Innovations in Clinical Cardiac Electrophysiology: From Conventional Approaches to Remote Magnetic Navigation

Aanwinsten in klinische elektrofysiologie van het hart: van een klassieke benadering tot magnetische navigatie op afstand

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Thesis

To obtain the degree of Doctor from the
Erasmus University Rotterdam
by command of the
Rector Magnificus

Prof.dr. S.W.J. Lamberts

and in accordance with the decision of the Doctorate Board.

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by

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To Amanda and the kids for all the bs

CONTENTS

Part 1

Conventional Approaches

Chapter 1:

Introduction

HISTORY: FROM UNDERSTANDING TO THERAPY

Clinical cardiac electrophysiology (EP) has progressed significantly since the first invasive electrophysiological studies were performed to study normal impulse formation and conduction in the heart and to confirm hypotheses regarding the causation of arrhythmias.

The first His bundle recordings in 1969,(1) and later, programmed atrial and ventricular stimulation(2) to induce tachycardia made detailed analysis of arrhythmias possible. This led to an understanding of reentrant and focal tachycardias on an atrial and ventricular level.

Subsequently therapeutic options became available when surgery entered the field with a approach for ventricular tachycardia (VT)(3) and ventricular preexcitation (WPW syndrome). Atrial fibrillation (AF) surgery was also successful but had a relatively high morbidity and a clear mortality risk. At this early stage no therapy could be given via the catheter. Subsequently direct current (DC) shock ablation of the AV node proved to be very successful and led to catheter ablation of ventricular tachycardia and accessory pathways (4). However, the complications of this technique were important. The arrival of radiofrequency was thought to be the solution for the more simple arrhythmias such as atrioventricular nodal reentrant tachycardia (AVNRT), WPW, idiopathic VT and atrial flutter(5). The development of better catheters allowed for successful therapy in excess of 85% in most cases of these arrhythmias(6, 7). The real challenges remained VT on a background of underlying heart disease, and AF in both the normal and abnormal heart. The arrival of mapping systems allowing detailed electro-anatomical mapping(8) helped strategies to develop for more complex arrhythmias. However these approaches are still time consuming and there remain some drawbacks.

WHERE ARE WE NOW: GOOD BUT COULD DO BETTER

Included in the above mentioned drawbacks are lower success rates for ventricular tachycardia and atrial fibrillation and difficulties in complex tachycardias relating to prior surgery whether for congenital, or non-congenital heart disease. There are also concerns about radiation exposure and safety of the patient as well as radiation concerns for the physician (9).

In the present thesis, we start to describe some of the most common arrhythmias in clinical cardiac electrophysiology in chapter 2. The diagnostic problems in atrial tachycardia remain huge. The role of the 12-lead ECG to assist in strategy and planning is important although perhaps less so than for the well known preexcitation syndrome and AV nodal re-entrant tachycardias. AF and atrial flutter are complex, inter-related and should often be treated together as we describe in chapters 3 and 4. The therapy of AF is now most often performed by isolating

the pulmonary veins (PVs) from the left atrium using a variety of techniques, as described in chapter 5 as originally proposed by the group from Bordeaux(10). These procedures are lengthy and expose both the patient and physician to significant amounts of ionising radiation. Apart from vascular complications, other complications include pericardial effusion, PV stenosis, stroke, and atrio-oesophageal fistulas(11). Despite these serious complications, patients with AF are often very motivated to undergo such a procedure. Some preliminary data indicate now that ablation may be better than drug therapy in normal hearts and should even be considered in patients with heart failure(12, 13). Atrial fibrillation ablation will almost certainly become a major burden for every electrophysiology centre.

WHERE ARE WE GOING:

It is clear from the previous statements that procedures should be improved and that we should develop a strategy to diminish the complication rate. One novel approach is remote magnetic navigation(14). This idea originated in the domain of clinical neurology in an effort to allow catheter access to various parts of the brain, allowing for potential delivery of magnetised material to stop bleeding in affected parts of the neurovascular system. It is not surprising that the first real developments in cardiology were made in clinical cardiac EP with the development of softer, floppy catheters with a magnetised tip. Two strong external magnets cause a magnetic field, allowing for the orientation of a magnetically enabled catheter tip in almost any direction (figure 1).

Figure 1. Overview of the initial room for magnetic navigation, with the patient lying between the external magnets, monitored by a nurse, with operator and technician behind the leaded screen (Niobe I, Stereotaxis, as built in the Erasmus MC, Rotterdam).

Theoretically the catheter is flexible enough to reach every part of the heart with a lower potential for perforation of the heart wall (figure 2). This complication is not uncommon when using rigid, multipolar catheters. A further advantage would be that automated mapping becomes

possible and that physicians and other personnel would receive lower ionising radiation doses.

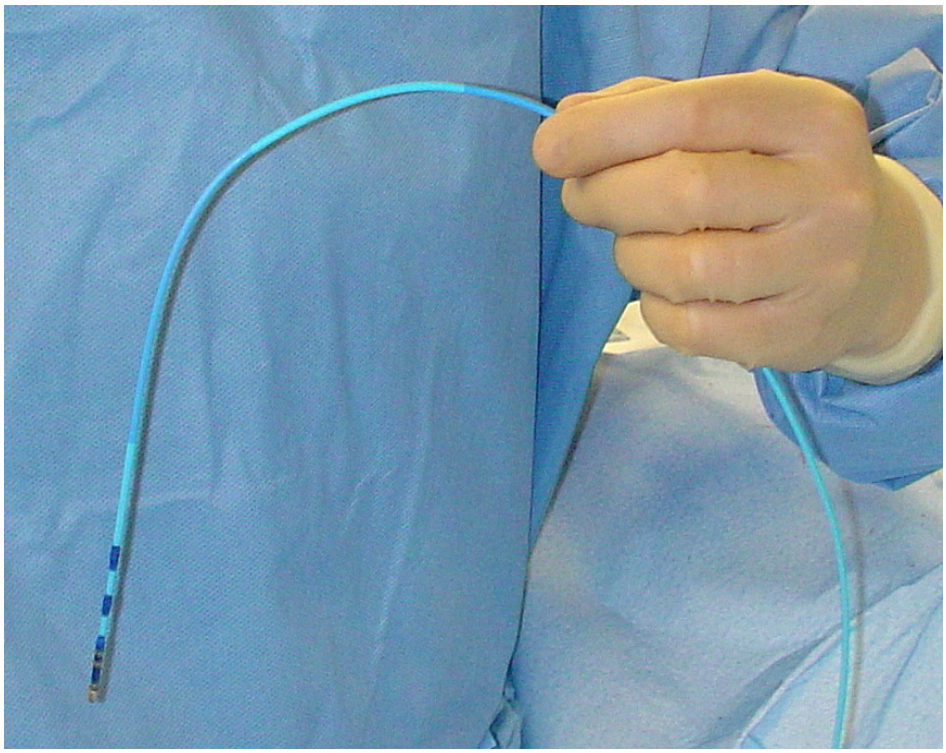

Figure 2. A 3-magnet ablation catheter. As opposed to conventional catheters it is floppy, because there is no internal steering wire.

After a description of potential uses for this technology in our domain of cardiology, chapter 6, we report the results of an animal study in chapter 7. It was not clear from the published and ongoing animal experiments whether a catheter which moved together with the heart would produce lesions that could be compared with those applied through a conventional catheter.

After an initial pilot study in one of the easiest substrates (AVNRT, as described in chapter 8) we moved to arrhythmias which required detailed mapping and very careful movements of the ablation catheter to detect the area of interest (chapters 9 and 10, addressing ventricular tachycardia). The right ventricular outflow tract (RVOT) sometimes poses difficulties to mapping, and is prone to catheter induced arrhythmias and is in a continuum with the pulmonary artery. Ablation in the RVOT has led in the past to serious complications. In idiopathic fascicular left ventricular VT "bumping" the fascicle may make the tachycardia non-inducible and therefore a soft touch is advisable as can be done with the magnetic catheter. Chapters 11 and 12 report

our experience with the system in the WPW syndrome. The fact that we could ablate using the retrograde (transaortic) approach, opened new perspectives for ablation in the left side of the heart.

In contrast to other investigators(15), we remained cautious in approaching atrial fibrillation as we felt that we needed better and safer catheters (8 mm tip and more specifically irrigated tip magnetically enabled catheters) to avoid thrombus formation(16). In the interim, we were able to access the left atrium and cannulate all the pulmonary veins with these catheters in a retrograde way, and could successfully ablate a focal left atrial tachycardia using a 4 mm tip catheter (chapters 13 and 14). As discussed in these chapters, this approach may be useful when transseptal puncture is contraindicated or difficult.

We end this thesis in chapter 15 with an overview of the potential applications in cardiac electrophysiology (as well as in cardiac resynchronisation therapy) and put this therapy in a broader perspective in chapter 16.

The availability of newer technologies such as alternative energy sources, mapping systems, robotics, magnetic navigation and the integration of real-time imaging into electrophysiology, should improve the outcomes as well as safety for both physician and patient. These evolving technologies will require new approaches to the techniques for ablation and catheter positioning and electrophysiologists will need to move beyond the "mind-sets" of present technology. Questions will inevitably arise about the cost-benefit of these technologies and how much they add, but this is a difficult subject as their benefit will vary considerably between units, with potentially less benefit in experienced high volume units and more benefit in less experienced low volume centres. This thesis is a look at early work in some of these new technologies.

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Chapter 2

Clinical aspects of atrial tachycardia, atrial flutter and atrial fibrillation

CLINICAL ASPECTS OF ATRIAL TACHYCARDIA, FLUTTER AND ATRIAL FIBRILLATION

(Aspects cliniques de la tachycardia atriale, du flutter et de la fibrillation auriculaire**)**

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EPIDEMIOLOGY

Atrial fibrillation (AF) is the commonest supraventricular arrhythmia encountered in daily clinical practice and is associated with substantial excess in morbidity and mortality.

Accurately determining the incidence and prevalence of this and other atrial tachycardias is complicated by a number of factors.

- The prevalence varies depending on the definitions, especially for atrial fibrillation. The fact that atrial fibrillation and flutter were often previously classified under one header has also increased the uncertainty of the incidence of each individual arrhythmia.
- These arrhythmias are frequently paroxysmal, so that a random measurement in time like a 12-lead electrocardiogram (ECG) or even a Holter ECG cannot be relied upon(1).
- The arrhythmia may be asymptomatic in a significant number of patients, making the history unreliable, leading to underestimation of the real prevalence(2).

ATRIAL FIBRILLATION

The prevalence of AF seems to be between 0.4%(3) and 1.9% of the population(4, 5). AF increases in prevalence with advancing age. It doubles with each decade beyond 50 years to around 10% in persons who reach 80 years(6). Around 70-80% of patients with AF will be in the age group 65-85 years with the median age of AF patients estimated to be 75 years. The prevalence is substantially higher in men than in women at all ages, with a 50% greater likelihood of AF in men than in women. Despite this the total number of men and women are almost equal because of the longer life expectancy of women. In addition, there may be a racial variation; patients of African descent may have a lower prevalence. The prevalence of so-called lone AF varies widely in published studies between 2.7% and 30% of all cases of AF(7, 8).

The incidence is approximately 0.1% per year in those less than 40 years of age up to greater than 1.5-2% per year in those over 80 years.

When one compares early, and later epidemiological studies it appears that the incidence is increasing in developed countries. Recent reports have described a 2-to 3-fold rise in the rate of hospitalisation for atrial fibrillation in recent years(9). This increase cannot be fully explained by the increasing age of the general population, or by an increase in the prevalence of underlying heart disease. One intriguing possibility is that a sharp rise in the incidence of obesity and obstructive sleep apnoea (known to be associated with an increased risk of developing atrial fibrillation) may be in part responsible(10). A sharp rise in the incidence is predicted for the coming five decades(11).

OTHER ATRIAL ARRHYTHMIAS

The exact prevalence and incidence of the so-called macro-reentrant atrial tachycardias (**atrial flutters**) is not entirely clear. Approximately 10% of patients presenting with supraventricular tachycardias do so with atrial flutter(12). What is known, however, is that 60% of atrial flutters occur during acute disease processes and may never recur. Approximately 25-35% of patients with AF will have atrial flutter at some time, either spontaneously or more commonly, induced by medication(13).

Sustained **focal atrial tachycardias** are relatively rare and overall make up only 10-15% of patients referred for radiofrequency (RF) ablation of SVT(14, 15). They are, however, more common in a paediatric population and especially in those with congenital heart disease(16, 17). Estimates of prevalence vary from 0.34% in asymptomatic patients to 0.46% in symptomatic patients(18).

NOSOLOGY

Definitions and Classification – Newer Classifications

Earlier classifications of atrial arrhythmias were based almost exclusively on the 12-lead ECG findings. A fairly crude classification of the atrial tachyarrhythmias was based on the atrial rate alone, as far as this can be assessed on the surface electrocardiogram. It is important to remember that these classifications refer to atrial rate and not ventricular rate on the 12-lead ECG. Atrial fibrillation was defined as an atrial tachycardia with a rate between 350 and 600 beats per minute. In atrial flutter the atrial rate was usually between 250 and 350 beats per minute. In atrial tachycardia the atrial rate was between 100 and 250 per minute(19). The presence of

an isoelectric baseline between atrial deflections was also used to assist classification between atrial flutter and atrial tachycardia, with an intermittent isoelectric baseline suggesting atrial tachycardia. Atrial tachycardia could be unifocal or multifocal.

These definitions were the time-honoured definitions traditionally used, however the distinction between the subtypes of atrial tachyarrhythmias may not always have been as clear as suggested. The use of intracardiac electrograms has been of great benefit in confirming some of the concepts developed by electrocardiographers as regards the mechanisms of some of these arrhythmias. As a result of our increased knowledge, newer definitions for the different atrial rhythms as well as sub-classifications of these have been proposed(20-23).

Atrial tachycardias can be classified as atrial rhythms at a constant rate > 100 beats per minute originating outside the sino-atrial node. The atrial arrhythmias can be roughly divided into the irregular atrial tachycardias or the atrial fibrillation group, and the atrial flutter and regular atrial tachycardia group (Table 1). This correlates to some degree with the concept of multiple circuit/foci tachycardias and single circuit/focal tachycardias, and also to a group of irregular, and a group of regular atrial tachycardia respectively.

One of the problems with any classification is that the characteristics of the arrhythmia may change over time or be modified by therapy, especially drug therapy, and conversion from one form to another is not uncommon. Furthermore, intracardiac recordings have revealed that there may be some overlap between these entities e.g. with left-sided disorganised rhythms (fibrillation) and right-sided organised rhythm (flutter). More recently the entity of pulmonary

Table 1 Classification of Atrial Arrhythmias

Irregular Atrial Tachycardias	
	Atrial Fibrillation
	Initial Event
	Paroxysmal
	Persistent
	Permanent
	Multifocal Atrial Tachycardia
Regular Atrial Tachycardias	
	Isthmus Dependent Flutters
	Typical Atrial Flutter
	Reverse Typical Atrial Flutter
	Non-Isthmus Dependent Flutters
	Scar/Incisional Flutter
	Left Atrial Flutter
	Focal Atrial Tachycardias

vein foci with tachycardia within the pulmonary veins driving the more clearly seen atrial fibrillation has been described(24, 25).

IRREGULAR ATRIAL TACHYCARDIAS

Irregular atrial tachycardias can be classified as irregular atrial rhythms at a constant rate > 100 beats per minute originating outside the sino-atrial node. Examples of these tachycardias are atrial fibrillation and multifocal atrial tachycardia.

Atrial Fibrillation

Atrial fibrillation has had numerous classifications applied to it over the years. Much clinical research has regarded AF as a single entity, while it clearly is not. In 2000 the Working Group on Arrhythmias of the European Society of Cardiology (WGA-ESC) and the North American Society for Pacing and Electrophysiology (NASPE) achieved some consensus on the terminology and classification of AF(22, 23). Recognising that an ECG classification would be unhelpful, and that a number of classifications based on for example epicardial mapping and other intracardiac recordings have also been made, it was felt that a clinically based classification would be more useful, and would assist both in therapeutic management and in future research. It is important to remember that no classification can take into account all features associated with AF, for example presence of underlying heart disease or not; associated features of onset etc.

The consensus defined AF as an atrial tachyarrhythmia with predominantly uncoordinated atrial activation with resulting deterioration in atrial mechanical function(26, 27). The classification that follows applies only to AF episodes that last longer than 30 seconds.

Initial Event – this can be self-terminating or non self-terminating and symptomatic or asymptomatic (although it may be difficult to know if prior episodes have been asymptomatic).

Recurrent AF – is defined as recurrent if the patient has two or more episodes. Within the recurrent group further subdivisions can be made:

- Paroxysmal – an episode of AF usually terminating with 48 hours but at longest in fewer than 7 days, since spontaneous cardioversion is unlikely to occur after this period and chemical cardioversion is also less successful.
- Persistent – an episode of AF lasting longer than 7 days. In this form sinus rhythm can usually be restored with electrical cardioversion.
- Permanent (Established) AF – when AF has been present for a prolonged period and fails to terminate with cardioversion or recurs repeatedly within 24 hours of cardioversion.

Accepted AF is a form of permanent AF when cardioversion has not been attempted or been refused.

In each case this may be the first form of AF or may be preceded by a less severe form.

It must be recognised that not infrequently, the physician may not know the temporal pattern. When atrial fibrillation is first diagnosed there is usually no way to know whether it is a persistent episode or a paroxysm that will shortly terminate. Even the distinction between frequent paroxysms and permanent atrial fibrillation may be impossible to make clinically.

This is clearly a time related classification and patients' AF often evolves from a paroxysmal to a persistent pattern and eventually to permanent AF.

Classifications based on the presence of particular disease states or characteristic onset and other associated features e.g. vagal vs. sympathetic, may be useful for choosing a particular medical therapeutic option(26, 27), but not in assessing broader management issues.

The ECG of atrial fibrillation can be characterised by the absence of consistent P waves and their replacement by waves that vary constantly in timing and appearance(28). The ventricular

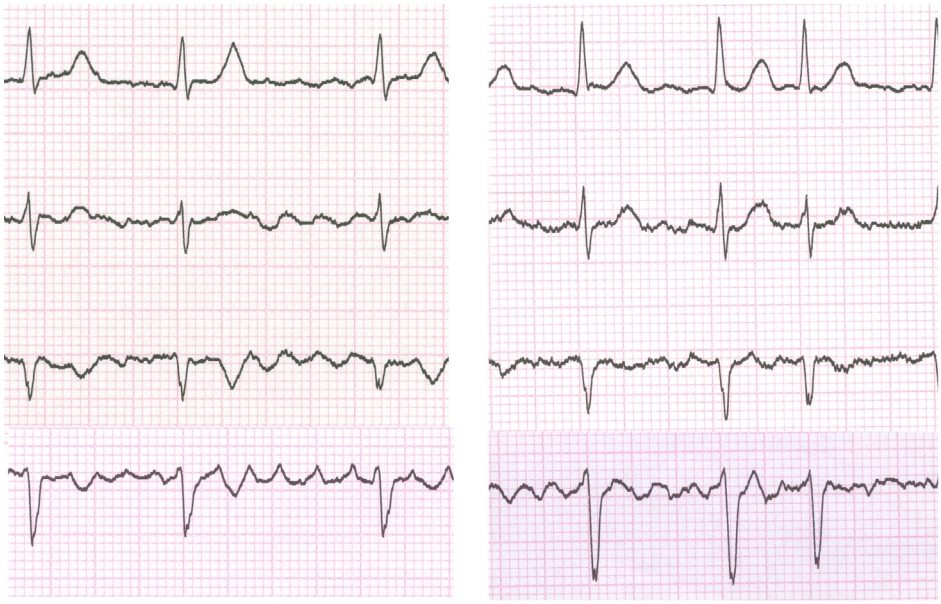

Figure 1: ECG (leads I, II, II, V_1) of atrial fibrillation (2 episodes). Note the completely irregular fibrillatory waves in this case of fairly coarse atrial fibrillation. There are no discernible P-waves and no clear isoelectric periods. The RR intervals and the rate are dependent on AV nodal conduction properties

response is generally irregular except in association with AV block and the ventricular rate depends on the AV nodal conduction properties (figure 1).

Multifocal Atrial Tachycardia

The diagnosis of multifocal atrial tachycardia is based on the finding of an irregular atrial tachycardia with 3 different P-wave morphologies, each at a different rate(29). It is often confused with atrial fibrillation but the atrial rates are usually slower than those in atrial fibrillation.

ATRIAL FLUTTER AND REGULAR ATRIAL TACHYCARDIAS

The recently published "Classification of Atrial Flutter and Regular Atrial Tachycardias" from a Joint Expert Group from the WGA-ESC and NASPE integrates the knowledge gleaned from electrophysiological studies with that from electrophysiological mechanisms(20, 21). This improved newer classification allows better prognostication as far as possible ablation therapy and its outcome are concerned.

This group includes regular atrial rhythms at a constant rate > 100 beats per minute originating outside the sino-atrial node. Basic clinical findings, particularly 12-lead ECG, can be used to assist in classification. Two further distinct groups can be defined

1. Macro-reentrant atrial tachycardias, including the various atrial flutters, and incisional and scar related "flutters".
2. Focal atrial tachycardias with an automatic, triggered or micro-reentrant mechanism.

Macro-reentrant Atrial Tachycardias including the Atrial Flutters

The mechanism of these arrhythmias is a single reentrant circuit around a central obstacle usually with a narrow area of conduction (isthmus) somewhere in the circuit. The obstacle can be a normal or abnormal structure and may be fixed or transient. Activation within the atrium is continuous and this is reflected by the lack of an isoelectric line on the surface ECG. These circuits can be entrained(30). The well-characterised macro-reentrant atrial arrhythmias are:

- The Inferior Vena Cava-Tricuspid Valve (IVC-TV) isthmus dependent flutters
- Typical (counter-clockwise) atrial flutter
- Reverse typical (clockwise) atrial flutter
- Lesion macro-reentrant tachycardias (incisional and scar flutter)
- Left atrial macro-reentrant atrial tachycardia (Left atrial flutter)
- Other variants such as "lower loop" and "double loop" reentry.

For practical and therapeutic purposes it is important to recognise the IVC-TV isthmus dependent flutters and lesion reentry flutters, as these are more easily amenable to ablation.

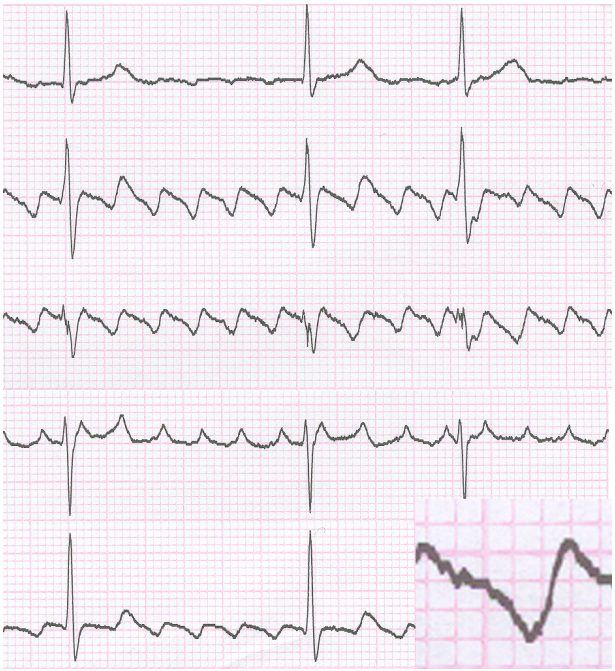

Figure 2: ECG (leads I, II, II, V_1 and V_6) of typical (counter-clockwise) atrial flutter. Note the typical features in the inferior leads (see also inset of lead III). The inferior leads show negative saw tooth waves and there are positive waves in V_1 and transition across the V-leads. In this case with AV block, decreasing the ventricular pacing rate allows for easier viewing of the flutter waves

Typical atrial flutter (counter clockwise flutter) circulates in a counter clockwise direction around the tricuspid annulus in the frontal plane and is constrained by constant anatomical structures within the right atrium (figure 2).

The ECG is characterised by dominant negative flutter waves inferiorly, classically described as showing a down sloping plateau, followed by a sharper negative deflection and then a sharp positive deflection with overshoot followed by the next down sloping plateau(31). In the chest leads there are positive flutter waves in V_1 and transition to a negative flutter wave in V_6. The rate is typically 250-350 bpm.

Reverse typical atrial flutter (also called clockwise or reverse flutter) circulates in the opposite direction around the tricuspid annulus but is constrained by the same structures as typical flutter (figure 3).

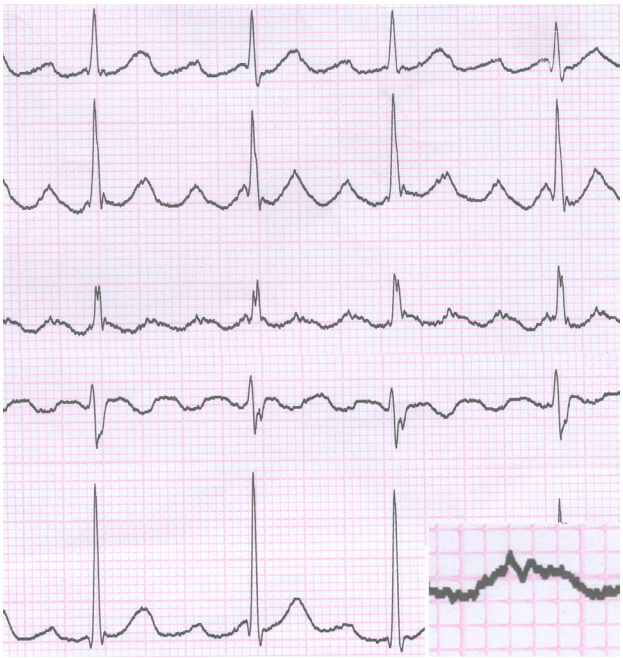

Figure 3: ECG (leads I, II, II, V_1 and V_6) of reverse typical (clockwise) atrial flutter. Note the difference in the inferior leads (see also inset of lead III). The inferior leads show positive saw tooth waves and there are negative waves in V_1 and transition across the V-leads

The ECG shows a rate which is similar to the above, but the flutter waves are now broad and positive, often notched in the inferior leads and negative in V_1 transitioning to positive in V_6(32).

The non isthmus dependent flutters include incisional flutter around scars from previous atriotomy incisions during cardiac surgery, flutter circulating around areas of fibrosis in the atria and flutter circulating around other anatomical or functional conduction barriers in the atria (figure 4).

The ECG in these flutters have no isoelectric baseline but do not fit into the above two clearly defined patterns, although differentiation may be difficult(32).

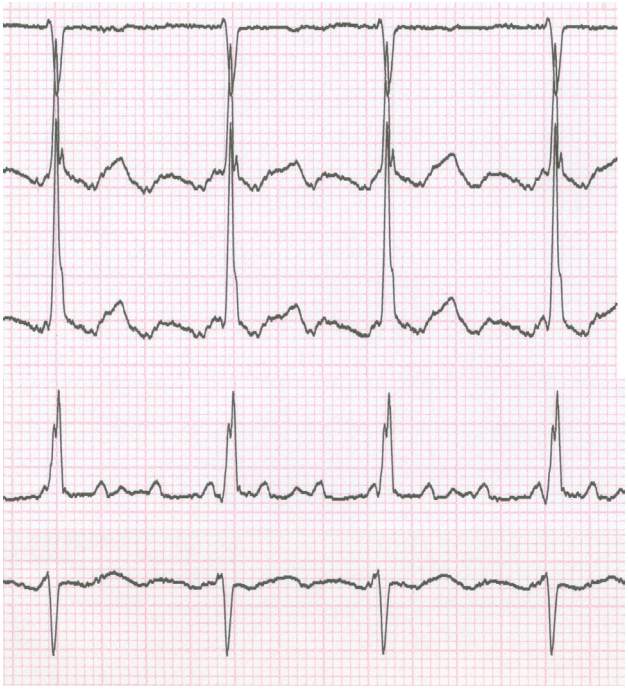

Figure 4: ECG (leads I, II, II, V_1 and V_6) of a non-isthmus dependent atrial flutter. Note the lack of an isoelectric line, but the absence of the features outlined in figures 2 and 3. In this case the patient has a surgical scar in the atrium and the flutter is circling around this scar.

Focal Atrial tachycardia

Unifocal and usually regular atrial tachycardias begin in a small area or focus in a rhythmical fashion. The commonest sites for these foci are the pulmonary veins, the crista terminalis and the entries of the SVC, IVC and coronary sinus(24, 25, 33). The ECG usually reflects the fact that there is a period of atrial electrical inactivity during the cycle, so that an isoelectric line can be seen on the ECG between P waves (figure 5). The P wave morphology of the individual tachycardia reflects the site of origin(34, 35). Focal atrial tachycardias usually have a rate $\leq$ 240 bpm (typically 130-240 bpm), although rates up to 300 bpm are occasionally seen. The tachycardia rate may vary over time. Automatic forms may warm up (progressively increase at onset) and cool down (progressively decrease at termination)(36). Adrenergic stimulation will also increase the rate in these arrhythmias. Automatic, triggered and re-entrant forms exist, but clinically the distinction may be impossible.

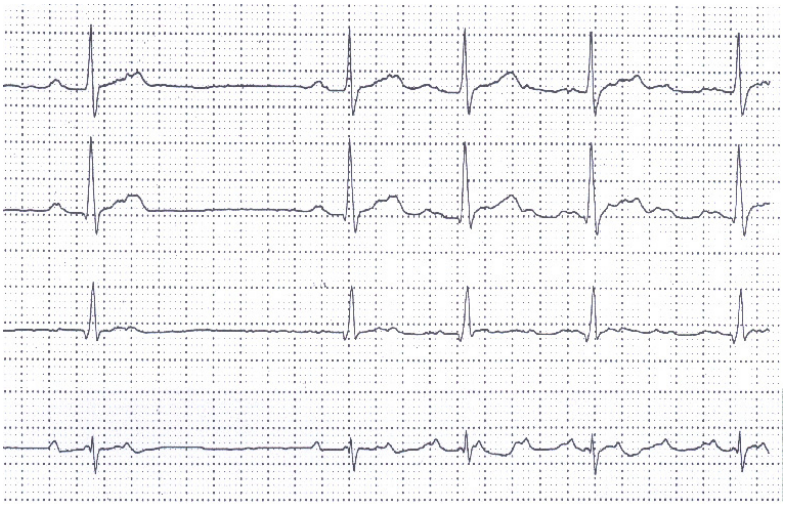

Figure 5: ECG (leads I, II, II, V_1) of a focal atrial tachycardia. There are unifocal P waves with a clear isoelectric line between. The morphology of the P-waves suggests an origin in the right upper pulmonary vein.

Other Atrial tachycardias

Unfortunately this classification is not entirely all encompassing as it leaves out inappropriate sinus tachycardia, sinus node reentry and what was previously known as type II atrial flutter(20, 21). Inappropriate sinus tachycardia appears to originate in the sinus node at rates above the physiologic range without proportionate relationship to physiologic requirements. Sinus node reentry tachycardia is a tachycardia with the same P wave morphology as sinus rhythm, which can be induced and terminated consistently by electrophysiogical stimulation. However it is possible that this is merely a micro-reentrant tachycardia originating near the sinus node. The exact electrophysiological background of type II flutter is not entirely clear.

AETIOLOGY

Atrial arrhythmias are not discrete disease entities, but rather syndromes that may be caused by a number of cardiac abnormalities or by a variety of as yet incompletely understood genetic abnormalities.

The causes of atrial fibrillation (table 2) can be roughly divided into the acute (sometimes referred to as secondary) causes, AF associated with heart disease, AF associated with autonomic triggers also known as neurogenic AF, and AF without associated heart or other systemic disease.

Table 2 Causes of Atrial Arrhythmias

Acute AF	Cardiac or other surgery, myocardial infarction, pericarditis, pulmonary embolism, toxic, metabolic and endocrine causes
AF associated with cardiac disease	Electrical – AVNRT, AVRT, Flutter, PV tachy Non-valvular – hypertension, coronary artery disease, CHF Valvular – especially rheumatic valvular disease
Autonomic/Neurogenic AF	Vagally mediated AF Adrenergic AF
AF without cardiac/other disease	Lone AF
AF due to genetic disease	Familial AF with various channelopathies

AVNRT – atrio-ventricular nodal reentry tachycardia, AVRT, atrio-ventricular reentry tachycardia, Flutter – atrial flutter, PV tachy – pulmonary vein focal atrial tachycardia, CHF – congestive heart failure

ACUTE AF

AF is frequently related to temporary and reversible acute events. Examples include AF associated with cardiac or other surgery, infarction, pericarditis, pulmonary embolism, toxic, metabolic and endocrine causes. Treatment of the associated condition is often associated with resolution of the AF without further recurrence. Post-cardiac surgery AF is the commonest complication of surgery. The pathogenesis is likely to be multifactorial (postoperative pericarditis, surgical trauma to the atria, myocardial ischaemia, inadequate atrial protection during cardiopulmonary bypass and high circulating levels of catecholamines)(37). AF associated with acute infarction tends to be associated with an adverse outcome in comparison to patients presenting in sinus rhythm or with pre-existing AF(38).

AF ASSOCIATED WITH HEART DISEASE

AF may be associated with both electrical, as well as structural cardiac abnormalities.

In the case of electrophysiological abnormalities it is known that patients with AVNRT(39) and AVRT have an increased risk of AF. With timeous therapy the risk can be reduced although not necessarily eliminated. Particularly in younger patients with AF an electrophysiological study may be an important part of the work up to exclude these potentially easily curable arrhythmias. It is also important to remember that AF may occur secondary to another atrial arrhythmia such as primary atrial flutter or focal atrial tachycardia (classically from a pulmonary vein focus), and

that these tend to be more easily treated by radiofrequency ablation. In addition, bradyarrhythmias and heart block are associated with atrial fibrillation. Pacemaker selection has a significant impact on the long-term incidence of AF; with trials having shown an increased risk of AF in those subjected to ventricular based pacing as compared to atrial based pacing, particularly in the presence of intact AV conduction(40, 41). The effect of this difference has not been as convincingly shown on mortality however.

Any process that infiltrates, irritates, inflames, scars or stretches the atria may cause atrial arrhythmias. Specific structural abnormalities associated with AF include hypertension, coronary artery disease and valve disease, especially mitral valve disease(5, 6). The ratio of these as underlying precipitators of AF varies across regions in the world. By convention the term "non-valvular" atrial fibrillation is restricted to cases where there is no rheumatic mitral valve disease or a prosthetic heart valve. AF is also associated with cardiomyopathies, hypertrophic and dilated, but also restrictive. Congenital cardiac abnormalities are associated with significant risk for atrial arrhythmias, as is pulmonary disease. Sleep apnoea syndrome as a cause of atrial, as well as ventricular arrhythmias, is increasingly being recognised. Obesity has also been associated with an increased incidence of AF, although whether this association is independent of other risk factors for AF is not yet clear. The ALFA study characterised the presentations and underlying causes of atrial fibrillation in general practice in a population of 756 patients(42). Cardiac disorders were found in 534 patients (71%). This included hypertension in 39%, coronary artery disease in 17%, and myocardial disease in 15%. In contrast to some other studies, the incidence of rheumatic valvular disease was low: 25% in women and 8% in men.

AUTONOMIC OR NEUROGENIC AF(43)

Some patients tend to develop atrial fibrillation during periods of high vagal tone, such as postprandially. So-called vagally mediated paroxysmal atrial fibrillation is typically seen in young men. Vagally mediated atrial fibrillation appears to respond more favourably to antiarrhythmic drugs with vagolytic properties such as Disopyramide.

In others the onset of atrial fibrillation occurs during periods of high adrenergic drive such as after or during exercise or during periods of sinus tachycardia. This is a more heterogeneous category and includes patients with ischaemic heart disease. In these patients it is reasonable to use adrenergic receptor blocking agents.

AF WITHOUT ASSOCIATED HEART OR OTHER KNOWN SYSTEMIC DISEASE

If no structural cardiac or systemic disease known to promote atrial fibrillation is present, it is called "lone atrial fibrillation". This term should however, be used only if no cause can be found after a thorough history, physical examination, basic laboratory investigations and echocardiography have revealed no predisposing factor. Even so, the diagnosis should repeatedly be reassessed and not infrequently, some cause only becomes apparent after a period of follow-up(8), in which case the term should no longer be applied.

Familial clustering of atrial fibrillation has been well described in a number of studies and is associated with a variety of ion channel and connexin abnormalities that affect the impulse generation and conduction properties of myocardial tissue(44-46). Affected individuals usually have structurally normal hearts and so it is reasonable to consider it as a subset of lone atrial fibrillation. As further research elucidates the mechanisms responsible, it is likely that the pathogenesis of most cases of lone atrial fibrillation will become clear.

CLINICAL FEATURES

Symptoms: The atrial tachyarrhythmias give rise to a number of symptoms with which the patient may present including palpitations, dyspnoea, reduced effort tolerance, chest pain and presyncope, to mention only a few. The expression of symptoms depends in part on the underlying cardiac disease, if present, as well as the characteristics of atrioventricular nodal conduction i.e. the rate and regularity of the ventricular response. The presenting symptoms may also relate to thromboembolic complications of atrial fibrillation.

Symptoms may vary between attacks and many episodes may be asymptomatic. In a study of symptoms in 600 patients approximately 80% were symptomatic and the symptoms varied between groups of patients(47, 48). Factors which seemed to predict symptoms were: young age, higher heart rates, higher systolic blood pressure, female gender, and no prior myocardial infarction. However individual symptoms were also associated with specific groups:

- Palpitations - in younger age, of female gender with higher rates and normal LV function;
- Cerebral hypoperfusion related symptoms such as light-headedness and dizziness - in those with smaller left atria;
- Dyspnoea - in those as expected with hypertension and larger left atria and ventricles, but also in those of female gender and younger age.
- Asymptomatic - those of an older age, with otherwise normal hearts and slower and more regular rates.

Signs: Patients with atrial arrhythmias should be examined for evidence of structural heart disease, systemic disease that may explain the occurrence of the arrhythmia and for complications associated with the arrhythmia itself, such as evidence of peripheral thromboembolism. Physical findings of the arrhythmia itself include in the case of atrial fibrillation, a slight variation in the intensity of the first heart sound, absence of a waves in the jugular venous pulse and an irregular ventricular rhythm with a so-called "pulse deficit" (a higher heart rate auscultated precordially than palpated peripherally) if the ventricular response is rapid.

COMPLICATIONS AND PROGNOSIS

Atrial tachyarrhythmias may give rise to a number of serious clinical sequelae:

The most definite and well-researched complication of atrial fibrillation and flutter is systemic thromboembolism. The incidence of this complication varies considerably depending on a number of modifying factors. Patients with valvular atrial fibrillation appear to have the highest risk, in the order of 4 to 6 % per year in patients with mitral stenosis. Young patients (less than 60 years) with lone atrial fibrillation have the lowest stroke risk, in the order of 0.5-1,5% per year(8, 49). By comparison stroke risk in older (>65years) lone AF patients is still probably elevated above that of age matched controls. In the Framingham study the impact of atrial fibrillation on the risk of stroke with increasing age was examined in 5184 patients(50). After 30 years of follow-up, chronic atrial fibrillation appeared in 303 persons. The proportion of strokes associated with this arrhythmia was 14.7%, 68 of the total 462 initial strokes, increasing steadily with age from 6.7% for ages 50 to 59 years to 36.2% for ages 80 to 89 years. In contrast to the impact of cardiac failure, coronary heart disease, and hypertension, which declined with age, atrial fibrillation was a significant contributor to stroke at all ages. Patients with paroxysmal atrial fibrillation appear to have an annualized stroke rate (3.2%) similar to those with chronic atrial fibrillation (3.3%)(51). The ALFA study found a 2.4% incidence of thromboembolism over a mean of 8.6 months of follow-up(42). Loss of active atrial transport appears to play some part in the risk of thromboembolism, but atrial fibrillation may also be merely a marker rather than a risk for thromboembolism in some cases.

