OPTIMIZING SAFETY AND EFFICACY OF CATHETER ABLATION PROCEDURES

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OPTIMIZING SAFETY AND EFFICACY OF CATHETER ABLATION PROCEDURES

Optimaliseren van veiligheid en effectiviteit van catheterablatie procedures

Proefschrift

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Het verschijnen van dit proefschrift werd mede mogelijk gemaakt door de steun van de Nederlandse Hartstichting.

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CHAPTER 1

General introduction

For millennia many cultures were fascinated by the human heartbeat, which first manifested as the peripheral pulse. The ancient Egyptian, Chinese, Greek and Roman scholars had many theories on the palpation of the peripheral pulse and how it might contribute to the correct diagnosis. From the remaining descriptions we know that ancient physicians were able to palpate a fast pulse and could relate the occurrence of the tachycardia to external stimuli. A systematic diagnosis and treatment was already described in the third century B.C. by the Greek physician Erasistratus of Ceos.[1] He was called to consult to treat King Seleucus' son who was suffering from severe palpitations and perspiration. After careful deliberation, Erasistratus found that these symptoms were caused by a strong affection for his exceptionally beautiful stepmother. He advised the king to divorce from his wife so his son could marry the woman. After this successful treatment the patient was free from any symptoms and lived happily ever after.

Cardiac electrophysiology underwent tremendous developments and more therapeutic options became available besides Erasistratus' successful therapy.[2-5] This revolution started when Willem Einthoven introduced the most fundamental tool for arrhythmia diagnosis in 1902: the electrocardiography.[6] This landmark in the history of electrophysiology paved the road for knowledge on the incidence, diagnosis, aetiology and treatment of cardiac arrhythmias.

After the establishment of the basic knowledge on the cardiac rhythm and arrhythmias, invasive electrophysiology was introduced. The work of the groups Durrer and Coumel in 1967 revealed the possibility to localize the site of origin and analyse the mechanism of cardiac arrhythmias.[7, 8] They demonstrated that by connecting intracardiac catheters to an external stimulator it was possible to reproducibly initiate and terminate clinically occurring tachycardias, and to identify the site of origin of the tachycardia. After the diagnosis was established by using percutaneous catheters, patients were still treated surgically. The first successful operation was reported in 1968 and a surgical interruption of the Bundle of Kent was performed.[9] After the successful treatment of patients suffering from Wolff-Parkinson-White syndrome and greater understanding of the aetiology, open surgical techniques were developed for the treatment of atrioventricular or accessory pathway mediated tachycardia, ventricular tachycardia and atrial fibrillation.[10-14]

When the value of percutaneous endocardial mapping was explored, the next revolutionary step in the development of invasive electrophysiology was based on

serendipity. In 1981 a pioneering electrophysiology group from San Francisco, USA, reported a patient who was undergoing an electrophysiological study following defibrillation.[15] During defibrillation the electrode accidentally came into contact with the intracardiac catheter located at the bundle of His, resulting in complete heart block. After this incident it became clear that catheter ablation could be the next step to cure cardiac arrhythmias. Direct current (DC) ablation was introduced where high-voltage discharges were applied to the myocardium.[16-18] Since these discharges were difficult to control, extensive damage to the tissue could occur leading to serious complications such as myocardial depression, unintended atrioventricular block, venous thrombosis, cardiac rupture and sudden death.[19] This revealed the importance of procedural safety and invasive electrophysiology has gone through major transformations to improve both safety and efficacy of catheter ablation procedures.

During the late 1980s technological developments led to the introduction of catheters that could deliver radiofrequency (RF) energy, which eventually replaced the use of DC ablation.[20-23] This development had major influence on how ablations were performed. First of all, procedures could be performed on conscious patients with minimal discomfort during energy delivery.[24] Furthermore, discrete lesions could be created due to local energy delivery and it allowed premature termination of ablation if complications occurred.[20, 25] Despite these significant advantages of RF ablation, its use in the ventricle or the systemic circulation was limited. High-power settings led to high temperatures, which increased the risk of perforation and thromboembolisms.[26, 27] After some time, new ablation systems allowed temperature monitoring and temperature control providing information regarding tissue heating and reduced the occurrence of coagulum formation and thromboembolism.[28-30] Further improvements included saline cooling at the distal electrode, which significantly improved procedural safety and allowed the creation of deeper lesions.[31-34] It became clear that multiple factors are responsible for the formation of the final lesion. Lesion size is dependent on the material of the catheter tip, the diameter of the distal catheter electrode, the delivered power, the use of saline irrigation at the catheter tip, the amount of blood flow, and the contact pressure of the electrode with the cardiac tissue. [26, 35, 36] Many studies have been performed to increase lesion size as much as possible, however, further optimization is required to achieve better procedural outcome without compromising the patient's safety.

Since the introduction of percutaneous catheter ablation and its revolutions it became a well-established therapy to treat arrhythmias. For several arrhythmias it even became the first-line therapy. [37] Our knowledge on the aetiology expanded and much more complex arrhythmias are currently treated (e.g. longstanding atrial fibrillation, arrhythmias in congenital heart disease, and hemodynamically instable ventricular tachycardia).[38-40] With an increasing eligible population suffering from (complex) arrhythmias, the safety of procedures is crucial to determine which technique should be used during ablation. Despite the major developments, there are still remaining challenges regarding safety, efficacy, efficiency and reproducibility. As technology evolved, new technological developments are available and could further improve catheter ablation procedures.

In this thesis new developments in the field of invasive electrophysiology are studied and discussed. The aim of this work is to find novel strategies to further improve safety and efficacy of catheter ablation procedures. Therefore, this thesis is composed of three parts each discussing a new technological development.

In the first part the use of robotics is discussed. One of the innovations is the remote magnetic navigation system that allows remote manipulation of the catheter in the heart.[41] In the chapters the use of this system is studied for several arrhythmias, including atrial fibrillation, ventricular tachycardia en arrhythmias in congenital heart disease.

In the second part another major development is evaluated: contact force sensing catheters. These catheters could measure the force between the catheter tip and the myocardium. As contact force is a major determinant for lesion formation it provides crucial information during catheter ablation.[42] Furthermore, since continuous force feedback is available it might also lead to safer ablation procedures.

Finally we studied the capabilities of a newly introduced catheter with a gold electrode and 12 irrigation holes. In this part we used an experimental model to investigate the features of this catheter compared to conventional ablation catheters. We aimed to answer the question if these new gold-tip catheters could improve lesion formation leading to better procedural success.

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PART I

ROBOTICS

CHAPTER 2

The magnetic navigation system allows safety and high efficacy for ablation of arrhythmias

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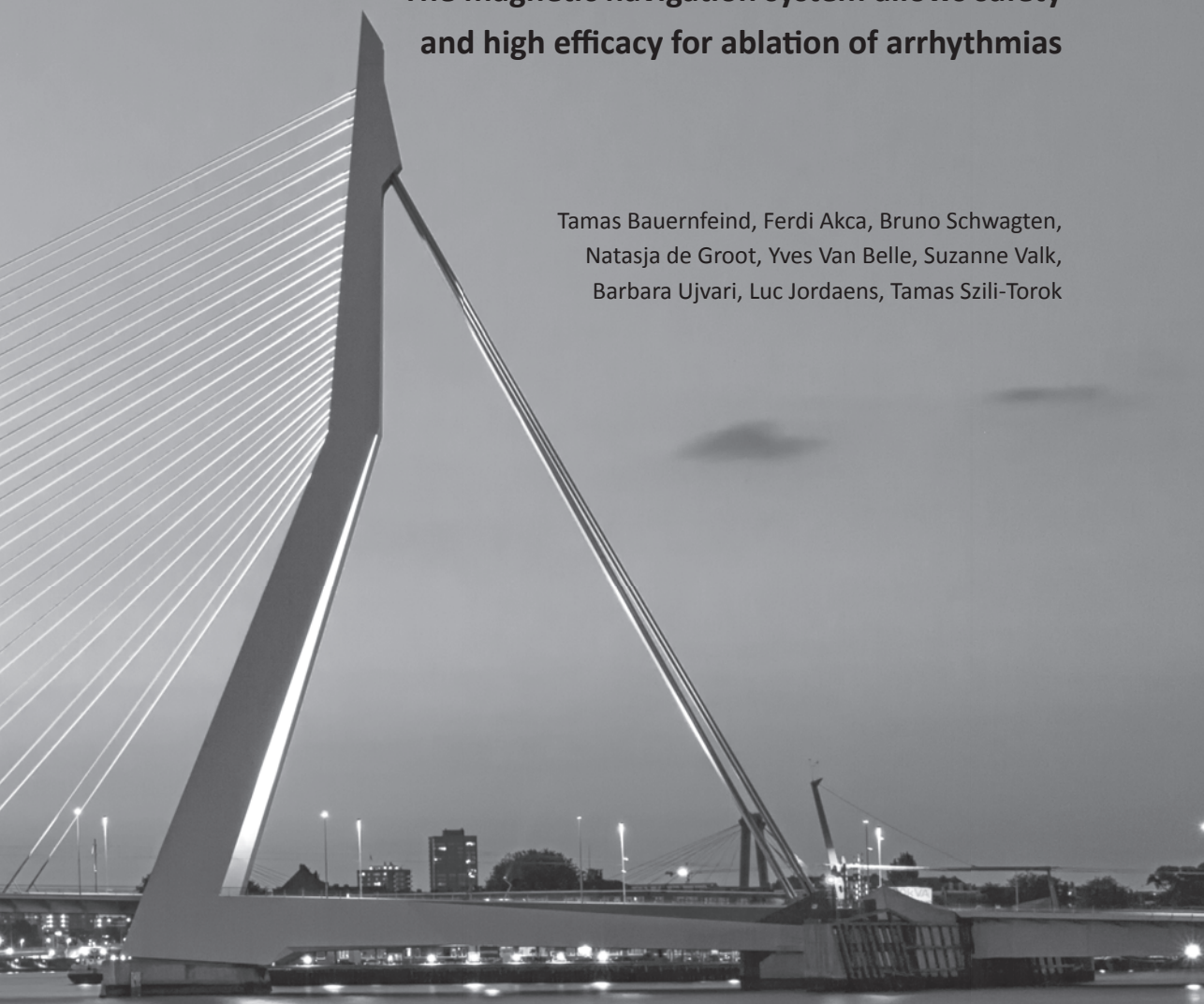

