours post-procedure prior to discharge.

Patients are followed up closely for the year following an ablation procedure. At 3, 6 and 12 months, patients are admitted to hospital for 24 hours and undergo clinical evaluation including exercise stress testing, ambulatory Holter monitoring and transthoracic echocardiography. After the procedure, warfarin is continued for at least six months, and guided thereafter by the presence or absence of conventional risk factors for thromboembolism and maintenance of sinus rhythm. Patients with a CHADS2 score ≥ 2 are kept on warfarin regardless of their rhythm outcome. All antiarrhythmic drugs are discontinued by 3-6 months except in case of recurrence. In such case, patients are offered a repeat procedure.

10. Complications

Serious complications can occur during an ablation for permanent atrial fibrillation, and it is important that these (and their rate of occurrence) are carefully discussed with the patients prior to him or her signing the consent form. The major complications are described in detail in the task force on atrial fibrillation (Calkins et al., 2007) and anybody carrying out these ablations should probably familiarize themselves with this document. Overall, tamponade, pulmonary vein stenosis, atrio-esophageal fistula and/or death (so far not existent at our centre), air emboli and cerebrovascular or peripheral-vascular complications compile to a cumulative 2-3% complication rate.

11. Procedural outcomes

The stepwise ablation of permanent atrial fibrillation leads to termination in 87% of patients (Haissaguerre et al., 2005a). In this series 23 of 53 patients had a repeat procedure for arrhythmia recurrence (mainly for 1 or more atrial tachycardias). After repeat ablation 95% of all patients were in sinus rhythm at 11± 6 months.

O'Neill (O'Neill et al, 2009) report similar results from a larger cohort (156 patients) achieving atrial fibrillation termination in 85% using the stepwise ablation approach in patients with persistent AF (ie termination by ablation alone, not requiring pharmacological and/or DC cardioversion). After 34 months follow up 95% of these patients were still in stable sinus rhythm, albeit 49% needed a repeat procedure. If AF termination was not achieved from ablation during the index procedure stable sinus rhythm was only found in 52% at 34 months, again albeit a redo procedure in 70%. In the AF termination group 89% have stopped anti-arrhythmic medication, whereas in the non-termination group only 25% stopped their AADs. Subsequent studies both from our group (Takahashi et al., 2007; Hocini et al, 2010) as well as studies published from other groups (Rostock et al., 2011) have reported the same findings; that the stepwise approach to ablation of persistent AF leads to unprecedented good clinical outcome.

11.1 Predictors of success

The duration of uninterrupted AF and AFCL has been shown to be independent factors predicting AF termination (O'Neill et al., 2009, Matsuo et al., 2009). If the duration of AF is less than 12 months there is a 90% chance of AF termination. This success rate gradually decreases to 54% if the duration of AF is more than 48 months. Similarly, the AFCL is a predictor of success, with a likelihood of AF termination of 95% if the AFCL is more than 161ms, gradually decreasing to 50% likelihood of success with AFCL of less than 120ms. Left atrial size is also predictor for termination of AF (Matsuo et al., 2009). Left ventricular ejection fraction, amiodarone use, troponin, procedure time and RF time did not reach statistical significance.

Termination of AF by ablation is also a strong predictor of success with up to 95% of patients remaining in SR after almost 3 years after 1.5 procedures (Takahashi et al., 2007; Rostock et al., 2011).

Fine atrial fibrillation, as measured by the fibrillatory (F-) wave on the surface ECG, has been shown to be a marker of longer lasting atrial fibrillation and larger left atrial size compared to patients with a more coarse AF. Coarse atrial fibrillation with F-waves $\geq 0.1\text{mV}$ in leads V1 and II of the surface ECG are correlated to younger age, a shorter AF history and a smaller left atrium. An F-wave amplitude of $\geq 0.7\text{ mV}$ predicts AF termination by ablation with a sensitivity and specificity of about 80%. Lastly, the smaller amplitude F-wave ($<0.05\text{mV}$) is associated with a higher AF recurrence rate as compared with higher F-waves ($\geq 0.5\text{mV}$) (Nault et al., 2009).

12. Conclusion

The stepwise ablation of permanent atrial fibrillation is a logical, patient tailored approach that is guided by electrophysiological endpoints. The method can lead to termination of AF in up to 85% of patients and render them arrhythmia free at least in the medium term, albeit

more than 50% of patients need more than 1 procedure to achieve sustained sinus rhythm. Termination of AF by ablation, mapping and ablation of all intermediate ATs, and linear blocks confirmed is associated with a better long-term clinical outcome than when AF is not terminated by ablation.

Predictors of success in restoration of acute and sustained sinus rhythm include the duration of the continuous AF, mean baseline AFCL, age and the amplitude of the surface ECG fibrillatory waves. Understanding further baseline characteristics, both clinically and electrophysiologically, may help improving outcome and lead towards better patient selection criteria.

It is not known how to forecast which patients will experience arrhythmia recurrence, but predictors are incomplete lines, either from recovery of conduction or deficient line-block at the time of creation. Both recovery of pulmonary vein conduction (Ouyang et al., 2005) and incomplete left atrial linear lesions (Knecht et al., 2008) are important factors for arrhythmia recurrence. However, this is by no means the cause of all recurrences, for example, about 20% of recurrence of atrial tachycardia following the index procedure occurred from sites not previously ablated (O'Neill et al., 2009).

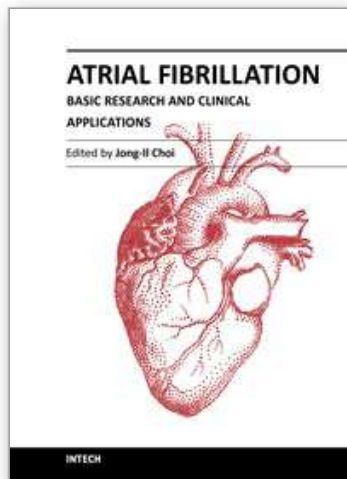
Despite unprecedented success of the stepwise approach to catheter ablation of permanent AF, ignorance remains particularly interpreting signals during chaotic activation in the atrium and this needs much more work. We still have only rudimentary tools to help identify the individual elements involved in AF and there is still a long way to go until we fully understand and master this arrhythmia.

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Atrial Fibrillation-Basic Research and Clinical Applications is designed to provide a comprehensive review and to introduce outstanding and novel researches. This book contains 22 polished chapters and consists of five sections: 1. Basic mechanisms of initiation and maintenance of atrial fibrillation and its pathophysiology, 2. Mapping of atrial fibrillation and novel methods of signal detection. 3. Clinical prognostic predictors of atrial fibrillation and remodeling, 4. Systemic reviews of catheter-based/surgical treatment and novel targets for treatment of atrial fibrillation and 5. Atrial fibrillation in specific conditions and its complications. Each chapter updates the knowledge of atrial fibrillation, providing state-of-the art for not only scientists and clinicians who are interested in electrophysiology, but also general cardiologists.

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