Recent trials of rate control versus rhythm control have shown that even in the rhythm control group there remains a significant risk for thromboembolism. The underlying risk factors, and risk of recurrence therefore need to be carefully assessed when deciding on the duration of anticoagulation post cardioversion. Age is often used as a deciding factor for anticoagulation(5). An age of 80 years has been used by some as a cut-off age, but it must be remembered that in the developed world approximately 30% of patients with AF will be older than 80 years.

The decision on what form of anticoagulation to give depends on a number of associated risk factors (table 3). Echocardiography is useful in risk assessment for thromboembolism but LV dysfunction appears to be a better predictor of risk than left atrial (LA) size. Transoesophageal echocardiography (TEE) is superior to transthoracic echocardiography, both in assessment of LA and left atrial appendage (LAA) thrombus as well as in detection of features such as reduced flow velocities in LA and LAA, as well as spontaneous echo contrast associated with increased risk of thromboembolism(52). The association of complex aortic atherosclerotic plaque on TEE with increased risk of thromboembolism shows that AF is both a risk factor, as well as an association with thromboembolism(53).

Table 3 Risk Assessment for Thromboembolism in Non-Valvular Atrial Fibrillation(26, 27)

Risk Factors	Relative Risk
Previous Stroke or TIA	2.5
Diabetes Mellitus	1.7
History of Hypertension	1.6
Coronary Artery Disease	1.5
Congestive Cardiac Failure	1.4
Advanced Age	1.4

TIA – transient ischaemic attack. Relative Risk compared to those with AF, but without these risks.

Functional deterioration has been well described in patients with persistent or permanent atrial fibrillation. Atrial fibrillation appears to be an independent predictor of functional decline and to be associated with increased mortality(54) in patients with underlying heart disease. Cardiac output can decrease because of loss of AV synchrony, irregular RR intervals(55, 56), and inappropriately rapid heart rates. A contribution of so-called tachycardia-induced cardiomyopathy in patients with persistently high ventricular response rates has been suggested(57).

Mortality appears to be independently associated with atrial fibrillation in large population studies such as the Framingham cohort. The presence of atrial fibrillation is associated with a doubling of mortality in both sexes, which is decreased to 1.5 to 1.9-fold after adjusting for associated cardiovascular conditions(6, 58). However, studies of lone AF patients suggest no difference in mortality between these patients and age matched population controls. Clearly however, the mortality in AF also relates to associated cardiac conditions that may be present.

COMPLICATIONS OF THERAPY

Even though the atrial tachyarrhythmias are associated with substantial morbidity and mortality it should not be forgotten that every form of therapy also carries with it a certain risk of adverse events. Antiarrhythmic drugs have a significant risk of proarrhythmia(59-61), anticoagulant

therapy a significant risk of bleeding complications and catheter ablation procedures a significant risk of a variety of complications inherent to the invasiveness of cardiac catheterisation.

CONCLUSION

The frequency of atrial arrhythmias is increasing in the general population. Interventional treatment is available, both for atrial fibrillation and focal, and macroreentrant atrial tachycardias, and as the approaches are different, it becomes important to recognise and differentiate the different arrhythmias. Electrocardiographic features allow one to assess whether a flutter is dependent on the cavo-tricuspid isthmus or not. All the atrial arrhythmias are closely related. In atrial fibrillation, therapy is presently more focused on rhythm and frequency control, and on prevention of thrombo-embolism. However, there is an increasing focus on intervention for atrial fibrillation which was previously reserved predominantly for focal and macroreentrant atrial arrhythmias.

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Chapter 3

Acute success and medium term follow up of catheter ablation of isthmus dependent atrial flutter : a comparison of 8 mm tip radiofrequency and cryothermy catheters

Acute success and short-term follow-up of catheter ablation of isthmus-dependent atrial flutter; a comparison of 8 mm tip radiofrequency and cryothermy catheters

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Abstract
Objectives To compare the acute success and short-term follow-up of ablation of atrial flutter using 8 mm tip radiofrequency (RF) and cryocatheters.
Methods Sixty-two patients with atrial flutter were randomized to RF or cryocatheter (cryo) ablation. Right atrial angiography was performed to assess the isthmus. End point was bidirectional isthmus block on multiple criteria. A pain score was used and the analgesics were recorded. Patients were followed for at least 3 months.
Results The acute success rate for RF was 83% vs 69% for cryo (NS). Procedure times were similar (mean 144±48 min for RF, vs 158±49 min for cryo). More applications were given with RF than with cryo (26±17 vs. 18±10, $p<0.05$). Fluoroscopy time was longer with RF (29±15 vs. 19±12 min, $p<0.02$). Peak CK, CK-MB and CK-MB mass were higher, also after 24 h in the cryo group. Troponin T did not differ. Repeated transient block during application (usually with cryoablation) seemed to predict failure. Cryothermy required significantly less analgesia ($p<0.01$), and no use of long sheaths ($p<0.005$).

The isthmus tended to be longer in the failed procedures ($p=0.117$). This was similar for both groups, as was the distribution of anatomic variations. Recurrences and complaints in the successful patients were similar for both groups, with a very low recurrence of atrial flutter after initial success.

Conclusions In this randomized study there was no statistical difference but a trend to less favorable outcome with 8 mm tip cryocatheters compared to RF catheters for atrial flutter ablation. Cryoablation was associated with less discomfort, fewer applications, shorter fluoroscopy times and similar procedure times. The recurrence rate was very low. Cryotherapy can be considered for atrial flutter ablation under certain circumstances especially when it has been used previously in the same patient, such as in an AF ablation.

Keywords Arrhythmia · Catheter ablation · Atrial flutter · Atrial fibrillation · Radiofrequency · Cryothermy

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1 Introduction

Atrial flutter is a common arrhythmia [1], difficult to suppress with medication [2], and is associated with significant symptoms. Since it was first proposed [3–5], ablation for atrial flutter has increasingly been used for its therapy, especially since induction of bidirectional cavotricuspid isthmus block was shown to be associated with better immediate outcomes and lower recurrence rates [6–11]. Failure to successfully ablate atrial flutter in the long-term may be due to particular anatomic problems [12–14], poor catheter stability in this region, and incorrect interpretation of isthmus block. Important developments in the field of atrial flutter ablation have been a better understanding of the anatomy of the isthmus, refinements of the definition of bidirectional isthmus block, and the arrival of new catheter technology.

Numerous studies have compared different energy types, different catheter tip sizes and different energy settings [15–19], as well as the use of advanced cardiac mapping

systems [20]. The preferred tools now are 8 mm, or irrigated tip catheters [21]. From a recent meta-analysis it would appear that these two technologies are equally effective with acute success quoted at 84% and 85% for the primary catheter chosen before changeover, whereafter final success rates of up to 99% can be achieved [22]. Not all studies have this high success rate and the preponderance of studies on ablation of atrial flutter suggest that these high success rates are not repeated in all centers [23]. Also of importance is a clinical recurrence rate, in the face of acute success, of at least 5 to 12% when using radiofrequency [19, 24, 25]. Disadvantages of radiofrequency (RF) energy include pain, overheating with "popping", char formation and risk to coronary arteries.

Cryoablation is a relatively recent addition to the transvenous ablation armamentarium and has been shown to be comparable to RF for some arrhythmias. It may have some advantages over RF, especially as regards discomfort during ablations [17, 26]. The development of 6 and 8 mm tip cryocatheters has increased the interest in this technology for atrial flutter ablation. As far as we are aware there have been no randomized comparative studies published comparing 8 mm tip cryocatheters with 8 mm tip RF catheters.

2 Methods

2.1 Patient population

Consecutive patients with ongoing symptoms and documented atrial flutter with or without fibrillation were included. At least one recent episode of atrial flutter (within the last 6 months) was documented on a 12 lead ECG and was suggestive for isthmus dependency. Patients with drug-induced flutter (and prior AF) could be included, and had their drug therapy continued after ablation. Patients were excluded if they had undergone a previous flutter ablation, if thrombus was present in the atria, or after previous cardiac surgery for valvular or congenital heart disease. Baseline investigations included a standard echocardiogram, a simple questionnaire asking about clinical well-being and a subjective assessment of the arrhythmia burden both in terms of duration and frequency. The study was approved by the ethics committee of our institution. All patients signed written informed consent.

2.2 Assessment before ablation

Antiarrhythmic drugs, except for AV nodal slowing agents, and amiodarone, were discontinued at least five half-lives prior to ablation. Patients were studied in the fasting, post-absorptive state. A coronary sinus (CS) catheter was inserted through the left subclavian vein, and a multipolar circular right atrial catheter with alternating 2–10–2 mm interelectrode distance was positioned from the right groin, with the tip positioned immediately lateral to the planned position of the isthmus line and anterior to the crista terminalis. Heparin 100 U/kg was given and a further 5 U/kg given if the procedure lasted longer than 180 min.

If the patient was in sinus rhythm, isthmus conduction was confirmed by pacing. If flutter was present, entrainment was performed to confirm isthmus dependence, and the patient left in flutter. If AF was present, the patient was cardioverted after a transoesophageal echocardiogram, and then isthmus conduction confirmed. Absence of isthmus conduction or non-isthmus dependence was not seen in the selected patients. No induction of arrhythmia was attempted if patients had sinus rhythm.

Radiological assessment of the right atrial isthmus was made in a right anterior oblique (RAO) 30°, and a left anterior oblique (LAO) 45° view (each with 40 cc at 18 cc/s). Angiograms were acquired digitally to allow for post-hoc analysis. The treating physician was able to view the angiographic findings to optimize the planned ablation line. The isthmus length was assessed from the inferior hinge point of the tricuspid valve to the IVC at the end of atrial diastole (the frame before opening of the tricuspid valve) [14]. Morphology was assessed visually as to the presence of a Eustachian valve or a recess, as well as to the general shape i.e. flat or concave.

2.3 Ablation procedure

The catheters were a 9Fr 8 mm tip catheter (FreezorMax, Cryocath Technologies Inc, Kirkland, Canada) with a cryoconsole for the cryoablation group, and a 7Fr 8 mm tip single sensor catheter (EPT Blazer II, Boston Scientific, Natick, MA, USA) with an EPT-1000XP generator for the radiofrequency group. A large curve was initially selected in both groups, with change out of catheter curve during the study only as necessary. Applications of −75°, for 4 min were given with cryothermy, and applications of 60 Watt, for 60 s, targeted at 60°C for RF. Lines were made with discrete applications between the tricuspid valve and the inferior vena cava at an approximately 6 o'clock position in LAO 45°, unless otherwise dictated. If termination of atrial flutter occurred, or if the patient was in sinus rhythm, continuous pacing from the proximal coronary sinus was employed to continually assess isthmus conduction. After the first line, a new assessment of conduction was performed. If conduction over the isthmus remained present, gaps were sought. If there was still isthmus conduction, a slightly more medial or lateral line was made. In no patient was an attempt made to perform a septal ablation line. Final assessment of acute block was confirmed after 30 min waiting.

The end point for successful ablation was induction of complete bidirectional isthmus block, defined as the presence of reversal of activation on the lateral and septal wall when pacing the CS os and low lateral RA, the presence of widely split potentials along the isthmus line, by activation mapping across the isthmus, and by differential pacing. All 4 were required before calling the ablation successful. In the case where bidirectional block was not achieved, ablation was stopped when no large, sharp signals could be identified over a broad area of the isthmus.

As pain perception was assessed, sedation was standardized. Before venous puncture 5 mg of diazepam was given intravenously, and repeated at the patient's request. Fentanyl 50 μg intravenously was given when the patient requested pain control and the physician considered this necessary. This was repeated as needed. Dosages of both diazepam and fentanyl were recorded.

In the initial 40 patients creatine kinase (CK) and CK-MB were taken before the procedure, 2 and 24 h after the start of the procedure. For the final 22 patients the laboratory had changed the measurement to CK mass. We then modified the protocol to measure CK-MB mass, Troponin T, and Myoglobin at 4 and 24 h after the start of the procedure.

No crossover, other than in catheter curve, was allowed in an attempt to remove any possible bias. Change over to an irrigated tip ablation catheter was also not allowed. In patients in whom no block could be induced, a repeat procedure was scheduled not earlier than 6 weeks after the initial ablation, at the physicians' discretion. The choice of energy source at that time was at the physicians' discretion.

Patients were all questioned with regard to pain perception using a visual analogue score, where patients are shown a line from 0 to 10, where 0 is no pain, and 10 is the highest pain level imaginable, and were asked to point to the position on the line where their pain level during ablation was.

2.4 Follow-up

All patients received an event-recorder for the first 6 weeks after the procedure and were requested to send at least daily strips as well as strips made during symptoms. Patients visited the outpatient clinic 6 weeks after the procedure. After this period all patients were asked to report symptoms and if these were present were given a further event monitor until documentation of symptoms was obtained. If at all possible a 12 lead ECG was also obtained. A second assessment with a questionnaire was performed after 3 months, again asking a question about general clinical well being and also symptom burden in regard to duration and frequency. Clinical files were followed up after 9 months.

2.5 Statistical analysis

For patients in whom another ablation was performed (AVNRT in two, and pulmonary vein ablation in six others) procedure and fluoroscopy times were limited to the flutter approach, which was done first, including 30 min waiting time. Biomarker assessment was not done in these patients. Continuous variables are expressed as mean ± standard deviation, with medians as necessary. Parametric and non-parametric tests were used where appropriate. A p-value of <0.05 was considered significant.

3 Results

3.1 Patient data

62 patients were included as planned, with clinical characteristics as outlined in Table 1. There were no significant differences in any of the parameters between the group assigned to radiofrequency (RF group) versus that assigned to cryotherapy (cryo group). The large number of patients with prior AF is due to the fact that we had initially taken a decision to perform isthmus ablation first in all patients with AF who had shown typical atrial flutter on any 12-lead ECG, prior to performing a left atrial procedure, initially in a separate procedure and only later in the same session.

3.2 Angiographic data

Right atrial angiography was not performed in 4 patients because of mild renal dysfunction or allergy to contrast material. The angiogram was of insufficient quality in eight others.

The mean isthmus length was 35.2±14.6 mm and its topography was assessed as being flat or only mildly concave in 28, markedly concave in 19 and showed a pit or aneurysm in 10. A clear Eustachian valve was seen on six angiograms.

Table 1 Demographics

	All	Cryo	RF	p value
Number	62	32	30	
Age (years±SD)	56±10	55±11	56±9	NS
Male/female	27/5	27/5	28/2	NS
Atrial fibrillation history	47 (76%)	25 (78%)	22 (73%)	NS

Cryo Cryoablation; *NS* not significant; *RF* radiofrequency; *SD* standard deviation

3.3 Ablation data

Assessment of acute results showed bidirectional isthmus block, using the criteria mentioned, in 47 of 62 patients (76%). This was in 25 of 30 patients (83%) of the RF group and in 22 of 32 (69%) of the cryo group (NS). In 1 patient in the RF group the procedure was terminated because of recurrent AF with early recurrence and inability to assess isthmus block. This patient was taken as a failure which was confirmed at the time of a subsequent AF ablation. Procedural data for all patients are given in Table 2.

In the successful patients the number of applications to ensure block in the whole group was 17±11. It was 23±13 in the RF group and 12±6 in the cryo group ($p<0.005$). Total ablation time was 1,283±777 s and 2,905±1,245 s ($p=0.0001$). In those in whom bidirectional block could not be achieved, the total number of applications was 33±14. For RF and cryo the values were 39±21 applications with a total time of 2,724±1,102 s vs 29±8 applications with a time of 5,873±1,337 s ($p<0.03$ and <0.0011, respectively).

In 22 of 30 in the RF group and 25 of 32 in the cryo group, a single line at approximately 6 o'clock was drawn. In the RF group two lines were drawn in seven, and three in one. In the cryo group two lines were made in four, and three lines in three. The need to draw more than one line was associated with failure of the procedure in four of eight in the RF group and five of seven in the cryo group (NS).

Short lived block, either recurring during the application or immediately thereafter, occurred in one patient in the RF group and in six in the cryo group, with a trend to statistical significance ($p=0.091$), with it being a predictor of failure if it occurred more than three times. In five patients in the RF group and one patient in the cryo group, conduction recurred later during a waiting period (with a median of 15 min) requiring further applications (NS). In only one patient in the RF group was late recurrence associated with failure to induce bidirectional block. In no patient in whom bidirectional block was present at the end of the 30 min waiting period did isoprenaline change this. The average power applied in the RF group was 52±6 W.

In the RF group the signal was significantly diminished at the end of each application whether isthmus block was present or not, while there tended to be preservation of signals on the cryoablation catheter after ablation across the isthmus until block occurred. Only then were low voltage signals seen.

Failures were not significantly associated with length of the isthmus (39.2±23.5 vs 34±9.0 mm in success, although there was a trend to this ($p=0.12$) There was no significant difference in anatomy between the two groups.

3.4 Procedure data and complications

The overall procedure time was 160±49 min, with no difference between 170±48 min in the RF group and 151±49 min in the cryo group. Overall fluoroscopy times were 28±14 min, with a difference between 33±15 min in the RF group and 23±11 min in the cryo group ($p<0.02$).

Change of catheter curve occurred in one patient in the RF group from large to standard curve. An SL1 sheath

Table 2 Procedure data and recurrent arrhythmias

	All	Cryo	RF	*p* value
Number	62	32	30	
Application number	22±13	18±10	25±16	0.05
Ablation time (s)	2,742±1,930	3,792±1,900	1,459±950	<0.001
Acute success	47 (76%)	22 (69%)	25 (83%)	NS
Single line	47 (76%)	25 (78%)	22 (73%)	NS
2 lines	9 (15%)	2 (6%)	7 (24%)	0.073
3 lines	4 (6%)	3 (9%)	1 (3%)	NS
Reversal of block during application	7 (11%)	6 (19%)	1 (3%)	0,091
Reversal of block during 30 min	6 (10%)	1 (3%)	5 (7%)	NS
Isthmus length (mm)	35±15	35±17	36±11	NS
Sheath usage	7 (11%)	0 (0%)	7 (23%)	<0.005
Recurrent arrhythmias				
Flutter (typical)				
After success	1 (2%)	0 (0%)	1 (4%)	NS
After failure	11 (73%)	7 (70%)	4 (50%)	NS
Flutter (atypical)	1 (2%)	0 (0%)	1(3%)	NS
Atrial tachycardia	5 (8%)	2 (6%)	3 (10%)	NS
Atrial fibrillation	28 (45%)	13 (41%)	15 (50%)	NS

The numbers are given with the standard deviation.
Cryo Cryoablation; *NS* not significant; *RF* radiofrequency

(Daig, Minnetonka, MN, USA) was used in seven patients in the RF group for stability, while no sheath usage occurred in the cryo group (p=0.005). During the procedure, six patients required cardioversion for induced AF, four in the RF group and two in the cryo group (NS). There were two small pericardial effusions seen on echocardiography without further significance (one in each group).

For the initial 40 patients there was a significantly higher peak CK and CK-MB after cryo (Table 3). This remained so after 24 h. For the last 22 patients we observed the same for CK-MB mass, but not for Troponin T (Table 3).

In assessing the level of comfort during the procedure and the pain experienced by patients, similar numbers from both groups assessed sedation as adequate (67% for RF and 63% for cryo). The pain scores given at the end of the procedure were not significantly different (42.9±24.0 for RF and 43.7±15.8 for cryo). Diazepam was given as standard at the beginning of the procedure and as necessary thereafter for discomfort related to having to lie still for protracted periods. The usage of diazepam was statistically similar in both groups (7.4±3.4 mg in the RF group and 8.0±3.1 mg in the cryo group). However, a significantly higher usage of fentanyl in the RF group was observed (70.0±44.9 μg vs 10.0±22.1 μg; p<0.01).

3.5 Follow-up results

Patients were followed up for between 90 and 411 days (138±81 days, median 90 days), which was similar in both groups (p=ns).

A total of 6 patients were taking no antiarrhythmic medication prior to ablation and this increased to 13 post isthmus ablation.

Table 3 Biomarkers after catheter ablation

	All	Cryo	RF	p value
Procedure values				
CK (U/l)	141±96	184±102	96±60	0.02
CK-MB (U/l)	27±16	36±17	18±8	0.011
CK-MB mass (μg/l)	18±21	33±24	4.4±1.2	0.004
Troponin T (μg/l)	0.49± 0.32	0.54± 0.38	0.39± 0.27	NS
Values after 24 hrs				
CK (U/l)	264±245	289±173	136±74	0.022
CK-MB (U/l)	37±28	51±30	18±6	0.011
CK-MB mass (μg/l)	8.4±7.3	12±10	5.16±3.3	0.07
Troponin T (μg/l)	0.44± 0.30	0.54± 0.36	0.38± 0.29	NS

The numbers are given with the standard deviation.
CK Creatine kinase; *Cryo* cryoablation; *NS* not significant; *RF* radiofrequency

Recurrent arrhythmias were frequent in both groups of patients. ECG documented recurrent flutter occurred only in one patient from the RF group. A further procedure confirmed recovery of isthmus conduction. This recurrence was seen at 14 months post ablation, whereas he had previously had monthly episodes of flutter. One other patient had symptoms with an apparently non-isthmus dependent flutter documented on ECG on day 1 post ablation and not since, and elected not to have a further procedure. We cannot exclude asymptomatic arrhythmias but at least during the first 6 weeks, patients sent in daily event monitor transmissions, which one would hope would have captured at least some asymptomatic recurrences, particularly of atrial flutter.

In 11 of 15 patients in whom the initial procedure failed, a redo procedure was performed after the elected period of 6 weeks because of documented recurrent flutter. The redo procedure required a small number of point touch ups in five patients (three in the RF group and two in the cryo group), while more extensive diffuse isthmus applications were required in six (one in the RF group and five in the cryo group). In those undergoing repeat ablation, success was achieved in all and during follow up no recurrent atrial flutter was noted.

Previously undocumented atrial tachycardias were also seen in both groups (three in the RF group, and two in the cryo group). ECG documented AF recurrence occurred in 28 patients, at a similar rate in both groups (15 in the RF group and 13 in the cryo group). The likelihood of asymptomatic recurrences is probably higher for atrial fibrillation but was not the primary focus of this study.

4 Discussion

4.1 Acute success

This study showed an acute success rate of 83% for an 8 mm tip RF catheter vs. 69% for an 8 mm tip cryocatheter. This non significant difference is clearly concerning. However, the cryoablation group required significantly less applications to achieve success, with a similar procedural duration, significantly lower fluoroscopy time, and with a much lower requirement for analgesia with fentanyl. Arrhythmia recurrences in the initially successful patients were similar with a very low flutter recurrence rate.

The acute success rate with 8 mm tip RF compares favorably with that found in the meta-analysis of Da Costa et al. [22]. However, the acute results for cryotherapy are lower than in previously published studies. The shorter fluoroscopy time using cryotherapy is related to cryoadherence during applications [26]. With the catheter firmly attached, no fluoroscopy to check position is required. This

is also reflected in the fact that no long sheaths were necessary. A lower requirement for analgesia has previously been described and this study confirms this finding [17, 26].

4.2 Difficulties during ablation

Recurrence during or shortly after ablation occurring more commonly in the cryo group probably relates to a reversible cooling effect at the periphery of the ice ball which recovers during or shortly after termination of ablation, while the central lesion acutely formed is more permanent. The more common recurrence during the waiting period after RF ablation probably relates to a longer reversal time of the acute RF effects (either edema or temperature effect).

4.3 Cryoablation for flutter

Cryoablation may have some advantages over RF in addition to those mentioned above such as less thrombogenicity [27], and maintenance of tissue architecture with homogenous well delineated lesions [28]. A 10Fr, 6.5 mm tip catheter showed acute success of 94–100% and 6 month recurrence rates of 0–25% [17, 29, 30]. A system with 7Fr, 6 mm tip catheters showed success in 87% to 88% using a septal line, without symptomatic recurrences, but with resumption of isthmus conduction at repeat study at 6 months in 30–35% [31, 32]. Using a 9Fr, 8 mm tip increased success rates to100% with symptomatic recurrence of 0% to 10% and recurrent conduction at 1 to 3 months in 19% to 32% [32–34]. There is some discussion as to whether 3, 4 or 8 min of ablation are needed for adequate lesion formation [33, 35].

Higher peak CK levels, confirmed by the high CK-mass in the last patients, suggest that the damage caused by cryotherapy may be more extensive despite the lower number of applications. Several explanations are possible. The first is that the CK levels may be underestimated after RF, which denatures proteins in another way than cryotherapy. Troponin T levels are more accurate in estimation of myocardial damage, but they also tended to be higher, be it not significantly. This may suggest that lesions are equal with both approaches.

4.4 Future developments

Newer data suggest that ablation per point guided by the maximal voltage may be a useful technique, but this has not been confirmed for cryotherapy [36].

4.5 Study limitations

This study was a single centre, largely single operator study involving a relatively limited number of patients with a high population of AF patients, making follow-up rather complicated. In present practice and later in this series, patients with the combination are often treated in one session, which still leaves physicians the choice whether cryo should be used for flutter, following its use for the pulmonary veins [37]. We only studied the acute and short-term success, while flutter recurrence may happen at more than 4 months of follow-up. While we attempted to exclude asymptomatic recurrences especially in the first 6 weeks, we cannot exclude the possibility of these, especially of AF and also late after the ablation. Isthmus conduction recovery is also possible in asymptomatic cases. In the RF group we limited the power to 60 W to ensure safety and this may be too conservative. Further, in our practice routine use of long sheaths was discouraged. At the time of this study use of an 8 mm tip with RF was considered as effective as irrigated tip ablation, so we elected to use this approach for the RF group. More recent studies have shown higher success rates than we obtained and have also suggested alternatives in the approach. These include the use of irrigated tip catheters and long sheaths as well as other technical issues and newer techniques such as maximal voltage guided ablation. A higher success rate for RF would clearly have been even more prejudicial to cryotherapy in this study. We were also extremely critical in our assessment of isthmus conduction, using multiple criteria. Angiograms were also performed in fixed views and not based on other catheter positions as has been suggested by others [14].

5 Conclusion

Acute success with cryotherapy for atrial flutter ablation, while non-statistically less effective in this study, requires fewer applications and is associated with a significantly lower requirement for pain relief. While our acute results for both cryotherapy and RF may not be as high as those in some comparable studies the recurrence rate was only 2.5% in the RF group, with no clinical recurrence in the cryo group. While cryotherapy cannot perhaps be advocated as first line therapy, it may be useful in certain circumstances. Certainly, if cryoablation is performed for AF, and if the isthmus needs to be ablated, cryotherapy might be used as well [37].

Conflict of interest statement No conflicts of interest exist.

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Chapter 4

Atrial flutter – watch and control

Atrial flutter: Watch and control?

Since the demonstration of the circuit of typical atrial flutter, and the recognition that an ablation line across the cavotricuspid isthmus could be a permanent cure for this arrhythmia [1,2], electrophysiologists have been attempting to improve the success rates for this procedure. The clarification of an acceptable end-point with relatively low risk for recurrence [3,4] has now led to an attempt to optimise the acute success rates, and thus also long-term efficacy, of this procedure. The introduction to the article by Hillock et al. [5] in this issue highlights some of the frustrations experienced by electrophysiologists attempting to ablate this region. The isthmus can be irregular and thick, and anatomical structures such as the Eustachian valve can make ablation both difficult and long [6]. In experienced centres there are always attempts to improve success rates. Furthermore, the success rates in excess of 90% with minimal radiation and short procedure times described by high volume units are presumably not always repeated by operators in less experienced centres, prompting attempts safely to improve these rates. Thus, there is a background which encourages operators to try new techniques not only to improve success rates, but also to shorten procedure and radiation times. Numerous authors have compared different energy types, different catheter tip sizes and different energy settings [7–11], as well as the use of advanced cardiac mapping systems [12], but the search for improved techniques continues.

Clearly it is important to balance the effectiveness of the procedure with the risks associated with the use of alternate techniques. As Hillock et al. have shown, the use of ''un-monitored'' very high power settings (>100 W) is associated with a significant risk of ''pops'' and subsequently of perforation and tamponade. These added risks were apparently not seen in other studies using long tip catheters and up to 100 W [10,11].

In the ablation of the cavotricuspid isthmus a number of features could potentially lead to an improvement in the success rate, while at the same time also improving safety.

What is needed pre-, or during ablation, is an accurate picture of the isthmus itself. These images would demonstrate anatomical variations which may prove to be an impediment to ablation, such as a markedly irregular or very thick isthmus, or the presence of deep pits or a large Eustachian ridge or valve. Detailed knowledge of the anatomy would allow for the planning of the best line so as to avoid difficult areas and move to the easier areas. Although an electroanatomic mapping system can be used to delineate anatomy, potential anatomical problems and to tag a line [12], perhaps this visualisation could be done better by direct imaging. Whether this enhanced anatomical knowledge is best based on a pre-study CT scan or MRI, or is made on the basis of intraprocedure angiography [13,14] or echocardiography [15] will become clearer in the future. Present techniques need to be further improved, because the resolution now is not always optimal (or cost effective) to make detailed plans.

In addition the optimal delivery of energy to cause lesions is also important. It is clear that the use of 4 mm tip radiofrequency catheters has become antiquated and that at the very least 8 mm tip or irrigated tip catheters are the preferred tools of most electrophysiologists [16]. The place of cryotherapy has yet to be fully established especially with the availability of large tip cryocatheters. Our experience of 8 mm tip cryocatheters is that the acute success rate over the last year appears to be as good of that of 8 mm tip radiofrequency catheters, with less pain experienced by the patients. This is the subject of an ongoing prospective study at our institution. The use of ''un-monitored'' high power radiofrequency

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energy has been the subject of a limited number of studies. It would appear from the present study, however, that the un-monitored use of energy greater than 100 W should probably not be attempted. The question is really, what is the optimal catheter type or energy setting to use, and whether better monitoring of energy delivery would assist in the formation of optimal lines of block. Ablation for atrial fibrillation complicated by the highly publicised risk of oesophageal fistula formation has refocused our attention on optimal energy delivery and optimal monitoring [17]. From the limited knowledge available, it seems that power may not be a good indicator of tissue temperature especially with the use of irrigated tip catheters, and assessment of micro-bubble formation for instance may be useful both for assessment of target tissue temperature and to decrease complications [18]. The ability to see lesions acutely and assess their placement and especially their adequacy, for example by intracardiac contrast ultrasound, helping us to place and form lesions, might also be a tool in increasing safety and efficacy in atrial flutter ablation.

All in all, despite what some electrophysiologists might think, we do need further study to improve the outcome in ablation of atrial flutter while improving patient safety and the efficacy of this ablation technique.

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Chapter 5

Pulmonary vein antrum isolation guided by phased-array intracardiac echocardiography

Pulmonary vein antrum isolation guided by phased-array intracardiac echocardiography

A third way to do PV ablation

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Background. **Pulmonary vein isolation (PVI) has emerged as an important strategy in the treatment of patients with atrial fibrillation (AF).The two most frequently used techniques are segmental PVI and left atrial circumferential ablation.**
Aim. **To describe and discuss pulmonary vein antrum isolation guided by phased-array intracardiac echocardiography (ICE) as an alternative approach, and to present initial results.**
Methods. **Patients with symptomatic AF were included. The antra (the larger circumferential area around the PVs) were isolated guided by ICE. ICE was also used to titrate the ablation energy.**
Results. **38 patients (3 with persistent AF) were included. Of the 35 patients with paroxysmal AF, 24 are without recurrences, and in six the incidence of paroxysms was significantly reduced after one procedure and a mean follow-up of 201 days. No major complications occurred.**
Conclusion. **Pulmonary vein antrum isolation guided by ICE is a promising technique in AF ablation and has the potential to avoid severe complications. (*Neth Heart J 2005*;13:439-43).**

Keywords: atrial fibrillation, PV isolation, intracardiac echocardiography

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Isolation of the pulmonary veins (PVI) has emerged as an important strategy in the treatment of patients with atrial fibrillation (AF). Several studies have demonstrated freedom from AF after complete PVI in 70% of patients presenting with paroxysmal AF.[1-3] In this paper we describe an intracardiac echocardiographically guided technique for PVI and report the initial results and complications of an ongoing study using this method, aiming at ablation of the antrum (the larger circumferential area around the PVs) rather than at the PV itself, to improve outcome and to prevent the occurrence of potentially serious complications.

Methods

Inclusion criteria

Patients with symptomatic paroxysmal AF despite at least two antiarrhythmic drugs, in the absence of significant heart disease, were included in an ongoing prospective clinical trial. Initially, patients with persistent AF could be included as well. Additional inclusion criteria were a left atrial dimension <55 mm, willingness to comply with invasive screening and follow-up procedures, and the absence of echocardiographic abnormalities during transoesophageal echocardiography (TOE) the day before the procedure. A multislice CT scan was performed to assess the anatomy and measure the diameter of the PVs.

Ablation procedure

A general outline of this procedure has already been given elsewhere.[4,5] A 10 Fr intracardiac echocardiography (ICE) catheter (Acunav, Siemens AG Inc., Malvern, PA, USA) is introduced through the left femoral vein and positioned in the right atrium. The subclavian vein is used to advance a decapolar stimulation catheter into the coronary sinus. Two long sheaths are advanced through the right femoral vein into the right atrium. Double transseptal puncture is carried out using a Brockenbrough needle guided by both ICE and fluoroscopy. ICE is also used to ensure a posterior transseptal approach. A circular mapping catheter is advanced and positioned in the antrum of the pulmonary veins (figure 1).

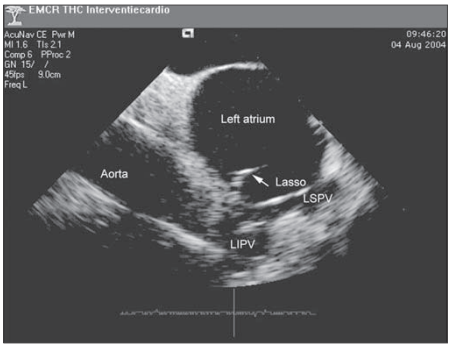

Figure 1. Phased-array intracardiac echocardiogram: circular multipolar catheter (Lasso) in the antrum of the left inferior pulmonary vein. LIPV=left inferior pulmonary vein, LSPV=left superior pulmonary vein.

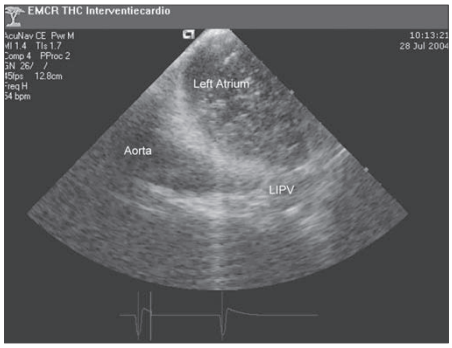

Figure 2. Phased-array intracardiac echocardiogram: microbubble formation during ablation, caused by overheating of the tissue, showing a 'brisk shower' and ablation is stopped immediately.

Radiofrequency energy is delivered using an 8 mm ablation catheter aiming at abolishing all PV potentials registered with the roving circular mapping catheter. RF energy is set at 30 Watts and 55°C and increased by 5-Watt steps to a maximum of 70 Watts or until microbubble formation (figure 2) occurs.

After isolation of all four PV antra the circular mapping catheter is placed in the superior caval vein (SVC) and this vein is also isolated. Ablation in the SVC is only carried out if there is no phrenic nerve stimulation while pacing at a high output in this vein. The day after the procedure a transthoracic echocardiogram is preformed to exclude pericardial effusion.

Anticoagulation protocol

All patients are treated with the coumadin preparation acenocoumarol for at least one month before the procedure, aiming at an INR of 2.5 to 3.5. Two days before the procedure, patients are admitted to hospital and the acenocoumarol is replaced by unfractionated heparin, aiming at an APTT ratio of three times the normal. A transoesophageal echocardiogram (TOE) is carried out the day before the ablation to exclude atrial thrombi. Two hours before the ablation, the heparin is stopped. After venous puncture and before transseptal puncture a 5000 E heparin bolus is given. After successful transseptal puncture another 5000 E heparin is given and a continuous titrated infusion of heparin is started. During the procedure the activated clotting time (ACT) is monitored every 30 minutes and is kept above 350 msec with bolus doses of heparin and adjustment of the infusion rate. After the procedure the patients are treated with heparin, and acenocoumarol is restarted. Heparin is stopped when the INR is above 2.5. Acenocoumarol is continued for at least six months.

Antiarrhythmic drug treatment after ablation

During the first two months after ablation all patients are treated with flecainide and bisoprolol to suppress atrial ectopy caused by the ablation. These drugs are stopped after two months if AF does not reoccur.

Follow-up methods

All patients are followed intensively in the outpatient clinic, including daily transtelephonic ECG monitoring from one month before until three months after ablation. Multislice CT scans are repeated at three months to evaluate the possible occurrence of PV stenosis, defined as a reduction in the diameter of more than 80%.[6]

Results

Patients

A total number of 38 patients (6 females), mean age 50.7 years (23 to 68 years), were included. Three of these patients had had persistent atrial fibrillation for more than one year and had to be cardioverted into sinus rhythm before ablation. Seven patients had previously undergone a right atrial isthmus ablation for atrial flutter. The mean LA dimension, as measured with transthoracic echocardiography, was 44.6 mm (32-53 mm). One patient had a fifth pulmonary vein on the right side. As the antra of the pulmonary veins often merge at the level of the atrium, this often creates the impression that there is a common origin of unilateral PVs.

Procedure and complications

All transseptal punctures were uneventful. In the first 38 patients, 150 pulmonary veins could be electrically isolated. All PVs were isolated in 36 patients. The

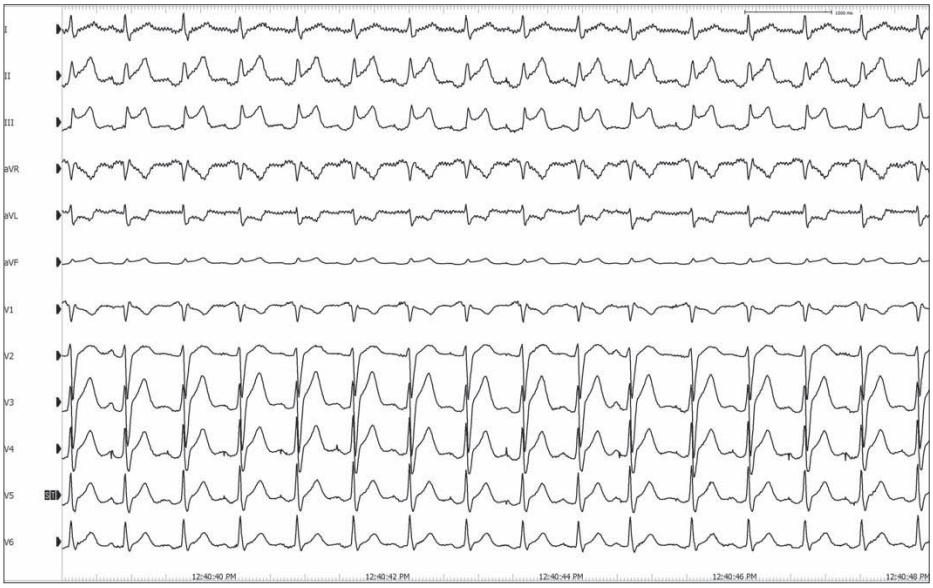

Figure 3. Transient ST elevation in the inferior leads after transseptal puncture.

average procedural time was 229 minutes (145-396) and the average fluoroscopy time 94 minutes (52-147). The average radiofrequency application time was 4098 seconds (1569-7999). The three patients with persistent AF were cardioverted several times during the ablation procedure. Of the other 35 patients, 17 were cardioverted once or twice during the procedure. In two patients, asymptomatic and transient ST elevation (figure 3) was observed after transseptal puncture.[7]

No echocardiographic evidence of myocardial infarction was observed. In four patients a right-sided isthmus ablation was carried out during the same procedure. In nine patients the superior caval vein (SVC) was isolated as well. This was not done in those patients undergoing phrenic stimulation during pacing in the SVC. In one patient an asymptomatic hemidiaphragmatic paralysis was seen immediately after ablation. No other complications occurred, except for two vagal reactions.