Europace. 2011;13(7):1015-21

ABSTRACT

Aims

We aimed to evaluate the safety and long-term efficacy of the magnetic navigation system (MNS) in a large number of patients. The MNS has the potential for improving safety and efficacy based on atraumatic catheter design and superior navigation capabilities.

Methods and Results

In this study, 610 consecutive patients underwent ablation. Patients were divided into two age- and sex-matched groups. Ablations were performed either using MNS (group MNS, 292) or conventional manual ablation [group manual navigation (MAN), 318]. The following parameters were analyzed: acute success rate, fluoroscopy time, procedure time, complications [major: pericardial tamponade, permanent atrioventricular (AV) block, major bleeding, and death; minor: minor bleeding and temporary AV block]. Recurrence rate was assessed during follow-up (15 ± 9.5 months). Subgroup analysis was performed for the following groups: atrial fibrillation, isthmus dependent and atypical atrial flutter, atrial tachycardia, AV nodal re-entrant tachycardia, circus movement tachycardia, and ventricular tachycardia (VT). Magnetic navigation system was associated with less major complications (0.34 vs. 3.2%, P = 0.01). The total numbers of complications were lower in group MNS (4.5 vs. 10%, P = 0.005). Magnetic navigation system was equally effective as MAN in acute success rate for overall groups (92 vs. 94%, P = ns). Magnetic navigation system was more successful for VTs (93 vs. 72%, P < 0.05). Less fluoroscopy was used in group MNS (30 ± 20 vs. 35 ± 25 min, P < 0.01). There were no differences in procedure times and recurrence rates for the overall groups (168 ± 67 vs. 159 ± 75 min, P = ns; 14 vs. 11%, P = ns; respectively).

Conclusion

Our data suggest that the use of MNS improves safety without compromising efficiency of ablations. Magnetic navigation system is more effective than manual ablation for VTs.

INTRODUCTION

Catheter ablation was introduced in clinical electrophysiology (EP) in the 1980s.[1,2] In past decades, it became well established as first-line therapy for many types of arrhythmias, including atrioventricular (AV) nodal re-entrant tachycardia (AVNRT), circus movement tachycardia (CMT), and cavotricuspid isthmus (CTI)-dependent atrial flutter (AFl), and as therapeutic option for the treatment of atrial fibrillation (AFib), atrial tachycardia (AT), and ventricular tachycardia (VT).[3] Further developments were implemented such as electroanatomical mapping, integration of cardiac imaging, and improved catheter design.[4,5] Until recently, all of the above-mentioned techniques were based on manual catheter navigation in the heart. The innovation of the remote magnetic navigation system (MNS) offered important theoretical advantages in safety due to the atraumatic catheter design and less physical stress and radiation exposure for the physician.[6 – 11] Higher efficacy is also expected due to the unrestricted and reproducible catheter movement, and improved catheter stability.[8,11 – 13] Numerous centers reported their initial experiences with MNS confirming its feasibility for ablation of most arrhythmias.[14 – 23] However, these early reports included only small numbers of patients, the follow-up periods were short, and they failed to demonstrate superiority of MNS in safety and efficacy.

The objective of the present study was to evaluate the safety and long-term efficacy of MNS as compared with conventional manual ablation techniques in a large number of patients with consistent technique and workflow.

METHODS

Patients

This study is an ongoing registry of the procedures performed in our clinic. Six hundred and ten consecutive patients underwent ablation from January 2008 to March 2010. All patients scheduled for EP study and ablation were distributed from the waiting list based on availability to the MNS-equipped or the conventional EP laboratory. Accordingly, ablation

was performed either using MNS (group MNS, 292 patients, age 48 ± 19 years, 166 males) or using conventional manual ablation (group MAN, 318 patients, age 52 ± 16 year, 197 males). The procedures were performed over the entire study duration by the same senior electrophysiologist group with the assistance of four fellows, trained for manual catheter navigation and for MNS as well. The attending physicians performed MNS and MAN procedures in equal distribution.

Electrophysiology studies – ablations

Written, informed consent for the ablation procedure was obtained from all patients. Resting 12-lead electrocardiogram (ECG), and laboratory tests, an X-ray thorax image, and a two-dimensional echocardiography were acquired from all patients within 1 month before and within 48 h following the procedure.

Local peri-procedural medication protocols were followed in all patients. In short, AVNRT, CMT, AT, and elective VT patients were instructed to stop taking antiarrhythmic drugs for a period of at least four half-lives prior undergoing the procedure. In cases of AFib, AV junction (AVJ) and emergency VT ablation medication remained unchanged. The procedures were performed during a fasting state, using local or general anaesthesia. Market-approved diagnostic and ablation catheters were used as clinically required at the discretion of the operator. The left heart could be accessed via the retrograde aortic route or transseptal puncture (TSP) based on the operator's preference. Generally, left-sided ventricular arrhythmias were performed via the retrograde approach (MNS 93%, MAN 89%; P = ns), left-sided atrial arrhythmias always via TSP, and left-sided accessory pathways distributed between the two methods (MNS 22% TSP, group MAN 20% TSP; P = ns). The use of three-dimensional mapping system was allowed in both groups if necessary. Intracardiac echocardiography (ICE) was used to guide TSPs in both groups.

Crossover from the magnetic navigation catheter to manual navigation catheter was allowed at the discretion of the investigator, although the crossover counted as an acute failure for the MNS group. Crossover from the MAN to the MNS group was not possible due to logistical reasons (see below).

The endpoints of procedural success were defined as the elimination of accessory pathway conduction for CMT, the elimination of inducibility and no more than single echo beats for AVNRT, complete AV block for AVJ ablation, bi-directional isthmus block for CTI- dependent AFl, and complete electrical pulmonary vein isolation for AFib. For VT patients; if the VT was inducible, non-inducibility was the endpoint, if only ventricular extrasystoles (VES) were present, then the complete abolishment of VES assessed by 24 h telemetry counted as acute success. The presence of a pacemaker (PM) or an implantable cardioverter defibrillator (ICD) was not considered as contraindication for MNS-guided ablations.

According to an institutional protocol for the treatment of patients with AFib, all paroxysmal AFib patients were ablated using the cryoballoon technique, the persistent AFib patients were ablated using cryoballoon or MNS, and all long-standing persistent (>12 months) AFib patients were ablated using MNS. Persistent and long-standing persistent AFib procedures included additional linear ablation in the left and/or right atrium. Whenever linear ablation was performed, conduction block was mandatory to be proven. Regardless of the type of AFib patients pulmonary vein isolation was mandatory in all patients. This was always controlled by a 'lasso-type' catheter. Also, atypical AFl and AT patients were ablated generally using MNS (50 of 56, 89%).

Magnetic navigation system-guided ablations

The procedures were performed in group MNS using the Stereotaxis Niobe II (Stereotaxis, Inc., St Louis, MO, USA) implemented in an EP lab equipped with a Siemens Axiom Artis (Siemens, Erlangen, Germany) fluoroscopy system. The following ablation catheters were used: for AVNRT, CMT and AVJ Celsius RMT (4 mm) (Biosense Webster, Diamond Bar, CA, USA), and for AFib NaviStar RMT ThermoCool (Biosense Webster), AFl/AT and VT Navistar RMT DS (8mm), NaviStar RMT ThermoCool (Biosense Webster), or Trignum Flux Gold-tip (Biotronik GMBH, Berlin, Germany). The use of an 8 mm tip RMT catheter was associated with a char formation in some patients. Therefore, after the thermocool RMT catheter became available the 8 mm tip catheter was no longer used.

When needed, electroanatomical mapping was performed using the CARTO RMT (Biosense Webster) system.

Manual-guided ablations

The procedures in the MAN group took place in an EP lab equipped with a Siemens Megalix (Siemens) fluoroscopy system. Electroanatomical mapping was performed using CARTO (Biosense Webster) or EnSite (St Jude Medical Inc., St Paul, MN, USA) system. The following ablation catheters were used: for AVNRT, CMT, and AVJ Biosense Webster B–D curve 4 or 8 mm tip (Biosense Webster), for AFib, AFl/AT, and VT Biosense Webster Navistar ThermoCool (Biosense Webster). The Artic Front cryoballoon catheters (Medtronic Inc., Minneapolis, MN, USA) were used for cryo-isolation of the pulmonary veins; Freezor Max (Medtronic Inc.) catheters were used in cases when complete electrical isolation could not be achieved with the balloon.

Data collection and analysis

The following parameters were analyzed both in group MNS and group MAN: acute success rate, fluoroscopy time, procedure time, and complications. Acute success rate was assessed according to the terms mentioned above. Fluoroscopy time and procedure time (latter began with subcutaneous injection application of lidocaine by the physician to the groin and ended when catheters were removed from the patient's body) were recorded in the clinical procedure log and included a 30 min waiting time. Any adverse event recognized by the operator during the procedure, by the attending cardiologist prior to hospital discharge, or by the general physician during follow-up was investigated by a trained electrophysiologist, and was considered as a complication if the event could be related to the procedure. Complications were categorized as major and minor [major: pericardial effusion or/and tamponade, permanent AV block, stroke, major bleeding (requiring blood transfusion or haemoglobin serum level drop of >20 g/L) or death; minor: minor bleeding, transient ischaemic attack, and temporary AV block].

Subgroup analysis of the above-mentioned parameters was performed for the following groups: AFib, AFl, atypical AFL (aAFl)/AT, AVNRT, CMT, AVJ, and VT. The AFib group was further divided into the following subgroups: paroxysmal, persistent, and long-standing persistent. Because different techniques were used for the treatment of paroxysmal and long-standing persistent AFib patients, paroxysmal and long-standing persistent AFib subgroups were not compared in efficacy; however, data from these groups were included

into the safety comparison (Tables 1 and 2). Patients included into the persistent AFib group were comparable (Tables 1 and 2). The VT group was further analyzed in subgroups of patients with and without structural heart disease (SHD and NSHD).

Follow-up

Follow-up visits were scheduled for all patients at the outpatient clinic of the Department of Cardiology, Erasmus MC 3 months following the procedure, and every 3 months thereafter, except for CMT, AFl, and AVNRT patients, when other than the first follow-up visit was scheduled only if the symptoms recurred. Atrial fibrillation patients were more rigorously followed at the AFib clinic of the department, including daily transtelephonic rhythm strips.

Statistics

Parameters obtained from the registry were analyzed using SPSS 15.0 (SPSS Inc., Chicago, IL, USA). Patient demographic and baseline characteristics were presented as mean ± SD. The two-tailed Student's *t*-test was used for comparing continuous unpaired samples, assuming unequal variances (age, fluoroscopy time, procedure time, and follow-up period). For categorical variables the X^2 test was performed (number of patients with different arrhythmias, gender, success rate, recurrence rate, and number of complications). Two-sided *P* values <0.05 were considered significant.

RESULTS

Patients

There were no differences in the gender and age between group MNS and MAN (Table 1). There were no differences in the number of patients enrolled into the subgroups based on the diagnosed arrhythmias, except for the subgroups mentioned in the Methods section—paroxysmal and long-standing persistent AFib and AFL/AT (Table 1). There was no difference in the presence of PMs or ICDs between the study groups (PM: 4 MNS vs. 6 MAN, P = NS; ICD 20 MNS vs. 21 MAN, P = NS). In, two patients (both in the VT group, both had abdominal implant) the ICD switched to magnet mode (asynchronous pacing). None of these patients

were PM dependent; therefore, temporary programming allowed electro-anatomical mapping without further problems. No long-term effect on ICD or PM function was observed.

Table 1
Patient demographics

	Group MNS	Group MAN	Total
Number	292	318	610
Age (years)	48 ± 19	52 ± 16	50 ± 18
Gender (male)	166 (57%)	197 (62%)	363 (60%)
AFib	56 (19%)	76 (24%)	132 (22%)
Paroxysmal	–	60 (19%)	60 (9.8%)
Persistent	23 (7.9%)	16 (5.0%)	39 (6.4%)
Long-standing persistent	33 (11%)	–	33 (5.4%)
AFl	40 (14%)	84 (26%)	124 (20%)
aAFl/AT	50 (17%)	6 (1.9%)	56 (9.2%)
AVNRT	29 (10%)	70 (22%)	99 (16%)
CMT	55 (19%)	45 (14%)	100 (16%)
AVJ	8 (2.7%)	8 (2.5%)	16 (2.6%)
VT	54 (18%)	29 (9.1%)	83 (14%)
VT-SHD	17 (5.8%)	15 (4.7%)	32 (5.2%)
VT-NSHD	37 (12%)	14 (4.4%)	51 (8.4%)

MNS, magnetic navigation system; MAN, manual navigation; AFib, atrial fibrillation; AFl, cavotricuspid isthmus-dependent atrial flutter; aAFl, atypical atrial flutter; AT, atrial tachycardia; AVNRT, atrioventicular nodal re-entrant tachycardia; CMT, circus movement tachycardia; AVJ, atrioventricular junction; VT, ventricular tachycardia; SHD, structural heart disease; NSHD, non-structural heart disease.

Table 2
Ablation results – acute success

	Group MNS	Group MAN	Total	*P* value
All arrhythmias	269/292 (92%)	298/318 (94%)	567/610 (93%)	0.904
AFib	52/56 (93%)	75/76 (99%)	127/132 (96%)	0.083
Paroxysmal	–	59/60 (98%)	59/60 (98%)	NA
Persistent	22/23 (96%)	16/16 (100%)	38/39 (97%)	0.398
Long-standing persistent	30/33 (91%)	–	30/33 (91%)	NA
AFl	38/40 (95%)	82/84 (98%)	120/124 (97%)	0.440
aAFl/AT	42/50 (84%)	4/6 (67%)	46/56 (82%)	0.295
AVNRT	29/29 (100%)	68/70 (97%)	97/99 (98%)	0.358
CMT	52/55 (95%)	39/45 (87%)	91/100 (91%)	0.075
AVJ	8/8 (100%)	8/8 (100%)	16/16 (100%)	–
VT	50/54 (93%)	21/29 (72%)	71/83 (86%)	0.013
VT-SHD	14/17 (82%)	10/15 (67%)	24/32 (75%)	0.306
VT-NSHD	36/37 (97%)	11/14 (79%)	47/51 (92%)	0.026

MNS, magnetic navigation system; MAN, manual navigation; AFib, atrial fibrillation; AFl, cavotricuspid isthmus-dependent atrial flutter; aAFl, atypical atrial flutter; AT, atrial tachycardia; AVNRT, atrioventicular nodal re-entrant tachycardia; CMT, circus movement tachycardia; AVJ, atrioventricular junction; VT, ventricular tachycardia; SHD, structural heart disease; NSHD, non-structural heart disease; NA, not applicable.
P values listed were calculated based on a two-sample *t*-test assuming unequal variances between group MNS and group MAN.