Follow-up

Mean follow-up in the described patients is 201 days (SD 10 days, 1-360 days). PV stenosis was not seen. Only one of the three patients with persistent AF was in sinus rhythm after the procedure. All three patients now have permanent AF. AF recurrences were seen in 11 of the 35 patients with paroxysmal AF. In six of these 11 patients the incidence of AF paroxysms was significantly reduced. AF was recorded in 34.6% of transmitted ECG strips before and 6.4% of transmitted ECG strips after PVI. Two patients developed a symptomatic atrial flutter, and were treated successfully with right-sided isthmus ablation.

Discussion

The first successful nonpharmacological treatment for AF, aiming at changing the substrate, was the Maze procedure.[8] Stimulated by the success of this procedure, initial ablation attempts were made to copy the Maze procedure, using transvenous ablation. The idea was to compartmentalise both atria by making long linear lesions. These procedures, however, were not successful because of technical difficulties in creating linear lesions, morbidity associated with this approach, long duration of the procedure and moderate effect on AF burden.[9] Two strategies for PV isolation emerged as more effective, and became major therapeutic options for patients with paroxysmal AF.

Classical techniques in radiofrequency AF ablation

Haissaquerre et al. drew attention to the role of focal activity within the pulmonary veins in triggering and maintaining AF.[10,11] Based on this knowledge he

originally performed radiofrequency (RF) ablations only at sites within the PVs where ectopic activity was recorded.[10] It is now accepted that the results of ablation improve if all PVs are completely isolated from the left atrium. Because the risk of PV stenosis with RF energy was substantial, ablation is now targeted at the ostia of the PVs. The endpoint of this approach (often referred to as the Haissaquerre approach or segmental PVI) is the elimination of all ostial PV potentials and the demonstration of complete entrance block. In this technique the ostium of the PVs is assessed by angiography.

Another successful approach in AF ablation, originally designed to isolate the PVs with a reduction in the risk of PV stenosis, is the circumferential pulmonary vein ablation.[3] This technique, developed by Pappone et al., is also known as left atrial radiofrequency circumferential ablation (LACA). Continuous circular lesions are made around each PV or around ipsilateral PVs with the help of a virtual three-dimensional (3D) electroanatomical mapping system. The ostium of the PVs is identified by fluoroscopy and during withdrawal of the catheter from the PV, with a simultaneous impedance decrease and appearance of atrial potentials. The endpoint of this approach is a low peak-to-peak bipolar potential (<0.1 mV) inside the circular lesion. The results of LACA are better when complete PV isolation, which can be considered to be a hybrid endpoint, is reached.[12]

Possible complications of PVI

Several complications of PVI have been reported. Severe thromboembolic complications are possible[13] and therefore good anticoagulation is warranted. PV stenosis has gained a lot of attention.[14] The incidence seems to decline with growing experience and with more proximal ablation.

Perforation, pericardial effusion and even tamponade have been described.[15] The left atrial appendage (LAA) is especially vulnerable to perforation and should be avoided during ablation. PVI can cause the appearance of new arrhythmias,[16,17] such as atrial tachycardia and left atrial flutter. The most feared complication nowadays is perforation at the posterior wall and the subsequent development of a left atrial-oesophageal fistula.[18-21]

Rationale for using intracardiac echocardiography

Intracardiac echocardiography (ICE) enables transseptal puncture and makes it safer.[22] Because ablation should target the ostia of the PVs, imaging of the pulmonary veins during the procedure is important. Angiography shows only the tunnel-shaped portion of the PVs, while in reality the PV antrum is more funnel-shaped, as can be seen on 3D multislice CT scan reconstructions (figure 4).

Real-time imaging of the PV antrum is currently only possible with ICE. Overheating of the tissue carries a risk of perforation and thrombus formation. Microbubble formation is a good indicator of excessive temperature and steam formation.[23] Monitoring microbubble formation with ICE can therefore be used to prevent overheating.[24] Ablation within the thin-walled LAA is prevented by the visualisation of this structure. ICE is the only tool available today to provide us with real-time imaging, making it possible to ablate in the antrum of the PVs and to ensure good wall contact. The use of ICE also holds promise for reducing fluoroscopy time; the fact that we could not demonstrate this is partly due to the learning curve involved in this technique. The average fluoroscopy time in more recent cases in our clinic has fallen below 60 minutes.

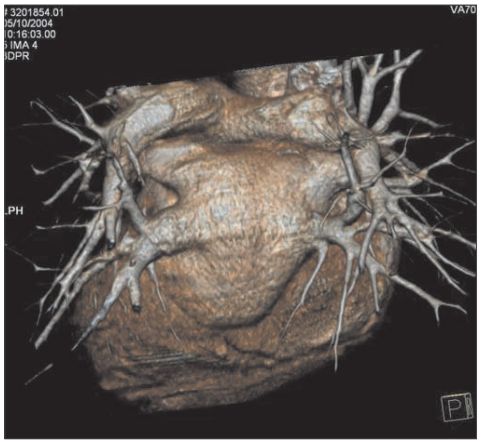

Figure 4. 3D reconstruction multislice CT scan. Posterior view. The tube-shaped portion of the pulmonary veins becomes funnel-shaped before entering the left atrium.

Merging techniques to improve efficacy and reduce complications

The differences between the two most frequently used techniques (segmental PVI vs. left atrial circumferential ablation) (figure 5) have often been passionately discussed. Pioneering groups using the segmental PVI reported freedom of AF without antiarrhythmic drugs in 70% of patients presented with paroxysmal AF.[25,26] This success rate was definitively lower compared with the LACA approach of Pappone et al.[3] reporting freedom of AF in 85% of patients. This was attributed to the reduction of electrically active tissue (substrate) with the wide encircling lesions. This difference between the two techniques disappears, however, with the more proximal ablation used today by those performing segmental ablation and with the complete PV isolation achieved with LACA. The electroanatomical mapping used in left atrial circumferential ablation has advantages because it creates a 3D map

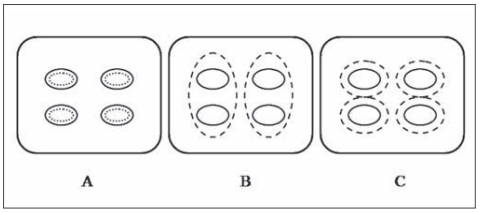

Figure 5. Schematic representation of the three described techniques. The PVs are drawn as four circles and the ablation lesions as dotted lines. A. Ostial PV isolation originally described by Haissaquerre et al. B. Circumferential ablation first described by Pappone et al. C. Typical lesions set after intracardiac echo-guided PV isolation.

enabling navigation. However, this 3D environment is virtual and often does not account for the funnel shape of the proximal part of the PV. The reported clinical results of the ICE-guided antrum ablation are very good, even in patients with structural heart disease.[27] The initial results of our ongoing experience are very promising. Despite the growing experience with the procedure and the improvement in success rate, PVI remains an invasive procedure and major and sometimes life-threatening complications can occur. We strongly believe that pulmonary vein antrum ablation guided by ICE has the potential to avoid several complications because it uniquely provides on-line visualisation of the left atrium together with the possibility to titrate energy in order to prevent overheating. This results in less PV stenosis and seems promising to avoid left atrial oesophageal fistulae. ■

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Part 2:

Remote Magnetic Navigation

Chapter 6

Potential applications of magnetic navigation in clinical electrophysiology

POTENTIAL APPLICATIONS OF MAGNETIC NAVIGATION IN CLINICAL ELECTROPHYSIOLOGY

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In spite of the high reported success rates, catheter ablation for supraventricular arrhythmias remains difficult, with early and late recurrences and complications. Several strategies to minimise the latter can be followed, as investigating alternative energy sources, using intracardiac echocardiography to monitor catheter handling and transseptal puncture, or as became possible only recently, stereotactic navigation of the catheter without manual force.

The restrictions of the present radiofrequency technology still are considerable. Apart from the fact that lesions are unpredictable and irreversible, catheters need a conductor to bring the energy to the tip, and additionally they are equipped with wires to deflect the catheter, sometimes in multiple directions. This explains why with such stiff, still poorly maneuverable catheters perforations of heart and vessels may occur. This results in hematomas, and pericardiac tamponade, not only in unexperienced hands. A further restriction is the lengthy procedure time, associated with high X-ray exposure, which is a potential hazard for the patient, and for the physician.

These considerations are especially important in more difficult situations, as in the presence of anatomic variations (e.g. complex congenital heart disease) or when a difficult target such as atrial fibrillation is approached. A similar problematic situation can be encountered when attempts are made to implant a biventricular pacing lead in the coronary sinus in a very large heart.

Automation, and remote navigation of flexible soft catheters might be an answer to some of these problems. This is made possible with the development of the so-called Stereotaxis system (St Louis), which makes it possible to steer a soft catheter with a magnetic tip in the heart, guided by two external, strong magnets producing a combined field strength of 0,08 Tesla at the place of interest.

In an experimental set up the tip prolapse push force on catheters was reduced from 240 to 132 g; the tip curl force (for alignment) was reduced from 45 to 15 g. This indicates indeed how the safety profile of this approach is very promising.The potential to advance and retract the catheter via robotics, or with a simpler system Cardiodrive^{TM} , was also developed by Stereotaxis. This combination permits perfect remote control over the catheter, and should result in less radiation for the physician.

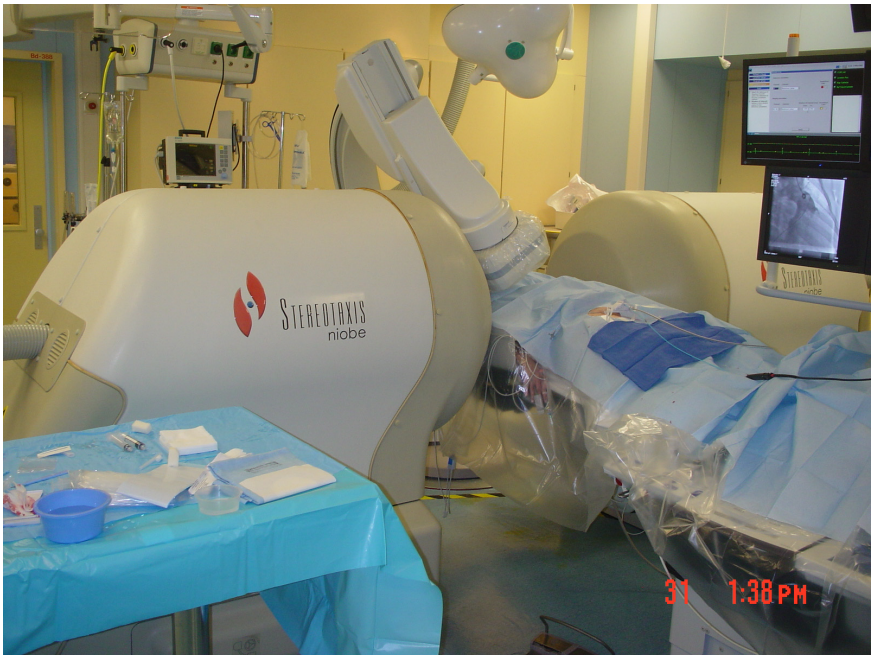

Figure 1. EP lab with two large magnets lateral of the patient table. The Cardiodrive advancer is inserted in the right femoral vein.

ELECTROPHYSIOLOGY (EP) STUDIES

It was shown that all basic steps for a diagnostic EP study can be taken with the described principle of magnetic navigation. If one wants to combine pacing and recording, a conventional catheter has to be inserted as well.

CATHETER ABLATION

Supraventricular tachycardia

We completed our learning curve for *AVNRT*, an arrhythmia with a simple anatomy in about 20 patients. The results were just as good as with conventional radiofrequency, or cryotherapy (table 1), with considerably less radiation for the patient as well.

Due to the magnetic field, less catheter movement with cardiac and respiratory cycles and during junctional rhythm were seen as with conventional approaches.We have used the system for *ectopic and incisional atrial tachycardia* and right and left sided *accessory pathways*. We used a retrograde approach for the latter, even with the actual catheters, which are floppy over the entire length, what creates some difficulties at the aortic arch and valve. Others have preferred

Table 1 – Comparison of ablation variables in AVNRT, using 3 different techniques

	Magnet ablation	Cryotherapy	RF
Number of ablations (median (range))	6 (1-22)	5 (2-16)	7 (2-28)
Total ablation time (s) (median (range))	240 (60-633)	633 (452-2599)	290 (90-895)
Success	19/ 20	12/12	5/5
Procedure time (min) (median (mean±sd))	163 (167±46)	148 (167±65)	159 (177±61)
Fluoroscopy time patient (min) (median (mean±sd))	12 (17±12)	17 (20±11)	30 (30±8.8)

the transseptal route, which may result in better appositioning of the catheter in the left lateral region.

Ventricular tachycardia

Ventricular tachycardia of non-ischemic origin can be addressed. In RV outflow tract tachycardia, conventional ablation poses some difficulties, as two opposite curves have to be accomplished, and precise mapping has to be performed in a relatively small area. This makes precision movement difficult, and often induces non-relevant arrhythmias. We have approached both left and right-sided idiopathic VT with magnetic navigation. This allows small steps, and very precise mapping with the floppy magnet catheter.

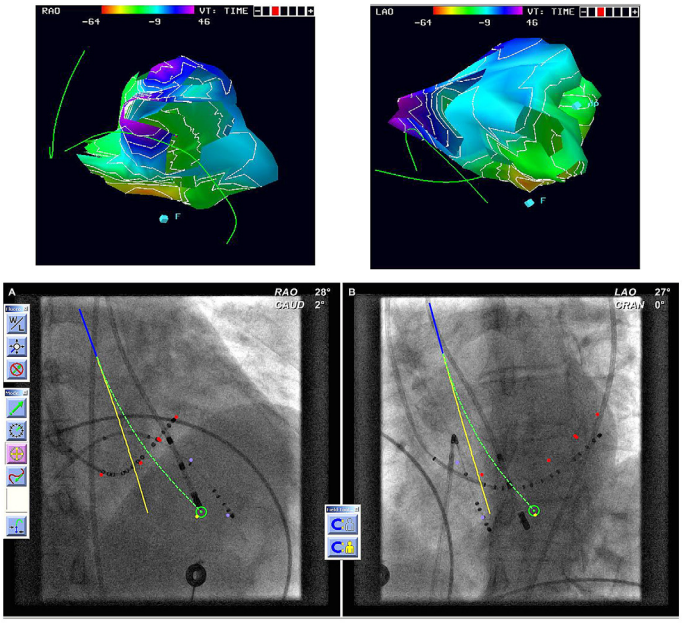

Figure 2. Left ventricular fascicular tachycardia. The upper panel shows the isolines in RAO and LAO, as acquired with the RPM mapping system, showing the apico-septal origin of the arrhythmia, with reference catheters in the coronary sinus and the right ventricular apex. The lower panel shows how the magnetic ablation lead (Helios 2, stereotaxis Inc) is moved from the yellow to the green line by magnetic forces. Here was a fascicular potential, and ablation was performed at this site. As both systems are not integrated, some imagination is left to the researcher. The angulations in RAO are not exactly the same.

Atrial fibrillation (AF)

AF is the real challenge today. Some attempts were made by Ernst et al to achieve pulmonary vein isolation. People tend to accept now that a wide circumferential approach is the best way to proceed. Pappone recently presented the first cases with integrated CARTO imaging, resulting in successful ablation of the AF substrate. The perspective should be that even the less invasive retrograde transaortic - transmitral approach should be considered.

Complex congenital heart disease.

Especially corrected complex congenital heart disease is frequently associated with arrhythmias. These can often be very difficult to control with conventional means. Reconstructed chambers, recesses, patches, and tubes make catheter manipulation and ablation very difficult. If there is a place for magnetic navigation, it is in these dilated, scarred tissues of operated aging hearts. Integration of anatomy, voltage mapping and activation mapping should assist in more performant ablation.

ADVANCED CARDIAC MAPPING

Electro-anatomic maps to guide the ablation process can now automated, more easily, be constructed aided by this remote technology. This will shorten the procedure time, and assist in assessing the success of otherwise lengthy procedures as pulmonary vein isolation.

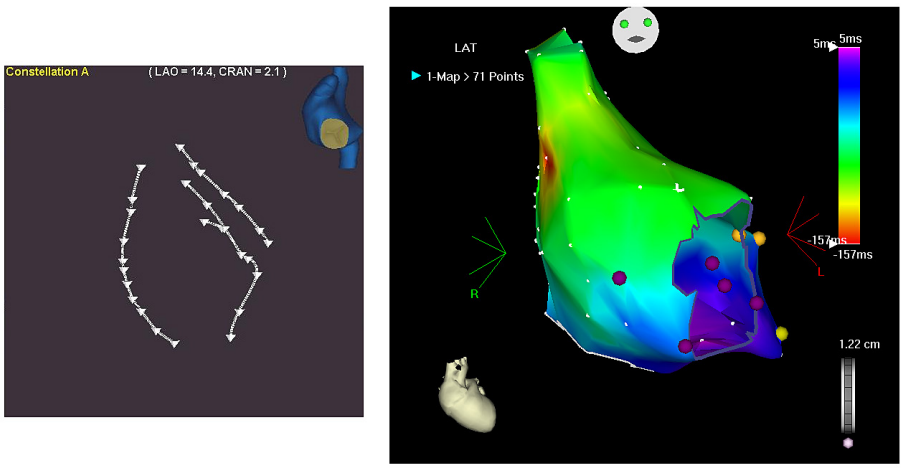

Figure 3. At the left designer lines as suggested by the investigator using the Navigant software (Stereotaxis Inc). At the right the CARTO map showing how these lines contributed to an electroanatomic map in sinus rhythm.

Attempts are now undertaken to merge (old) MRI and multislice CT images in on-line electro-anatomic maps. The overlay seems acceptable. All want to believe hat this is progress. Real image integration in the EP domain will be realized when on-line integration of a 3-dimensional image with the online EP data becomes a fact. This will probably be realized with 3D echo, but if developments in X-ray and MRI are fast, these techniques have a chance to be involved as well.

CARDIAC RESYNCHRONISATION THERAPY (CRT)

Implanting a biventricular pacing lead in the coronary sinus (CS) can be very time consuming. These procedures can require extensive fluoroscopic screening. This is partly due to difficulties in cannulating the CS, and once the guide wire or the lead is in the CS, partly to attempts to reach the potentially best side branch, and finally because the lead has to remain there after it is advanced over the magnetic guide wire, and when the guide wire is retracted. Further, complications as dissection of the CS and pericardiac tamponade exist. The idea to cannulate the CS with a sheath into the mid right atrium or without a sheath at all should be tested with dedicated guide wires.

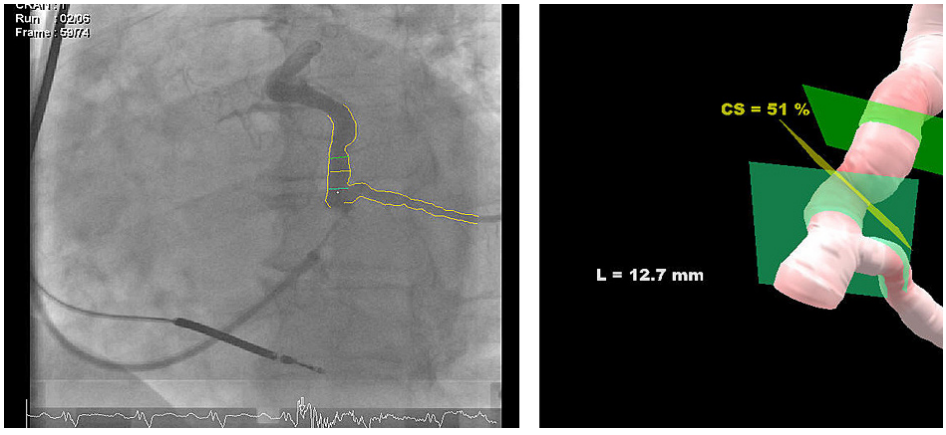

Figure 4. At the right coronary sinus venogram using dedicated software to reconstruct a 3D image (at the left) what can be used to direct the guide wire.

Further, target side branches should be reached with the assistance of magnetic navigation, once the vessel is engaged. Magnetic force should be able to keep the guide wire in position when advancing the pacing wire. Most of these principles were tested already in our lab, and hold great promise.

FUTURE CONCEPTS

It is expected that with the incorporation of catheter registration technology or echocardiography to this system or using these technologies in parallel procedure and radiation times will decrease. Combining this technology with other new technology such as cryotherapy and the other mapping technologies mentioned above, may significantly improve outcome, as well as reducing the number of applications, and associated collateral tissue damage. The potential for other areas in cardiology is there: stem cell therapy, difficult coronary artery procedures, congenital heart disease. Even when this system is only a first step on the road to performant magnetic navigation, the tested principles so far seem to confirm that the concept is valid, and should be considered a milestone in the development of safer and automated procedures.

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Chapter 7

An in-vivo comparison of cardiac radiofrequency lesions formed by standard, and magnetically steered 4 mm tip catheters

AN IN-VIVO COMPARISON OF RADIOFREQUENCY CARDIAC LESIONS FORMED BY STANDARD, AND MAGNETICALLY STEERED 4 MM TIP CATHETERS

Magnetic versus standard ablation lesions

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In preparation

ABSTRACT

Background:

In-vivo comparison of cardiac radiofrequency ablation lesions between standard and magnetically steered 4 mm tip catheters has not been reported. We therefore compared lesions in the porcine right atrium (RA) and right ventricle (RV) using both techniques. Methods:

High and low RA free wall, isthmus, and RV free wall and outflow tract lesions were studied macroscopically and microscopically at 5 days after lesion formation in 7 pigs. We compared lesions characteristics including shape, size and thrombus formation, as well as ablation parameters, using standard and magnetically enabled catheters. The effect of minimal, medium and high wall contact was assessed by a contact measurement utility for the magnetically enabled catheters.

Results:

All 14 RA free wall lesions were transmural with similar epi- and endocardial surface area. In the RV, epicardial surface area usually appeared smaller than endocardial with standard, compared to magnetically enabled catheters. Isthmus lesions were difficult to assess for transmurality. There was no significant difference in endocardial surface area in the first 4 animals: standard: 39 mm^2 (range 16-82 mm^2) vs. magnetic: 36 mm^2 (range 23-111 mm^2). If the catheter tip was perpendicular to the tissue, lesions from magnetically enabled catheters were significantly more often round or oval (8) than those from standard catheters (3), which were more often elongated ($p < 0,05$). When the catheter tip was parallel to the tissue, such as in the isthmus, lesions tended to be elongated with both catheter types. Microscopic characteristics were similar. The contact utility was not useful. The average impedance ($p<0.0001$) and average energy delivered ($p<0,05$) were less in the magnetically enabled catheter group.

Conclusions

Lesions from magnetically enabled catheters are transmural, of similar size but with less variability and a more rounded or oval appearance, than standard catheters, especially when the tip is perpendicular rather than parallel to the tissue. Microscopic characteristics are similar. Lesion formation with magnetically enabled catheters was associated with lower impedance and average energy delivery. Magnetically enabled catheters appear to have a more stable tip to tissue contact, and may allow for more predictable lesions.

KEY WORDS

arrhythmias, catheter ablation, radiofrequency energy, magnetic navigation

INTRODUCTION

Radiofrequency (RF) lesions are created during ablation due to resistive heating as RF current passes through tissue. Lesion size is dependent on tissue temperature which relates to a number of factors, of which some are called controllable or non controllable.(1) The controllable factors include catheter tip size and more specifically tip surface area, electrode tip orientation, power settings, energy application time, and catheter temperature cut-off. The non-controllable factors have included cooling of the catheter tip by chamber blood flow and tissue contact. The majority of these factors have been studied extensively.(1-6)

Recently a magnetic system (Niobe, Stereotaxis Inc., St. Louis, MO, USA) was introduced which allows for the use of floppy magnetic tip catheters which are steered and advanced remotely using an applied magnetic field and an external advancer system. The floppy magnetic catheters may have advantages not only in positioning in difficult anatomy, but also by maintaining position during ablation. Conventional catheters with stiff shafts may pose difficulties in maintaining tip contact on a fixed point when the heart is moving during the cardiac cycle and with respiration. This movement during ablation may cause elongated or "brush" lesions. Improved catheter flexibility with floppy magnetic catheters during the cardiorespiratory cycle, may allow for more stable tissue contact during ablation. As the characteristics of standard and remote magnetically enabled catheters are so different, it is hypothesized that the lesion characteristics will also differ significantly, in favor of the use of magnetic catheters.

A difference between in-vitro and in-vivo models may be the effect of cardiac and respiratory motion on catheter tissue contact. A comparison using preparations such as the thigh muscle may be very useful for comparing standard catheters with similar construction and different energy sources, tip lengths and settings.(4-6) The unique and different way in which Stereotaxis directs the catheter against the tissue and the nature of the floppy shaft of this catheter meant

that we needed to compare the efficacy of standard versus magnetic catheters using the same type of ablation tip and energy settings in an in-vivo model, as there is no other model which mimics cardiorespiratory movement. To date there has been no direct in-vivo comparison between lesions produced by standard catheters and magnetically steered catheters.

The magnetic system has also recently been integrated with an electroanatomical mapping system (CARTO RMT, Biosense Webster, Diamond Bar, CA, USA), such that information is sent from the one to the other. The combined system has a contact indicator monitor which attempts to indicate the contact which the catheter makes with the tissue surface. This tissue contact utility has also not been assessed in-vivo.

The purpose of this study was therefore to prospectively compare the safety and size of lesions produced by standard and magnetically enabled 4 mm tip catheter, in the RA and RV of the porcine heart. We also wanted to assess the impact of the CARTO RMT tissue contact utility when forming lesions.

METHODS

Introduction

Eight Yorkshire farm bred pigs with a mean weight of 40 kg, underwent transvenous ablation with a predetermined protocol (Figure 1), with sacrifice planned 5 days after the procedure. This experimental protocol was approved by the Animal Ethics Committee at the Erasmus University, and also conformed to the guidelines published in the "Guide for the Care and Use of Laboratory Animals." (NIH publication No. 85-23, revised 1996).

Initial Procedure

All animals received pre-procedural sedation with ketamine 20mg/kg and midazolam 0.5 mg/kg intramuscularly. Once sedated, maintenance anesthesia was instituted with midazolam 2mg/kg/hour and fentanyl 10 µg/kg/hour supplemented as necessary by isoflurane and an oxygen/nitrous oxide inhalation (1:2) gas mixture. A cuffed endotracheal tube was introduced after successful induction and the animals were then mechanically ventilated with a tidal volume of 13 ml/kg. Body temperature was maintained at 37 to 38 degrees Celsius with warming blankets.

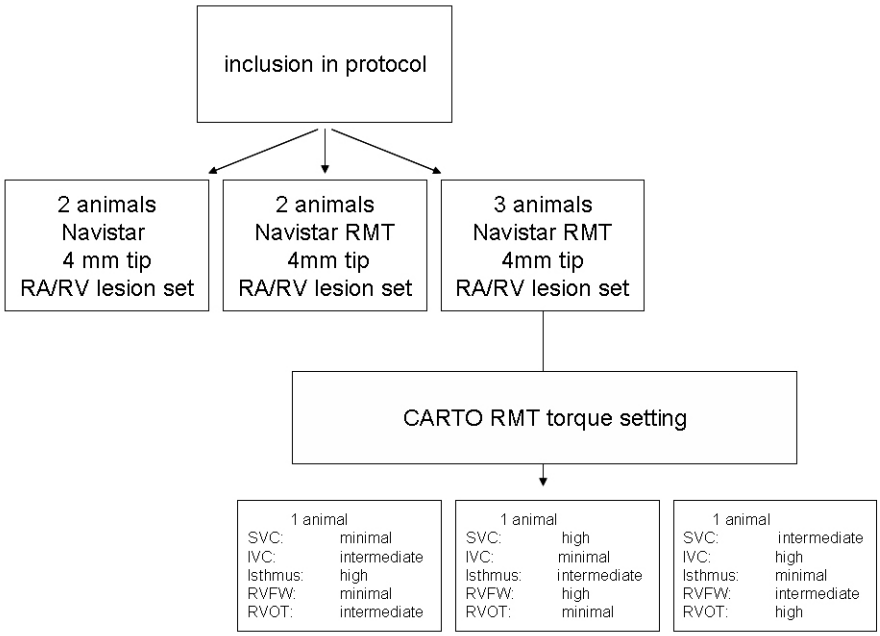

Figure 1. Flow chart of the study. The first 4 animals were a comparison with a conventional (Navistar) catheter and a magnetic catheter of the same size, but with magnetic properties (Navistar RMT).The last 3 animals were submitted to various torque contact settings. IVC = inferior vena cava, RA = right atrium, RMT = remote, RV = right ventricle, RVFW = right ventricular free wall, RVOT = right ventricular outflow tract, SVC = superior vena cava.

An introducer sheath was placed into the right femoral vein by direct cut-down and the ablation catheter under study was advanced to the heart. All animals received a single dose of 150 IU/kg of heparin sulfate at the beginning of the procedure, followed after 1 hour with an additional 500 IU/hr.

Magnetic Navigation

Magnetic navigation was undertaken as previously described using the Niobe system.(7) In short the Niobe I magnetic navigation system (Stereotaxis Inc.) was combined with a mono-plane angiography system (AXIOM Artis, Siemens, Erlangen, Germany). The Niobe I system has 2 large permanent magnets with a combined field strength of 0.08 Tesla in navigation mode, on either side of the patient. The magnets and the generated field are controlled via a computer workstation (Navigant, Stereotaxis Inc.) to allow for changes in the direction of a stable magnetic field within the heart of the patient. The ablation catheters have magnets in the distal shaft and these align the catheter tip with the field produced by the external magnets. Remote catheter advancement and retraction is performed using a catheter advancer system (Cardiodrive^{TM}, Stereotaxis Inc.), positioned on the thigh. After the magnets are brought in next to the patient

or experimental subject in navigation mode, remote control of all of the components of the system can be performed from the control room.

Ablation – standard vs. magnetic

In the first 4 animals ablation was performed using either a standard Navistar 4 mm tip, (2 animals) or a magnetic Navistar RMT 4 mm tip catheter (2 animals) both from Biosense Webster (Diamond Bar, CA, USA). Serial RF lesions were produced in each of the following areas: high right atrial free wall, low right atrial free wall, right ventricular free wall, right ventricular outflow tract, and inferior vena cava-tricuspid annulus (IVC-TA) isthmus, in the same sequence in each animal. Radiofrequency energy was delivered using an EP Shuttle generator (Stockert GmbH, Freiburg, Germany) with maximum set values of 58 degrees Celsius, 50 Watts and 60 seconds. Current was applied between the electrode at the distal end of the ablation catheter and a standard dispersive electrode placed on the animal's back. Continuous recording prior to, during, and immediately after ablation was made from the ablation catheter. During the ablation, recordings were made of the ablation site, both radiologically, as well as on the Stereotaxis system when this was used. Adequate tissue contact was determined by the physician on the basis of the radiographic images.

Ablation – contact indicator use

The combined Stereotaxis and CARTO RMT system tries to assess contact by looking at the difference between the magnetic field orientation, as determined by the Stereotaxis system, and the localized catheter orientation, as determined by the CARTO RMT system. As the difference between applied magnetic field orientation and the localized catheter orientation increases, the contact indicator value increases on a scale from 0 to 4. When advancing a catheter perpendicularly into a wall, the contact meter will only rise when the flexible catheter begins to prolapse.

In the last 3 animals ablation was performed at the same sites as noted earlier, using the same generator settings, while trying to achieve a predetermined contact indicator setting for each given position. Attempts to change the contact indicator setting were made by modifying the magnetic vector and/or advancing the catheter into the wall. The attained contact obtained, as well as comments in this regard, were recorded.

Lesion formation characteristics

As noted above, during each RF application continuous measurements were taken of steady-state power, energy, temperature and impedance during ablation. Average measurements were then compared.

Sacrifice

After 5 days the animals were again sedated with ketamine and midazolam with doses as described above, and anesthetized with pentobarbitol 12mg/kg after endotracheal intubation. The chest was opened and the heart exposed. The animals were euthanized using an overdose of pentobarbitol and the heart fibrillated using direct current. The heart was then explanted and opened.

Lesion assessment - macroscopic

Both the epicardial and endocardial surfaces of the heart were examined macroscopically for lesion characterization and the individual lesions photographed. The qualitative assessment included a description of shape (round, oval or elongated), the presence of cavitation and surface thrombus and whether the lesion was transmural. Epicardial and endocardial features were noted, as was done with evidence of any collateral damage such as to pericardium, pleura or lung. A quantitative assessment of endocardial surface area was made by 2 independent observers, and included use of planimetric software (Clemex Vision PE software, Clemex Technologies Inc., Longueuil, Canada).

Lesion assessment - microscopic

The lesions were dissected and fixed in 10% formalin. After processing, the tissue was embedded in paraffin. A section was obtained perpendicular to the surface at the maximum diameter and stained with haematoxylin and eosin as a routine stain, and resorcin-fuchsin as elastin stain. The lesion was analyzed using the same planimetric software as noted above to assess for diameter, maximum depth, area of necrosis and inflammation and the presence of thrombus.

Statistics

Data were expressed as median, with ranges. Comparisons among groups were performed with a two-tailed analysis of variance. Comparisons of simple proportions between two groups were made with a Fisher's exact test. A p value of ≤ 0.05 was considered to be statistically significant.

RESULTS

Animal data

One animal developed VF and then electromechanical dissociation during the first RF application and died. All other animals completed the protocol. In total, 35 lesions were created at the high and low RA free wall and isthmus, the RV free wall and outflow tract in the 7 surviving pigs. There were no complications of ablation. In 4 animals we compared 19 lesions using standard and magnetically enabled catheters – 1 RV free wall lesion could not be found back. In 3 animals

the contact measurement utility was assessed, with 1 high, medium and low contact ablation made at each of the 5 predetermined sites (15 lesions).

Macroscopic Lesion Assessment

Standard vs. magnetically enabled catheters

In the first 4 animals 19 lesions were compared. All RA free wall lesions were transmural with similar epi- and endocardial surface area. In the RV, the epicardial surface area appeared smaller than the endocardial with both standard, and magnetically enabled catheters. Isthmus lesions were difficult to assess as regards transmurality due to the complex anatomy of this region. There was no significant difference in endocardial surface area between standard and magnetic catheters as assessed with the planimetric technique: 39 mm^2 (range 16-82 mm^2) vs 36 mm^2 (range 23-111 mm^2). Lesions from the 3 other animals were included in the analysis of table

Table 1: Macroscopic and microscopic assessment of the lesions

	Magnetic	Conventional	p
Macroscopic assessment endocardium			
Total number	(24)	(9)	
Area (mm2)			
Observer 1	43 (21-83)	38 (20-164)	NS
Observer 2			
(quantitative analysis)	48(18-120)	39 (16-82)	NS
Perpendicular to RA/RV	(8)	(7)	
Round/ Oval*	5 / 3	1 / 2	0,05
Elongated*	0	4	
Microscopic assessment at the middle of the lesion			
Total number	(24)	(9)	
Thrombus (nr)	15/24	7 / 9	NS
Number for analysis	(21)	(9)	
Diameter (mm)	10,59 (5,55-18,6)	8,90 (3,76-15,7)	NS
Maximal depth (mm)	3,64 (1,78-8,13)	3,78 (1,32-7,38)	NS
Necrotic area (mm2)	17,44 (4,59-57,01)	7,05 (2,32-50,17)	NS
Inflammatory area (mm2)	2,84 (4,70-14,34)	3,26 (0,41-10,33)	NS
Total area (mm2)	21,46 (5,26-69,87)	10,22 (2,70-59,80)	NS
Thrombotic area (mm2)	0,25 (0-5,02)	0,33 (0-5,87)	NS

The median and range are given. NS: not significant; RA: right atrium; RV: right ventricle
* isthmus lesions have been excluded

1. After exclusion of the isthmus, with perpendicular applications to RA and RV, lesions from magnetically enabled catheters were significantly more often round or oval (8) than those from standard catheters (3) which were more often elongated ($p<0,05$). This is also shown in figure 2. When the catheter tip was parallel to the tissue, for example in the isthmus, or some lesions in the RVOT, lesions tended to be elongated with both catheters, although less so with the magnetic catheters.

Contact utility comparison

In the 3 animals (15 lesions) where the contact measurement utility was assessed (table 2), it did not appear particularly useful at assessing high or low contact as compared to radiographic assessment. With all three contact assessments there was a similar amount of oval and elongated lesions.

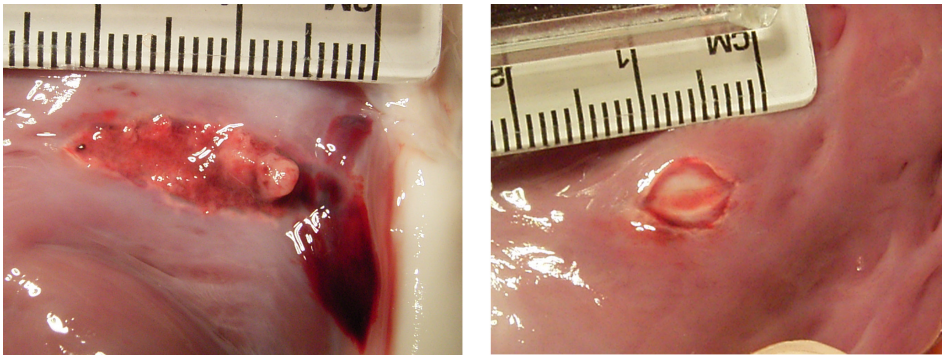

Figure 2. Macroscopic aspect of lesions in the right ventricle with a conventional catheter (left) and a magnetically enabled catheter (right).

Table 2: Comparison of lesion shape with different contact utility settings

	Low	Medium	High
HRA	elongated	elongated	oval
LRA	elongated	round	round
RV	oval	oval	oval
RVOT	oval	oval	elongated
Isthmus	oval	elongated	elongated

HRA: high right atrium; LRA: low right atrium; RV: right ventricle RVOT: right ventricular outflow tract

Microscopic assessment

Lesions were transmural in 15/24 magnetic cases and in 4/9 conventional procedures. This limited correct depth assessment. Three lesions from one animal were excluded from quantitative histological analysis for technical reasons. Microscopic assessment did not suggest any significant difference in lesions caused by standard or magnetically enabled catheters. There

was no significant difference in maximum diameter, maximal depth, the area of necrosis, the area of inflammation, and the combined area of inflammation and necrosis between magnetic and standard catheters respectively. Thrombi were seen in 15 of 24 magnetic lesions and 7 of 9 conventional lesions.

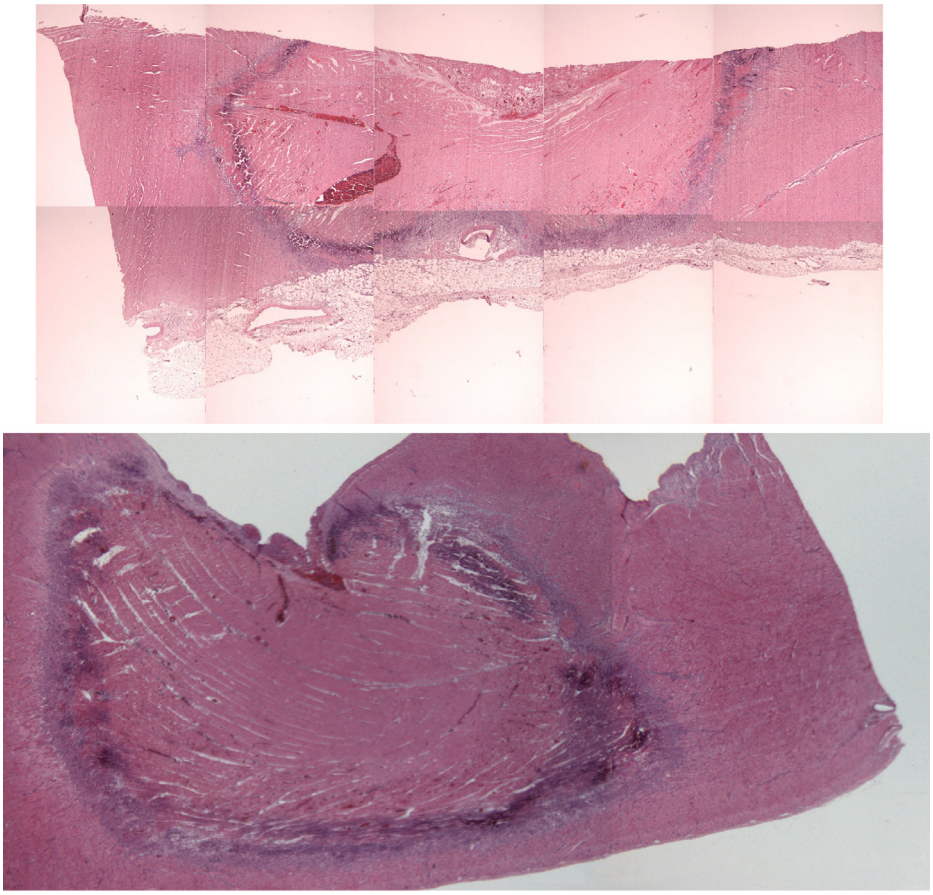

Figure 3. Histological aspect of lesions in the right ventricle, as prepared for planimetric analysis. Haematoxilin eosin stain. Both sections show a large necrotic area, with an inflammatory margin, with a small central thrombus in the upper one. The upper lesion is the result of a magnetic guided application; the lower one from a conventional catheter, with a more retracted aspect.

Radiofrequency ablation characteristics

The data on steady-state power and impedance during ablation are presented in table 3. Average impedance was significantly lower for lesions created using magnetically enabled catheters ($p < 0{,}0001$) as was average energy used ($p < 0{,}05$). This might suggest more efficient lesion formation.

Table 3: Measured ablation parameters

	Magnetic	Conventional	p
Duration (sec)	60(51-60)	60(60-60)	NS
Temperature (°C)	53(51-60)	53(49-53)	NS
Power (Watt)	19(5-37)	16(2-42)	NS
Impedance (Ohm)	118(105-128)	131(121-225)	0,0001
Energy (Joules)	970(327-2228)	1799(963-2525)	0,05

The median and range are given. NS: not significant

DISCUSSION

General

Catheter ablation is successful in treating a large number of cardiac arrhythmias. In recent years technologies have evolved to treat more complex arrhythmias such as intra-atrial reentry tachycardias, atrial fibrillation, and ventricular tachycardia, as well as to improve the results in other tachycardias, such as atrial flutter. These technologies include catheter designs allowing higher energy usage, and significant developments in arrhythmia mapping systems including image integration. New systems for remote navigation, both magnetic and mechanical have been incorporated into combined systems.

RF lesions depend on controllable and non-controllable factors, and the Stereotaxis-CARTO RMT system described here uses a radically different way of maintaining catheter tissue contact than standard catheters or the mechanical remote navigation system, (8, 9) and this has effects on how lesions are formed and may make a previously poorly controllable factor, catheter tip tissue contact, more controllable. This has as yet not been shown at a clinically obvious level as yet, where the clinical effects so far seem similar.(7, 10-16)

Comparison of standard vs. magnet

As can be seen from the results, ablation lesions formed by magnetically enabled catheters have similar characteristics to those from standard catheters. The only significant differences appears to be that the lesions from magnetically enabled catheters are more round or oval rather than elongated, suggesting more constant catheter tissue contact. There is less likelihood of "brush lesions" when the catheter tip is perpendicular to the tissue, but these may still occur to a lesser extent when the catheter tip is parallel to the tissue such as in the isthmus. This may have advantages when it is important to limit the lesion and disadvantages when "brush lesions" are actually advantageous, for example in linear lesions in the isthmus or atria.

Tissue contact can be better described as the relationship between contact area and contact force. With magnetically enabled catheters the contact area appears to be decreased with the tip being more constantly related to a specific area, as shown by this study. However there have been questions about the tissue force able to be generated by these floppy magnetically

enabled catheters and available data would suggest that a lower maximum contact force can be applied.(11)

RF lesion size relates to the generated tissue temperature, which relates to the amount of energy delivered. The energy delivered to the tissue itself relates to the amount of energy delivered by the generator and the its proportion entering the tissue. This again depends on the electrode tissue contact and the degree of external cooling.(1) Constant tissue area contact should mean that the energy is more effectively delivered to the underlying tissue of that area. In the case of magnetically enabled catheters the tip contact force may be less, meaning that the tip is less deeply buried in the tissue than a standard catheter, allowing for more cooling of the exposed area of the tip. However, the tip is almost certainly applied constantly to the tissue therefore preventing cooling to this contact area. The question therefore is how much one predominates over the other. The lower impedances during ablation may relate to different engineering within the catheters, as the internal impedance makes up a significant part of the total, but the lower impedance may also confirm the better tissue contact seen visually and implied by the macroscopic features seen. Lower system impedance may mean that less energy is necessary to cause similar size lesions. The lower average energy may also relate to impaired cooling of the tip and thus higher tip-tissue temperatures which inhibit maximum energy delivery, but conversely more effective delivery of that lower energy to the tissue may mean that lesion formation is as effective as suggested by the comparative findings.

It is important to point out that while thrombus was seen microscopically, we had no sudden impedance rises during RF energy application or pops, and no visible thrombus was seen macroscopically when using magnetically enabled catheters.

Examining the effects of these differences in tissue contact will require significant further evaluation both in-vivo but also in-vitro. Models may need to be developed for in-vitro study which take into account cardiac and respiratory movement.

Contact utility assessment

Use of the contact force utility showed that the entire range of forces was associated with a high likelihood of "brush lesions". In fact, during catheter contact assessed by radiographic and electrogram review, the contact utility seemed to show average contact most of the time. It was also noted that the tissue contact assessment was perhaps more useful when the tip was not perpendicular to the tissue. When the catheter is entirely perpendicular to the tissue the mechanical "push" of the catheter into the tissue wall is not measured by the contact indicator.

Study limitations

This study looks at only a relatively limited number of lesions in an animal model. The number of lesions formed using a standard catheter was small. It was not feasible to assess lesion volume and therefore the findings are unfortunately a little more subjective than those using a thigh muscle preparation but we feel reflect more accurately clinical RF lesions.

CONCLUSION

Magnetically enabled 4 mm tip RF ablation catheters perform as well as standard 4 mm tip RF ablation catheters as assessed by lesion size. The lesions show less "brush" effect and are more predictably oval or round. The contact utility assessment in the system seemed not to be very useful in its present form. The finding that impedance was lower and that less energy was required is intriguing and needs further assessment. It may be that magnetically enabled catheters may need a different set-up than standard catheters. Similar comparisons will need to be performed for magnetically enabled 8 mm tip and irrigated tip catheters.

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DISCLOSURES

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Chapter 8

Magnetic navigation in AV nodal reentrant tachycardia study : early results of ablation with 1- and 3-magnet catheters

Magnetic navigation in AV nodal re-entrant tachycardia study: early results of ablation with one- and three-magnet catheters

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KEYWORDS
Arrhythmias;
AV nodal re-entrant tachycardia;
Catheter ablation;
Magnetic navigation;
Stereotactic therapy

Aims Steering soft, flexible catheters using an external magnetic field could have advantages for heart catheterization, especially for therapy of tachyarrhythmias. Our aims were to assess the feasibility of magnetic navigation to Koch's triangle and reliable ablation of atrioventricular nodal re-entry tachycardia (AVNRT) with a magnetic catheter.
Methods and results Consecutive patients with AVNRT were mapped and ablated with a magnetically enabled catheter (Helios I or II), with, respectively, one and three magnets at the tip. The catheter was remotely advanced with the Cardiodrive™ system and orientated with the Navigant™ control system. After initial positioning with the external magnets, adjustment was made in 5° steps. Success rates, procedure, and fluoroscopy times were analysed, and compared with a local contemporary series of conventional AVNRT ablations. Magnetic navigation was feasible in all 20 patients. Targets were easily reached. Catheters remained stable in position during accelerated junctional rhythms. Ablation was successful in 18/20 procedures (90%). No significant complications occurred. Median patient fluoroscopy time was 12 min, median physician fluoroscopy time was 4 min. Fluoroscopy times tended to be shorter than that in the conventionally treated group. Procedure duration decreased significantly over time, median procedure time was similar to that in the conventional group.
Conclusion AVNRT can be successfully mapped and ablated using magnetic navigation. A learning curve was evident, unrelated to catheter type, but to increasing operator experience. Physician radiation times were one-third of patient times. No complications occurred. Procedure time is comparable with that of conventional ablation.

Introduction

Although catheter design in electrophysiology has undoubtedly improved the handling of standard steerable diagnostic catheters, these are still fairly stiff, and have to be manoeuvred by means of a catheter handle, from outside the vascular system and the body. Standard catheters can be rotated manually and, by use of a pull-wire or wires, flexed and extended as necessary. Manipulation of these catheters to certain targets can be almost, or totally impossible, especially in complex anatomy. Application of manual force to ensure reliable contact with the myocardium is associated with a certain risk including perforation,[1] especially in some locations, such as the left atrial appendage, or in structurally weaker tissue, such as aneurysms. Maintenance of a constant force can also be extremely difficult in a moving structure such as the heart. The ability to steer a soft, flexible catheter by the use of an external magnetic field may, therefore, have certain fundamental advantages. Studies have shown the ability of magnetic navigation to place catheters in difficult anatomical positions and to maintain good tissue contact throughout the cardiac and respiratory cycles, without additional risk of perforation.[2,3] This new technology to map and ablate atrioventricular nodal re-entry tachycardia (AVNRT) has been used in only a relatively limited number of patients.[3–5] In the largest series to date by Ernst *et al.*,[4] only a single-magnet catheter was used.

We report our initial experience in 20 consecutive cases of AVNRT, 11 with a single-magnet catheter and the other 9 with a similar three-magnet catheter. The goal was to study the feasibility of magnetic navigation to map a well-known region in the heart and to assess the possibility of reliable ablation of AVNRT in both catheter types.

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Methods

Patient population

Between February and August 2004, we enrolled a total of 20 consecutive patients with proven AVNRT at electrophysiological study. An additional two patients gave consent, but were found to have left-sided arrhythmias. No patient had a contraindication to the use of magnetic navigation (such as an implanted metallic device or claustrophobia). This study forms part of the safety and efficacy study approved by the Ethics Committee of the Erasmus Medical Centre. We compared our ablation data, results, procedure, and fluoroscopy times with those obtained in a contemporary group of 17 patients treated in 2004 for AVNRT, immediately before and after this study.

Electrophysiological study

Patients were studied in the fasting, post-absorptive state under light sedation using intravenous boluses of diazepam and fentanyl as necessary. A standard conventional, diagnostic, electrophysiological study was performed using three transvenous catheters, placed from the subclavian and femoral veins in the coronary sinus, right ventricular apex, and the His bundle region. Standard techniques were used to measure conduction properties and to induce tachycardia. In all patients, typical AVNRT was induced either before or after the use of isoprenaline. The presence of dual AV-nodal conduction was assessed, and accessory pathways were excluded. Once the diagnosis was confirmed, an additional femoral access sheath was used to manually advance a magnetic navigation ablation catheter with a 4 mm tip to the right atrium. Catheters used for ablation were the 8 Fr Helios I, with a single magnet of 1.8 mm at the tip, or Helios II, with three 1.8 mm magnets at the tip and the distal shaft (Stereotaxis Inc., St Louis, MO, USA). The choice was determined by availability. Electrograms were recorded using a standard recording system (Sensis, Siemens, Erlangen, Germany).

Magnetic navigation

The Niobe magnetic navigation system (Stereotaxis Inc.) is combined with a monoplane fluoroscopy system (AXIOM Artis, Siemens). The Niobe system consists of two permanent magnets situated on either side of the patient, which are computer-controlled via a workstation (Navigant, Stereotaxis Inc.) to allow for changes in the orientation of a stable magnetic field within the chest of the patient. A combined field strength of 0.08 T is produced in navigation mode. As navigation is best performed with a fixed table position, this must be optimized prior to the start of magnetic navigation. When the magnets are positioned next to the patient, only limited angulation of the C-arm is possible (~28° in the right and left anterior oblique angulations). Remote catheter advancement and retraction from the control room was performed using a catheter advancer system, Cardiodrive™ (Stereotaxis Inc.), positioned on the high anterior thigh (*Fig. 1*). Remote control of the fluoroscopy system is also performed from the control room. The ablation catheters, with a single or multiple magnets within the distal tip segment, align themselves with the field produced by the external magnets, allowing effective catheter orientation. After the magnets are brought in next to the patient, the physician is free to leave the room and performs the rest of the procedure from the control room. A single nurse remains with the sedated patient to monitor vital signs and administer drugs when required.

Mapping and ablation

Mapping of the low right atrial septum in the region of the coronary sinus os (Koch's triangle) was performed combining an anatomical approach with an attempt to obtain electrograms suggestive of a slow pathway potential. Radiofrequency ablation was delivered via the 4 mm tip of the Helios I or II catheter using temperature-controlled ablation from an EP Shuttle RF generator (Stockert GmbH, Freiburg, Germany) with settings of 55°C, 60 s and power titrated from 15 to 50 W to obtain the set temperature. Radiofrequency applications were stopped after 20 s if no accelerated junctional rhythm was seen. These applications were included in

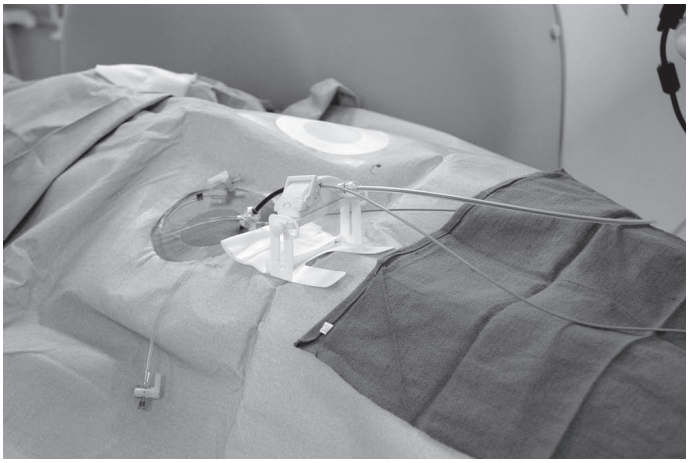

Figure 1 The catheter advancer system (Cardiodrive) is placed on the anterior thigh and used remotely to advance and retract the catheter. It uses a simple cogwheel system and is driven by a fixed rate motor attached via a flexible drive cable. An adaptor between the Cardiodrive and the sheath prevents buckling of the catheter.

the total number of applications. The generator was also operated remotely from the control room allowing the electrophysiologist to manage all aspects of the procedure.

Endpoint for ablation

The endpoint for ablation was non-inducibility of tachycardia using standard electrophysiological manoeuvres and evidence of slow pathway modification or ablation in those where this was possible. Isoprenaline was given after all apparent successful applications. Manoeuvres were repeated after a waiting period of 30 min. Procedure times were defined from the time the patient was put on the table until removal of the sheaths, 30 min after the last application, and include the time for the standard diagnostic electrophysiological study. Fluoroscopy times were measured for the patient and separately for the physician.

Statistical analysis

All continuous variables are expressed as mean $\pm$ standard deviation. When appropriate, median values are reported and non-parametric tests were used.

Results

Patient data

The patient group consisted of 4 males and 16 females, with a mean age of 54 $\pm$ 12 years. Apart from inducible typical AVNRT, a jump in the AH interval of $>$50 ms was detected in 16 of the 20 patients. At baseline, isoprenaline was necessary for reproducible induction in 4/20 patients. There were no significant differences in clinical data between the study group and the conventional treatment group, which consisted of 17 patients, who were treated with a standard approach (using either standard cryotherapy or radiofrequency catheters).

Remote navigation and mapping using the magnetic navigation system

We were able to obtain a satisfactory position using the advancer and magnetic navigation in all 20 patients (*Fig. 2*). This implied that the initial target was situated in the low septum, at the level of the coronary sinus os. Modification of the position was based on electrogram criteria such as the AV relationship and the presence of potentials. Adjustment was made magnetically in 5° steps, laterally and vertically.

Ablation data

Ablation was acutely successful in 18/20 patients. Junctional rhythm was seen in all patients. During this rhythm, the catheter remained entirely stable, as assessed on fluoroscopy and assessment of the intracardiac electrograms (*Fig. 3*). In 16 patients, clear dual AV nodal physiology, as shown by a jump in AH interval, was present at some time during the procedure. After ablation, no further slow pathway conduction could be demonstrated in 11 of 15 (73%) successful cases, whereas only modification of the slow pathway was obtained in the other four patients in whom this could be completely assessed. There was no difference on the basis of catheter type.

In the two failed patients, 22 and 15 application attempts were made, respectively; also there was no difference in the incidence of junctional rhythm. In one of these patients, in whom the area of interest appeared close to the region of the His bundle and in whom RF application was associated with fast accelerated junctional rhythm, a transient, minor delay in AV conduction was observed. The transient AV delay was thought to be due to the initial catheter position and not to catheter displacement. Cryocatheter ablation in the same position was associated with slow pathway ablation without impairment of AV conduction. In the other, with a very large coronary sinus os, cryotherapy failed.

The median number of RF applications in the successful cases was 6 (range 1–22). The total RF ablation time was a median of 240 s (range 60–633 s). There was no significant difference between the single- and three-magnet catheter approach.

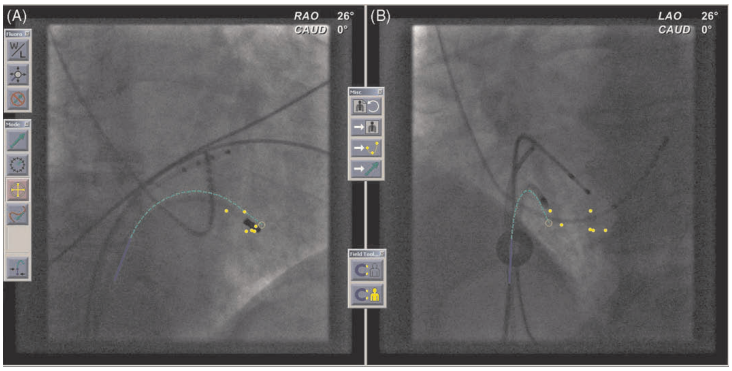

Figure 2 Part of the working screen of the Navigant workstation. The two radiographic views, with the His bundle, coronary sinus, and right ventricular catheters, are used with target-based navigation to indicate where the catheter should be placed. Previous positions are indicated by the closed yellow dots. The predicted catheter position, as shown in green, (with catheter shaft and pivot point in blue) is slightly different from where the catheter has finished and this sometimes requires some correction. The screen includes some of the tools used for different navigation modes.

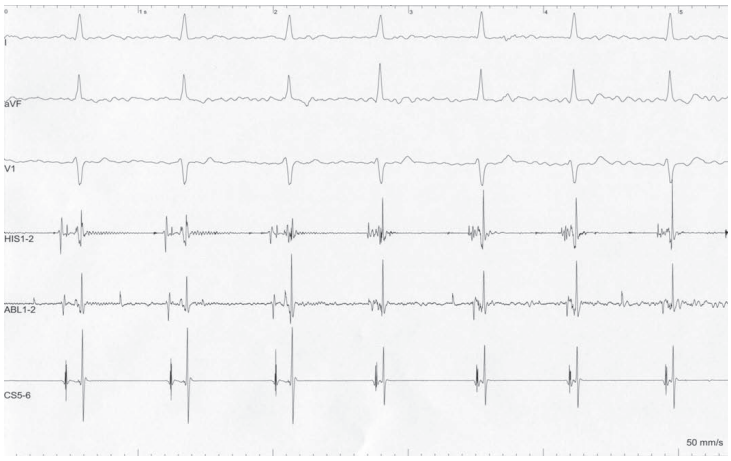

Figure 3 Accelerated junctional rhythm with leads S1, aVF, and V_1 and three intracardiac registrations as noted on the figure. Three sinus beats are followed by junctional rhythm with a cycle length of 800 ms. The ablation catheter signals remained stable during the transition.

Procedure data

The mean procedure time (including the waiting time) was 167 $\pm$ 46 min (median 163 min) with a patient fluoroscopy time of 17 $\pm$ 12 min (median 12 min). Of the total fluoroscopy duration, the physician was exposed only during introduction of the sheaths and positioning of the catheters, which averaged 5 $\pm$ 2 min (median 4 min). The evolution of the procedure and fluoroscopy times is given in *Fig. 4*. The procedure time decreased significantly in a linear fashion ($R^2 = 0.2541$). There was no significant difference in procedure and fluoroscopy time between those patients in whom the single-magnet catheter or the three-magnet catheter was used.

Comparison with the control group

Table 1 shows a comparison of ablation data, results, procedure, and fluoroscopy times between the magnetically treated group as a whole, and broken down into one- and three-magnet groups, and the non-magnetically treated patients. The control group had the same ablation settings as those used in the magnetically treated group. No significant differences were observed between magnet and conventional groups or between the one- and three-magnet groups.

Follow-up results

No complications related to the advancer or the magnetic system occurred. Neither AV block nor distal conduction disturbances were observed. AH and HV intervals remained comparable. One complication, a pectoral haematoma, was a sequel of the subclavian puncture and did not require intervention. During a follow-up of 90 days, there have been no recurrences of AVNRT in the 19 (18 radiofrequency and 1 with additional cryotherapy ablation) successful procedures.

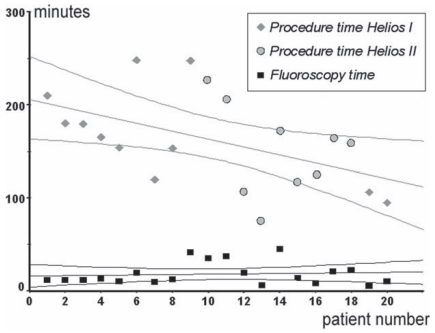

Figure 4 Intervention time (including waiting times) and fluoroscopy time vs. the consecutive number of patients. Regression lines are plotted, along with 95% confidence intervals, for procedure and radiation times. For the procedure time, the $R^2 = 0.2541$, whereas for radiation time, $R^2 = 0.0077$.

Discussion

Although AVNRT can be successfully ablated with success rates of the order of 95% and with a 1–2% risk of complete AV block,[1,6] there are other catheter-based procedures which are much more difficult because of anatomical and technical issues. Patients with corrected congenital heart disease and patients requiring left atrial procedures for atrial fibrillation therapy are good examples.

The possibility of using floppy catheters with new technology in association with magnetic navigation and remote ablation is therefore appealing.

We have shown that using this technology we can achieve success rates equalling those with more conventional

Table 1 A comparison of ablation data, results, procedure, and fluoroscopy times

	Total magnet group	One-magnet group	Three-magnet group	Control group
Number of patients	20	11	9	17
Number of ablations [median (range)]	6 (1–22)	4.5 (1–22)	8.0 (1–21)	5 (2–28)
Success	18 (19)/20	10/11	8 (9)/9	17/17
Slow pathway ablation	11	5	6	11
Slow pathway modification	4	1	3	3
No jump pre-ablation	4	4	0	3
Procedure time (min) [median (range)]	163 (69–260)	160 (106–260)	166 (69–235)	159 (83–290)
Fluoroscopy time (min) [median (range)]	12 (4.5–37.4)	11 (4.5–18.3)	19 (7–37.4)	18 (9–51)

technology without significant complications and with reasonable patient radiation exposure.

Procedure time

It is important to note that our procedure times are not from initial sheath placement, but from time on table to removal of sheaths; this adds approximately 15–20 min. Procedure time also includes the time for the initial diagnostic study and an observation period of 30 min after the last application.

This explains the difference with a prior study using magnetic navigation performed in the same substrate.[4] However, the procedure time was comparable with that in our control group. The time to set up the advancer was short, and it would have been interesting to log the duration of different parts of the procedure to have a better understanding of the time effects of this new technology.

Fluoroscopy time

Of great significance is the fact that in a procedure with relatively little radiation the physician radiation time was less than one-third of that of the patient. Although individual patient radiation exposure is not increased in comparison with other trials, it is evident that physician dosage is significantly decreased. In more complex procedures with longer exposure times, this will be of even more significance.

Part of the somewhat long radiation time relates to initial unease about the stability of the catheter during ablation and junctional rhythm. The time did not decrease as might be expected, because of the second learning curve due to the transition to three-magnet catheters. We wished to check on the stability of these catheters as well.

Catheter stability

It must be noted that catheter position was extremely stable when compared with standard catheters, even when patients tended to take deep breaths, and during accelerated junctional rhythm.

One-magnet vs. three-magnet catheters

A clear learning curve is evident. There was no apparent benefit in this ablation situation with a three-magnet when compared with a single-magnet catheter. This may reflect partly the learning curve, but probably the relative ease with which a catheter can be placed in the slow pathway region.

The orientation of the three-magnet catheter appears somewhat different. With all three magnets orientated in the field, the distal part of the catheter is straighter than with the single-magnet catheter. In one patient, this did seem to cause some instability of the catheter position as the straightening caused the more proximal portion to buttress against the IVC–RA junction. The catheter tended to move backwards and forwards over the annulus during respiration. This was not a noticeable problem in the other patients.

It is possible that in more complex anatomy and more challenging positions the three-magnet catheter may perform better than the one-magnet version.

Advantages in AVNRT

The slow pathway region is easy to reach and mappable with the magnetic navigation system. The success rate is in the range expected with conventional technology. There was no incidence of permanent AH or PR prolongation. We had no evidence of any fast pathway modification. The high ratio of slow pathway ablation vs. modification compares favourably with that seen with cryoablation[7] and is the inverse of that seen in the only other published magnetically ablated series.[4]

Future concepts

Combining standard catheters with systems such as LocaLisa and CARTO resulted in shorter radiation times in prior studies.[8,9] It is expected that with the incorporation of catheter registration technology or echocardiography[10] into this system, or using these technologies in parallel, procedure and radiation times will further decrease.

Combining this technology with other new technologies, such as cryotherapy and the other technologies mentioned previously, may significantly improve outcome, as well as reduce the number of applications, and associated collateral tissue damage.[11]

Conclusions

AVNRT can be successfully mapped and ablated using magnetic navigation with comparable risks and benefits as obtained when using standard catheters. A learning curve was evident, not related to the catheter type, but to increasing experience. Physician radiation times were only

one-third of patient radiation times and are therefore significantly reduced. No complications occurred. Our results show that magnetic navigation in Koch's triangle is feasible, easy to learn, and can assist in successful ablation.

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Chapter 9

Remote magnetic navigation to map and ablate right ventricular outflow tract tachycardia

Remote magnetic navigation for mapping and ablating right ventricular outflow tract tachycardia

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BACKGROUND Navigation, mapping, and ablation in the right ventricular outflow tract (RVOT) can be difficult. Catheter navigation using external magnetic fields may allow more accurate mapping and ablation.

OBJECTIVES The purpose of this study was to assess the feasibility of RVOT tachycardia ablation using remote magnetic navigation.

METHODS Mapping and ablation were performed in eight patients with outflow tract ventricular arrhythmias. Tachycardia mapping was undertaken with a 64-polar basket catheter, followed by remote activation and pace-mapping using a magnetically enabled catheter. The area of interest was localized on the basket catheter in seven patients in whom an RVOT arrhythmia was identified. Remote navigation of the magnetic catheter to this area was followed by pace-mapping. Ablation was performed at the site of perfect pace-mapping, with earliest activation if possible.

RESULTS Acute success was achieved in all patients (median four applications). Median procedural time was 144 minutes, with 13.4 minutes of patient fluoroscopy time and 3.8 minutes of physician fluoroscopy time. No complications occurred. One recurrence occurred during follow-up (mean 366 days).

CONCLUSION RVOT tachycardias can be mapped and ablated using remote magnetic navigation, initially guided by a basket catheter. Precise activation and pace-mapping are possible. Remote magnetic navigation permitted low fluoroscopy exposure for the physician. Long-term results are promising.

KEYWORDS Arrhythmia; Catheter ablation; Magnetic navigation; Mapping; Right ventricular outflow tract; Ventricular tachycardia

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Introduction

In normal hearts, idiopathic ventricular tachycardia (VT) originates most commonly from either the outflow tract region or the fascicles of the left ventricle.[1–3] The right ventricular outflow tract (RVOT) is the most common site of origin, although an increasing number of these arrhythmias now are demonstrated to arise from the left ventricular outflow tract (LVOT) and even from above the pulmonary valve.[2,4,5] Ablation has a high success rate (reportedly 85%–100%) for both frequent VT and repetitive ventricular ectopy.[6–11] It usually is performed on the basis of simple activation and pace-mapping. Some reports have questioned the use of this approach.[12] Changes in autonomic tone during and after ablation that alter the pattern of spontaneous arrhythmias could make activation mapping difficult. In addition, technical problems with pace-mapping may limit its accuracy.[13,14] Even small changes within the RVOT can lead to marked changes in the paced QRS.[15,16] The ability to map carefully within such small areas and to return to the best sites is important. Multielectrode catheters and noncontact mapping systems have been introduced in an attempt to improve the success rate, in particular to improve the ease of the procedure and decrease procedural duration.[17] Cardiac perforation and cases of fatal tamponade related to perforation or late rupture have been described.[18,19]

Floppy magnetically enabled catheters have been developed, which can be steered by manipulation of an external magnetic field and advanced or retracted remotely by means of a mechanical external advancer system. This technique, called *remote magnetic navigation,* may allow easier movement in the RVOT compared with standard catheters. Standard catheters must be negotiated through two curves before mapping can be performed (the curve from the right atrium to the right ventricle, and then the curve from the main right ventricular cavity to the outflow tract), and this requirement hinders precise point-by-point navigation within the RVOT.

We postulated that a 64-polar basket catheter in association with a floppy magnetically enabled catheter would allow us to quickly target an area within the RVOT, to navigate easily to this site, to map more carefully within this area, and to perform accurate pace-mapping, with success rates for ablation at least equal to those obtained using standard catheters and with the potential to decrease procedural and fluoroscopy times.

Methods

Patient selection

Between June 2004 and February 2005, eight consecutive patients with left bundle branch block, inferior-axis VT suggestive of RVOT focal origin were admitted for electrophysiologic mapping and ablation. No patient had a contraindication to use of magnetic navigation (such as an implanted metallic device or claustrophobia). This study forms

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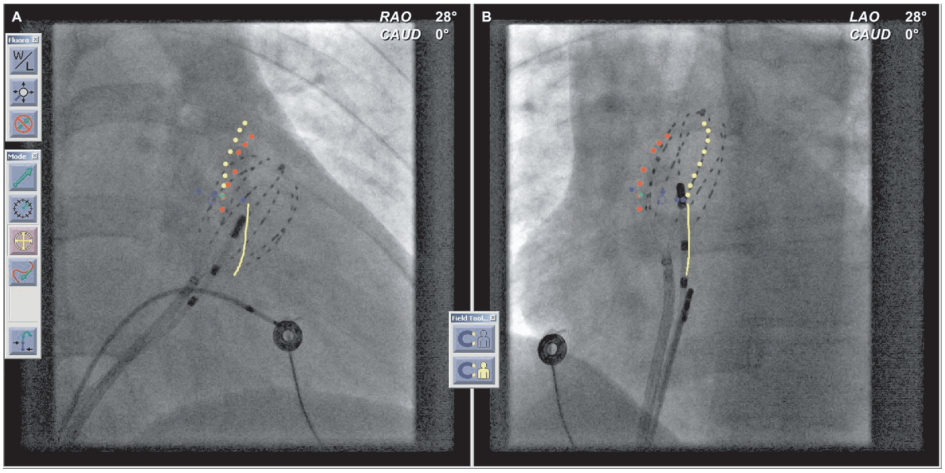

Figure 1 Navigant screen showing the two radiographic views obtained (right anterior oblique [RAO] on the **left,** left anterior oblique [LAO] on the **right).** The basket catheter with its eight splines can be seen within the right ventricular outflow tract with a temporary bipolar ventricular pacing lead. The magnetically enabled catheter has been navigated to a more anteroseptal position on the *horizontal line of blue dots* (previous mapping positions). Two of the splines have been marked on the Navigant software *(yellow and red dots).* The effect of respiration on the image acquisition can be seen in the RAO radiographic image. The *yellow line* indicates a virtual catheter drawn where the software identifies the catheter should be located according to the applied magnetic field.

part of the safety and efficacy study approved by the ethics committee of the Erasmus Medical Centre. All patients gave informed consent for the procedure.

Electrophysiologic study

Patients were studied in the fasting, postabsorptive state under little or only light conscious sedation, with intravenous boluses of diazepam and fentanyl administered as necessary. Electrograms were recorded using a standard recording system (AXIOM Sensis, Siemens, Erlangen, Germany). Prior to introducing catheters, an attempt was made to register spontaneous or isoprenaline-induced ventricular ectopy or nonsustained VT with a morphology similar to the clinical arrhythmia. This was used as a template for all mapping. Occasionally, an additional pacing catheter was introduced for atrial or ventricular burst or for programmed pacing. A long sheath (5662, Boston Scientific Corporation, San Jose, CA, USA) was positioned in the RVOT. A 38-mm, multielectrode basket catheter consisting of eight self-expanding splines and a total of 64 electrodes (Constellation, Boston Scientific Corporation) was inserted through the sheath to record and measure intracardiac electrograms from this region. The site of earliest activation was defined as the position with the longest interval from the local ventricular electrogram to onset of the earliest deflection of the QRS on the surface ECG during tachycardia. Earliest activation of target ventricular ectopy or VT was localized on the basket catheter (Figure 1) and marked using two orthogonal radiologic views on the Navigant system (Stereotaxis Inc., St. Louis, MO, USA). Once a suitable target area was identified, a second femoral access sheath was used to advance a three-magnet, 4-mm-tip radiofrequency (RF) ablation catheter (8Fr Helios II, Stereotaxis Inc.) to the RVOT. Heparin was given after venous puncture according to a weight-based nomogram. Activated clotting times (ACTs) were measured regularly with the aim of maintaining ACT at 250 seconds.

Magnetic navigation

The technique for magnetic navigation has been previously described.[20,21] In brief, the Niobe magnetic navigation system (Stereotaxis Inc.) is combined with a monoplane flat-panel fluoroscopy system (AXIOM Artis, Siemens). The Niobe system consists of two permanent magnets positioned on either side of the patient. The magnets are computer controlled via a workstation (Navigant) to effect a change in the orientation of a stable magnetic field within the patient's chest. A combined field strength of 0.08 Tesla is produced in navigation mode. Because navigation is best performed with a fixed table position, the table position should be optimized and isocentered before starting magnetic navigation. When the magnets are positioned next to the patient, only limited angulation of the C-arm is possible (approximately 28° in the right and left anterior oblique angulations). Remote catheter advancement and retraction from the control room are performed using a catheter advancer system (Cardiodrive, Stereotaxis Inc.) positioned on the high anterior thigh. Remote control of the fluoroscopy system also is possible from the control room. The ablation catheter (Helios II, Stereotaxis Inc.), which contains three

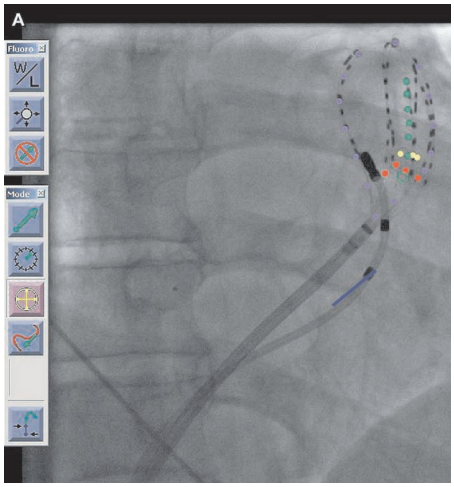

Figure 2 Angiographic right anterior oblique (RAO) view from the Navigant software screen showing the two curves. The basket is delineated in *purple,* the spline of interest with *green dots,* the pace-map points in *yellow,* and the ablation points as *red dots.* The *blue line* is the virtual pivot point of the catheter.

magnets within the distal tip segment, aligns with the field produced by the external magnets, allowing effective catheter orientation. Once the external magnets are in position, the physician can leave the room and perform the rest of the procedure from the control room. Only one nurse remains with the lightly sedated patient to monitor vital signs and administer drugs when required.

Mapping and ablation

Mapping was performed using a 12-lead ECG of the clinical tachycardia as the basis. Electrograms with early activation were combined with a pace-mapping approach. The site of earliest activation on the multipolar basket catheter was labeled as a navigation target using the Navigant software (Figure 2). The ablation catheter was introduced into the right ventricle by application of sequential magnetic vectors and then to the target within the RVOT using target-based navigation. When the general area of interest was reached, pace-mapping was performed to confirm that the paced QRS corresponded well to that of the clinical arrhythmia.[16] If a good pace-map was not obtained, the catheter was maneuvered in small increments around the area of interest using the Navigant software. Pace-mapping was performed at each site until an acceptable (at least 11/12) pace-map was obtained, with early activation of ectopy if possible. RF ablation was delivered using temperature-controlled ablation from an EP Shuttle RF generator (Stockert GmbH, Freiburg, Germany) with settings of 55°C, 60 seconds, and power titrated from 15 to 40 W to obtain the set temperature. The generator was also controlled remotely. RF applications usually were stopped after 20 to 30 seconds if no short runs of VT were observed. After apparently successful ablation, up to three additional applications, guided by the target site and magnetic navigation, were administered to the region around the successful site. These applications are included in the total number of applications and total RF time. Procedural time was defined as the period from the beginning of venous puncture until removal of the sheaths, 30 minutes after the last application. Fluoroscopy times were measured separately for the patient and for the physician.