Ablation

Magnetic navigation system was equally effective as MAN in acute success rate for the overall groups (Table 2). In the subgroups only VT results were different, where MNS was more successful (Table 2). The success rate in the NSHD-VT subgroup was higher in MNS group, whereas the difference in VT subgroup with SHD did not reach statistical significance (Table 2). For the other subgroups no differences were observed in success rates (Table 2). Crossovers occurred only before the availability of irrigated tip MNS catheters, whereas one CMT patient and two AFl patients underwent crossover from MNS catheters (4 mm for CMT, 8 mm for AFl) to manual guided irrigation tip catheters. Following the crossover all the three patients were ablated successfully. However, the MNS still proved to be non-inferior for the ablation of AFl and CMT. Overall, less fluoroscopy was used in group MNS (Table 3). In the AVNRT and VT subgroups, less fluoroscopy was used in group MNS, otherwise there were no differences between the two groups (Table 3). There were no differences in procedure times between group MNS and MAN. Concerning subgroups, procedure times were higher using MNS in AFl, but were shorter in the VT subgroup.

Table 3
Summary of mean fluoroscopy and procedure times for group MNS and MAN

	Fluoroscopy time (min)			Procedure time (min)		
	MNS	**MAN**	***P* value**	**MNS**	**MAN**	***P* value**
All arrhythmias	30 ± 20	35 ± 25	0.009	168 ± 67	159 ± 75	0.119
AFib	44 ± 17	40 ± 22	0.278	248 ± 59	191 ± 81	0.001
Paroxysmal	–	36 ± 19	NA	–	168 ± 52	NA
Persistent	42 ± 15	54 ± 28	0.061	232 ± 41	276 ± 107	0.088
Long-standing persistent	46 ± 19	–	NA	264 ± 70	–	NA
AFl	27 ± 13	32 ± 24	0.198	152 ± 44	123 ± 47	0.005
aAFl/AT	37 ± 23	47 ± 20	0.361	188 ± 51	208 ± 53	0.464
AVNRT	12 ± 8.8	25 ± 20	0.001	114 ± 39	136 ± 55	0.068
CMT	28 ± 18	32 ± 27	0.428	134 ± 50	146 ± 57	0.314
AVJ	6.5 ± 2.4	7.7 ± 3.7	0.472	72 ± 7.5	86 ± 21	0.147
VT	27 ± 21	56 ± 31	0.001	166 ± 54	222 ± 97	0.009

MNS, magnetic navigation system; MAN, manual navigation; min, minutes; AFib, atrial fibrillation; AFl, cavotricuspid isthmus-dependent atrial flutter; aAFl, atypical atrial flutter; AT, atrial tachycardia; AVNRT, atrioventicular nodal re-entrant tachycardia; CMT, circus movement tachycardia; AVJ, atrioventricular junction; VT, ventricular tachycardia; NA, not applicable. *P* values listed were calculated based on a two-sample *t*-test assuming unequal variances between group MNS and group MAN.

Complications

The use of MNS was associated with a lower complication rate (4.5 vs. 10%; P = 0.005). Moreover, concerning major complications the difference was also significant between the two groups (0.34 vs. 3.2%; P = 0.01). One permanent AV block occurred in the MNS and one in the MAN group. The other nine major complications in the MAN group were either pericardial effusion or pericardial tamponade, whereas no effusion/tamponade occurred in the MNS group. There was a trend towards lower minor complications in the MNS group as well, but it did not reach statistical significance (4.1 vs. 6.4%; P = ns) (Figure 1). Two temporary AV block were observed in the MNS group, one in the MAN group, the rest of the minor complications were femoral bleeding/haematoma in both groups.

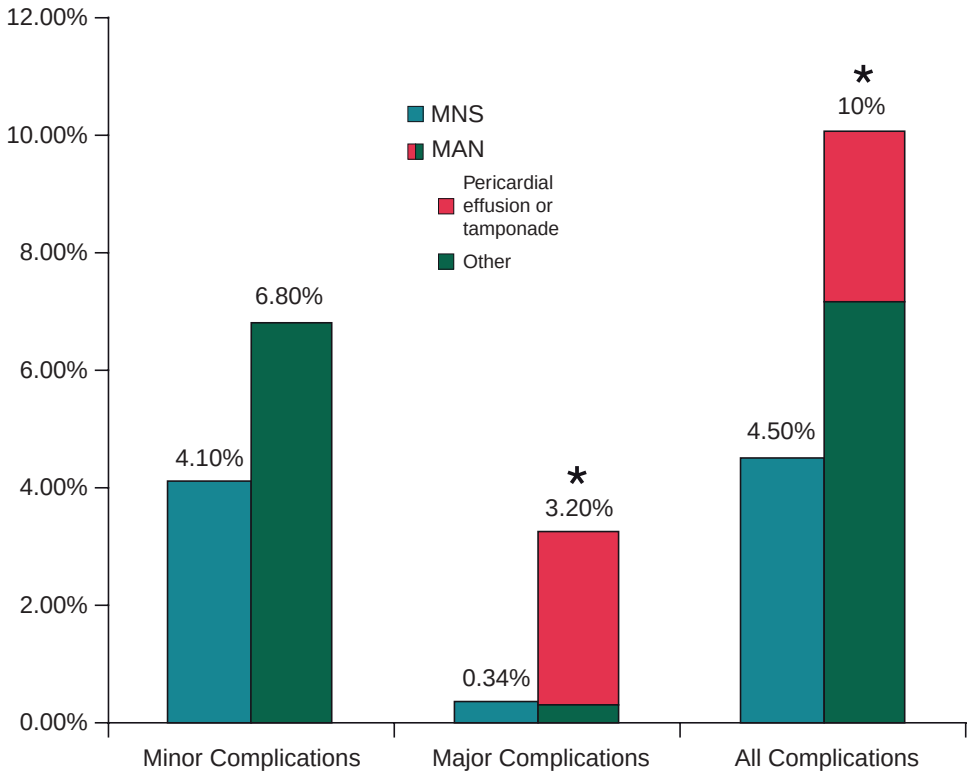

Figure 1: Complications – Comparison of minor, major, and all complications between magnetic navigation system and manual navigation groups. Pericardial effusion/tamponade is coloured red. Asterisk indicates *P* < 0.01.

Follow-up

There were no differences in follow-up periods between group MNS and MAN (15 ± 9.5 vs. 14 ± 9.5 months, P = ns). There were no differences in recurrence rates between group MNS and MAN in overall (14 vs. 11%, P = ns) or in any of the subgroups [(AFib persistent 14 vs. 19%) (AFib paroxysmal — vs. 16%) (AFib long-standing persistent 33 vs. 0%) (aAFL/AT 14 vs. 25%) (AFl 13 vs. 11%) (AVNRT 6.9 vs. 7.4%) (CMT 7.7 vs. 5.2%) (AVJ 0 vs. 0%) (VT 14 vs. 14%), P = ns].

DISCUSSION

This is the first study that assesses the efficacy and safety of ablations using MNS vs. manual navigation involving statistically equivalent, large-scaled patient groups. Our series includes all types of arrhythmias, arising from all four heart chambers. There are three major findings of this study. First, MNS proved to be equal to manual ablation not only in acute success rate, but for a reasonable follow-up period in a broader aspect of arrhythmias. Second, MNS was superior in safety as compared with manual navigation resulting in lower number of complications as well as less fluoroscopy times. Third, MNS was found to be better for the ablation of VT.

Rationale of using MNS for ablations

The success of catheter ablation procedures depends on accurate substrate location, followed by optimal delivery of energy provided by good tissue contact.[24] Manual navigation of catheters in the human heart has limitations: some regions are difficult to reach, and compromised catheter positioning may result in insufficient lesion formation.[13,24] Catheter movement in some positions is accompanied by the risk of major complications, including pericardial effusion or tamponade.[7,24] Although several pre-defined catheter curves were introduced to help appropriate lesion delivery, there are no optimal curves available for the treatment of paediatric patients with small hearts, patients with complex congenital heart defects, or some type of VTs.[25] The introduction and utilization of MNS was aimed at surmounting these difficulties. It provides improvement of safety by the flexible catheter design, and no pericardial effusion or tamponade was reported related to catheter

navigation using MNS.[20] Magnetic navigation system also provides better navigation capability, which is not limited by preformed or evolved catheter curves.[19,25,26] Theoretically, non-fluoroscopic imaging and recently built-in automated functions (AutoMap, stored magnetic vectors) allow less fluoroscopy time (to both operator and patient).[18] Stored magnetic vectors also make it possible to re-navigate to spots defined and stored during the procedure.[26] Promising initial results were published concerning these above-mentioned issues.[22,23,25,27] In our experience, automated map function was used in all AFib, aAFl/AT and VT patients undergoing MNS ablation. Manual correction was performed after automated mapping, which could be completed in 5–6 min on average.

Acute success rates and recurrences

Based on the theoretical advantages mentioned above, MNS could be superior to manual navigation in the analyzed parameters. Reports until now focused more on feasibility rather than assessment of efficacy of MNS.[10,11,15,17,23,25 – 30] Contrary to this, we aimed at comparing large groups of patients treated using MNS or MAN, with a long follow-up period. We confirm that MNS is feasible for ablation of different kinds of arrhythmias, and clearly demonstrate that it provides better safety and uses less fluoroscopy than manual navigation (see below). Furthermore, superiority in acute success rate can be achieved in the VT subgroup (see below).

Certainly, some issues are still to be solved that may play a role in limiting of MNS. The delivered contact force is unknown relative to manual catheters in which it had been shown to affect adequate lesion formation. However, based on the high acute success and low recurrence rates found in all subgroups during the reasonably long follow-up period, it does not seem to effect patient outcomes. Preparation of the system consumes considerable time (isocentering, registration, merging with CARTO, checking magnet movement). However, it does not result in significant prolongation of the procedures in overall. Although improvements were made recently, we also lack of fully automated functions (no need or automated isocentering; reliable, well-defined automapping) yet.

Crossovers

In our series, we encountered only three patients, where crossover to manual navigation became necessary (one CMT and two AFl patients). Although the endpoint could be reached using manual navigation in all three cases, no difference was found in general between MNS and MAN concerning the acute success rates in these subgroups. Also, it is important to notice that these crossovers happened before the availability of irrigation tip catheters for MNS.

Safety of ablations

The use of atraumatic, flexible designed ablation catheters combined with magnetic field-guided navigation resulted in significantly reduced number of complications. No pericardial effusion or tamponade was observed in the MNS group, whereas in the MAN group these proved to be the most frequent major complications. All TSPs were guided by ICE, and none of these complications were related to them. This finding is consistent with previous reports, but these reports failed to substantiate it with significant statistical difference. Two atrioventricular blocks (AVB) occurred in the MSN group (one in a patient with parahisian AT; the risk was discussed with the patient after the diagnosis of the tachycardia was established. The other AVB occurred in a patient with AVNRT during an application near the ostium of the coronary sinus. In this case, our hypothesis is either an ectopic fast pathway or the occlusion of the AVN artery).

Concerning minor complications—dominantly minor bleeding related to the femoral punctures, we also found somewhat higher number in the MAN group, which could be explained by the greater diameter of sheaths used for manual ablation such as cryoballoon sheaths and decreased movement of the sheath at the puncture site during remote catheter manipulation.

The high manoeuvrability and atraumatic design of the MNS-guided ablation catheter allows navigation without constant fluoroscopy control, while re-imaging is typically required after each repositioning of the manual-guided catheter.[18] Furthermore, stored MNS vectors also help to navigate the catheter without repeated fluoroscopic pulses.

As we mentioned in the Methods section, our clinic is an academic center, and the fellows are taking part of the procedures, including femoral vein and artery punctures, and diagnostic catheter positioning. This significantly influences fluoroscopy or procedure times, and minor complication rates in both groups. Although our data may seem too high at first glance concerning these parameters, they are not really deviated from recently published available data.[31]

Transseptal puncture or retrograde aortic approach

In our center, standard approach for left-sided VT is retrograde aortic ablation. Also, in case of left-sided accessory pathway the retrograde aortic approach is preferred. In our experience, this method helps to avoid the chance for serious complications (pericardial effusion/tamponade) and/or the need for expensive diagnostic tools (ICE).

Ablation of ventricular tachycardia

This is the first large-scale study to prove the superiority of MNS for ablation of VT compared with manual navigation. This is demonstrated in most of the analyzed parameters, such as acute success rate, and procedure and fluoroscopy times. There are multiple reasons to explain this finding. The MNS-guided catheter retains its manoeuvrability even in difficult positions, e.g. in cusp-related VTs, papillary muscle-originated VTs, where the capabilities of manual navigation are seriously limited by the multiple curves of the catheter.[11] The MNS controls the tip of the catheter, which means that the unavoidable curves of the catheter do not hinder the positioning of the tip, and good contact can be achieved, resulting in appropriate lesion formation.[13] An MNS-guided catheter has no pre-defined curve, which also contributes to the high manoeuvrability. Moreover, catheter stability using MNS is improved due to the constant magnetic force directing the tip unchanged during application.[13] The above-mentioned capabilities are especially beneficial for patients in whom the arrhythmia substrate is located in a difficult position (i.e. posteroseptal wall in the right or left ventricular outflow tract) or where stability is the major issue (i.e. papillary muscle VTs). Two patients had papillary muscle-originated VT, and five patients had aortic cusp VT in the MNS group, all the seven patients were ablated successfully. This can explain the difference in success rates between the VT subgroups, whereas statistical significance could be only proven for the NSHD-VT subgroup.

Limitations of the study

Although this registry is not a randomized, prospective trial, there was not any difference between the two groups and the assignment of the patients to the groups was independent of the operators. However, because of local protocols for the treatment of AFib patients, there were no paroxysmal patients treated with the MNS, and there were no long-standing persistent AFib patients treated manually. This means that only persistent AFib subgroups were comparable, and these groups were not different indeed.

CONCLUSION

The MNS is equal in terms of acute and long-term success rates compared with MAN, whereas MNS-guided procedures can be performed with a lower complication rate and using less fluoroscopy. For the ablation of VT, MNS is superior to MAN.

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CHAPTER 3

Outcomes of repeat catheter ablation using magnetic navigation or conventional ablation

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ABSTRACT

Aims

After initial catheter ablation, repeat procedures could be necessary. This study evaluates the efficacy of the magnetic navigation system (MNS) in repeat catheter ablation as compared with manual conventional techniques (MANs).

Methods and Results

The results of 163 repeat ablation procedures were analyzed. Ablations were performed either using MNS (n = 84) or conventional manual ablation (n = 79). Procedures were divided into four groups based on the technique used during the initial and repeat ablation procedure: MAN–MAN (n = 66), MAN–MNS (n = 31), MNS–MNS (n = 53), and MNS–MAN (n = 13). Three subgroups were analyzed: supraventricular tachycardias (SVTs, n = 68), atrial fibrillation (AF, n = 67), and ventricular tachycardias (VT, n = 28). Recurrences were assessed during 19 ± 11 months follow-up. Overall, repeat procedures using MNS were successful in 89.0% as compared with 96.2% in the MAN group (P = ns). The overall recurrence rate was significantly lower using MNS (25.0 vs. 41.4%, P = 0.045). Acute success and recurrence rates for the MAN–MAN, MAN–MNS, MNS–MNS, and MNS–MAN groups were comparable. For the SVT subgroup a higher acute success rate was achieved using MAN (87.9 vs. 100.0%, P = 0.049). The use of MNS for SVT is associated with longer procedure times (205 ± 82 vs. 172 ± 69min, P = 0.040). For AF procedure and fluoroscopy times were longer (257 ± 72 vs. 185 ± 64, P = 0.001; 59.5 ± 19.3 vs. 41.1 ± 18.3 min, P < 0.001). Less fluoroscopy was used for MNS-guided VT procedures (22.8 ± 14.7 vs. 41.2 ± 10.9, P = 0.011).

Conclusion

Our data suggest that overall MNS is comparable with MAN in acute success after repeat catheter ablation. However, MNS is related to fewer recurrences as compared with MAN.

INTRODUCTION

Nowadays, catheter ablation is a well-established technique that has an important role in the treatment of many arrhythmias. It has become the first-line therapy for arrhythmias such as atrioventricular nodal re-entrant tachycardia (AVNRT), circus movement tachycardia (CMT), and cavotricuspid isthmus (CTI)-dependent atrial flutter (AFl).[1] Furthermore, it is used as therapeutic option for the treatment of atrial fibrillation (AF), atrial tachycardia (AT), and ventricular tachycardia (VT).[1] In the past years, the magnetic navigation system (MNS) has been evaluated for treatment of different arrhythmias.[2 – 4]

Studies showed that the design of MNS has some advantages such as an atraumatic catheter design that allows safe catheter ablation, a reduced amount of radiation exposure to both the patient and physician, unrestricted and reproducible catheter manoeuvrability, and improved catheter stability.[5,6] However, MNS is related to longer procedure times in some cases and may result in more expensive procedures.[7] Several studies demonstrated that MNS offers at least equally effective catheter ablation and for particular arrhythmias (e.g. non-structural VT) even improved outcomes as compared with manual ablation.[2,8,9] All performed studies evaluated the acute or long-term success and no data are available on the effectiveness of MNS in repeat catheter ablation specifically.

The objective of this study was to evaluate the efficacy of MNS in repeat catheter ablation for different arrhythmias as compared with conventional ablation techniques in a large series of patients. Because of the prior described advantages of MNS our primary hypothesis was that MNS would lead to higher success rates after prior unsuccessful ablation procedures.