Endpoint for ablation and definition of acute success

The endpoint for ablation was absence of clinical ventricular arrhythmias during monitoring and noninducibility of arrhythmia using isoprenaline and burst pacing. Maneuvers were repeated after a 30-minute waiting period. All patients underwent continuous 24-hour monitoring after the procedure, and acute success was defined only if no ventricular ectopy was observed during this period.

Follow-up

A 24-hour Holter ECG was recorded 6 weeks after ablation. All patients were followed clinically for at least 9 months after the procedure.

Statistical analysis

All continuous variables are expressed as mean ± SD. Median values are reported where appropriate.

Results

Patient data

The study group consisted of eight patients (six men and two women; mean age 44 ± 8 years). Ventricular ectopy and/or bigeminy were the presenting arrhythmia in three patients; longer runs of nonsustained (n = 4) or sustained VT (n = 1) were seen in the remaining five patients (Table 1). One patient had undergone one previous procedure, and another patient had undergone three previous procedures at two different institutions. One patient had what was described as a vague morphologic abnormality of the right ventricle close to the outflow tract noted on echocardiography but no other suggestion of arrhythmogenic right ventricular cardiomyopathy.

Remote navigation and mapping using the magnetic navigation system

In one patient, no site of early activation could be identified from the RVOT. This patient refused left-sided mapping. In the remaining seven patients, a region of early activation was determined from the electrograms of the basket catheter. Using pace-mapping, the clinical arrhythmia ultimately was well matched in all seven patients (Figure 3). The site of early activation after confirmation with an acceptable pace-map preceded the QRS by a mean time of 20 ms (range −12 to −36 ms). This final site was clearly septal in four patients and in the transition from posteroseptal to free

Table 1 Clinical and Mapping Characteristics

Patient no.	Sex	Age (yr)	Arrhythmia	Twelve-lead ECG assessment	Position from basket electrogram	Final x-ray position	Pace-map accuracy	Activation signal (ms)
1	M	45	VT	High PS-FW	Mid S-FW	Mid PS to FW	11/12	−13
2	M	37	Ectopy	High PS-FW	M-L PS to FW	M-L PS to FW	11/12	−36
3	M	58	NSVT	High PS	High AS	High AS	12/12	−19
4	F	45	NSVT	Mid PS-Mid S	M-L PS to S	M-L PS	11/12	−35
5	M	30	Ectopy	High AS	High AS	High AS	11/12	−12
6	M	45	NSVT	High PS	Mid PS	Mid PS to FW	12/12	−14
7	F	45	NSVT	Septal LVOT/epicardial	NA	NA	NA	NA
8	M	49	Ectopy	High AS	High AS	High AS	12/12	−12

AS = anteroseptal; F = female; FW = free wall; LVOT = left ventricular outflow tract; M = male; M-L = mid to low; NA = not applicable; NSVT = nonsustained ventricular tachycardia; PS = posteroseptal; s = septal; VT = ventricular tachycardia.

wall in three. A satisfactory and stable position for pace-mapping and ablation was obtained in all seven patients using the advancer and magnetic navigation. This position corresponded to the site of earliest activation in six cases.

Ablation data

Ablation was undertaken with the patient in sinus rhythm with or without ectopic beats or short runs of nonsustained VT, as sustained VT was only inducible with intravenous isoprenaline. During the early part of successful ablations, accelerated ventricular rhythm was always seen and the catheter remained stable during this rhythm and the transition to sinus rhythm. Ablation was acutely successful in all seven patients in whom an early signal could be defined in the RVOT (Table 2). From 2 to 10 (median 4) RF applications were applied, with a total RF duration of 174 to 554 seconds (median 240 seconds). These figures include the one to three extra RF applications administered to the area around the presumed successful site in most cases. After ablation, no further arrhythmias occurred spontaneously or could be induced. No arrhythmias were noted during the first 24 hours of continuous ambulatory monitoring (Figure 4).

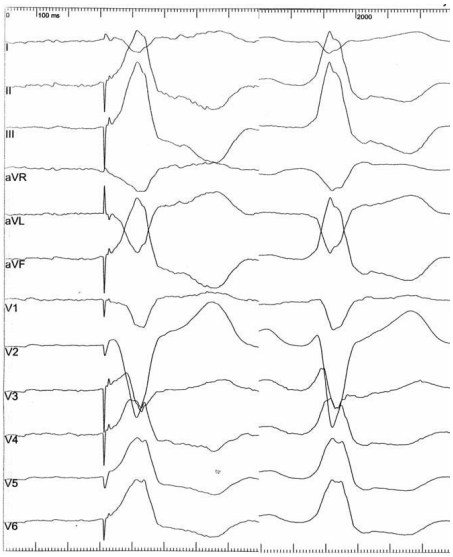

Figure 3 Twelve-lead ECG of a pace-map at a successful site obtained using the magnetic system. The **left** side of the image shows the QRS generated by pace-mapping; the **right** side shows the spontaneous ectopic beat used as the template. The paced beat is an acceptable pace-map of the clinical ectopic beat.

Procedure data

The mean procedural time (including waiting time) was 151 ± 35 minutes (median 144 minutes), with a patient fluoroscopy time of 12.5 ± 5.8 minutes (median 13.4 minutes). Of the total fluoroscopy duration, the physician was exposed only during introduction of the sheaths and positioning of the catheters (average 3.5 ± 1.3 minutes, median 3.8 minutes).

Follow-up results

No complications related to the advancer or the magnetic system occurred, and no other complications were noted. The patient with presumed LVOT origin refused further interventional therapy. Mean clinical follow-up is now 366 days (310–497 days). Four weeks after initial ablation, one patient presented with recurrence of symptoms, manifested as nonsustained VT in contrast to the sustained VT preablation. He subsequently underwent further ablation. Of the remaining six patients, five have been entirely asymptomatic throughout follow-up. The remaining patient initially had symptoms related to other ventricular and atrial ectopic beats, but the symptoms ultimately resolved with the patient off all medication. None of the six patients had any clinical ventricular ectopy or VT on Holter ECG at 6-week follow-up (Table 2).

Discussion

Pharmacologic therapy for outflow tract tachycardia may fail in some cases.[7,22] Catheter ablation using standard catheters has some limitations. Acute failure may be related to

Table 2 Ablation, Procedure and Follow-Up Characteristics

Patient no.	Application no.	RF duration (s)	Outcome	Procedure duration (min)	Fluoroscopy time for patient (min)	Fluoroscopy time for physician (min)	Clinical follow-up	Follow-up Holter
1	3	180	S	154	22.9	6.8	NSVT	NSVT and ectopy
2	8	436	S	148	13.8	3.7	Asymptomatic	Some ectopy—different
3	7	358	S	138	9.1	3.5	Asymptomatic	Normal
4	4	240	S	160	6.5	3.4	Asymptomatic	Left ventricular ectopy
5	4	240	S	95	11.1	3.2	Asymptomatic	Normal
6	10	554	S	156	15.5	3.5	Asymptomatic	Normal
7	4	77	F	203	19.9	2.3	Symptomatic	No change
8	3	174	S	98	8.4	4.0	Asymptomatic	Normal

F = failed ablation; NSVT = nonsustained ventricular tachycardia; RF = radiofrequency; S = successful ablation.

the lack of inducibility of the clinical arrhythmia during the study, failure to appreciate that the focus lies elsewhere, or difficulty in manipulating the catheter in the constrained region of the outflow tract.

Using remote magnetic navigation, we were able to easily and successfully navigate to selected points in the RVOT based on initial signals detected by a multielectrode catheter. The prematurity of the signals obtained with more detailed mapping was, on average, a little less than reported in some published studies[23–25] but nevertheless was associated with good pace-mapping. The clinical success rate achieved in this study is equivalent to the rates reported in the published studies.

Procedure parameters

The mean procedural time is favorable to the times reported for standard procedures (mean 99.4–166.9 minutes), especially when compared with some studies in which advanced mapping was used (mean 107.1–275 minutes).[16,23] The mean total radiation time also compares favorably to values reported in other studies using standard catheters (mean 15.4–66.5 minutes) or advanced mapping systems (mean 45.8–68.4 minutes).[15,16,23] In addition to the highly favorable patient radiation times, the physician radiation times were significantly less (<4 minutes), which is beneficial in the long term. The mean of four RF applications in this study, including the debatable additional applications, compares well with published figures (mean 4–7.1 applications).[15,23,26–28] The additional applications probably should be avoided and would further decrease the number of applications. Both the acute complete success rate and the low recurrence rate (14%) mirror those of other studies (85%–100% and 0%–19% respectively).[16,23,26,27] The ease of this new approach is reflected in the short procedural and radiation times, even considering the learning phase associated with applying the remote magnetic navigation system.

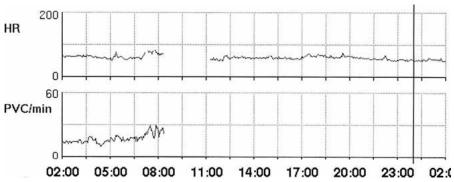

Figure 4 Ambulatory monitoring before and after ablation. **Top graph** shows the heart rate (HR) trend. **Bottom graph** shows the number of ectopic beats per minute (PVC/min). The gap in the recordings shows the time when the patient was disconnected during the ablation procedure.

Advantages and disadvantages of remote magnetic navigation

No complications related to these procedures occurred, and use of a floppy, rather than stiff, ablation catheter should decrease the risk for perforation.

In this study, we showed that magnetic navigation to a preselected site in the RVOT is feasible, with the ability to perform highly accurate mapping, leading to a good pace-map in all patients. The ability to move the floppy catheter in extremely small steps is a clear improvement over the conventional approach where the electrophysiologist repositions a stiff catheter across two curves and then applies a force to ensure close contact when applying RF energy. Such a technique severely limits the ability to move the catheter in small steps. In addition, more pressure likely is applied to the myocardium when conventional catheters are used, which is not without danger in a structure such as the RVOT, where the wall can be relatively thin. Early and late perforations have been described, with potentially fatal outcomes. This complication may be related both to local catheter trauma as well as to the effects of RF applications. Therefore, it seems logical that as few applications as possible should be given. The relatively smooth RVOT may favor the magnetic catheter by allowing for smooth mapping in small increments, but other investigators have shown that these catheters also are useful in the more trabeculated parts of the ventricles.[20]

Advantages and disadvantages of multipolar recording

Reports of advanced mapping techniques showed longer, not shorter, procedural and radiation times. Spontaneous

ectopy can be rare, and its absence may predict failure of the procedure. Therefore, when designing this approach, we believed a basket electrode catheter would be useful in directing us to the general area of interest because simultaneous multisite recording for activation mapping is one of the few solutions for infrequently occurring arrhythmias. A drawback of this approach is that the basket catheter itself is quite stiff and may cause perforation or induction of nonclinical ectopy. In addition, it usually requires use of a long sheath. The relatively fixed shape may preclude good contact with certain areas of the RVOT. Noncontact mapping has largely similar disadvantages.

Study limitations

This study involved a limited number of patients, with a preponderance of men and isolated ectopy. The study looked only at acute and short-term success, and recurrence may occur after 6-month follow-up. Late results could be more disappointing.

Conclusion

In this study, we showed that remote magnetic navigation to a preselected site in the RVOT is feasible and that successful ablation of foci within the RVOT can be performed with short procedural and fluoroscopy times. Use of this system appears to improve efficiency and safety when performing ablation for this type of arrhythmia.

If this technology shows similar benefit in more complex procedures, then incremental improvements in efficacy and safety can be expected. With the recent availability of integrated electroanatomic mapping and image integration, we are hopeful that the procedure can be further improved.

Acknowledgments

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Chapter 10

Use of advanced mapping and remote magnetic navigation to ablate left ventricular fascicular tachycardia

Use of Advanced Mapping and Remote Magnetic Navigation to Ablate Left Ventricular Fascicular Tachycardia

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Ablation of idiopathic left ventricular, or fascicular tachycardia can be aided by electroanatomical mapping. The addition of a floppy, magnetically enabled ablation catheter may improve maneuvering as well as decrease mechanically induced arrhythmias and mechanical block. We describe a case of fascicular tachycardia in which both these modalities were used in a sequential fashion. Integration of these modalities should prove even more helpful. (PACE 2006; 29:685–688)

ablation, ventricular tachycardia, mapping, magnetic navigation

Advanced activation mapping can be helpful for ventricular tachycardia requiring a focal approach. A typical example is fascicular tachycardia where ablation can be guided by the presence of Purkinje potentials, both during sinus rhythm and during tachycardia. However, this is not always very easy, as patients can be noninducible or other arrhythmias (e.g., catheter-induced) can interfere with the interpretation of the findings.

This case report shows the use of activation mapping to guide a magnetically enabled catheter, retrograde across the aortic valve, to the site of left-sided fascicular tachycardia, using remote magnetic navigation.

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Case Report

A 57-year-old woman was referred for catheter ablation. She was known to have ventricular arrhythmias for the past 5 years. Initially, heart failure was present and mitral regurgitation was detected. Coronary arteries were normal at

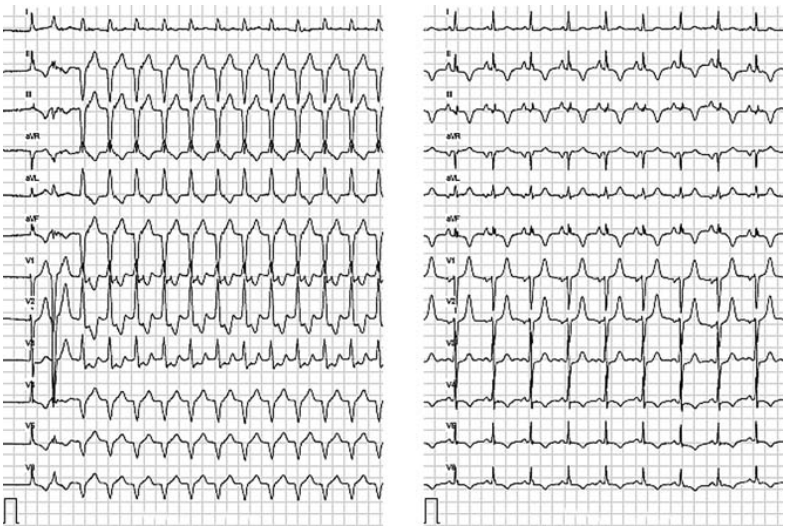

Figure 1. *ECGs (25 mm/s) during ventricular tachycardia and in sinus rhythm. Note the inverted T-waves in leads II, III, and aVF during sinus rhythm.*

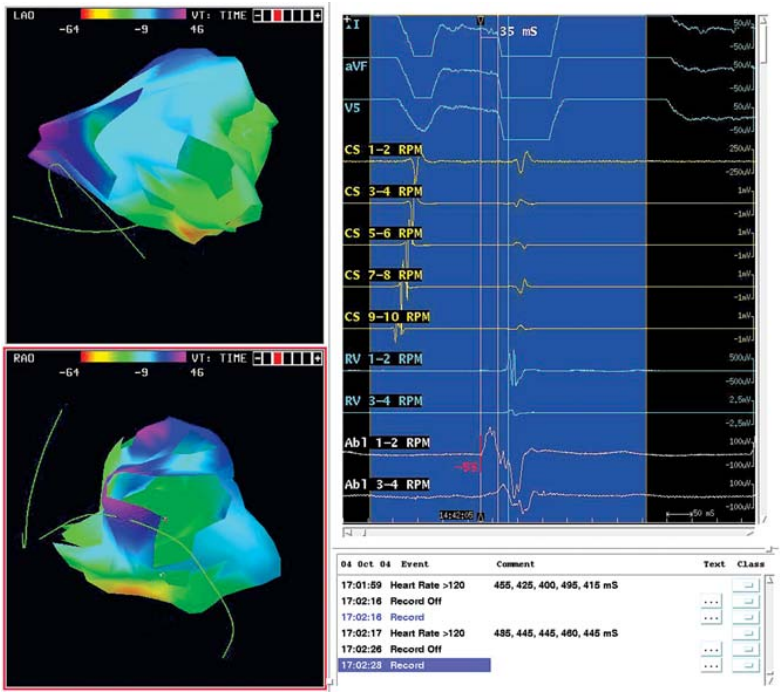

Figure 2. *RPM screen, showing activation maps in left anterior oblique (LAO) (upper left panel) and right anterior oblique (RAO) (lower left panel) views, along with the endocardial signal at the right, displaying an early activation (55 ms before the right ventricular signal and 35 ms before the QRS of the surface ECG) of a ventricular premature beat. The earliest site on the activation maps is in the yellow-red region.*

angiography. She was treated for heart failure, received sotalol and improved, but 2 years later was shown to still have exercise-related sustained ventricular tachycardia which was asymptomatic. She was readmitted 2 years later in July 2003 with recurrent symptomatic arrhythmias, and Amiodarone was administered to suppress the ventricular tachycardia. The tachycardia had a rate of 150 beats/min, showed a right bundle branch block pattern with left axis (−94°) and QS pattern in the inferior leads. The resting ECG was normal. Fascicular tachycardia from the left posterior fascicle was suspected, and demonstrated during exercise. Radiofrequency ablation aided by LocaLisa (Medtronic, Inc, Minneapolis, MN, USA) was attempted in August 2003. Mapping guided the way to fascicular potentials in the mid-posterior septal region. A total of 43 applications were given in this area. The radiation time was 70 minutes with a procedure time of 258 minutes. Two early short-lasting recurrences were a reason to continue amiodarone therapy. Seven months later amiodarone was stopped as hyperthyroidism was detected. Ventricular tachycardia then became incessant, albeit at slower rates (Fig. 1).

In October 2004 she was therefore, resubmitted for mapping and ablation, aided by an advanced mapping system, the real-time position management system (RPM, Boston Scientific Corporation, Natick, MA, USA). In this way the left ventricle was mapped retrograde transaortically during sinus rhythm and tachycardia or premature beats using a 4-mm tip EPT Blazer RPM catheter (Boston Scientific Corporation). The site of interesting Purkinje potentials was again inferoposterior on the activation map (Fig. 2). Stability of the mapping catheter was a problem during repeated runs of tachycardia and we postulated

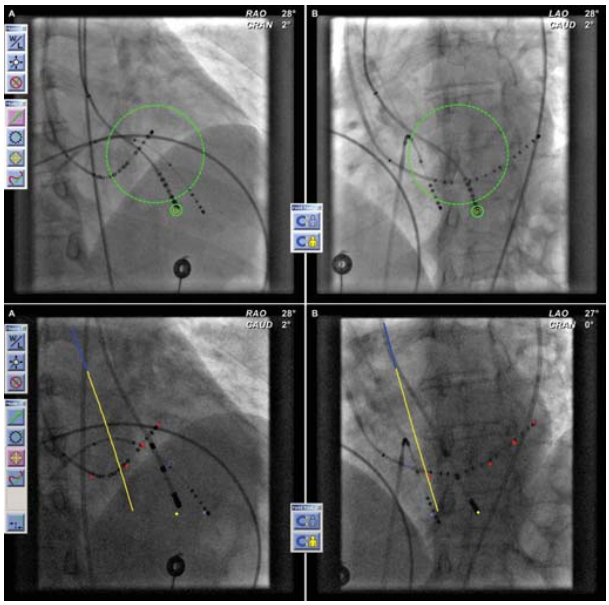

Figure 3. *Two Navigant screens, above and below, with RAO and LAO views. In the upper half of the figure the manual mapping catheter as well as the right ventricular and coronary sinus catheters can be noted in RAO and LAO views. The tip of the RPM mapping catheter is labeled by the green dot. In the lower half of the figure the magnetically enabled Helios ablation catheter is brought to the desired spot (green dot with circle) in approximately the same views. The green dot and circle is now represented by the yellow dot. The blue and yellow lines are those drawn by the operator and the software on the navigation screen. The blue line is drawn by the operator and forms a catheter base reference for the software; because the catheter is not fixed in the aorta the reference may differ from the actual catheter position. The yellow line is a virtual catheter representing the applied field needed to navigate the catheter to the desired point. The virtual and actual catheter positions differ partly due to the change in the reference base and partly because of a need sometimes for manual correction to get to a point of interest.*

that the use of very flexible magnetically steered catheters might be of benefit in this situation. The external magnets of the Niobe system were activated, with the accompanying Navigant software (Stereotaxis Inc, St Louis, MO, USA). The radiographic position of interest of the initial mapping catheter tip was imported into the Navigant software and labeled in two views (upper half of Fig. 3). The initial mapping catheter was then replaced by a 4-mm tip Helios catheter (Stereotaxis Inc.) which was introduced and then advanced across the aortic valve using the catheter advancer system (Stereotaxis Inc.). Subsequent magnetic vectors oriented the catheter tip toward the point of interest (lower half of Fig. 3). A total number of 17 applications was given in the region of interest, and no further tachycardia or premature beats were observed. The radiation time was 50 minutes with a procedure time of 225 minutes.

She remains without symptoms or documented tachycardia on multiple Holter ECGs for more than 12 months now.

Discussion

Fascicular tachycardia can be treated with conventional radiofrequency catheter ablation. The presence of Purkinje potentials may guide the physician in targeting a critical area of the reentrant circuit.[1,2] Conventional catheters may pose a problem, as they cannot always be easily directed

to the site of interest when using a retrograde approach, and mechanical block may also occur during manipulation. Using floppy catheters developed to be guided by external magnets may help to avoid these problems, as manipulation in the ventricle becomes easier.[3] Furthermore, one may assume that it is less prone to mechanically induced arrhythmias caused by manipulation. However, mapping remains necessary, and we present here a well-described electro-anatomical mapping tool that functioned well in the magnetic environment, and assisted in localizing the target area before introducing the magnetically enabled catheter.[4] Once in the ventricle, the magnetically guided catheter was maneuvered without difficulty to the target area, where Purkinje potentials were present.

Drawbacks of the magnetic catheter in this position include some initial difficulty crossing the aortic valve, and marked mobility of the magnet catheter in the left ventricular cavity during contraction and relaxation of the left ventricle, before good left ventricular wall contact was made. Once good wall contact was achieved the catheter stability was excellent despite regular transition between tachycardia and sinus rhythm. Ideally, the mapping system should be integrated with the magnetic navigation system.

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Chapter 11

Magnetic navigation in left sided AV reentrant tachycardias : preliminary results of a retrograde approach

Magnetic Navigation in Left-Sided AV Reentrant Tachycardias: Preliminary Results of a Retrograde Approach

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Retrograde Magnetic Ablation of Accessory Pathways. ***Introduction:*** **A novel magnetic navigation system allows remote guidance of floppy radiofrequency (RF) ablation catheters. We evaluated the feasibility of mapping and ablation of left-sided accessory pathways (APs) using the retrograde transaortic approach with this system. This might open the gate to retrograde ablation of left atrial arrhythmias.**

Methods and Results: **Twenty consecutive patients were included. A Helios II was used in five and in 15 a Celsius RMT RF catheter with higher magnetic mass and different flexibility was used. Mapping and ablation were attempted. The learning curve was analyzed. Ablation was acutely successful in 60% of the patients using the Helios II and in 80% using the Celsius RMT. Median procedure time was 158 minutes, with median patient and physician fluoroscopy times of 26 and 4 minutes. In the last 10 patients, procedure times became significantly shorter (median 122 minutes, only Celsius RMT catheters) and standard catheters had to be used only twice. No complications occurred.**

Conclusions: **Remote retrograde transaortic RF ablation of left-sided APs is feasible, safe, and reduces the physician's fluoroscopy exposure. There is a very steep initial learning curve, with the success rate increasing from 50% in the first 10 cases to 80% in the last 10 cases. Different catheter configurations may influence the outcome.** *(J Cardiovasc Electrophysiol, Vol. 18, pp. 467-472, May 2007)*

arrhythmias, AV reentrant tachycardia, catheter ablation, magnetic navigation, stereotactic therapy, Wolff-Parkinson-White syndrome

Introduction

Since transvenous ablation of accessory pathways (APs) was described,[1] more recently with radiofrequency (RF) energy,[2-4] nothing really substantial has changed in the catheter technique.

Ablation of left-sided pathways can be undertaken in both a retrograde transaortic fashion as well as via a transseptal approach.[5-8] The two approaches have their advantages, disadvantages, and complications. The success rate is comparable. Procedure and fluoroscopy time, and complication rates are similar.[8-13] The choice is therefore mainly dictated by the preference of the physician and his experience with transseptal puncture.

The magnetic navigation system (Niobe, Stereotaxis Inc., St. Louis, MO, USA) makes it possible to steer soft, flexible catheters and guide-wires by the use of an external magnetic field.[14-18] These catheters may allow for reliable contact with the myocardium, without increased risks such as perforation, and to maintain that contact throughout the cardiac cycle even in the face of changes in rhythm. In addition, it may help to access difficult anatomy, for example, in corrected complex congenital heart disease. This new technology to map and ablate has only been described in a relatively limited number of patients with left-sided APs,[19] and then mainly via a transseptal approach, using first-generation magnetic catheters.

We assessed the feasibility of a retrograde approach to ablation of left-sided APs using a magnetic navigation system. We also compared the efficacy of two catheters with different magnetic mass and configuration and different shaft flexibility, as well as the learning curve required for this approach. With increasing experience, this approach opens a route to less invasive access of left atrial arrhythmias, as transseptal puncture may become unnecessary.

Methods

Patient Population

We enrolled 20 consecutive patients with proven symptomatic left-sided APs, including 14 with overt preexcitation. No patient had a contraindication to the use of magnetic navigation. This study forms part of the safety and efficacy study approved by the ethics committee of the Erasmus Medical Centre. All patients gave informed consent for the procedure.

Electrophysiological Study

Patients were studied in the fasting, postabsorptive state under light sedation. A diagnostic electrophysiological study confirmed the diagnosis of a left-sided AP. Electrograms were recorded using a standard recording system (Sensis, Siemens, Erlangen, Germany). An additional femoral arterial access sheath was placed and heparin 100 units/kg body weight was given. We maintained an ACT above 250 s throughout the

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procedure. Through the sheath, a magnetic navigation ablation catheter with a 4-mm tip was advanced manually to the descending aorta distal to the origin of the left subclavian artery. The catheter was then inserted into the catheter advancer system (Cardiodrive™, Stereotaxis, Stereotaxis Inc.) and the magnets were brought in. The catheters used were the 3-magnet low magnetic mass catheter, Helios II (Stereotaxis, Stereotaxis Inc.), and another 3-magnet, more flexible and higher magnetic mass catheter, Celsius RMT (Biosense Webster, Diamond Bar, CA, USA), which became available later. The choice was determined by availability.

Magnetic Navigation

The Niobe I magnetic navigation system (Stereotaxis Inc.) is combined with a monoplane angiography system (AXIOM Artis, Siemens).[17] The Niobe I system consists of two large permanent magnets with a combined field strength of 0.08 Tesla produced in navigation mode, situated on either side of the patient and controlled via a computer workstation (Navigant, Stereotaxis Inc.) to allow for changes in the orientation of a stable magnet field within the chest of the patient. The ablation catheters have magnets in the distal shaft that align themselves with the field produced by the external magnets, allowing for effective catheter orientation. Only limited angulation of the C-arm is possible (approximately 28° in the right and left anterior oblique angulations), due to the position of the magnets. Remote catheter advancement and retraction is performed using a catheter advancer system (Cardiodrive™, Stereotaxis Inc.) positioned on the thigh. After the magnets are brought in next to the patient, remote control of all of the components of the system, including the RF generator, stimulator, and recording equipment, is performed by the physician from the control room. A nurse remains with the sedated patient to monitor vital signs and administer drugs when required.

Using the Navigant software, the catheter is manipulated across the aortic valve. The mitral annulus is mapped from the ventricular side to locate the position of the pathway. If this fails, the atrial side of the annulus is accessed and the annulus mapped in this fashion. Crossover to a standard RF ablation catheter using the retrograde approach during the same procedure is possible, at the discretion of the treating physician.

Procedure times are defined from the start of venous access until the end of testing after a 30-minute waiting period. Fluoroscopy times are measured separately for the patient and the physician.

Mapping and Ablation

RF energy was delivered via the 4-mm tip of the ablation catheter using an EP Shuttle RF generator (Stockert GmbH, Freiburg, Germany) with settings of 55°C, 60 seconds and power titrated up to 50 W to obtain the set temperature. RF applications were stopped 10 seconds after adequate temperature was obtained if no effect was seen. Temporary success was considered as success for mapping with the system. The end point for ablation was absence of AP conduction and noninducibility of tachycardia using standard electrophysiological maneuvers and isoprenaline. Maneuvers were repeated after a waiting period of 30 minutes.

Follow-Up

All patients received heparin intravenously for 24 hours after the procedure and aspirin 80 mg per day for 6 weeks following the ablation. Each patient had an echocardiogram before discharge. All patients were seen at 3 months postablation, when a history was taken and ECG performed.

Statistical Analysis

All continuous variables are expressed as mean ± standard deviation. When appropriate, median values are reported and nonparametric tests used.

Results

Patient Data

The patient group consisted of 14 males and six females, with a mean age of 42 ± 15 years (17–70 years), all having normal hearts. All patients had left-sided APs, with two patients having two anatomically separate left-sided pathways. The 22 pathways were left anterolateral (1), left lateral (14), left posterolateral (1), and left posterior (6). The patients with two pathways both had a left lateral and a left posterior pathway and were treated in the Helios II catheter group. Helios II catheters were initially the only catheters available and were used in cases 1–4 and 9.

Remote Navigation and Mapping Using the Magnetic Navigation System

Traversing the aortic arch, we used two vectors to go anteriorly and to the right, and then inferiorly, to position the catheter above the aortic valve. Initially, we attempted to cross the aortic valve by forming a loop and advancing, or by pushing the catheter into one of the sinuses of valsalva and then trying to prolapse it across the valve. The former often ended with the catheter tip back in the arch and the most advanced part still just above the valve, while with the latter the catheter entered the left ventricle (LV), but with the tip remaining above the valve (Fig. 1). The LV was accessed in all, but after the first three cases, we advanced the soft tip catheter in a straight fashion across the valve, using a vector aimed at the apex in a left anterior oblique (LAO) view and at the mid-posterior septum in a right anterior oblique (RAO) view (Fig. 2), thus avoiding accidental coronary artery cannulation. Once stabilized, the tip was retracted and freed up, usually without losing the catheter from the LV. Either target navigation, or recently, the 3-D anatomic model was then used to target areas around the annulus. The catheter sometimes moved easily, while in others the catheter would have to be straightened and then a different target or vector selected. In the last nine cases, we were able to manipulate the catheter through the mitral valve into the LA and also map the annulus from the atrial side. This enabled easier mapping but, visually, contact on the annulus was not good, and trying to increase contact often caused the catheter to fall back into the LV. Good contact could be obtained under the mitral valve by "over-advancing" the catheter until a little buckling was seen more proximally in the catheter.

Procedure Data

The mean procedure time (including the 30 minutes waiting time) was 162 ± 56 minutes (median 158 minutes), with a patient fluoroscopy time of 31 ± 22 minutes (median 26

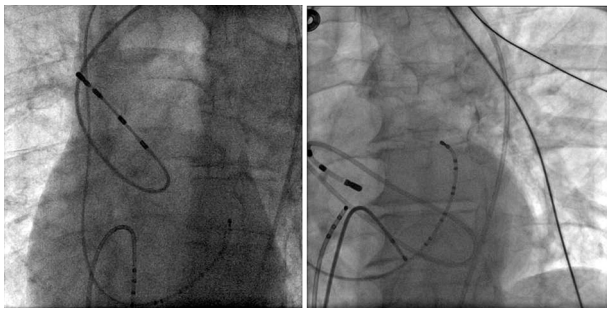

Figure 1. *Left: LAO view, with the catheter position after trying to form a loop in the proximal ascending aorta. The floppy catheter (Celsius RMT) is completely curled up with the tip in the distal ascending aorta. Right: LAO view, with the catheter position after trying to prolapse the catheter across the aortic valve. The floppy catheter (Helios (II) has prolapsed across the valve, but the tip of the catheter remains supra-valvar.*

minutes). For successful magnetic ablation cases, the mean procedure time was 130 ± 41 minutes (median 111 minutes), with a patient fluoroscopy time of 21 ± 16 minutes (median 14 minutes). Of the total fluoroscopy duration, the physician was only exposed only during sheath introduction and diagnostic catheter positioning, or when standard ablation catheters were used. This was for a mean of 9 ± 11 minutes (median 4 minutes) in all patients, but only 4 ± 3 minutes (median 4 minutes) in the cases were only a magnetic catheter was used.

Ablation Data

Data are shown in Table 1. Ablation was generally performed either during sinus rhythm in those with an overt pathway or during ventricular pacing in those with concealed pathways. In one patient with a concealed AP, any ventricular pacing immediately induced tachycardia. He was ablated in tachycardia. Termination was not associated with displacement of the catheter.

Mapping for ablation was acutely successful with magnetic navigation in 15 of 20 patients (75%) and 22 pathways (68%). In the Helios II group, acute success was achieved in three of five patients (60%), and seven pathways (43%). In the Celsius RMT group, 12 of 15 patients and pathways (80%) were successfully mapped for ablation.

This included one patient (13) with recurrence after 30 minutes. Using the ablation catheter and stored vectors, it was easy to get back to the area with permanent block. In two patients, only temporary block was obtained on several occasions with a magnetic catheter, and the pathways were easily ablated retrogradely with a standard catheter on the identified site.

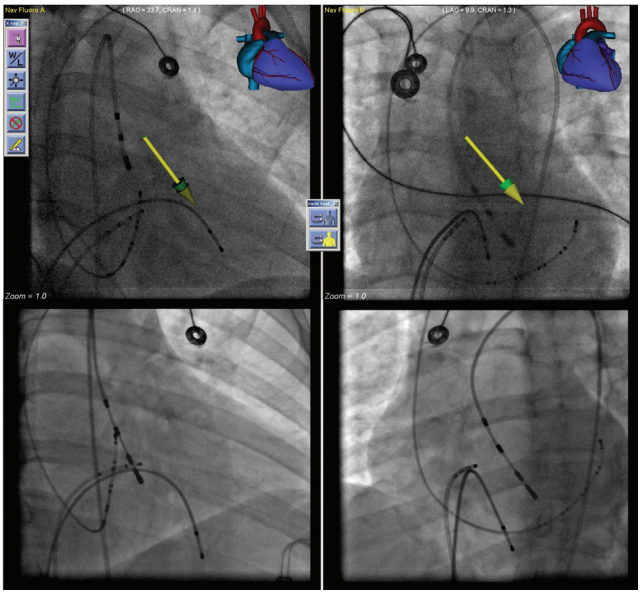

Figure 2. *Crossing of the aortic valve with a magnetic catheter. The two views above are from the Navigant screen showing the selected vector with the fluoroscopy on the left (RAO), updated before advancing across the valve, and the fluoroscopy on the right (LAO), showing just after crossing the valve with the catheter kept straight. The yellow arrows with green and yellow arrowhead show that the selected vector for crossing the aortic valve has been applied. The two images below are RAO and LAO fluoroscopic images (left and right, respectively), showing how a magnet catheter has just crossed the aortic valve.*

TABLE 1

Overview of Patient, Catheter, and Procedure Data

No.	AP Site	Catheter Type	Success	Proc. Time (Min)	# RF M	M Time (Sec)	# RF S	S Time (Sec)	Final Success	Fluoro Time Patient	Fluoro Time Physician
1	LL	Helios II	Y	191	6	420				43.9	12.0
2	LL	Helios II	T	230	5	324	1	21	Y	30.1	7.3
3	LL, LP	Helios II	N	265	20	405	20	779	Y, Y	24.0	5.1
4	LL, LP	Helios II	N	197	9	290	13	341	Y, N	58.2	22.1
5	LP	C RMT	Y	180	8	170				53.5	3.5
6	LP	C RMT	T	225	29	550	2	145	Y	52.0	3.5
7	LL	C RMT	Y	130	7	318				14.2	2.6
8	LL	C RMT	Y	110	4	126				7.8	1.0
9	LL	Helios II	Y	105	7	199				19.1	3.8
10	LL	C RMT	N	170	11	204	14	292	N	74.2	41.0
11	LL	C RMT	Y	103	12	202				12.5	3.6
12	LL	C RMT	Y	93	5	169				16.0	5.0
13	LP	C RMT	Y	189	4	163				28.2	8.0
14	LL	C RMT	Y	136	1	60				10.0	2.3
15	LAL	C RMT	Y	146	4	104				35.9	2.1
16	LL	C RMT	Y	108	1	60				7.3	1.1
17	LL	C RMT	Y	90	1	60				9.3	5.2
18	LPL	C RMT	N	196	12	221	6	94	N	55.0	16.0
19	LP	C RMT	Y	112	2	76				4.1	2.6
20	LL	C RMT	N	260	13	368	18	359	N	66.0	30.3

AP = accessory pathway; C RMT = Celsius RMT catheter; Fluoro time = fluoroscopy time in minutes; LAL = left anterolateral; LL = left lateral; LP = left posterior; LPL = left posterolateral; M = magnetic catheter; N = no success; No. = patient number; Proc. = procedure; # RF = number of RF applications; S = standard catheter; T = temporary success; Y = permanent success.

In the five patients in whom no temporary success could be obtained, crossover to standard catheters with the same approach was successful in two during the same procedure. One of these had a left lateral AP ablated with a standard catheter, but a left posterior AP could not be ablated. She remains completely asymptomatic. This gave a complete procedural success rate after crossover to a standard catheter of 17 of 20 patients (85%) and 19 of 22 (86%) APs. The three remaining patients had either left lateral (two) or left posterolateral (one) APs, which were successfully ablated using a transseptal approach and standard catheters at a subsequent procedure.

The median number of RF applications was seven (range 1–40), with a median RF time of 201 seconds (range 60–1,184). In the successful cases using magnetic catheters, the median number of RF applications was four (range 1–12), with a median RF time of 163 seconds (range 60–420). If more than seven applications were not associated with at least temporary effect, then permanent success was never achieved with magnetic catheters.

Learning Curve or Catheter Type

There was a significant decrease in procedure and RF time between the first and last 10 patients, with a tendency to decreased patient fluoroscopy time and the number of RF applications (Table 2). There was also a significant decrease in procedure and RF time and a tendency to a better outcome in ablation of APs in the Celsius RMT group compared to the Helios II group (Table 3). There was no significant difference in any of the parameters between the first seven and the second eight patients treated with Celsius RMT catheters.

Follow-Up Results

No complications occurred during the procedure. Echocardiograms done on the day after the procedure were normal. A pulmonary embolus, 2 weeks after the procedure, occurred in the patient with two pathways in whom only one could be ablated. This was despite adequate anticoagulation both during the procedure and for 24 hours thereafter. All patients were seen at 3 months' follow-up. No recurrences of tachycardia or delta waves were observed when initial success was obtained.

Discussion

Both the transseptal and transaortic approaches to left-sided APs have been used. Each has its own specific advantages and disadvantages. Comparisons of these two approaches using standard catheters have generally shown similar success rates, procedure and fluoroscopy times, and complication rates.[8–13] There is, however, a greater acceptance of the transseptal approach. This may be explained by studies showing somewhat shorter fluoroscopy and procedure times

TABLE 2

Comparison of the First 10 Versus the Last 10 Patients

	First 10	Last 10	P Value
No. patients (APs)	10 (12)	10 (10)	
Helios/Celsius RMT	5/5	0/10	
Success patients	5/10	8/10	NS
Success APs	5/12	8/10	0.099
Proc. time (min)	180 ± 53	137 ± 48	0.038
Patient fluoro time (min)	33.7 ± 21.8	24.4 ± 21.5	0.078
Physician fluoro time (min)	10.2 ± 12.5	7.6 ± 9.1	NS
# RF applications	15.9 ± 12.6	7.9 ± 9.8	0.076
RF time (sec)	458.4 ± 317.7	193.6 ± 204.5	0.028

APs = accessory pathways; Fluoro = fluoroscopy; min = minutes; No. = number; NS = not significant; Proc. = procedure; RF = radiofrequency; sec = seconds. Success is defined as permanent success with the magnet catheter.

TABLE 3
Comparison of the Two Catheter Groups

	Helios II	Celsius RMT	P Value
No. patients (APs)	5 (7)	15 (15)	
Success patients	2/5	11/15	NS
Success APs	2/7	11/15	0.074
Proc. time (min)	198 ± 60	145 ± 47	0.029
Patient fluoro time (min)	35.1 ± 15.9	29.7 ± 24.2	NS
Physician fluoro time (min)	10.1 ± 7.4	8.5 ± 11.8	NS
# RF applications	16.8 ± 14.5	10.9 ± 10.8	NS
RF time (sec)	542 ± 400	249 ± 223	0.026

APs = accessory pathways; Fluoro = fluoroscopy; min = minutes; No. = number; NS = not significant; Proc. = procedure; RF = radiofrequency; sec = seconds. Success is defined as permanent success with the magnet catheter.

with the transseptal approach and more complications in the transaortic approach.[10] It has also been stated that contact is better via the transseptal approach. On the other hand, some have demonstrated an increased number of complications, especially major complications, in the transseptal approach, although this was not statistically significant.[12]

The use of a magnetic navigation system to map and ablate left-sided pathways has only been described in a relatively limited number of patients,[19] and then mainly via a transseptal approach, using single magnet and low magnetic mass catheters (Helios). We elected to study the retrograde approach again using a magnetic navigation system. Magnetically enabled catheters may allow us to maintain reliable contact with the myocardium without increased risk, such as perforation of the aorta or myocardium, or damage to valves, and to maintain that contact throughout the cardiac cycle even in the face of changes in rhythm.

The procedure and fluoroscopy times in this study compare favorably with those in published studies, especially the radiation time for the physician, which is certainly significantly less than that which would normally be experienced. Our success rates overall and for both catheters, especially the low magnetic mass catheter, are less than that which would normally be expected. The success increased to 80% in the last 10 cases. This may well have related to our learning curve. There are significant technical differences between standard and magnetic catheters, which result in different handling characteristics. Learning how to overcome some of these differences and use these to our advantage remains a challenge. We believe this led to the very steep, but short initial learning curve. The short learning curve may reflect our experience with this system in other arrhythmias, but other operators have also described a short learning curve for this system for atrial fibrillation.[20] While a real comparison of the two catheters used is not really possible here, subjectively, we are in no doubt as to the better features of the higher magnetic mass, more flexible catheter.

Limitations of the Study

This study has been undertaken in a small number of cases and merely shows feasibility. We cannot reliably compare the outcome to either a transseptal approach using either magnetic or standard catheters, or to a retrograde approach using standard catheters, as the initial learning curve is steep. Having climbed the initial hump of the learning curve, we now need to compare the outcomes with a transseptal approach using magnetic catheters, as well as to use of standard catheters.

Conclusions

APs can be successfully mapped and ablated retrogradely, using magnetic navigation. A very steep initial learning curve was evident, with an ongoing but less steep curve. The use of newer, higher magnetic mass, more flexible catheters made the ablation easier. Procedure and fluoroscopy times are comparable to standard approaches even at this early stage, but physician fluoroscopy times are significantly shorter than would be expected.

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Chapter 12

A left sided accessory pathway revisited with remote retrograde magnetic navigation

A Left-Sided Accessory Pathway Revisited with Remote Retrograde Magnetic Navigation

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Accessory pathways can be ablated with a high success rate. Occasionally, recurrences appear after successful procedures, sometimes shortly after the end of the procedure. We describe a successful ablation using remote magnetic navigation of a single catheter using stored vectors after recurrence of accessory pathway conduction while the patient was still in the electrophysiology laboratory. (PACE 2007; 30:573–576)

accessory pathway*, *ablation*, *arrhythmia*, *magnetic navigation

Introduction

Returning to a given ablation point once one has moved the catheter can sometimes be quite challenging, certainly when using radiographic imaging alone. This can be even more difficult if using a single catheter approach,[1] without other references. Registration of the successful point would be useful, and could be done using a mapping system. Another possibility is to register the successful position to radiological images on a magnetic navigation system and then ask this system to return a magnetically enabled catheter to this point.[2]

Case Report

A 21-year-old man with a long history of paroxysmal palpitations with a regular narrow complex tachycardia and electrocardiographic evidence of preexcitation suggestive of a posteroseptal accessory pathway was studied under light conscious sedation and intravenous heparin. The left subclavian vein and right femoral vein were cannulated for right ventricular apex (RVA) and coronary sinus (CS) catheters. The presence of a left posterior pathway was confirmed, with an anterograde effective refractory period less than 300 ms, and inducible orthodromic atrioventricular reentrant tachycardia (AVRT).

A retrograde transaortic approach with remote magnetic navigation of a floppy magnetically enabled ablation catheter was used. A 3 magnet, 4-mm tip ablation catheter (7 Fr Celsius RMT, Biosense Webster, Diamond Bar, CA, USA) was inserted through an 8-Fr sheath in the left femoral artery. It was advanced up the aorta as far as the origin of the left subclavian artery. The magnetically enabled catheter was connected to the remote catheter advancer system (Stereotaxis, St. Louis, MO, USA) and the external magnets (Niobe, Stereotaxis) brought in. The rest of the procedure was performed remotely from the control room using the Navigant workstation (Stereotaxis).

The ablation catheter was advanced across the aortic valve using what is known as vector-based navigation. The mitral valve annulus was mapped from the ventricular side using target-based navigation. Both the vectors necessary to cross the aortic valve as well as the targets for successful ablation were stored on the magnetic navigation system. At a site associated with good signals, a radiofrequency application was made with temperature-controlled ablation from a remotely controlled EP Shuttle radiofrequency (RF) generator (Stockert GmbH, Freiburg, Germany) with settings of 55°C, 60 seconds, and power titrated up to 50 W. During the first application, accessory pathway conduction disappeared after 15 seconds, but at 21 seconds, the catheter became displaced by ventricular ectopy induced by the ablation, an unusual occurrence as catheter stability is otherwise usually very good. Conduction returned quickly. Repositioning the catheter was performed by withdrawing and then again advancing the catheter with a little extra loop in the ventricle. Application of energy (application 2) was associated with disappearance of the accessory pathway within 5 seconds and continued bidirectional accessory pathway block (see position in Fig. 1). After 10 minutes of accessory pathway block, the ablation catheter was removed and after 30 minutes block was still present, even with isoprenaline, and with complete atrioventricular (AV) and ventriculoatrial (VA) block after administration of adenosine. At this time, the catheters were withdrawn and venous sheaths removed and preparations made to move the patient back to his room. At this time, the electrocardiogram (ECG) was again noted to show preexcitation with the same characteristics as at the beginning of the procedure.

As the arterial sheath was still in situ because of the significantly prolonged ACT, it was decided to return to the successful site using the vec-

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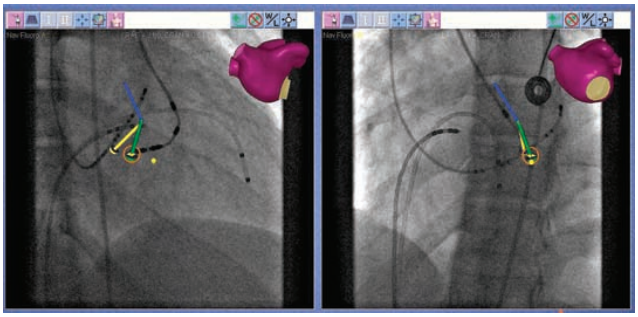

Figure 1. *Navigant work screen with LAO 24° (at the right) and RAO 32° (at the left). Catheters are in the right ventricular apex, the coronary sinus and in the AV ring. The blue line is where the catheter shaft was based; the yellow line is the vector as programmed; the green line ends within the orange circle, which is around the successful site of ablation.*

tors and target previously stored on the Navigant system. This was possible as the patient had not changed position. The CS catheter was not repositioned as the venous sheaths had already been removed. The catheter returned easily to the area of interest (Fig. 2), although with a slightly larger atrial signal suggesting a slightly more atrial position on the annulus (Fig. 3A,B). Radiofrequency application resulted in disappearance of accessory pathway conduction 8.5 seconds into the application (application 3). The accessory pathway conduction remained absent for 40 minutes. There was no delta wave either the following day, or at 6 weeks follow-up.

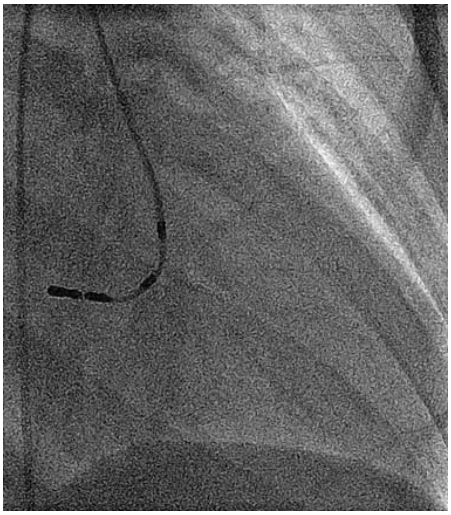

Figure 2. *RAO view with the single ablation catheter, similar position as compared to Fig. 1.*

Discussion

This report is the first describing how stored magnetic vectors in the Niobe system (Stereotaxis Inc) can be used to revisit the area of successful ablation. No other landmarks were in place at this time. It was possible to position the catheter in the region of interest and to successfully reablate this pathway in less than 5 minutes, including time for catheter reintroduction and magnet redeployment. That the signals at the final position are suggestive of a somewhat more atrial position show that the vectors are only part of the positioning process and that slightly different advancement or retraction of the catheter also influences the position. The ability to return to an area of interest using a few mouse clicks may prove useful in some cases.

The Stereotaxis system can store previous magnetic vectors, which are then used, together with the catheter advancer system, to maneuver the catheter back to a specific target. How close the catheter gets to that spot depends on a number of factors, such as whether the patient has moved, whether the prespecified catheter pivot point has moved and whether the catheter advancer system has been used to advance or retract the catheter sufficiently to allow it to get to that point. The Stereotaxis system, as a stand alone system, has stored fluoroscopic views with superimposed targets, and other visual clues, as a reference to en-

A LEFT-SIDED ACCESSORY PATHWAY REVISITED

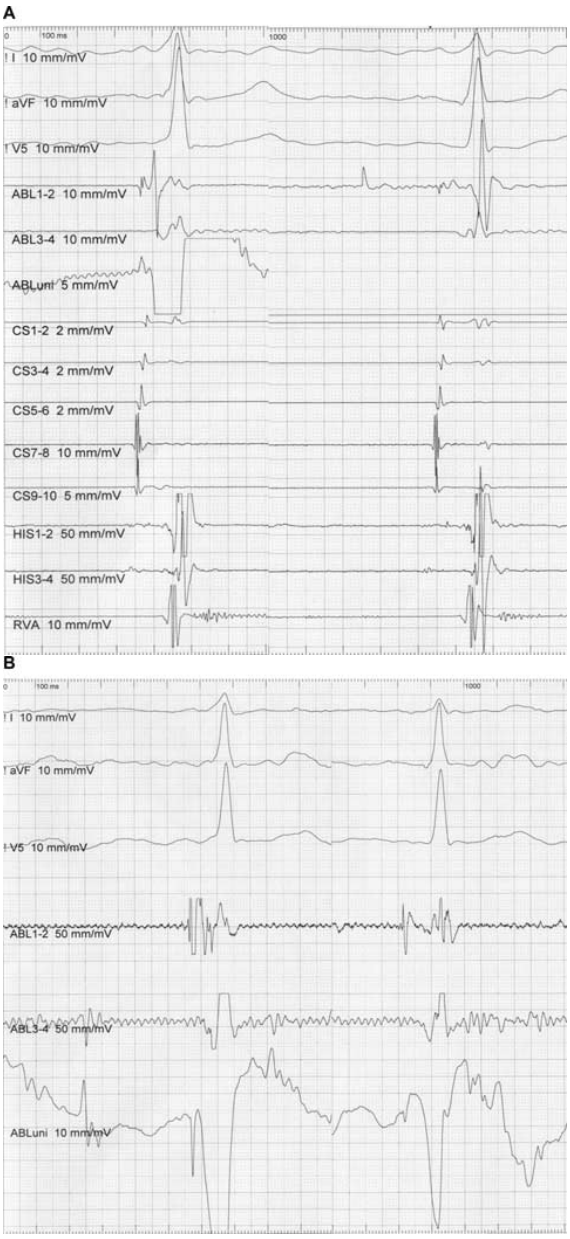

Figure 3. *(A) Electrograms from the initial successful site (application 2), before the ablation on the left, and after the ablation on the right. (B) Electrograms from the final site (application 3), before the ablation on the left, and after the ablation on the right.*

sure that the catheter returns to a given location. While reproducing the catheter movement that enabled the target to be reached, the stored image is a fairly inaccurate way of ensuring that the catheter has in fact returned to the target. Electroanatomic mapping systems compute a point in space using a magnetic, electrical, or ultrasound field, and if reference catheters have not moved, we can show with an accuracy of a few millimeters whether a catheter has returned to that point. However, with most of these systems, the catheter has to be manually returned to that point and this may or may not be easy. Combining the two systems i.e. storing the vectors used to manipulate a catheter to a point as well as accurately storing the target point would mean easier and more accurate navigation to a point, and that system is now available with the combination of the Stereotaxis system with the CARTO RMT system (Biosense Webster).

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Chapter 13

Preliminary data showing feasibility of retrograde transaortic left atrial and pulmonary vein access using remote magnetic navigation

Preliminary data showing feasibility of retrograde transaortic left atrial and pulmonary vein access using remote magnetic navigation

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Submitted

KEY WORDS

atrial fibrillation; catheter ablation; magnetic navigation; transseptal puncture

ABSTRACT

Background: Left atrial access for electrophysiological procedures may not always be possible using a transseptal approach. Other approaches need to be developed. We evaluated the feasibility of accessing the left atrium and pulmonary veins in a retrograde transaortic fashion, using magnetic navigation.

Methods: Access to the left atrium and pulmonary veins was undertaken via a retrograde approach using a magnetically enabled ablation catheter and remote magnetic navigation. Once in the left atrium we attempted to cannulate the pulmonary veins using the preset vectors in the system.

Results: In 9 consecutive patients left atrial access was successfully achieved. The pulmonary veins could be cannulated using the magnetic system and preset vectors (with or without minor modification) developed for a transseptal approach in all 5 patients in whom this was attempted. The mean time needed to advance the catheter from the aorta to the left atrium was 13.8 ± 3.6 minutes with a screening time of 4.9 ± 2.2 minutes. Subsequent cannulation of all the pulmonary veins took 1.4 ± 0.2 minutes. No complications occurred.

Conclusions: In this small, observational series, feasibility of a retrograde transaortic approach to the left atrium and pulmonary veins, using a magnetically enabled floppy catheter, was successfully demonstrated with no complications in all patients in whom it was attempted.

1. INTRODUCTION

Access to the left atrium for catheter interventions using transseptal puncture was first described in the late 1950s and early 1960s.[1-3] Transseptal puncture has increasingly been used to access the left atrium for electrophysiological procedures.[4-8] Increased experience, and newer techniques, particularly imaging, have increased the safety of this procedure, and removed some of the risks associated with this procedure.[9-11] Some contraindications remain and a newer contraindication to transseptal puncture relates to closure of atrial septal defects (ASD) and patent foramen ovale (PFO) with percutaneous closure devices.[12-14]

Standard steerable diagnostic catheters introduced in a retrograde fashion can be placed on the atrial side of the mitral annulus for ablation of accessory pathways, however there is then almost no way of manipulating the catheter further within the left atrium (LA) for atrial fibrillation ablation, or for treatment of other complex left atrial arrhythmias.[15]

The recent development of floppy magnetically steered catheters directed by the use of an external magnetic field might allow for this approach. We have been evaluating a retrograde approach to left sided accessory pathways using the magnetic navigation system.[16] We will discuss the small consecutive series in which we accessed the LA and then the pulmonary veins (PVs) in a retrograde fashion to test its feasibility.

2. MATERIALS AND METHODS

2.1 Patient Population: Left atrial access was attempted in 9 consecutive patients undergoing a retrograde transaortic approach to a left sided accessory pathway using remote magnetic navigation, for mapping of the atrial side of the mitral annulus. In 5 of these, during the waiting period after ablation of the accessory pathway, the catheter was then drawn back to above the aortic valve and the LA was again accessed from above the aortic valve, and cannulation of the PVs was subsequently attempted. Approval was given by the institutional review board of the Erasmus MC to use the system for mapping and ablation. All patients gave written informed consent.

2.2 Magnetic Navigation System: The Niobe I magnetic navigation system [16-19], combined with the monoplane AXIOM Artis angiography system (Siemens, Erlangen, Germany) was used together with the remote catheter advancer system (Cardiodrive^{TM}, Stereotaxis Inc., St Louis, MO, U.S.A.), positioned on the anterior thigh, to navigate a 4 mm tip ablation catheter (Celsius RMT, Biosense Webster, Diamond Bar, CA, USA). The magnetically enabled ablation catheter was manually advanced up the descending aorta to the origin of the left subclavian artery. Remote control of all of the components of the system in the electrophysiology laboratory

was then performed from the adjacent control room. Access to the LA via the aortic and mitral valves was attempted using the magnetic navigation system.

2.3 Accessing the left atrium retrogradely: Access was gained to the left ventricle (LV) using the technique we have used for a retrograde approach to left sided accessory pathways. [16] This was done by keeping the catheter straight and choosing a vector aimed at the mid-posterior septum in RAO and the apex in LAO, while advancing and retracting the catheter with minor modification around this (figure 1). Mimicking standard techniques was less successful in our hands, with the catheter either curling up even more with the tip moving up into the arch, or the catheter body prolapsing into the LV, while the tip remained supra-valvar. Using the catheter in this straight orientation ensures that there is little chance of coronary artery cannulation, as their initial course is more horizontal or superior.

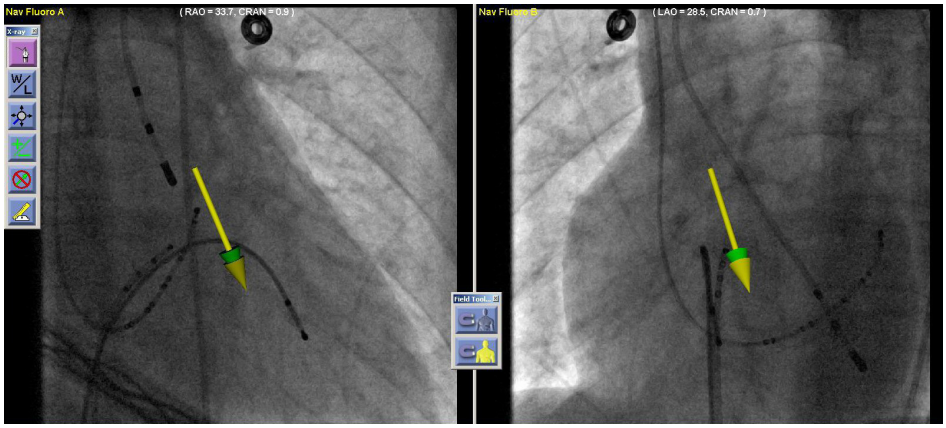

Figure 1:
This clip from the Stereotaxis screen shows 34 degree RAO, and 28 degree LAO fluoroscopic views with the selected vectors which we found most useful when advancing the catheter in a straight orientation across the valve. In the RAO view the catheter is still above the valve, while in the LAO view it has entered the LV.

Once across the aortic valve, by loosening the catheter tip from the LV apical wall and then choosing a vector aimed at the anterolateral portion of the mitral valve orifice and advancing the catheter, the floppy catheter was directed across the mitral valve into the LA (figure 2). All these vectors can be stored for repositioning if this is necessary.

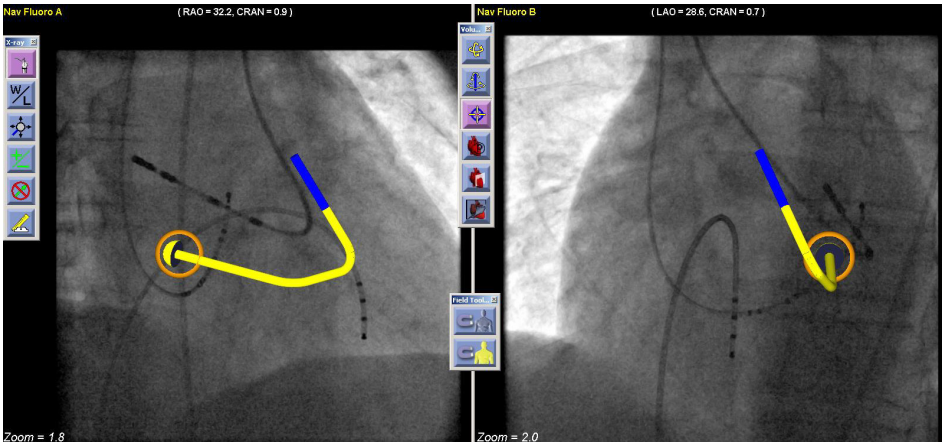

Figure 2:
Similar views to those in figure 1 showing the selected vectors for accessing the LA from the LV. In both views the catheter has already advanced across the anterolateral mitral valve commissure into the LA.

In the 5 patients in whom left atrial access was gained again during the waiting period, cannulation of the PVs was attempted using the preset vectors developed for cannulation of the PVs using a transseptal approach, without or with minor modification. We subjectively assessed catheter stability and attempted to manipulate the catheter around the ostia of the PVs, on the roof of the LA, around the opening of the left atrial appendage and around the body of the LA down to the mitral annulus. Electroanatomic mapping was not undertaken in this group.

4. RESULTS

3.1 Cannulation of the left atrium: Left atrial access was successful in all 9 patients in whom it was attempted, with a retrograde transaortic approach using magnetic navigation. In all 5 patients in whom left atrial access was again attempted during the waiting period after ablation of the accessory pathway this was successful, as was cannulation of the PVs. In no case did we fail to access the LA or the PVs when this was attempted.

3.2 Left atrial access and mapping: Once in the LA, the catheter appeared stable and could be manipulated around the ostia of the PVs, on the roof of the LA, around the opening of the left atrial appendage and on the upper parts of the septum, and anterior and posterior walls without difficulty and with apparent good stability. In our early experience, mapping closer to the mitral annulus seemed to be associated with a risk of falling back into the LV. All 4 PVs in each patient were cannulated using the preset vectors for a transseptal approach without or with minor modification (figure 3). Minor modification was required in 2 patients for the left upper pulmonary vein and in 1 for the left inferior pulmonary

vein, with a median number of 4.6 ± 0.9 vectors for all 4 veins. No complications occurred.

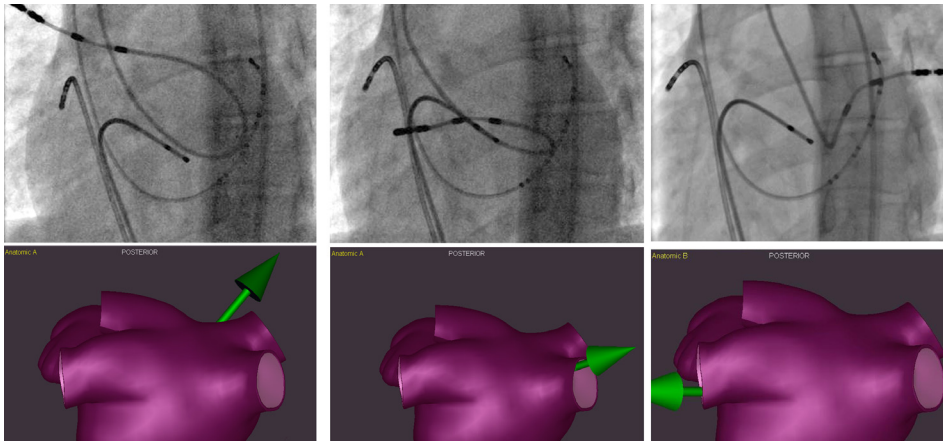

Figure 3:
This series of figures shows a fluoroscopic view, above – in all cases 28 degrees LAO, and the corresponding view from the Navigant system, below, showing the selected vector used to cannulate respectively from left to right, the right upper pulmonary vein, the right inferior pulmonary vein, the left inferior pulmonary vein and the left upper pulmonary vein. The vector has been selected using a software model of the left atrium created by Stereotaxis (the 3D anatomic model). The vectors selected are either the presets or minor modifications thereof.

3.3 Procedure and screening times: These are shown in figure 4. The procedure time needed to advance the catheter from the aorta to the LV was 4.3 ± 4.2 minutes (median 2.9 minutes, range 1.7 to 15.0 minutes) with a fluoroscopy time of 3.5 ± 3.9 minutes (median 2.6 minutes, range 0.6 to 13.6 minutes). The time required to access the LA from the aorta was 13.8 ± 3.6 minutes (median 12.7 minutes, range 11.0 to 20.0 minutes) with a fluoroscopy time of 4.9 ± 2.2 minutes (median 4.8 minutes, range 2.2 to 8.4 minutes). Once in the LA, access time for all 4 PVs was 1.4 ± 0.2 minutes (median 1.3 minutes, range 1.2 to 1.8 minutes) with a fluoroscopy time of 0.1 ± 0.1 minutes (median 0.1 minute, range 0.1 to 0.3 minutes)

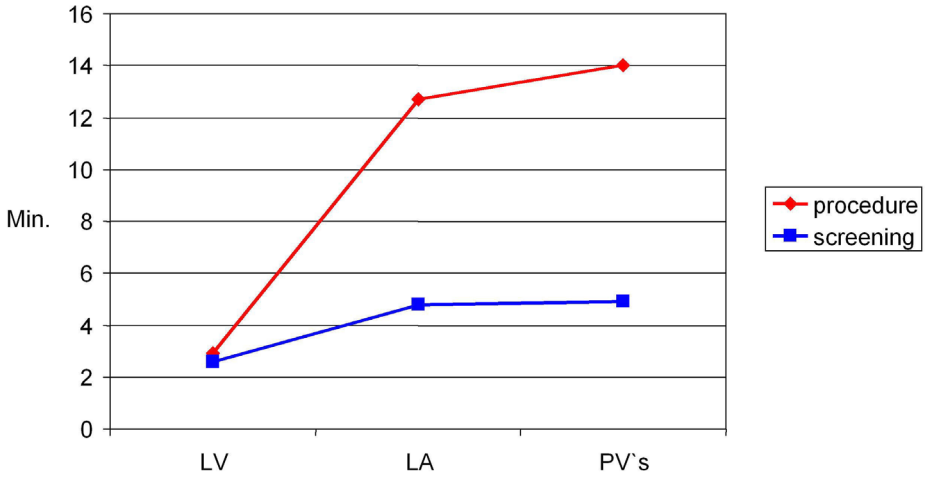

Figure 4:
Median cumulative access and screening times with a retrograde magnetic approach. Times (in minutes) are taken from when the catheter is initially positioned in the aortic root. LA = left atrium, LV = left ventricle, min. = minutes, PVs = pulmonary veins.

5. DISCUSSION

Access to the LA by transseptal puncture is increasingly being used for electrophysiological procedures,[8] and this has recently risen exponentially with the advent of a successful ablation therapy for atrial fibrillation.[4-7] Since its introduction there have been some risks associated with this procedure,[11] and some contraindications. The risks include perforation of the free wall of the heart and of the aorta,[20] air embolism,[21] and cerebrovascular accidents. Increased risk may be associated with insufficient landmarks or individual variations in cardiac position. Relative contraindications include a dilated aortic root or coronary sinus, cardiac malpositions, distorted contours of the interatrial septum and a thick or fibrosed muscular septum.[8,22] An increase in experience,[9,10] and newer techniques, particularly echocardiography, have increased the safety of this procedure, and removed some of the problems.[23] While the success rate of attempted transseptal puncture is high, usually above 95%, it occasionally fails.[9,10,24] In some patients with congenital heart disease access to the pulmonary venous atrium or to the "other" side of a baffle may also be very difficult.[15]

The increasing use of ASD and PFO closure devices for prevention of recurrent paradoxical emboli,[12-14] has led to a new contraindication to transseptal puncture. While newer occlusion devices may be made from biodegradable materials, for the present these are generally metallic. With the demonstration of a relationship between migraine and PFO, and the compelling but not yet robust potential to treat this by closing the PFO,[25] the number of young

patients who will have absolute or relative contraindications to transseptal puncture may rise in the coming years. There is a risk that this same group of patients may continue to be at risk for atrial arrhythmias.[26]

There is a need for another, non-surgical, approach to be found to access the LA, failing which an increasing number of patients who are otherwise eligible for percutaneous left atrial ablation as therapy for atrial fibrillation or another atrial arrhythmia but have an impediment to transseptal puncture, may have to forego this.

Magnetic navigation can position catheters despite difficult anatomy and maintain good tissue contact throughout the cardiac and respiratory cycles, without additional risk of perforation. [17,18] In a recent report of successful PV isolation in a porcine model, mention is made in the discussion of PV cannulation in 30 of 30 veins in 5 canines using a retrograde transaortic magnetic enabled approach.[19] We have now confirmed the feasibility in humans. The procedure and fluoroscopy times were acceptable and should decrease further with increased experience. No complications occurred and we also felt that the flexible nature of the catheter made the risk of complications lower than that when using standard catheters. Specifically we felt that using the described method that the risk of inadvertent coronary artery cannulation was lower than using either a standard catheter or a floppy catheter when the tip is prolapsed superiorly. There have been some concerns about catheter entrapment in the mitral apparatus, but to date that has not been reported. We felt that entrapment was less likely as long as with each attempt to cross the mitral valve we disengaged the magnets and allowed the catheter tip to return to the apex before trying a different vector. We did not feel that there was any more likelihood for entrapment with magnetic catheters than with standard catheters.

Limitations include that this is a small, non-randomised series. The ability to access the LA and cannulate the PVs does not necessarily mean that atrial fibrillation ablation will be possible, as this was not tested. Additional lines, especially the mitral isthmus line might also be difficult due to instability. In addition clearly only the ablation catheter could access the LA, but we felt that using intracardiac echocardiography would assist in catheter placement and ensuring stability and tissue contact. We also need to show that it will be as easy to access the LA and PVs with 8 mm tip and irrigated tip magnetic catheters which could be used in ablation within the LA.

In conclusion, this small series shows that using a magnetically enabled floppy catheter one can gain access to the LA and to the PVs using a retrograde transaortic approach. Access to the LA and PVs can be undertaken successfully in a reasonably short time. Using the approach described above and the soft magnetic catheters we feel that the risks are low. In the presence of contraindications to, or problems with transseptal puncture, left atrial electrophysiological

procedures may still potentially be possible. Further investigation is required to determine whether accurate mapping of the LA and ablation of the left atrium or isolation of the pulmonary vein ostia can also be undertaken safely and efficiently.

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Chapter 14

Ablation of a focal left atrial tachycardia via a retrograde approach using remote magnetic navigation

Ablation of a focal left atrial tachycardia via a retrograde approach using remote magnetic navigation

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Case report

A 66-year-old man who had undergone successful ablation of typical atrial flutter subsequently developed a left atrial tachycardia. A trans-septal approach was proposed, but not performed due to risk. He was referred to us with the suggestion that a retrograde procedure could be attempted using a magnetic navigation system (Niobe, Stereotaxis Inc, St Louis, MO, USA) installed in our institution.

We performed multi-slice computed tomography (CT) with three-dimensional reconstruction to allow for use of the CARTO RMT Merge system (Biosense Webster, Diamond Bar, CA, USA). The patient was sedated with diazepam and fentanyl. Heparin was used to maintain the activated clotting time of above 300 s. After placing diagnostic catheters, we approached the left atrium (LA) in a retrograde fashion using a 4 mm tip magnetically enabled ablation catheter (Navistar RMT, Biosense Webster), advancing it to just below the subclavian artery manually. The ablation catheter was then manoeuvred across the aortic and mitral valves using remote magnetic techniques developed while accessing left-sided accessory pathways in a retrograde fashion.[1] Left atrium via the aortic and mitral valves was accessed within 12 min, with 5 min and 24 s of screening. We then performed anatomic and activation mapping of the LA during tachycardia. On assessing the activation map, it was clear that the area of interest was the roof of the LA between the upper pulmonary veins, towards the right (*Figure 1*). Mapping was concentrated in this area with an adequate map of the area of interest completed within a further 15 min (*Figure 2*). A complete map of the LA was not deemed necessary. The 'design-a-line' facility was used to fill in areas on the CARTO map where points had not been taken. Points on the

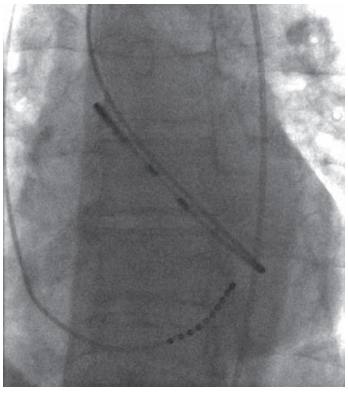

Figure 1 Left anterior oblique fluoroscopic view of the site of successful ablation with the catheter positioned in the left atrium roof via the aortic and mitral valves.

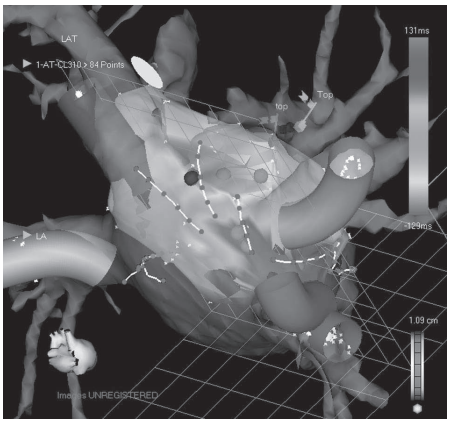

Figure 2 CARTO merge map looking from supero-posterior and slightly from the right. The red dot marks the successful ablation site. The roof of the left atrium and around the pulmonary vein ostia has been mapped, but not closer to the mitral valve. The white lines with blue dots are the 'design lines'.

design line are transferred to the Niobe system and this then directs the catheter to these positions. One could also use the 'click and go' facility for this purpose. The CARTO RMT map obtained was merged with the reconstructed CT image.

Features suggested a focal tachycardia, and we ablated at the point of earliest activation using settings of 60°C, 30 W for 60 s. This resulted in slowing (at 8 s) and termination of the arrhythmia (at 12 s) during the first application. Catheter stability was excellent. We were unable to reinduce any atrial arrhythmia even with aggressive pacing and isoproterenol, and after waiting 20 min. Follow-up to date (20 months) has shown no arrhythmia recurrence. Total procedure time was 157 min and total fluoroscopy time was 27 min.

Discussion

Trans-septal puncture is most often used for electrophysiological procedures in the LA.[2] Newer techniques and increased experience have improved the safety of this procedure and reduced some of the risks.[3] Although the success rate of trans-septal puncture is usually above 95%, it occasionally fails,[2,3] especially when repeat trans-septal puncture is necessary.[4] In some patients, contraindications may also be present. Given the number of patients presenting for percutaneous left atrial ablation, it is therefore important that alternative, non-surgical approaches be found to access the LA.

Standard steerable catheters can be placed retrogradely on the atrial side of the mitral annulus for the ablation of accessory pathways, but further manipulation within the atrium is then difficult. Magnetic navigation can place catheters, despite difficult anatomy and maintain good tissue contact throughout the cardiac and respiratory cycles, without additional risk of perforation.[1] In a recent report,[5] mentioning is made of cannulation in 30 of 30 pulmonary veins in five canines using a retrograde transaortic magnetic-enabled approach. We managed LA access in this patient and were able to successfully ablate an atrial tachycardia, thus moving a further step forward.

Conclusion

Although we would not advocate this approach as a first-line option, this case demonstrates that when trans-septal puncture cannot be undertaken, for whatever reason, alternatives exist. Although this technique proved useful in the ablation of this focal left atrial tachycardia, it is not yet clear whether ablation around the pulmonary vein ostia, using recently available irrigated tip catheters, can be undertaken using this approach.

Conflict of interest: A.S.T. and L.J.J. have received speaker's fees from Stereotaxis Inc., St Louis, MO, USA.

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Part 3

Overview

Chapter 15

Magnetic assisted navigation in electrophysiology and cardiac resynchronisation: a review

Magnetic Assisted Navigation in Electrophysiology and Cardiac Resynchronisation: A Review

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Conflicts of interest: A. Thornton is a consultant and proctor for Stereotaxis, Inc, while L. Jordaens and Erasmus MC have received a research grant from Stereotaxis, Inc.

Abstract

Magnetic assisted navigation is a new innovation that may prove useful in catheter ablation of cardiac arrhythmias and cardiac resynchronization therapy. The ability to steer extremely floppy catheters and guidewires may allow for these to be positioned safely in previously inaccessible areas of the heart. The integration of other new technology, such as image integration and electroanatomic mapping systems, should advance our abilities further. Although studies have shown the technology to be feasible, with the advantage to the physician of decreased radiation exposure, studies need to be performed to show additional benefit over standard techniques.

Key Words: Arrhythmias, catheter ablation, radiofrequency energy, magnetic navigation, cardiac resynchronisation therapy

Introduction

Where are we now in catheter ablation and resynchronisation therapy?

Catheter based ablation of cardiac arrhythmias has advanced significantly since its inception, with progress both in the technology, as well as in our understanding of both simple and complex arrhythmias. Newer approaches to ablation such as in atrial fibrillation and ventricular tachycardia, as well as more defined endpoints for these procedures, has meant that success rates, both acutely as well as in the long term, have improved. Success rates for less complex procedures such as AVNRT, accessory pathways and atrial flutter ablation are above 95%, while those for more complex intraatrial reentry, ventricular tachycardia and atrial fibrillation are, in the best hands, around 80%.

Notwithstanding these excellent results there is still a not insubstantial failure rate. In addition, in certain anatomies, such as repaired complex congenital heart disease, ablation of some arrhythmias can be extremely challenging. Besides the intellectual challenge these arrhythmias may pose, there is still a marked technical challenge in manipulating conventional catheters to sites which need to be reached. Today's catheters, while a significant advance on

prior generations, are still fairly stiff, as they use pull-wire technology to bend and straighten the catheter in a fixed curve, and require twisting of the catheter to rotate the tip. This stiffness decreases their manoeuvrability in certain situations and increases the risk of perforation when compared to softer catheters. New developments such as electroanatomical mapping systems mean that even more technology needs to be incorporated into the design of modern ablation catheters.