METHODS

Patients

A total of 163 repeat catheter ablation procedures were included in this study. The median age of the study population was 55.0 years [interquartile range (IQR), 42.0 – 65.0 years] and

64% was male. Sixty-seven patients had ablation for AF, 16 for AT, 18 for CTI-dependent AFl, 15 for AVNRT, 18 for CMT, 28 for VT, and 1 for atrioventricular junction (AVJ) ablation. These arrhythmias were combined in three subgroups: supraventricular tachycardias (SVTs, n = 68), AF (n = 67), or VTs (n = 28). Three types of AF were classified according to the ESC 2010 guidelines:[10] paroxysmal (self-terminating AF within 7 days), persistent (AF lasts longer than 7 days or required termination by cardioversion), and long-standing persistent (AF being persistent for 12 months or longer). In the AF subgroup 48 patients suffered from paroxysmal AF, 15 patients had persistent AF, and 4 patients had long-standing persistent AF (Table 1).

Table 1
Patient demographics and arrhythmia distribution between MNS and MAN

	MNS	**MAN**	***P* value**
Total patients	84	79	–
Age (years)	49.6 ± 18.2	52.8 ± 15.2	0.231
Gender (% male)	64.3	64.6	0.551
Number of VT	18	10	0.101
Number of AF	33	34	0.372
Paroxysmal (%)	75.8	67.6	0.321
Persistent (%)	15.2	29.4	0.134
Long-standing persistent (%)	9.1	2.9	0.295
Number of SVT	33	35	0.118
AFl (%)	27.3	25.7	0.551
AT (%)	42.4	5.7	< 0.001
AVNRT (%)	9.1	34.3	0.012
AVRT (%)	21.2	31.4	0.249
AVJ (%)	0.0	2.9	0.515

The mean left atrium (LA) size of AF patients was comparable for MNS and manual conventional technique (MAN) patients (43.1 ± 6.4 vs. 44.9 ± 6.4mm, P = 0.282). Ablation was performed either using MNS (84 patients) or conventional manual techniques (group MAN, 79 patients). Only patients who underwent repeat catheter ablation for the identical arrhythmia as targeted in the initial procedure were included in this study. Data of patients with either an unsuccessful initial procedure or recurrence after an initially successful ablation were analyzed. Investigators were not involved in the decision as to whether a patient was scheduled in the MNS-equipped laboratory or MAN-equipped laboratory. Patient age, gender, and number of SVT, AF, and VT were equally distributed between the

two groups (Table 1). The ablation procedures were performed by the same group of electrophysiologists experienced with both manual and MNS techniques.

Electrophysiology studies – ablation strategy

Written informed consent for the ablation procedure was obtained from all patients. Resting 12-lead electrocardiogram, and laboratory tests, a chest X-ray image and a two-dimensional echocardiography were acquired from all patients within the month prior to and 48 h following the procedure. A transoesophageal echocardiogram was performed if considered necessary. Standard peri-procedural medication protocols were followed in all patients. For AVNRT, AT, CMT, and elective VT patients were instructed to stop taking antiarrhythmic drugs for a period of at least four half-lives prior undergoing the procedure. In cases of AF, AVJ ablation, and emergency VT ablation medication remained unchanged. The procedures were performed during a fasting state, using local or general anaesthesia.

The left heart could be accessed via the retrograde aortic route or trans-septal puncture (TSP) based on the operator's preference. Generally, left-sided ventricular arrhythmias were performed via the retro-grade approach (MNS 100%, MAN 75%; P = ns), left-sided atrial arrhythmias always via TSP, and left-sided accessory pathways distributed between the two methods (MNS 14% TSP, group MAN 67% TSP; P = ns). Intracardiac echocardiography was used to guide TSPs in both groups.

The endpoints of procedural success were defined as the elimination of accessory pathway conduction for CMT, the elimination of inducibility and no more than single echo beats for AVNRT, complete AV block for AVJ ablation, and bidirectional isthmus block for CTI-dependent AFl. The endpoint for paroxysmal and persistent AF was complete electrical pulmonary vein isolation (PVI) and, if necessary, additional linear lesions to achieve sinus rhythm. For long-standing persistent AF, first all PV's were isolated, linear lines were created (first roof line, then mitral line, and lastly postero-inferior line), and electrogram-based ablation in the LA and coronary sinus was performed. After restoration of sinus rhythm bidirectional block was assessed at every line using differential pacing methods. Arrhythmia induction was not part of this protocol. Additional linear ablation was performed in 19 patients and was higher for the MNS group than the MAN group (39.4 vs. 17.6%, P = 0.044).

For VT patients, if the VT was inducible, non-inducibility of the clinical VT was the endpoint, if only ventricular extrasystoles (VESs) were present, then the complete abolishment of VES assessed by 24 h telemetry counted as acute success.

Magnetic navigation system-guided ablations

Magnetic-guided ablation procedures were performed using the Stereotaxis Niobe Magnetic Navigation System (Stereotaxis, Inc) in an electrophysiology (EP) lab equipped with a Siemens Axiom Artis (Siemens) fluoroscopy system. The principles and use of the MNS has previously been described.[4] The Niobe II MNS consists of two permanent magnets situated on both sides of the patient. The system uses a computer-controlled workstation (Navigant, Stereotaxis, Inc.) to allow changes of the magnetic field orientation in order to navigate the ablation catheter. Combined field strength of 0.08 or 0.1 T was used. During the procedures the following ablation catheters were used: for AVNRT, AVJ, and CMT the Celsius RMT (4mm) (Biosense Webster); for AF the NaviStar RMT ThermoCool (Biosense Webster); and for AT and VT the Navistar RMT DS (8 mm) or NaviStar RMT ThermoCool (Biosense Webster). However, after the thermocool RMT catheter became available the 8 mm tip catheter was no longer used because of char formation. Electroanatomical mapping was performed using the CARTO RMT (Biosense Webster, Inc.) system.

Manual-guided ablations

Procedures in the manual group were performed in an EP lab equipped with a Siemens Megalix (Siemens) fluoroscopy system. Electroanatomical mapping was performed using CARTO (Biosense Webster) or the EnSite NavX system (St Jude Medical, Inc.). The following ablation catheters were used: for AVNRT, AVJ, and CMT the Biosense Webster B–D curve 4 or 8 mm tip (Biosense Webster); for AF, AT, and VT the Biosense Webster Navistar ThermoCool (Biosense Webster). The Arctic Front cryoballoon catheters (Medtronic Inc.) were used for cryo-isolation of the PVs; Freezor Max (Medtronic Inc.) catheters were used in cases when complete electrical isolation could not be achieved with the balloon. For recurrent AVNRT a Cryo-cath 4 or 6 mm catheter was used as well when it was judged that cryoenergy was the appropriate choice. Ablation parameters were excluded from analysis, if the repeat procedure was performed using cryoenergy.

Crossovers

Crossover from the magnetic navigation catheter to manual navigation catheter was allowed if preferred by the operator. Any crossover was counted as an acute failure for the MNS group. However, no crossover occurred during this study and therefore it was not taken into account in the analysis.

Data collection and analysis

Procedures were divided into four groups based on the technique used during the initial and repeat ablation procedure: MAN–MAN (n = 66), MAN–MNS (n = 31), MNS–MNS (n = 53), and MNS–MAN (n = 13). Direct post-procedural success rates were analyzed and subgroup analysis was performed for the subgroups SVT, AF, and VT. Acute success was assessed according to the criteria described before. Procedural parameters such as total application, fluoroscopy and procedure time, and the number of radiofrequency (RF) applications were analyzed as well. Procedure time was defined as the time between the first subcutaneous injection application of lidocaine to the groin and the removal of all catheters from the patient's body. A waiting time of 30 min was included.

Follow-up

During a follow-up period of 19 ± 11 months recurrence rates were assessed between the overall group and the subgroups. Follow-up visits were scheduled for all patients at the outpatient clinic of the Department of Cardiology, Erasmus MC, starting at 3 months after the procedure, and every 3 months thereafter, except for CMT, AFl, and AVNRT patients, when other than the first follow-up, visits were scheduled only if the symptoms recurred.

Statistics

Normality of distribution was determined by using the Kolmogorov–Smirnov test. Continuous variables were expressed as mean ± SD, if normally distributed, and compared with the Student's *t*-test for independent samples. In case of non-normal distribution of data, medians and IQRs were reported and the Mann–Whitney U test was used for data comparison. Categorical data were expressed as percentages and compared with the X^2-test or Fisher's exact test when appropriate. Event-free survival rates were determined using the Kaplan–Meier method and differences were evaluated by the log-rank test. Statistical

analysis was performed using SPSS 15.0 (SPSS Inc.). Statistical significance was defined as $P < 0.05$ (two-tailed).

RESULTS

Overall

Repeat procedure using magnetic navigation system

When a repeat procedure was performed using MNS, independent of the approach used during the previous procedure, similar success rates were achieved as compared with MAN (89.0 vs. 96.2%, P = 0.078; Figure 1). However, when a procedure was successful, significantly fewer recurrences were experienced in the MNS group (25.0 vs. 41.4%, P = 0.045; Figure 2). During these procedures the median number of RF applications was higher when using MNS compared with MAN [19, IQR (6–58) vs. 6.5, IQR (3–21), P = 0.002]. No differences were observed for application time [720 s, IQR (245–1710 s) vs. 581 s, IQR (113–1201 s), P = 0.116], fluoroscopy time (37.4 ± 26.3 vs. 36.6 ± 17.5min, P = 0.859), and total procedure time (199 ± 87 vs. 164 ± 61min, P = 0.063). Figures 3 and 4 represent the freedom of recurrence for the overall groups of MNS and MAN and the four subgroups, respectively. After analyzing the survival curves no significant difference was reached between the groups.

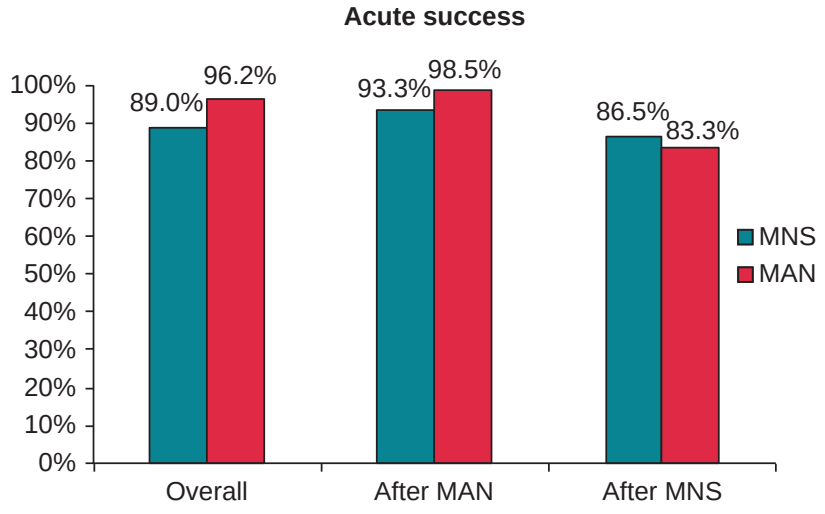

Figure 1: Overall acute success rates and after initial MAN or MNS ablation procedures.

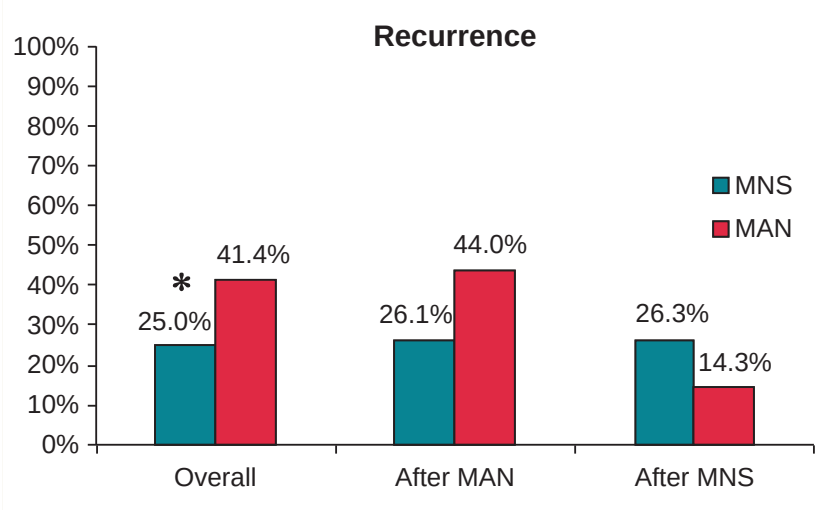

Figure 2: Overall recurrence rates and after initial MAN or MNS ablation procedures. The asterisk indicates *P* < 0.05.

After initial manual conventional technique procedure

For the two groups that included patients who had a prior manual ablation there was no difference in acute success depending on the use of MNS or MAN during the repeat procedure (93.3 vs. 98.5%, P = 0.229). Recurrence rate was comparable as well between MAN – MNS and MAN – MAN (26.1 vs. 44.0%, P = 0.114). When a patient experienced any recurrence, the time until this event was comparable for the two groups (3.9 ± 3.2 vs. 3.0 ± 2.5 months, P = 0.411). Using MNS for the repeat procedure is associated with a higher number of RF applications [41, IQR (9 – 68) vs. 5.5, IQR (3 – 21), P = 0.001] and more use of fluoroscopy (49.6 ± 24.8 vs. 36.3 ± 18.3 min, P = 0.007). When the use of fluoroscopy was corrected for the type of arrhythmia this difference could be explained by a significantly lower fluoroscopy use during MAN ablation in AF (40.0 ± 16.6 vs. 61.3 ± 16.8 min, P < 0.001). Other arrhythmias did not contribute to this difference. Total RF application time (1575 ± 1563 vs. 801 ± 853s, P = 0.052) and procedure time (219 ± 102 vs. 174 ± 68min, P = 0.057) was not statistically different between MNS and MAN.

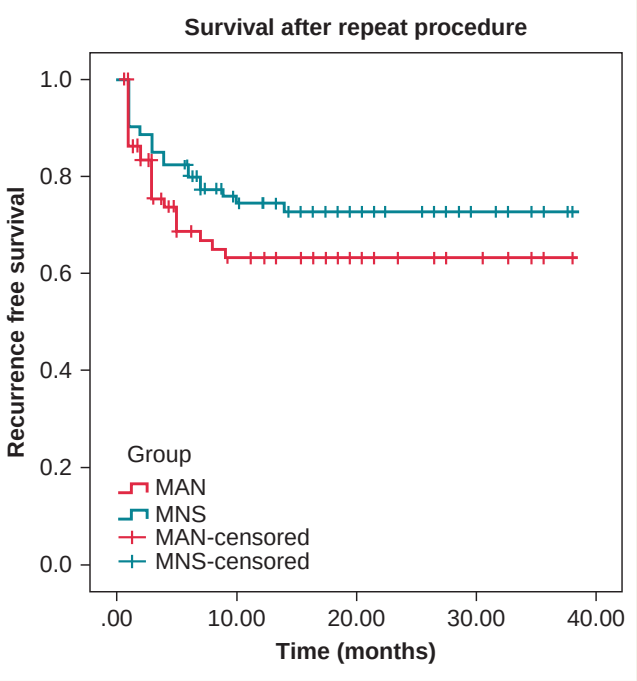

Figure 3: Survival plots for recurrence-free survival between MAN and MNS after repeat catheter ablation.

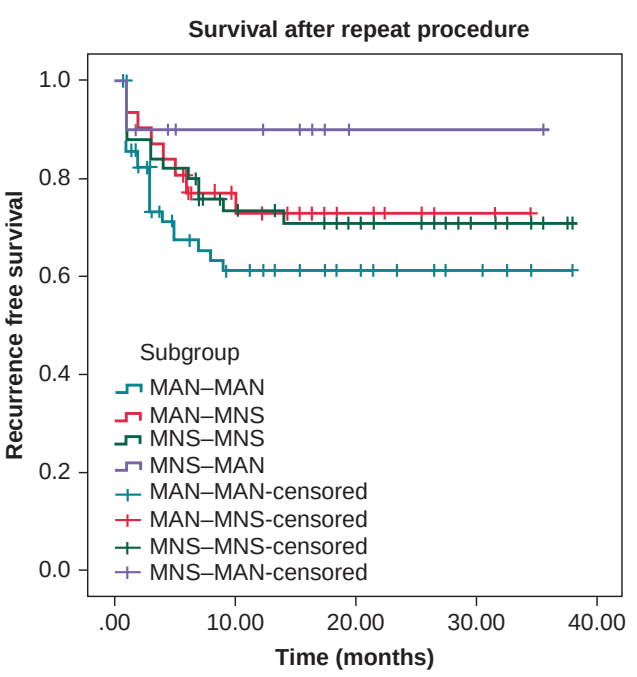

Figure 4: Survival plots for recurrence-free survival in the subgroups after repeat catheter ablation.