A recent innovation in heart failure therapy is that of cardiac resynchronisation therapy (CRT), where, in addition to the standard pacemaker or ICD leads, an additional lead is used to pace the left ventricle. In most cases the left ventricular lead is placed via the coronary sinus (CS) and its branches so as to pace the epicardial surface of the left ventricle. In approximately 90% of patients this is successfully achieved, but there may be a number of impediments to success. The anatomy of the CS and its tributaries is extremely variable, in normal individuals, and even more so in patients with underlying cardiac disease. Entering the CS os, and then manipulating the lead into the targeted side branch can be time consuming and in some cases impossible due to tortuousity or angulation of the CS or its side branches. Even if one is able to access the targeted side branch there may a high threshold or phrenic nerve stimulation. This may then require repositioning of the lead into another side branch. In CRT we have been forced to use some of the skills of our interventional colleagues to improve our success rates, most particularly by learning to manipulate coronary guidewires in order to be able to access some of the coronary veins. The CS differs significantly in its diameter from the coronary arteries and thus the use of guidewires is more difficult. Invariably after one has used a curve to engage a particular side branch, a different curve to the tip of the guidewire might be useful to advance the guidewire further. Using the "normal" guidewire this is not possible without removing and reshaping it. This may either not be possible or extremely time-consuming. Technology has developed significantly since the inception of this therapy, with the development of better leads and improved delivery systems. The search continues however for further improvement in success rates, as well as for a decrease in procedure, and associated fluoroscopy time.

Of course, whether it is a catheter ablation or CRT, the operator is standing, or perhaps sitting next to the patient, wearing a lead apron, but still being exposed to radiation. The risk from radiation imposed by newer X-ray systems is significantly less than with older systems, but we should still strive for less, both for the patients and of course, with the cumulative exposure, for ourselves. The stress imposed on the musculoskeletal system, particularly to the lumbar spine, by the standing and the weight of the lead apron has caused a premature end to some careers.

What alternatives would we like to have?

This is by no means an exhaustive list, but amongst those to be considered are:

- More steerable and softer catheters which could be manipulated to previously inaccessible or markedly problematic areas while improving safety.
- Catheters which could be manipulated with better precision so as to improve the quality of arrhythmia mapping.
- Coupling these desired alternatives with the latest technology, such as image integration and electroanatomic mapping, to increase success rates in the therapy of increasingly complex arrhythmia substrates.
- New guidewire technology to allow access to difficult CS anatomy and allow delivery of pacing leads to these areas.
- A system which would reduce the X-ray exposure of the operator and would improve operator comfort and safety. A system which would allow us to perform the procedure remotely from a comfortable chair in the control room would be ideal.

What is magnetic assisted navigation (MAI)?

One of the options which may provide a solution to some of the concerns and give us some of the alternatives discussed above is magnetic assisted navigation. A system has been developed which uses a powerful external magnetic field to orientate tiny magnets contained in the tip of extremely flexible catheters or guidewires with the large external magnetic field. Orientating these tiny magnets points the tip of the catheter or guidewire to where you want it to go, and by using an advancer/retractor system the catheter or guidewire can then be manoeuvred around inside a cardiac chamber or a vessel, such as the coronary sinus or a coronary artery. It is important to emphasise that the external magnetic field does not pull or push the tiny magnets and the catheters or guidewires in which they are contained. By understanding the physical characteristics of the catheter or guidewire, and how it moves in the heart or vessel, software can be developed to allow the cardiologist to direct the movement of the tip of the catheter or guidewire to access the region of interest.

Magnetic assisted navigation - the system

The basic system developed by Stereotaxis (St Louis, MO, USA) for magnetic assisted navigation (MAI) consists of a number of different parts:

1. The Niobe system (Stereotaxis) consists of 2 large permanent external neodymium-iron-boron magnets located on both sides of the patient table (**Figure 1a and b**). In the Niobe 1 iteration these can only be swung in (active navigation) or stowed, while in the Niobe II the magnets have a different housing and can also be tilted to allow for more angulation of the single plane C-arm imaging system. The magnetic field generated by interaction of these two magnets forms a uniform field of 0.08 tesla (T) within a spherical volume with a diameter of 15 to 20cm; sufficient to encompass the heart when the patient is properly positioned.

Figure 1a: The Stereotaxis room with the Niobe I magnets and single plane C-arm. The limited angulation of the C-arm can be seen. In this case CARTO RMT is being used to map. As can be seen, all aspects of the study are being performed from the control room. There is a nurse maintaining contact with the patient and monitoring the patient's haemodynamics.

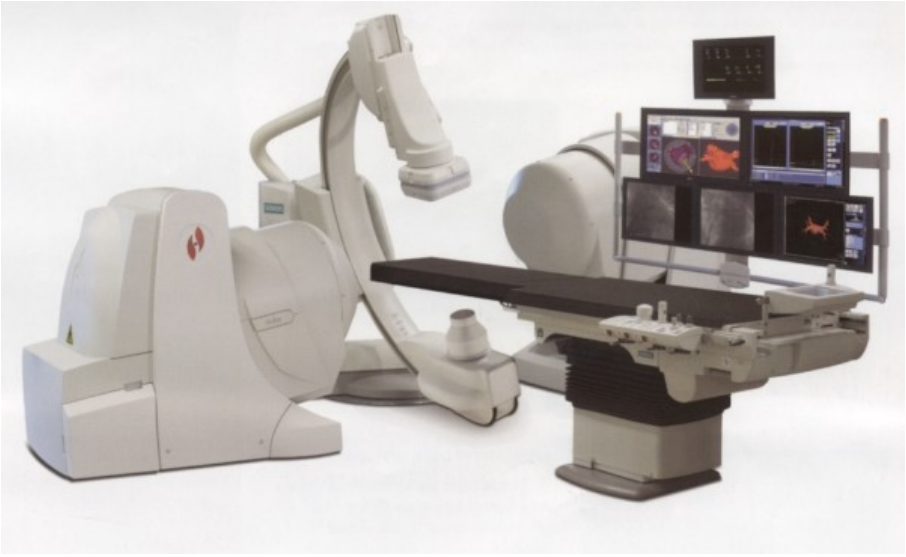

Figure 1 b: Niobe II with magnets which can be tilted thus increasing the angulation possible with the C-arm.

2. The Navigant system (Stereotaxis) is the computerised graphical user interface system and includes the software used for image integration, and for control of the magnetic fields that orientate the catheter within the heart (**Figure 2**). Software has been developed which, by understanding the characteristics of the catheter or guidewire and how it moves in the heart or vessel, allows the cardiologist to direct the movement of the tip of the catheter or guidewire to access the region of interest. The operator can access an area of interest using either vector based navigation or target based navigation. In vector based navigation the operator tells the system, by drawing a vector in virtual 3D space on the computer, what orientation of the magnetic field he requires. In target based navigation a target is placed on a specified point using the stored orthogonal fluoroscopic views, and the system then calculates the vector required to access this target. Each time a vector is selected or a target is marked, the computer sends information to the magnets which changes their relative orientation, and with it the orientation of the uniform magnetic field in the chest, so that catheter orientation is then changed within a matter of a few seconds. The software contains a number of preset vectors selected by the manufacturer, after careful appraisal of multiple CT images and reconstructions, for positioning the catheter at various anatomic landmarks. In addition the software can be used to automatically map various chambers of the heart.

3. Once the catheter is orientated it may need to be advanced or withdrawn in order to approximate the area necessary. This is done using a simple mechanical advancer, the catheter advancer system (Stereotaxis) (**Figure 3**). At present a commercially available advancer system is only available for use with ablation catheters. Guidewires need to be advanced and retracted by hand, although we and others have modified the present system to also be able to advance and retract guidewires remotely. A commercial advancer system for guidewires is in development.

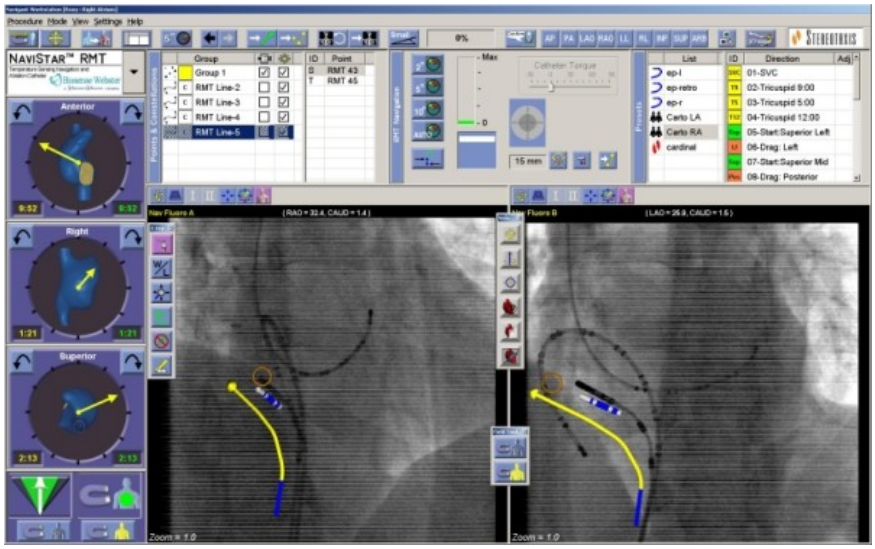

Figure 2: The Navigant screen. The fluoroscopic images at the bottom (RAO on the left and LAO on the right) can be stored at the start of the procedure, but in this case have been recently updated. The yellow line is the virtual catheter which the software has placed on the image. The blue and white catheter tip is the virtual catheter which the CARTO system places in the Navigant screen. As can be seen the virtual catheter is overlying the actual fluoroscopic catheter shadow. The other features on the screen are aids to navigation.

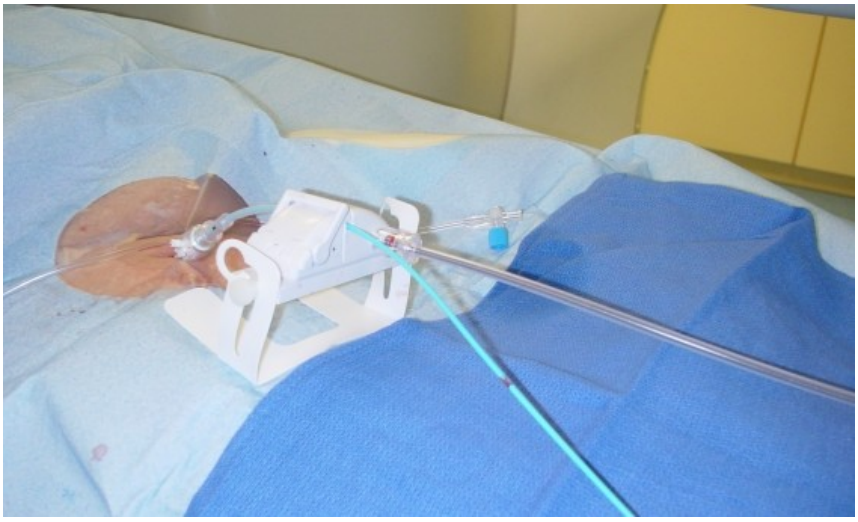

Figure 3: The catheter advancer system. The catheter runs through this simple mechanical cogwheel system and advances or retracts depending on the direction of movement of the cogwheel. An adapter connects the catheter advancer to the sheath to prevent prolapse of the catheter between the two.

4. The next parts of the system, and of great importance, and the reason for all the above complex technology, are the electrophysiology ablation catheters and the guidewires. These are extremely flexible distally, especially the distal shaft of the ablation catheters, and have tiny magnets (single or multiple in various configurations) inserted in their distal portion (**Figure 4**). The catheters and guidewires are made either by Stereotaxis or partner companies.

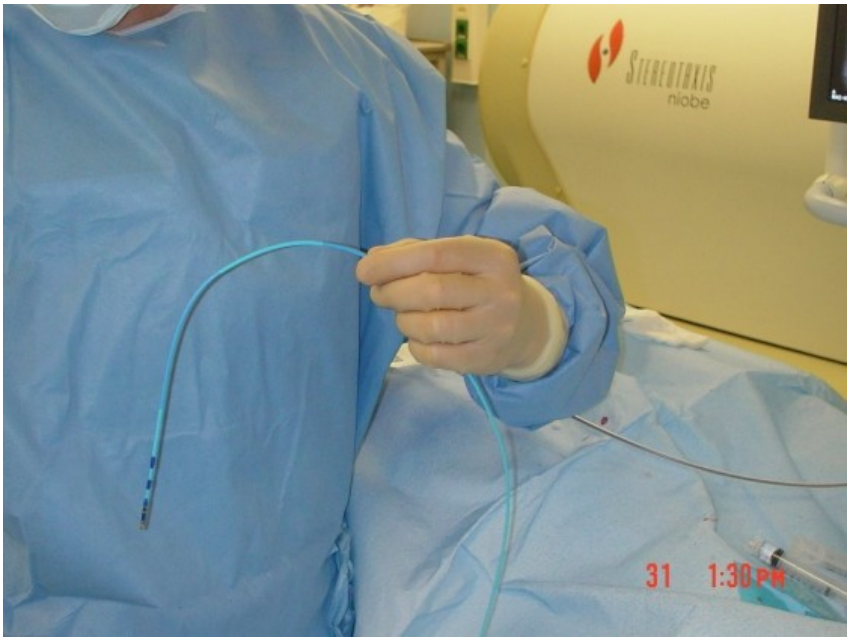

Figure 4: A magnetic catheter outside the magnetic field. It is extremely flexible. There are magnets in the tip and underneath the two blue markers on the distal shaft just proximal to the tip.

The latest catheters have 3 tiny magnets distributed along the distal shaft and the tip of the catheter to increase responsiveness of the catheter to the magnetic field generated. The maximum tissue force which can be applied by one of these flexible catheters is less than the average, and significantly less than the maximum which can be applied using a standard catheter.[1] It would appear almost impossible to perforate a vessel or chamber with one of these catheters, and this has not been described to date. At present only a 4mm tip radiofrequency ablation catheter is available, but irrigated RF, and 8mm tip RF catheters are due for release within the next year. Already available are catheters which can be used with an electroanatomical mapping system (CARTO, Biosense Webster, Diamond Bar, CA, USA) - see below.

The initial guidewires available were essentially standard floppy PTCA guidewires to which a magnet had been attached to the end and although usable, were not ideal. The newest generation of guidewires have been better designed to work with the system and retain a fairly floppy tip with a magnet, but have significantly more support - very useful when trying to track an LV lead over the wire into a CS side branch.

5. Of course the system is combined with an X-ray system - mainly a monoplane unit because of the limitations imposed by the magnets, although a biplane system can be installed for use when

the magnets are stowed and not in use. Because of the magnets, the rotation of the imaging system is limited to approximately 30 degrees RAO and LAO in Niobe I and nearly 45 degrees with Niobe II.

6. Finally, an electroanatomic mapping system and image integration have also been integrated with the system both for ablation, and , in the case of image integration, for coronary artery and coronary sinus interventions.

a. In the case of ablation this is with the CARTO system - now known as CARTO RMT (**Figure 5)**, which has been specifically redesigned to work in the magnetic environment of Stereotaxis. CARTO RMT includes all the latest updates such as CARTO Merge, where a 3D reconstruction of a CT or MRI can be integrated into the electro-anatomic map. With the CARTO integration there is communication between the two systems allowing for real time catheter orientation and positioning data to be sent from CARTO to the Stereotaxis system, and for the catheter tip to be displayed on the saved images stored on the Navigant system. This permits tracking of the ablation catheter without having to update the radiographic image as often. Magnetic vectors can also be applied from the CARTO screen. A feature called design line can be used to send a line of points - either for mapping a specific area, or potentially as a line of ablation points. "Click and go" is a utility allowing for one to click on an area of the map to set a target and have the system guide the catheter to this point. As Stereotaxis and CARTO have feedback integration, the CARTO system is able to feed back to the Stereotaxis system if the exact point is not reached, allowing for further automatic compensation by the software until the desired point is reached.

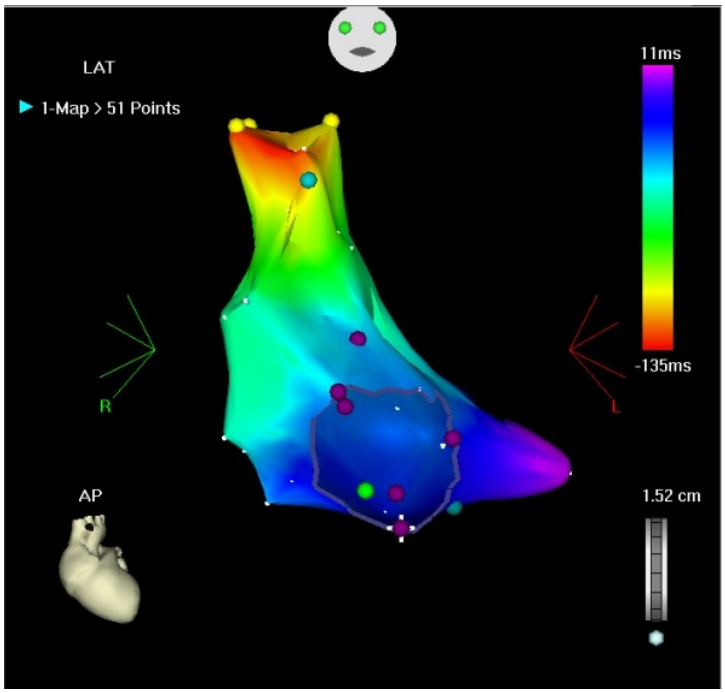

Figure 5: CARTO RMT - a 51 point map which reflects the right atrial anatomy reasonably well. This map was made in 10 minutes and shows a focal SVC tachycardia.

b. In the case of CRT or interventional coronary work PAIEON (Paieon, Haifa, Israel) (**Figure 6)** is a system which allows one to make a 3D reconstruction of a vessel from 2 or more radiographic views. Once this has been done virtual fly-though views can be generated which, after registration of the catheter tip on the image, assist in navigation of the catheter up to and into a side branch os.

Figure 6: PAIEON - This image again shows the Navigant screen with the reconstruction overlaid on the radiographic images saved during the angiogram. The image above the LAO radiographic image shows the 3D reconstruction and the image above the RAO shows a fly-through image from the reconstruction. This is then used to navigate the magnetically enabled guidewire into the CS side branch. The other features which can be seen are aids to navigation.

What does it offer us?

All the components of the MAI as well as the X-ray, ablator, and stimulator can be operated from the control room. Therefore, after initial placement of sheaths and catheters, the entire procedure, in the case of ablation, can be performed remotely from the control room. This eliminates the exposure to radiation for the physician and also decreases the strain from standing next to the bed for long periods wearing a lead apron. In the case of CRT the benefit of remote navigation is less as most of the procedure cannot be performed with Stereotaxis and at present the guidewire still needs to be advanced and retracted manually. The latter problem will be solved by the availability of a commercial advancer system.

Using the above components it is possible to move the catheter or guidewire in extremely small increments of 1 degree or 1mm within the heart and vessels, making mapping more accurate. All vectors and targets selected can be saved, as can relative positions of the catheter advancer system, allowing one to reproducibly revisit specific areas in the heart or side branches of vessels. Because of the flexibility of the catheters, perforation is extremely unlikely and has not been described to date.

Studies on magnetic assisted navigation to date

The studies to date on using MAI in catheter ablation, CRT or coronary intervention have largely been feasibility studies and there have been no large-scale comparisons with manual manipulation of catheters or guidewires. Initial studies have also tended to focus particularly on mapping or ablation of less complex arrhythmias, where the advantages of MAI would be more difficult to demonstrate. Given that a recurring theme in all the papers is that there is a steep learning curve, it would also seem warranted to get over this first before comparing this new technology with established therapies. We will review here the studies published to date as well as discuss some of our own feelings on MAI.

Catheter ablation

The initial studies in catheter ablation were performed with an older 0,15 T magnet version of the system, initially in animal, and then in human studies.[1,2] These studies were mainly mapping studies, where floppy magnetically enabled catheters were navigated to pre-specified sites with good success, both on the right and left sides of the heart. The electrogram signals obtained were comparable, as were the stimulation thresholds. In addition catheter stability was thought to be good during the cardio-respiratory cycle as well as during tachycardia. In one of these studies 13 patients with SVT were studied.[2] Of these 5 had manifest accessory pathways, right lateral in one and left sided in 4 (3 were mapped transseptally, and 1 retrograde), while 7 were AVNRT and 1 was flutter. 2 of the WPWs and 5 patients with AVNRT underwent successful ablation.

Using MAI for ablation of AVNRT has been shown to be feasible without complications in almost 100 published cases, with similar procedure times and success rates. In those where there was a comparison with standard catheters there was significantly reduced radiation exposure for the physician.[3-5] Even in the early studies without comparison to standard catheters it immediately became clear that physician fluoroscopy times are significantly reduced as the physician is exposed only during advancement of catheters to the heart. These procedures are already those with fairly short fluoroscopy times, and the added benefit in procedures commonly associated with much longer fluoroscopy times is obvious. Of importance is that even at this early stage of our experience fluoroscopy times for the patients were not prolonged and it can be anticipated that these will shorten even further, especially when the system is used together with non-fluoroscopic electroanatomic mapping systems. Catheter stability, even during junctional rhythms, appears to be excellent. In one of the studies there was a trend to decreased radiofrequency ablation time.[5] Slow pathway modification has even been performed using this system in patients with somewhat more challenging anatomy such as with a persistent left sided SVC.[6]

Very little has been published to date on ablation of accessory pathways, however some of this data has been presented in abstract form. The usual variety of accessory pathways have been ablated using MAI including anteroseptal accessory pathways,[7] with success rates generally as expected from manual catheters. Mapping may in fact be enhanced by the ability to move more precisely around the annulus of either the tricuspid or mitral valve. The ability to return to a given point accurately using stored vectors adds to the ease of mapping, and given the fact that less force is applied with these catheters the risk of mechanical block is probably decreased. Catheter stability has again been seen to be excellent. We have shown that a retrograde approach to left sided accessory pathways is feasible and gives us alternatives when a transseptal approach cannot be used for some reason.

We have published a study on the use of MAI in RVOT VT, as well as a case study we used the system to ablate an idiopathic left ventricular fascicular VT.[8,9] When ming RVOT VT ablations we found that mapping of the RVOT was markedly facilitated of the remote magnetic navigation, enabling very fine movements to be made in order to ze activation- and pacemapping. In addition, the use of such a floppy catheter avoided the er induced extrasystoles that are sometimes troublesome during these procedures. The are good and again physician fluoroscopy time was markedly reduced. We have not d ischaemic VTs with this system, but have used it for the initial mapping, in the RV and oth retrograde and transseptal. A retrograde approach to left ventricular VT appears a little difficult because of catheter stability across the aortic valve, however the transseptal ich has given excellent maps with good resolution.

Greenberg et al first published results of pulmonary vein isolation using the magnetic n in an animal model.[10] They successfully isolated the upper pulmonary veins in 7 dogs it complication or long term stenosis using a transseptal approach. Because these lures were performed remotely the radiation exposure of the physician was significantly d. They also noted that they had been able to navigate to 30 of 30 pulmonary veins oted in 5 dogs using a retrograde approach. Pappone et al have described in detail their human experience using Stereotaxis together with the CARTO RMT system to perform nferential pulmonary vein ablation.[11] They found the system very useful for making the while acquiring more points in less time than would have been possible doing a manual They felt that the initial learning curve was extremely steep but fairly short and that despite procedure times in this initial group of patients, that mapping and ablation times were r and that they had a similar success rate. Ablation times for the right pulmonary veins ularly were shorter than when using standard catheters. There were no complications. They at using the system made the ablation potentially less operator dependent, although this is to be proven.

Our own experience, part of which is detailed above, is now over a 100 cases, and vide is over 2000 cases. The only limiting factor to routinely performing other types of ons (typical atrial flutter, AF ablation, ischaemic VT, etc) is the lack of availability of ed tip, and 8mm tip ablation catheters. As mentioned above, we have also used the system ively for mapping in combination with CARTO RMT and have found it extremely le, with the ability to easily form accurate and detailed maps both in the atria and the cles. The possibility of using a retrograde approach for ablation of atrial fibrillation and ex corrected congenital heart disease is being explored.

ac resynchronization therapy

MAI is increasingly being used for positioning a guidewire in the target CS side branch in placement of the left ventricular lead in pursuit of CRT. In a small published series[12] we d that using MAI and the first generation of guidewires, procedure and fluoroscopy times similar, as was success compared to manual placement of the guidewire. Pacing and g characteristics did not differ between the two groups. No complications occurred. We also used MAI for placement of LV leads without the use of a CS sheath.[13] This may be in decreasing the hardware use and cost as well as decreasing the risk of perforation of the ide of the heart or coronary sinus dissection. While this approach is feasible, the procedure the presently available guidewires is longer, with more radiation exposure for the patient, t the physician. The difficulties with the original guidewires was that positioning in the d side branch was somewhat complicated by a lack of stiffness of the guide wire with buckling at the SVC - right atrial junction and within the right atrium. Two further

ems with using MAI for CRT are that the magnets are unfortunately situated directly where ould stand and thus cause an impediment, and that at present there is no commercially ble guidewire advancer. The latter means that someone has to manually advance and t the wire to command. The availability of an advancer will significantly improve this on.

We are presently assessing the utility of the PAIEON system in conjunction with newer to improve the success rate of side branch cannulation, with a decrease in fluoroscopy A further potential advantage of MAI is that the vectors used to access a particular side n can be stored thus allowing for investigation of multiple side branches for optimal oning without extracardiac stimulation, and then a rapid return to the best site. This needs e confirmed in clinical investigation.

ıary intervention

We have not gone into detail here as this is beyond the scope of our interaction with the n. The initial problems we experienced with the guidewires have to some extent been red by the interventional cardiologists, who were able to access difficult anatomy with the wire, but were then unable to deliver balloons and stents to this area. Newer wires are oming this problem and there are an increasing number of publications regarding the utility AI for coronary interventional work.[14-17]

lusion

We have, in this review, highlighted the present situation with regard to catheter ablation rdiac arrhythmias and cardiac resynchronization therapy, and where we might like vements. We have also provided an overview of what magnetic assisted intervention is and uipment which is presently available to perform this. In addition, we have reviewed the hed literature and hopefully given an insight into the experience with this new technology. nportant to emphasise that the initial enthusiasm for this technology needs to be reinforced y large trials in experienced centres comparing it to accepted practice.

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Chapter 16

Advances in the approaches to ablation of complex arrhythmias

Advances in the Approaches to Ablation of Complex Arrhythmias

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Ablation of Complex Arrhythmias. A complex arrhythmia is one where successful ablation represents a serious challenge to the treating physician, and in this situation an advanced solution such as the combination of imaging with mapping and the ability to deliver a newer energy form using remote navigation may be a combined option some may wish was presently available. As will be discussed, there have been many advancements in the armamentarium of the electrophysiologist, and the above scenario may not be too far removed. This is not an exhaustive review, but serves to highlight some of the issues. Hopefully some, if not all, of the advances discussed will assist us in improving success rates, while decreasing risks and complications. The ability to allow less experienced and busy electrophysiology centers to perform complex ablation with similar success and risk as more experienced labs may also be a possibility. *(J Cardiovasc Electrophysiol, Vol. 18, pp. S2-S10, Suppl. 1, January 2007)*

catheter ablation, ventricular tachycardia, voltage mapping, interventional navigation, magnetic navigation, atrial fibrillation, atrial tachycardia

Introduction

The topic of this manuscript begs the questions: What are advances and what is complex?

The definition of *complex*, or difficult, is not defined and will vary from center to center. Some have suggested its use for redo ablations using advanced mapping after failed conventional ablation,[1] others as patients where more than one arrhythmia is present,[2] and yet others as ablation resting on anatomic considerations where extensive lesions are required.[3] Cosio et al. described complex re-entrant circuits as those that demand of the electrophysiological team a deep knowledge of anatomy and a great deal of experience in the correlation of activation patterns with anatomic landmarks.[4] Undoubtedly, everyone will have his or her own opinion, and it could be defined merely as a case in which successful ablation represents a serious challenge to the treating physician. Complexity would seem to relate best to two areas: substrate complexity and intellectual complexity. Substrate complexity includes normal but challenging anatomic areas such as the left atrium, small hearts such as in children, and also altered hearts either due to disease, surgery or both (e.g., corrected congenital hearts). Substrate complexity may also relate to areas where pathological structures lie close to normal structures, for example septal accessory pathways.[5] The ability to create complete linear lines of block is increasingly required for ablation of arrhythmias and presents both an anatomical and, frequently, an intellectual challenge. Substrate complexity also relates to unstable arrhythmias, either hemodynamic instability or arrhythmias that are difficult to initiate or maintain. Intellectual complexity relates partly to the number of channels required to be displayed on an EP system in arrhythmias where the circuit itself is complex. In addition, the entire circuit is not always endocardial, but may be subendocardial or even epicardial, or there may not be adequate access to be able to record electrograms at all sites. In these cases, it can be an intellectual challenge to picture the focus or circuit in a particular arrhythmia.

The definition of *advances* is also a personal one and depends from where one is starting. If one only has a limited recording system, then a simple mapping system is advanced, while if one already has a mapping system, then advanced is perhaps the combination of imaging with mapping and the ability to deliver newer energy forms using remote navigation. In both cases the aim is to improve ablation outcome while improving safety. The focus of this paper will be on various techniques that may be used, singly or in combination, in complex cases of arrhythmia.

While we are looking to improve outcome and safety, it should not be forgotten that one aspect of safety is a decrease in fluoroscopy exposure for patient and physician. Long fluoroscopy times are associated with a small but measurable increase in the long-term risk of malignancy,[6] and keeping this to a minimum is essential both for patient and staff.

In a recent editorial it was asked whether many of the modalities mentioned here should be considered as "tool or toy." It must be remembered (to paraphrase) that many toys of yesterday are the tools of tomorrow.[7]

It would be presumptuous to attempt to cover all aspects of these topics, so only a few have been selected. These include advances used in the treatment of intra-atrial re-entry (predominantly post surgical congenital heart disease), atrial fibrillation ablation and ablation of ventricular tachycardia, particularly of ischemic origin.

Imaging

Perhaps the dream of all electrophysiologists is to have good imaging. We have adapted over the years to the use

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of fluoroscopic images and have become relatively adept at interpreting two-dimensional (2D) images in combination with electrogram signals to tell us where we are in the heart. Fluoroscopy does not show us complex anatomy and anatomic variations though and is unable to show whether lesion sets are contiguous in order to form complete lines of block. Use of a model (computer generated), or better still actual anatomy, to show both spatial and activation detail simultaneously would obviously be enormously helpful (Fig. 1). Clearly, there are advances in imaging that are taking us further in the treatment of arrhythmias, not only by allowing for treatment of ever more complex arrhythmias, but at the same time by improving the safety of these same ablations. They also decrease radiation exposure for both patient and physician, which can be substantial in ablation of complex substrates.[8]

Nonfluoroscopic Mapping Systems

The arrival of nonfluoroscopic mapping systems, roughly 10 years ago, was one of the initial developments that allowed for advances in cardiac mapping. CARTO (Biosense-Webster, Diamond Bar, CA, USA), RPM (Boston Scientific, Natick, MA, USA), LocaLisa (Medtronic, Minneapolis, MN, USA), and EnSite-NavX (St. Jude Medical, St. Paul, MN, USA) have all been used to allow for positioning of catheters in virtual three-dimensional (3D) space in an online fashion with decreased use of fluoroscopy and with enhanced safety of procedures.[9,10] All of these systems have been well described elsewhere, as have their advantages and disadvantages,[11] but all of these mapping systems primarily require catheter movement to form geometry and cannot predict anatomy on their own. It has been increasingly realized that the 3D geometry created was definitely virtual and very operator dependent; and they have not been as effective as initially thought, especially in preventing some complications, e.g., pulmonary vein (PV) stenosis during PV isolation procedures.[12] The 3D surfaces drawn by these maps rely on detection of the catheter tip, and the surface is formed by the maximum excursion of the catheter within the chamber of interest.[13] If insufficient points are taken in forming a map the map will not be accurate and may underestimate the chamber size and be of little use. If sufficient force is applied, then the chamber may well become deformed, and thus the surface and volume will be an overestimate of the reality.[14] It is important to remember that the information put into a mapping system determines what it puts out. Thus, in nonanatomic ablation with re-entry, an intimate knowledge of electrophysiological principles is still required to differentiate from any number of potential circuits. For example, in corrected congenital hearts where typical isthmus-dependent flutter and one or more actual or potential scar re-entry circuits may coexist, entrainment maneuvers are often necessary. Conversely, in some cases where entrainment is possible over a wide area, a mapping system is very useful for delineating a narrow isthmus for ablation. A mapping system is often very useful for delineating conduction block over an isthmus line, especially in the case of a nonconventional isthmus.[15] In some cases, though, fluoroscopy may still have some benefit while using a mapping system, for instance in assisting with localization of the true PV ostium—left atrium (LA) junction,[16] although real-time image integration and other modalities, such as impedance maps, may be useful in this context. Some systems are ideally used with hemodynamically stable, sustained tachycardias, e.g., CARTO, NavX, and RPM, while others are suited for single beat mapping or mapping of unstable tachycardias, e.g., EnSite.[1] While some studies have continued to show relatively long procedure and fluoroscopy times, these have been attributed to the complexity of the cases being attempted. In direct comparative studies the procedures are not prolonged, but fluoroscopy times are significantly shorter than those where fluoroscopy alone is used, even for relatively straightforward procedures such as AVNRT and AVRT.[17] This benefit is even greater in more complex procedures such as atrial flutter where there is also relative cost neutrality in certain cases.[18] Despite some remaining questions, groups still feel that these mapping systems provide significant benefit, particularly in the congenital heart disease patient,[1,19] where anatomical and intellectual challenges are often severe and combined.

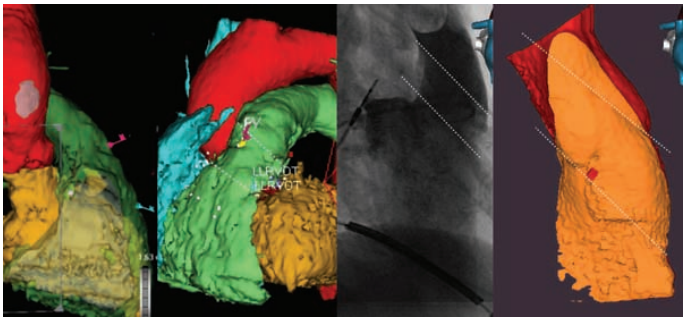

Figure 1. *This figure is in four sections with the left two sections showing a 3D reconstruction from a multislice CT in right lateral and then LAO views, showing how the RVOT (in green) curves around the left ventricular outflow tract (in yellow) and aorta (in red) such that the "septum" is not in a single "flat" plane as suggested by the angiographic image, but actually runs from the anterior RVOT inferiorly to the posterior RVOT superiorly. The course of the RVOT is highlighted by the dotted lines in the three images on the right. The impression of the aorta can also be seen on the virtual endoscopic view on the far right.*

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Preoperative Standalone CT and MRI Imaging

The recent use of CT and MRI as stand alone modalities has reminded us of the importance of anatomy and anatomic variables, for example, in LA-PV anatomy. They have also helped in the planning of ablations in more complex anatomy by providing road maps for the procedure.[20] While CT is technically simpler in that it is quicker and easier to obtain images of the beating heart, MRI potentially has more applications. MRI has the ability to obtain images with similar spatial resolution and detail to those obtained with CT, without the ionizing radiation or nephrotoxic contrast agents.

Interventional Cardiac MRI

The development of MR intervention means that procedures may, in the near future, be guided by MR, thus obviating the risk from ionizing radiation. In the case of electrophysiology, more work needs to be done on MRI compatible electrodes, but these are in development[21] while other technical challenges, such as real-time multislice acquisition and 3D display, amongst many others, still remain. A number of preliminary studies and a limited number of cases have been performed using these systems. In the interim, a number of hybrid X-ray MRI (XMR) suites combining these technologies have been installed.[21,22]

Image Fusion with Nonfluoroscopic Mapping Systems

The ability to combine CT or MRI reconstructions with nonfluoroscopic mapping systems, such as with CARTO in CARTOMerge, and with the EnSite-NavX system with DIF (digital image fusion) has further improved the accuracy of the virtual anatomies on which electrophysiologists are working, and allows for real-time navigation in these improved virtual anatomies. DICOM images are imported into a mapping system, following which software, as has been described elsewhere,[3] is used to segment the 3D geometries of the different cardiac chambers from the volume as a whole. Further software is then required to perform registration, which performs a fit between the electroanatomical map formed and the 3D reconstruction. This is usually performed by linking a set number of points on both images that are easily identifiable (landmark registration), followed by surface registration in order to create the smallest average distance between the two data sets. There are limitations to these systems, and while accuracies in the order of a few millimeters can be obtained (with surface to surface errors of 2–3 mm[3,14]), these levels of accuracy cannot be reproduced in all cases. A number of factors contribute to inaccuracy in image registration: inaccuracies in the electroanatomical map; inaccurate or poor quality scans; physiologic differences such as different rhythms during the scan and the electrophysiological study; differences in the respiratory phase at which images are acquired;[23] changes in fluid status; and registration errors. As mentioned, some of the differences in registration may occur due to incorrect identification of registration points on either the scan image or the electroanatomical map made and may be less with the use of certain structures such as the aorta,[24] or possibly other vascular structures such as the venae cavae, the pulmonary artery, or PV branches.[14] Solutions may exist in being able to use CT/MRI images overlaid with fluoroscopy and then combined with nonfluoroscopic mapping systems, further increasing the accuracy of maps.[25,26] Complications frequently relate to extracardiac structures,[27] and the ability to include the esophagus, phrenic nerve, and coronary arteries on reconstructions made using CT or MRI may further improve safety by decreasing complications. What we do not have in large numbers are trials with image integration in nonfluoroscopic mapping systems that confirm the impressions noted above. Early studies using these newly available integrated image and mapping systems have not confirmed significantly shorter radiation times nor have they shown improved outcome, but these have been mainly feasibility studies.[28] What we hope is that being able to navigate an area like the narrow ridge between the left-sided PV and the left atrial appendage will prove useful and improve outcome while decreasing complications such as perforation of the left atrial appendage (LAA) or ablation within the PV in an attempt to avoid the LAA. Newer software versions are also able to show impedance maps and fractionation and dominant frequency maps in atrial fibrillation—all utilities to improve safety and improve success rates particularly as regards AF ablation.

Intracardiac Echocardiography (ICE)

ICE allows for real-time 2D imaging of anatomy with the possibility for some assessment of catheter position, catheter-wall contact and for controlling delivery of energy. ICE has proven very useful in positioning mapping and ablation catheters relative to the PV ostia.[29] It has already been used to assess both anatomy and lesions formation, particularly when combined with the use of myocardial contrast agents.[30,31] Both radiofrequency and cryoablation lesions can clearly be visualized, and this technology could be used to confirm positioning of lesions so as to ensure complete linear lesion sets are formed. While on-line 3D transthoracic and transesophageal echocardiography is already available and proving useful,[32] on-line 3D intracardiac echocardiographic imaging is still in development. When available, it could herald a new era in real-time, real anatomy imaging in electrophysiology. At present, 3D-ICE requires off-line reconstruction and thus has less utility than other 3D image sets.

Intracardiac MRI

In a similar way to intracardiac ultrasound, intravascular and, more particularly, intracardiac MRI may also prove useful in the future as a method of obtaining real-time 3D anatomic images of the heart. In addition, its ability to characterize tissue may also be extremely valuable in real-time assessment of lesion formation allowing for formation of linear lesions without gaps. Following the evolution of lesions during ablation may confirm that sufficient energy is given without causing too much damage, in order to prevent the occurrence of complications. Already, MRI has been used to assess lesions quantitatively as well as qualitatively after ablation,[33] and intravascular MRI has been used to assess vessel wall histology.[34]

Rotational Angiography

While high speed rotational angiography may be useful for the coronary arterial and venous anatomy,[35] it is unlikely to be useful for imaging of the chambers.

Real-Time 3D Imaging

The advent of increasingly sophisticated imaging forms with improvements in echocardiography, CT, and MRI have enabled us to acquire reasonable online 2D images using echocardiography, and good 3D off-line imaging using CT and MRI. However, the ultimate goal must be on-line, real-time 3D imaging that we can use to navigate through the heart, to position our catheters, and to visualize our lesions.[28] In addition, the ability to show myocardial contraction, viability, scar, and other physiological parameters may further enhance the utility of and may possibly replace some features already present in the nonfluoroscopic mapping systems.

3D Image Visualization

Of course, the problem with any 3D image is projecting it on a 2D screen, where it undoubtedly loses some of its potential. Virtual reality labs using holograms have been used to visualize other 3D data sets, allowing the physician to "enter" the image of interest. In these labs an animated hologram is created, and, by wearing special glasses, the physician can have depth perception. The physician can then interact with the image in a number of ways. Recently, its use has been demonstrated in data sets acquired using 3D transthoracic echocardiography.[36] While presently requiring use of a "small" room, this will certainly develop and miniaturize. Other potential approaches include use of a head-mounted display with tracking cameras that has been used to allow for potential CT-guided interventions.[37]

Navigation

Having good imaging and efficient energy forms is of little use if we are unable to navigate our catheters to the required position and then maintain stable catheter contact on this tissue.[38] While our standard catheters have undoubtedly developed, they still are relatively thick and inflexible. The diameter of the catheters is dictated to some extent by the need for electrical connections between the tip and the connector in order to acquire the signals used for diagnosis and positioning of therapy. In the case of standard catheters, there is an additional requirement for a steering mechanism. In EP catheters this is by the use of one or more pull wires. The necessity to steer the catheter means that the shaft is relatively stiff. In cases where the anatomy is complex, for example, in patients who have undergone Mustard, Senning, or Fontan repairs, there may be a significant part of the circuit or a focus that is poorly accessible to a standard ablation catheter, thus increasing the complexity of ablation or precluding or decreasing the chance of success for ablation.[39,40] In addition, using inflexible catheters in a constantly moving heart may predispose to catheter movement during ablation, with the formation of elongated or "brush" lesions with a risk of complications and destruction of unnecessary tissue. There have been a number of recent developments in terms of delivering catheters to difficult anatomic areas.

Remote Magnetic Navigation

A remote magnetic navigation system (Niobe, Stereotaxis, St. Louis, MO, USA) has been developed that uses large external magnets to form a stable magnetic field in which an extremely flexible catheter with magnetic mass in the tip and distal shaft can be maneuvered. This system has been described extensively elsewhere.[41] In short, the Niobe system is managed by a computer interface system (Navigant) that changes the magnet orientation and the magnetic field and thus the catheter tip orientation. The catheter is advanced and retracted by a mechanical advancer system (Cardiodrive). Using these components in association with a dedicated fluoroscopy system, one can move the catheter in extremely small increments of 1° and 1 mm within the constraints of the heart. Once catheters are in the heart, all further catheter maneuvering can be performed in a fully remote fashion from the control room. Magnetic vectors used, and areas targeted, can be saved, and this detail used at a later stage to return to points of interest. This can be extremely useful. The highly flexible catheters can be navigated throughout all chambers after an initial, relatively steep learning curve, and perforation has never been described using this system. The system has proven to be equal to standard ablation for the management of such supraventricular tachycardias (SVT) as AVNRT and AVRT,[41–44] as well as in idiopathic VT.[45] More recently, publications have emerged showing its feasibility in the more complex field of ablation of AF, both in experimental models and in humans.[38,46] This system has now been combined with an electroanatomic mapping system (CARTO RMT), which was specially modified to be able to function in this magnetic environment (Fig. 2). With the inclusion of the Merge facility within CARTO RMT, one is able to combine all the features mentioned above under imaging with a remote navigation system. With this combination system, information is sent between systems so that particular points can be targeted. A function called "design line" can be used to fill in areas on a

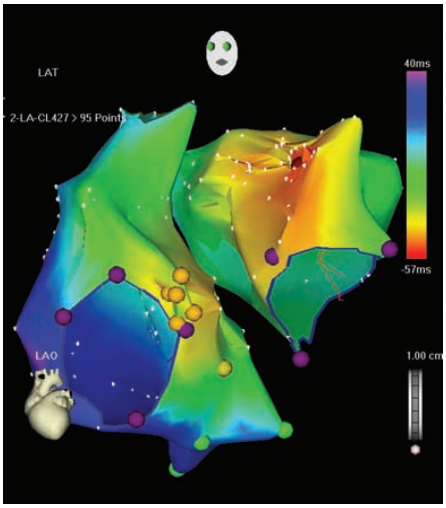

Figure 2. *A CARTO RMT biatrial map. This map was made in 2 stages, the second stage with the LA map has 95 points and took just over 10 minutes to make. The map was made using an automated mapping function present in the Navigant software specifically made for mapping of the LA. Additional points have been taken manually in the area of interest accounting for the clustering of points in that area.*

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map and potentially to plan ablation lines. "Click and go" is a utility whereby a point on the CARTO map is highlighted and, via feedback through both systems, the magnetically navigated catheter is moved accurately to this point. In their paper on AF ablation using this system,[38] Pappone et al. felt that the combined system was very useful for constructing an accurate electroanatomical map while acquiring more points in the time usually taken for a map made by hand. Although there is an extremely steep initial learning curve, the soft catheters can be navigated precisely and safely in the LA even in challenging sites, while reducing fluoroscopy exposure for the operator. Procedure times were a little longer than manual cases, but this was again early in their learning curve. It was felt that AF ablation using this system is less operator dependent than when performed manually. Although some have found a retrograde approach to the left heart difficult,[38] this again is part of a learning curve. We have been able to access the left ventricular (LV) in all patients in whom this was attempted, and more recently to access the left atrium both for mapping (Fig. 3) and for ablation of a focal tachycardia in the roof of the left atrium. It is entirely plausible that AF ablation could be performed in a retrograde transaortic fashion, either as an alternative approach or as first line therapy. Also, maneuvering a catheter around complex congenital anatomy may be possible. In addition, in a recent animal series, we have seen better delineation of lesions without the "brush" phenomenon, suggesting that catheter stability during cardio-respiratory movement is superior to that with manual catheters, and may increase the selectivity of the tissue that we ablate and thus decrease collateral damage and complications.

Robotic Navigation

The Hansen robotic system uses a different philosophy for navigation of catheters in 3D geometry, although it also aims to provide fine catheter control, to access complex anatomy, to easily repeat procedure steps, and to maintain catheter stability. In this system, a robotic catheter control system, essentially a steerable sheath, is used to navigate within the cardiac chambers. This system can also be maneuvered remotely with a slave system at the patient's side that then steers the catheter control system. Through the sheath a standard catheter is placed in order to perform mapping and/or ablation. The system can be fitted in existing labs, is significantly smaller than the magnetic navigation system, and thus requires no specialized construction. It is relatively mobile and can be moved between labs. Potential drawbacks could include a risk of perforation from the relatively stiff steerable sheath (a risk inherent in all steerable sheaths), the risk of thrombus formation within the sheath lumen, and the requirement for a standard catheter to be placed through the sheath that potentially could limit any remote ablation capability. To date, only a limited number of

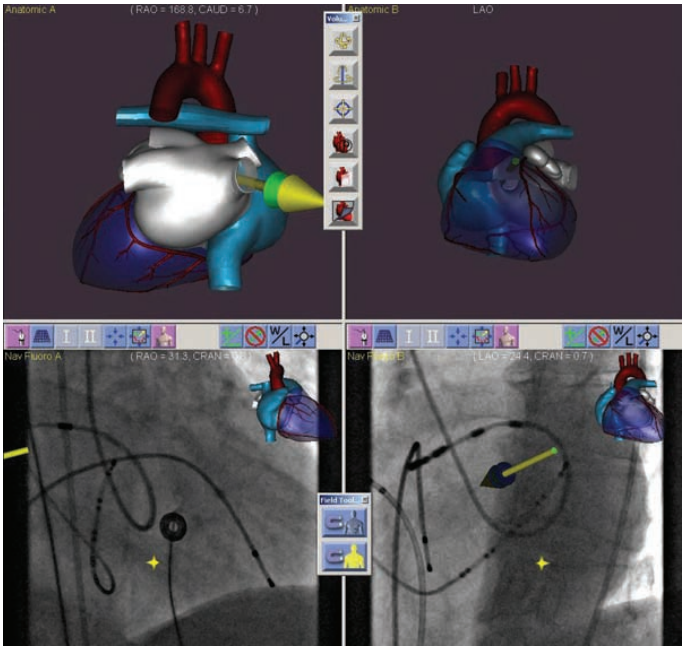

Figure 3. *Retrograde access to the right inferior pulmonary vein (RIPV). Having gained access via the aortic valve and through the mitral valve to the left atrium, presets in the Navigant system have been used to gain access to the PV. Left above is an area indicating the vector used by the preset to access the RIPV while below are RAO and LAO fluoroscopic images taken over from the X-ray system.*

feasibility studies in animal models and a small number of humans have been published, with no complications having occurred.[47,48]

Both of the above technologies have elicited a significant amount of interest, and further large-scale studies are awaited.

Lesion Formation

Having navigated to the area of interest, we must be able to apply a safe, reliable, and effective energy form with a high chance of success and a low risk of complications.

Cooled Radiofrequency Ablation

In the case of complex congenital heart disease, particularly late postoperative, lesion formation can be problematic. Reasons may include hypertrophied and fibrosed myocardium; and particularly in those where chamber function is very poor, blood flow (and thus catheter tip cooling) may be especially poor, making it difficult to deliver adequate energy to the tissue to allow for sufficient lesion dimensions to ensure successful ablation.[15,19] The use of passive cooled (8 or 10 mm tip), or active cooled (irrigated tip) catheters has certainly proved useful in this regard, as well as in the treatment of ventricular tachycardia[49] and atrial flutter.[50] There is some evidence to suggest that irrigated tips may be better than long tips in low flow states as regards energy delivery to tissue,[2] and a number of studies have suggested benefit from the use of especially open irrigated tip catheters (frequently in association with a mapping system) for the ablation of intra-atrial re-entrant tachycardias post cardiac surgery for congenital heart disease.[15,19,51] The use of these catheters may be associated with a risk of more collateral damage due to deeper lesions, but this has not been confirmed; and although the incidence of pops is higher, this does not seem to be associated with a significant increase in the risk of perforation and tamponade. Some degree of uncertainty still remains as to whether open or closed irrigation are similar in efficacy and complication rate. A recent animal study suggested that lower blood-tissue interface temperature, thrombus and steam pop occurred with open irrigation especially in low flow situations such as would be expected in heart failure and in atria after surgery, while lesion depth and surface area were similar.[52] This might suggest more clinical safety with open irrigation, although this clearly needs to be studied further.

Cryoablation

Electrophysiologists are increasingly ablating near normal conducting tissue or where collateral damage to coronary arteries, and extra cardiac tissue such as the esophagus, bronchus, and phrenic nerve, is possible. With the use of radiofrequency energy, especially in the coronary sinus, damage to coronary arteries has been described.[53] While much of the narrowing that has been seen is asymptomatic, the long-term outcome following such narrowing is still not known, and given the frequency with which it can be induced in the experimental laboratory, it is well worth watching out for.[54] With the attention given more recently to ablation near the mitral annulus and, quite frequently, within the coronary sinus in patients undergoing ablation for atrial fibrillation, especially the chronic forms,[55] we might expect to see another complication of this type of ablation appearing. It has been shown that the use of cryoablation within the coronary sinus, while associated with similar size lesions as well as medial necrosis of the circumflex artery, is only associated with mild intimal hyperplasia without significant stenosis as yet.[54] Clearly, with expansion of ablation to more and more pediatric patients and to sites closer to the normal conducting system, the potential benefits of cryomapping before ablation have been looked at. In AVNRT ablation in the pediatric population the success rates were similar while the recurrence rates were a little higher, although this did not reach significance.[56] No complications occurred, although we know that there is a small but well-known risk of atrioventricular (AV) conduction block using radiofrequency energy, which can be avoided using cryothermal ablation. In septal accessory pathways the use of cryothermy has decreased some of the fears associated with using radiofrequency in this area, with similar success rates to those using radiofrequency.[5] Although in this study there were no cases of AV block in either the RF or cryo group, a 4% incidence of AV block during RF application in this area is quoted. While safety is potentially improved, a somewhat more disturbing figure is the recurrence rate that was significantly higher in the cryotherapy group. This was felt by the authors possibly to relate to lesion characteristics, with more focused necrosis with cryoablation. As the authors note, though, recurrence is much less of a clinical problem than permanent AV block. Most recently, the use of cryoablation has been described for ablation of right ventricular outflow tract tachycardia where it seems, at least in the short term, to be comparable to radiofrequency but with the advantage of virtual absence of pain associated with the ablation.[57]

Balloon-Delivered Ablation Therapy

Balloons are being combined with newer energy sources such as microwave and ultrasound in the pursuit of circumferential lesions around the PV. However, as these energy sources also generate heat, and a balloon can easily advance into the PV if not correctly sized and positioned, there is a potential for PV stenosis and there remain some issues before these balloons and energy forms become fairly mainstream. The balloon-energy source that has been fairly widely used in the last 2 years is the Arctic Front (Cryocath Technologies, Inc., Kirkland, Canada) cryoballoon. While there is encouraging animal data on the use of cryoballoons for PV isolation,[58] there are no published clinical data outside of abstracts. Judging from data discussed at congresses and from our own experience with this balloon, the results are encouraging. The ability to isolate all 4 PV with a limited number of applications using the balloon is an advantage of the balloon technology, although some questions must remain about the level of the isolation within the PV-LA junction, and the long-term results. As with all of the balloons, there is a risk of damaging the right phrenic nerve during isolation of the right upper PV; and techniques have been used, such as intermittent pacing of the phrenic nerve, to detect this and then to stop the application immediately, after which recovery usually occurs (Fig. 4). The risk of PV stenosis with cryoablation seems extremely small, and this is a potential advantage. Whether there is a decreased risk of atrio-esophageal fistula remains open to conjecture. Short and medium to longer term data should become available in the near future.

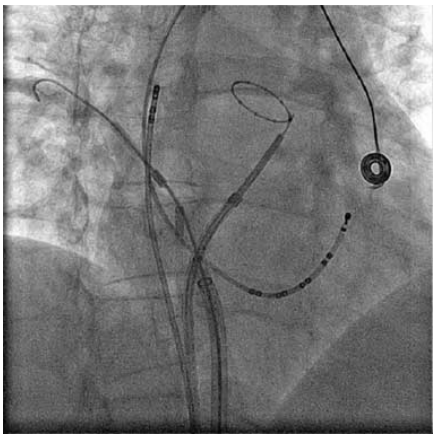

Figure 4. *An Arctic Front cryoballoon can be seen inflated within the ostium of the right upper PV but inside the heart shadow in the RAO fluoroscopic projection. A quadripolar catheter can be seen at the high right atrium-superior vena cava junction, and is being used to stimulate the phrenic nerve to identify any phrenic nerve injury early. A multipolar circular mapping catheter is lying free within the left atrium and a decapolar catheter is present in the coronary sinus.*

Other Advances

Not to be forgotten are developments in accessing the heart and certain chambers in the case of limited standard access, especially in patients with corrected as well as uncorrected congenital heart disease.

Epicardial Access

In many cases, circuits or foci are epicardial or partly so both in ischemic and nonischemic VT, and thus the development of epicardial approaches has also been a major advancement.[1,59] In addition, some SVTs have parts of their circuits epicardially, and the presence of ganglionic plexuses in the epicardial fat pads of the atria mean that an epicardial approach may also be required for mapping and ablation of some SVTs.[60] Damage to the phrenic nerve and epicardial vessels is a risk, and there is also a risk of pericarditis, but with adequate precautions the risk of the first two can be minimized.[61]

Alternative Methods for Access to Cardiac Chambers

In patients with congenital heart disease, especially those with prior surgery, access to some chambers may be difficult or almost impossible, and in addition the number of catheters that can be placed may be severely reduced. The use of alternate access sites may involve transhepatic puncture to obtain venous access when the inferior vena cava (IVC) is occluded,[62] and puncture of conduits or baffles. Access to the pulmonary venous atrium in patients with lateral Fontan tunnels has also been obtained by direct transthoracic puncture.[39] While this sounds risky and has been associated with both hemo- and pneumothorax, it does provide an alternative for some patients.

Conclusions

Generally what are required are good studies to confirm what we feel: that these new technologies are not just toys, but add significantly to the success rates of increasingly complex rhythm problems, while improving safety and decreasing radiation exposure for physician and patient. Also of importance of course in the days of financial constraints is showing that these technologies are cost effective by increasing turnover in the lab, decreasing costly complications, and improving efficacy of this therapy. It will become increasingly important when considering this long list of extremely expensive hardware and software that we prove which of these systems gives us the most "bang for our buck" and which is appropriate in a particular situation.

Even more intriguing is the possibility that using these technologies may, as has been stated by others,[11,38] be an equalizer, leveling the playing field and allowing for more complex procedures to be carried out by less experienced operators in low volume laboratories with similar success and complication rates to those of highly experienced operators in high volume centers.

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Part 4

Summary and conclusion (English / Nederlands)

Summary and conclusions

SUMMARY AND CONCLUSIONS

The aims of this thesis were to summarise the status of catheter ablation with conventional approaches in atrial flutter and fibrillation and to understand the problems related to this conventional approach. With this starting point we then investigated the role of remote magnetic navigation in the domain of cardiac catheter ablation.

In Chapter 2 we discuss clinical aspects of atrial arrhythmias and their accurate diagnosis allowing for practical decisions on therapy. The differential diagnosis between atrial tachycardia, atrial flutter and atrial fibrillation (AF) is not always easy. The presence of an underlying cardiomyopathy influences the clinical picture and requires more intensive therapy, including anticoagulation. In patients with congenital heart disease, especially the operated group, it is often difficult to characterise the circuit of macro-reentrant atrial tachycardia and its location.

The objective of Chapter 3 was to compare the acute success and short-term follow-up of ablation of atrial flutter using 8 mm tip radiofrequency (RF) and cryocatheters. The acute success rate for RF was slightly (but not significantly) higher than for cryo. Procedure times were similar although fluoroscopy time was longer with RF. More applications were given with RF, but indicators for myocardial damage were similar. The isthmus tended to be longer in the failed procedures. Recurrences and complaints in the successful patients were similar for both groups, with a very low recurrence of atrial flutter after initial success, in comparison to some groups who have reported higher initial success rates but also higher recurrence rates.

In chapter 4 we allude to the fact that despite what some electrophysiologists might think, in atrial flutter the ongoing publication of studies aiming to improve success rates suggests that we do need further study to improve the outcome in ablation of atrial flutter, while improving patient safety and the efficacy of this ablation technique. In the meantime such attempts have been undertaken with maximal voltage guided ablation and we feel that this should also be studied with remote magnetic navigation using the new high power catheters.

In chapter 5 we describe our early experience with ablation for AF. The two most frequently used techniques at that time were segmental pulmonary vein isolation and left atrial circumferential ablation. We discuss our approach using pulmonary vein antrum isolation guided by phased-array intracardiac echocardiography (ICE) and its initial results. Of the patients with paroxysmal AF, 69% were without recurrences after one procedure at a mean follow-up of 201 days. No major complications occurred with this technique, which was however associated with a very long procedure and radiation time despite the use of ICE. The promise of high power and irrigated magnetically enabled catheters means that we can hopefully investigate the use of magnetic navigation in AF in the near future.

Following this look at some conventional approaches to ablation we move on to the use of remote magnetic navigation in the field of clinical cardiac electrophysiology.

Chapter 6 is a brief review of the problems of conventional ablation methods. The very early experience with remote magnetic navigation is also described. We also look at the potential for its use in clinical cardiac electrophysiology and cardiac resynchronisation therapy for the management of heart failure.

In chapter 7 the lesions formed by remote magnetic navigation and standard catheters in the right atrium or right ventricle of a porcine in-vivo model were compared. Transmural macroscopic lesions with magnetic navigation were more often oval or round (versus elongated after standard ablation) suggesting less potential for "brush" lesions and more precise lesion formation. The microscopic assessment revealed no significant differences. However, the lesions with magnetic navigation could be achieved with lower energy and impedances, possibly suggesting more effective energy delivery. The need for a different in-vitro model taking into account cardiorespiratory movement is highlighted.

Chapter 8 then describes our very early work with the system in one of the easily accessible arrhythmias – atrioventricular nodal re-entry tachycardia (AVNRT). Our aims were to assess the feasibility of magnetic navigation to Koch's triangle and reliable ablation of AVNRT. Consecutive patients were mapped and ablated with early generation magnetically enabled catheters with one or three magnets at the tip. The catheter was remotely advanced with the Cardiodrive™ system and orientated with the Navigant™ control system. After initial positioning with the external magnets, adjustments were made in small steps. Success rates, procedure, and fluoroscopy times were analysed, and compared with a local contemporary series of conventional AVNRT ablations. Magnetic navigation was always feasible. Targets were easily reached. Catheters remained stable in position during accelerated junctional rhythms. Ablation was successful in 90% of procedures. No significant complications occurred. Median patient fluoroscopy time was 12 min, while median physician fluoroscopy time was 4 min. Fluoroscopy times tended to be shorter than those in the conventionally treated group. Procedure duration decreased significantly over time, and the median procedure time was similar to that in the conventional group.

Navigation, mapping, and ablation in the right ventricular outflow tract (RVOT) can be difficult. The purpose of the study in Chapter 9 was to assess the feasibility of RVOT tachycardia ablation using remote magnetic navigation to allow for more accurate mapping and ablation. Mapping and ablation were performed in eight patients with outflow tract ventricular arrhythmias. Tachycardia mapping was undertaken with a 64-polar basket catheter, followed by remote activation and pace-mapping using a magnetically enabled catheter. The area of interest was

localized on the basket catheter and remote navigation of the magnetic catheter to this area was followed by pace-mapping. Ablation was performed at the site of good pace-mapping, with earliest activation if possible. Acute success was achieved in all patients with a median of four applications. No complications occurred. One recurrence occurred during 1 year of follow-up. Remote magnetic navigation permitted low fluoroscopy exposure for the physician and the long-term results are promising with very accurate, high resolution mapping being facilitated by remote magnetic navigation.

Ablation of idiopathic left ventricular fascicular tachycardia can be aided by electroanatomic mapping, and the addition of a floppy, magnetically enabled ablation catheter improved manoeuvring in a case of fascicular tachycardia. In Chapter 10, both these modalities were used in a sequential fashion. Mechanically induced arrhythmias and mechanical block could be avoided. Integration of these modalities would have proved even more helpful, and this has since become available.

We evaluated the feasibility of mapping and ablation of left-sided accessory pathways (APs) using the retrograde transaortic approach with this system in Chapter 11 in the hope that this might open the gate to retrograde ablation of left atrial arrhythmias. Twenty consecutive patients were included and two magnetic catheters with different magnetic mass and different flexibility were used. Ablation was acutely successful in 60% of the patients using the Helios II and in 80% using the Celsius RMT. Median procedure time was comparable to conventional approaches. Physician fluoroscopy time was only 4 minutes. In the last 10 patients, procedure times became significantly shorter. There was a very steep initial learning curve, with the success rate increasing from 50% in the first half to 80% in the second half. Different catheter configurations may influence the outcome. Transseptal approaches clearly remain of value and a transseptal remote magnetic approach is presently being compared to this retrograde magnetic approach.

Occasionally recurrences appear after successful procedures, sometimes shortly after the end of the procedure. In Chapter 12 we describe successful ablation of a very early recurrence of accessory pathway conduction while the patient was still in the electrophysiology laboratory. We used remote magnetic navigation with a single catheter, and targeted the accessory pathway using the stored magnetic vectors from the initial applications.

Left atrial access for electrophysiological procedures may not always be possible using a transseptal approach. Alternative approaches need to be developed. As a further step in the assessment of the feasibility of this approach, in Chapter 13, access to the left atrium and pulmonary veins was undertaken via a retrograde approach using a magnetically enabled ablation catheter and remote magnetic navigation. Once in the left atrium we cannulated

the pulmonary veins using the preset vectors in the system and were repeatedly successful in a small series of patients. The mean time needed to advance the catheter from the aorta to the left atrium and for subsequent cannulation of all the pulmonary veins was acceptable. No complications occurred.

In Chapter 14, ablation was successful in the roof of the left atrium in a patient with focal left atrial tachycardia, who refused transseptal puncture, using the approach described in the previous chapter. This adds to our work looking at the feasibility of left atrial ablation for atrial tachycardia and potentially atrial fibrillation using an alternate approach should transseptal puncture be contraindicated or problematic.

The next chapters summarise the early work done using remote magnetic navigation (chapter 15) as well as many other new innovations in clinical cardiac electrophysiology (chapter 16).

In the work put forward in this thesis we have shown that new innovations in terms of image integration and energy sources can prove useful in improving outcomes in clinical electrophysiology when using fairly conventional equipment. In the later studies we have shown that an approach using remote magnetic navigation is at least equivalent to a conventional approach. Some potential advantages were shown in these early studies such as the ability to perform remote mapping and ablation thereby decreasing physician radiation exposure and the need for heavy lead aprons; the ability to reproducibly and easily return to a previously assessed site, the ability to perform accurate and high resolution mapping; and finally, the ability to access otherwise potentially inaccessible areas of the heart such as the left atrium when transseptal puncture is contraindicated or areas of the heart which are difficult to access in operated congenital heart patients.

In the future the opportunity exists, with image integration, for fully automated remote mapping and potentially ablation. This would clearly be of potential benefit in ablation for atrial fibrillation and in other complex arrhythmias such as macro-reentry atrial or ventricular arrhythmias after cardiac surgery. The potential also exists for remote assistance whereby an experienced operator with a set-up elsewhere could assist with mapping or ablation should that become necessary. Clearly, more complex substrates may become ablateable increasing the pool of patients with arrhythmias who may benefit from ablation. Increasing the patient pool, while improving success rates and keeping the risk low are obviously all beneficial. As mentioned in the introduction, these new innovations may allow less experienced and less busy electrophysiology centres to perform complex ablations with similar success and risk as more experienced electrophysiology laboratories. The unresolved question, to quote one of the articles, is determining how much "bang we get for our buck" with these new technologies.

This will only be determined in the future and with trials involving both high and low volume, and experienced and less experienced operators.

OVERZICHT EN BESLUITEN

Het doel van deze thesis is een overzicht te geven van de status van katheterablatie met conventionele benaderingen bij ritmestoornissen als o.a. atriale flutter en fibrillatie en de problemen te beschrijven die gerelateerd zijn aan deze conventionele benadering. Vanuit dit uitgangspunt hebben wij de rol van stuurbare magnetische navigatie in het spectrum van cardiale katheterablatie onderzocht.

In hoofstuk 2 bespreken wij de klinische aspecten van atriale ritmestoornissen en de accurate diagnose ervan met een praktische discussie over therapie. De differentiale diagnose tussen atriale tachycardie, atriale flutter en atriale fibrillatie (AF) is niet altijd gemakkelijk. Het bestaan van onderliggende hartziekten beïnvloedt het klinisch beeld en vereist individueel aangepaste therapie, zoals anticoagulatie. In patienten met congenitale hartafwijkingen, vooral de geopereerde groep, is het vaak moeilijk het circuit van `macro-reentrant` atriale tachycardie te onderscheiden en te lokaliseren.

Het onderwerp van hoofdstuk 3 is het acute succes en de opvolging op korte termijn van ablatie van atriale flutter, bestudeerd in een vergelijking van een 8 mm radiofrequentie (RF) en een gelijkaardige 8 mm cryothermiekatheter. Het acute succes voor RF was iets (maar niet signifikant) beter dan voor cryo. Proceduretijden waren vergelijkbaar, maar fluoroscopietijden met RF waren langer. Er zijn meer applicaties gegeven met RF, maar indicatoren voor myocardschade waren vergelijkbaar. Bij de mislukte procedures leek de isthmus langer te zijn. Terugval en klachten bij de succesvolle patiënten waren vergelijkbaar in beide groepen, met een zeer lage terugval naar atriale flutter na het initiële succes, in vergelijking tot sommige groepen die meer initieel succes maar ook meer terugval hebben gerapporteerd.

In hoofdstuk 4 stellen we dat, ondanks wat sommige elektrofysiologen misschien denken, er wel degelijk meer studies nodig zijn om het resultaat bij atriale flutterablatie te verbeteren en om tegelijk de patiëntveiligheid te verhogen. Ondertussen zijn dergelijke pogingen ondernomen met ablatie gericht door het maximale voltage, en ons gevoel is dat dit onderzocht zou moeten worden met stuurbare magnetische navigatie en de nieuwe katheters met geïrrigeerde tip.

In hoofdstuk 5 beschrijven we onze vroege ervaring met AF ablatie. De twee meest gebruikte behandelmethodes waren toen segmentale pulmonaire vene isolatie en linker atriale circumferentiële ablatie. We bespreken onze benadering met gebruik van pulmonale antrum isolatie

begeleid met intracardiale echografie (ICE) en de eerste resultaten hiervan. Van de patienten met paroxysmale AF, hadden 69% geen recidieven tijdens een gemiddelde opvolging van 201 dagen na een procedure. Er waren geen grote complicaties als gevolg van deze techniek, maar deze benadering ging wel gepaard met lange procedure- en stralingstijden ondanks het gebruik van ICE. De recente beschikbaarheid van magnetisch stuurbare katheters met geïrrigeerde tip betekent dat we in de nabije toekomst het gebruik van magnetisch navigatie voor AF kunnen onderzoeken.

Na deze analyse van conventionele benaderingen van ablatie gaan we verder het gebruik van magnetische navigatie voor klinische elektrofysiologie bespreken.

Hoofdstuk 6 geeft een kort overzicht van de complicaties van conventionele ablatiemethodes. De eerdere ervaring met stuurbare magnetische navigatie wordt ook beschreven. We hebben ook gekeken naar het potentiele gebruik ervan in cardiale resynchronisatie therapie voor de behandeling van hartfalen.

In hoofdstuk 7 is een vergelijking gemaakt van de laesies met gebruik van op afstand stuurbare magnetische navigatie en een standaard katheter in het rechte atrium of rechter ventrikel van een in-vivo varkensmodel. De transmurale macroscopische laesies onder magnetische navigatie waren vaker ovaal of rond (tegen geëlongeerd bij standaardablatie) wat potentieel minder kans geeft voor "brush" laesies en meer voor precieze laesievorming. Microscopisch onderzoek naar de diepte van de laesie heeft geen significante verschillen laten zien. De laesies met magnetische navigatie werden bereikt met lagere energie en impedantie, wat betere energieoverdracht naar het weefsel suggereert.

Hoofdstuk 8 omschrijft ons eerdere werk met het magnetische navigatiesysteem in een gemakkelijk te bereiken ritmestoornis – atrioventriculaire nodale re-entry tachycardie (AVNRT). Ons doel was de haalbaarheid van het magnetisch navigeren naar de driehoek van Koch te onderzoeken en de betrouwbaarheid van ablatie. Twintig opeenvolgende patiënten werden in kaart gebracht en behandeld met gebruik van met magneten uitgeruste katheters met één of drie magneten in het distale deel. De katheter werd op afstand naar voor of naar achter bewogen door middel van het `Cardiodrive$^{TM}$ systeem` en georiënteerd met gebruik van het `Navigant$^{TM}$ ` controle systeem. Na initiële positionering met de externe magneten, werden veranderingen in positie gemaakt in kleine stappen. Succes, procedure- en fluoroscopietijden werden geanalyseerd en vergeleken met een lokale eigentijdse reeks conventionele AVNRT ablaties. Magnetische navigatie was altijd mogelijk. Het vooropgezette doel was gemakkelijk te bereiken. Katheters bleven stabiel op hun plaats tijdens geaccelereerde junctieritmes. Ablatie was een succes in 90% van de gevallen. Er werden geen significante complicaties gezien. De mediane fluoroscopietijd voor de patiënt was 12 min, voor de interventiearts slechts 4 min. Er

was een tendens naar kortere fluoroscopietijden vergeleken met de conventioneel behandelde groep. De proceduretijd nam significant af in de loop van de studie, en de mediane proceduretijd was vergelijkbaar met deze van de conventionele groep.

Navigatie, mappen en ablatie van de rechter ventriculaire outflow tract (RVOT) kan moeilijk zijn. Daarom was de bedoeling van hoofdstuk 9 om te kijken naar de haalbaarheid van RVOT tachycardie-ablatie met gebruik van op afstand bestuurde magnetisch navigatie. Mapping en ablatie werd uitgevoerd in acht patienten met kamer-ritmestoornissen uit het uitstroomgebied. De tachycardie werd in kaart gebracht met een 64-polige `basket`-katheter, gevolgd door een van op afstand gestuurde, met magneten uitgeruste katheter om de vroegste activatie te vinden en pace-mapping te doen. Acuut succes werd bereikt bij alle patiënten met een mediaan van 4 applicaties. Er waren geen complicaties. Er was één recidief gedurende gemiddeld één jaar follow-up.

Ablatie van idiopathische linker ventriculaire fasciculaire tachycardie kan ook vergemakkelijkt worden door elektro-anatomische mapping. Het gebruik van een zachte, magnetisch geactiveerde, ablatiekatheter verbeterde de stuurbaarheid in een geval van fasciculair tachycardie (hoofdstuk 10). Mechanisch geïnduceerde ritmestoornissen en mechanisch block konden vermeden worden. Integratie van deze modaliteiten zou behulpzamer zijn geweest, en is intussen ook beschikbaar.

We hebben de haalbaarheid van mappen en ablatie van linkszijdige accessoire bundels met gebruik van een retrograde trans-aortische benadering met dit systeem ge-evalueerd in hoofdstuk 11, in de hoop dat dit de weg zou kunnen openen naar retrograde ablatie van ritmestoornissen van het linker atrium. Twintig op elkaar volgende patiënten werden hierbij bestudeerd en twee magnetisch katheters met verschillende magnetische massa en flexibiliteit werden gebruikt. Ablatie was succesvol bij 60% van de met de Helios II katheter behandelde patiënten en bij 80% behandeld met de Celsius RMT katheter. De mediane proceduretijd was vergelijkbaar met conventionele benaderingen. De fluoroscopietijd van de interventiearts was maar 4 minuten. Bij de laatste 10 patiënten werden de proceduretijden significant korter. Er was in het begin een steile leercurve met successen van 50% in de eerste helft van de studie, tot 80% in de twede helft. Verschillende katheterconfiguraties hebben mogelijk invloed op het resultaat. Transseptale benaderingen blijven duidelijk waardevol en op dit moment wordt een transseptale, op afstand bestuurbare benadering vergeleken met deze retrograde magnetische benadering.

Af en toe ziet men na een succesvolle procedure de abnormale geleiding terug optreden. In hoofdstuk 12 beschrijven wij de succesvolle ablatie van een accessoire bundel met reconductie, terwijl de patiënt nog steeds in het elektrofysiologisch lab was. Met magnetische navigatie en

één enkele katheter hebben wij de bundel teruggevonden met gebruik van de geregistreerde vectoren van de oorspronkelijke applicaties.

Toegang tot het linker atrium is niet altijd mogelijk via de transseptale benadering. In hoofdstuk 13, werd retrograde toegang tot het linker atrium en de pulmonaalvenen gezocht via een met magneten uitgeruste katheter, en op afstand bestuurbare magnetische navigatie. Eénmaal in het linker atrium, werden de pulmonaalvenen gecannuleerd met gebruik van de vooraf geprogrammeerde vectoren van het systeem. We waren telkens succesvol in een kleine serie patiënten. De gemiddelde tijd om de katheter van de aorta naar het linker atrium te brengen en voor de daarop volgende cannulatie van alle pulmonaalvenen was acceptabel. Er waren geen complicaties.

In hoofdstuk 14 blijkt ablatie in het dak van het atrium te slagen met gebruik van de benadering uit het voorgaande hoofdstuk bij een patiënt met focale atriale tachycardie. Deze laatste twee hoofdstukken dragen bij aan ons doel om te bekijken of mapping en ablatie van linkszijdige atriale tachycardie en atriale fibrillatie via deze alternatieve magnetische benadering haalbaar is.

De volgende hoofdstukken geven een overzicht van vroeger werk dat verricht werd met gebruik van op afstand stuurbare magnetische navigatie (hoofdstuk 15), en van andere vernieuwingen in de klinische elektrofysiologie van het hart (hoofdstuk 16).

In het werk in deze thesis hebben we laten zien dat innovaties op het gebied van beeldintegratie en energiebronnen de resultaten in klinische elektrofysiologie kunnen verbeteren zelfs wanneer tamelijk conventionele middelen worden gebruikt. In de latere studies hebben wij laten zien dat een benadering met van op afstand stuurbare magnetische navigatie minstens even goed is als een conventionele benadering. Sommige potentiele voordelen zijn hierbij de verminderde blootstelling aan straling van de arts, en de verminderde noodzaak een zware loodschort te dragen; de mogelijkheid om herhaaldelijk en gemakkelijk te kunnen terugkeren naar eerder behandelde gebieden in het hart; het vermogen om accuraat en met hoge resolutie het hart in kaart te brengen; de mogelijkheid om naar anders niet zo toegankelijke delen van het hart zoals het linker atrium te gaan, wanneer transseptale punctie niet gewenst is, of bij geopereerde congenitale hartpatiënten.

In de nabije toekomst wordt (met beeldintegratie) geheel geautomatiseerde mapping en potentieel ablatie op afstand mogelijk. Dit zou duidelijk een voordeel zijn bij ablatie van atriale fibrillatie en bij andere complexe ritmestoornissen zoals macro re-entry, of atriale of ventriculaire ritmestoornissen na hartchirurgie. Ook bestaat de mogelijkheid voor assistentie op afstand waarbij een ervaren operator, met een systeem op een andere plaats zou kunnen

assisteren bij mapping of ablatie. Het is duidelijk dat meer complexe substraten behandelbaar worden. Toename van het aantal behandelbare patiënten, en tegelijk een grotere kans op succes met behoud van een laag interventierisico, biedt duidelijke voordelen voor de zorg. Zoals reeds gezegd, zouden deze innovaties minder ervaren en minder drukke elektrofysiologische centra de mogelijkheid geven om complexe ablaties uit te voeren met vergelijkbaar succes en risico als meer ervaren elektrofysiologische labaratoria. Hier is uiteraard nog veel onderzoek voor nodig, en ook is de meerwaarde van deze dure technologieën nog steeds niet helemaal duidelijk.

Part 5

Miscellaneous

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Curriculum Vitae and Publications

Andrew Thornton was born in Durban, South Africa and brought up in Yorkshire, England and Uitenhage, South Africa where he matriculated at Muir College Boys' High School. He attained the degree MBBCh at the University of the Witwatersrand and then did his internship at the J.G. Strijdom Hospital in Johannesburg before performing his national service in the Department of Cardiology at 1 Military Hospital in Pretoria. He then specialised in internal medicine and subsequently cardiology through the Johannesburg teaching hospital complex and the University of the Witwatersrand. After an initial grounding in electrophysiology he then spent one year training in electrophysiology at St. George's Hospital, in London, UK under Prof A.J. Camm and Dr. E. Rowland, before returning to the Johannesburg General Hospital in South Africa. He then left clinical medicine to work with Medtronic in South Africa for 18 months as a business unit manager before being tempted back into clinical electrophysiology at the Thoraxcentre in Rotterdam where he worked for 4 years as a cardiologist in clinical electrophysiology. In 2006 he returned to South Africa where he is a cardiologist with a special interest in electrophysiology at the Sunninghill Hospital in Johannesburg.

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