After initial magnetic navigation system procedure

If a patient underwent a prior MNS procedure there was no difference in acute success if the repeat procedure was executed using MNS or MAN (86.5 vs. 83.3%, P = 0.539). No difference was observed in recurrence rate (26.3 vs. 14.3%, P = 0.445) and the time until recurrence (3.9 ± 4.3 vs. 0.3 ± 0.6 months, P = 0.185). When procedural parameters were compared between the MNS–MNS and MNS–MAN group there was no statistical difference in total number of RF applications [17, IQR (5–41) vs. 9.4, IQR (1 – 23), P = 0.215], total RF application time (942 ± 946 vs. 622 ± 684 s, P = 0.512), fluoroscopy time (32.4 ± 25.1 vs. 40.7 ± 24.5 min, P = 0.444), and procedure time (194 ± 79 vs. 160 ± 76 min, P = 0.417).

Supraventricular tachycardia

In the subgroup with patients suffering from SVT, a lower acute success was observed using MNS compared with MAN (87.9 vs. 100.0%, P = 0.049; Figure 5). The recurrence rate for this subgroup was comparable for MNS and MAN (17.2 vs. 31.4%, P = 0.155; Figure 6). In the SVT subgroup, repeat ablation procedures using MNS were associated with comparable numbers of total RF applications (15.1 ± 18.9 vs. 10.3 ± 10.5, P = 0.251) and longer procedure time (205 ± 82 vs. 172 ± 69 min, P = 0.040). No difference was observed for total RF application time [317 s, IQR (195 – 740 s) vs. 537 s, IQR (143 – 976 s), P = 0.670] and fluoroscopy time (42.4 ± 27.1 vs. 36.7 ± 19.7 min, P = 0.206).

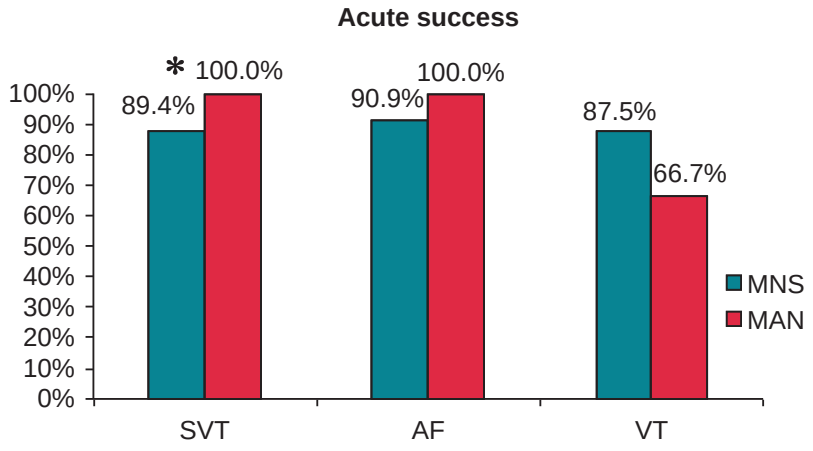

Figure 5: Acute success rates for SVT, AF and VT. The asterisk indicates *P* < 0.05.

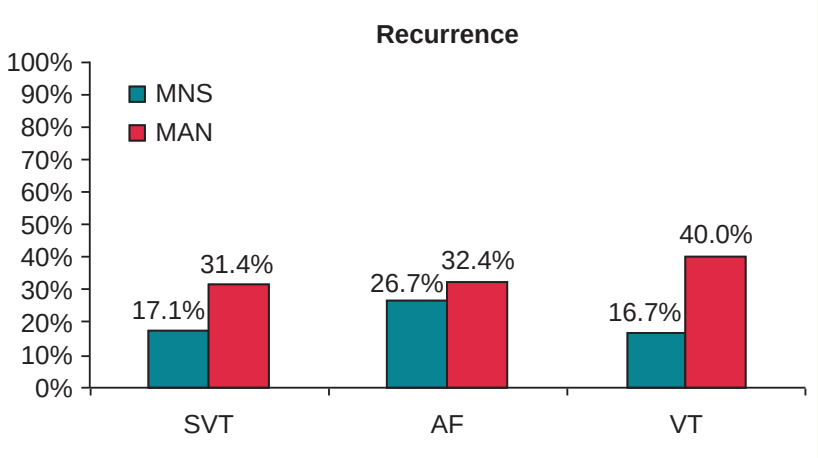

Figure 6: Recurrence rates for SVT, AF and VT.

Atrial fibrillation

In patients with AF, MNS achieved comparable acute success rates as MAN (90.9 vs. 100%, P = 0.114) with equal recurrence rates (26.7 vs. 32.4%, P = 0.413). For patients who underwent PVI alone, success rates were comparable for MNS and MAN patients (95.0 vs. 100.0%, P = 0.417). The time until recurrence was comparable for both groups (5.1 ± 4.2 vs. 3.0 ± 2.5 months, P = 0.177). When procedural parameters were analyzed MNS was associated with longer fluoroscopy times (59.5 ± 19.3 vs. 41.1 ± 18.3 min, P < 0.001) and longer procedures (257 ± 72 vs. 185 ± 64 min, P < 0.001).

Ventricular tachycardia

Patients who were classified in the VT subgroup had comparable rates for acute success and recurrence when compared between MNS and MAN (87.5 vs. 66.7%, P = 0.230; 16.7 vs. 40.0%, P = 0.330, respectively). There was no difference between MNS and MAN for the median number of RF applications (13.0 vs. 9.0, P = 0.392), total RF application time [481 s, IQR (214–990 s) vs. 270 s, IQR (51 – 1200 s), P = 0.495], and procedure time (181 ± 100 vs. 190 ± 62min, P = 0.891). During these procedures, MNS was associated with decreased fluoroscopy use (22.8 ± 14.7 vs. 41.2 ± 10.8 min, P = 0.011).

DISCUSSION

This is the first study that reports on the effectiveness of MNS for repeat catheter ablation. For the efficacy during initial ablation procedures the MNS has been well investigated.[11 – 13] However, since this system is so well implemented into modern electrophysiology, understanding of the usefulness for repeat catheter ablation is very important for clinical practice. Our data suggests that the use of MNS offers comparable success rates after repeat catheter ablation as MAN for the overall study population. In this group, MNS results in fewer recurrences after long-term follow-up. Furthermore, after subgroup analysis MNS leads to similar acute and long-term success as manual ablation, independent of what technique has been used during the initial procedure. For the ablation of recurrent SVT's, MNS procedures resulted in a lower acute success than manual-guided procedures.

As a result of the improved catheter manoeuvrability and stability using MNS, our hypothesis was that MNS would lead to higher success rates after prior unsuccessful ablation procedures. Based on the findings of this study our conclusion is that MNS does not increase efficacy for repeat catheter ablation. Future improvements of this system could enhance the efficacy of the system by implementing a force-sensing catheter that is currently not available. This might lead to more effective ablation procedures by providing feedback regarding lesion formation. However, when the MNS procedures were successful the effect sustained over time and this is reflected in the decreased recurrence rate in the overall population.

The findings of our study demonstrate that MNS is associated with lower acute success in treatment of recurrent SVT. However, in the MNS group a significant higher percentage of the patients had ATs and the MAN group included more AVNRT's. The difference in complexity in the ablation of these arrhythmias could have influenced the acute success rate. Subgroup analyses on AT or AVNRT specifically would lead to too small groups that have very less value for clinical practice.

Clinical implications

The outcomes of this study have important clinical implications for the use of MNS in repeat catheter ablation. Since the acute outcomes of MNS are comparable with MAN the question rises if the magnetic system has advantages for use during repeat procedures. In some particular situations the special capabilities of the MNS could be beneficial during the ablation procedure. For example, when the site of origin is very difficult to approach or could not be reached at all using manual ablation catheters (e.g. right inferior PV) the superior manoeuvrability of the magnetic catheter could allow navigation to this specific site. Other groups have published these advantages of the MNS in tip delivery as well.[14,15] However, for repeat catheter ablation in a large series of a mixed patient population this advantage could not be demonstrated. Therefore, more research is required to evaluate the true value of MNS in repeat procedures for complex atrial arrhythmias.

Certainly more purposes of the MNS could be mentioned for repeat catheter ablation despite the similar acute outcome. Many reports have demonstrated the improved safety using MNS.[5,16 – 19] For complex situations or an unknown cardiac anatomy in congenital heart disease patients the atraumatic catheter design could be valuable. In addition, the use of fluoroscopy could be important to decide whether to choose MNS or MAN for repeat procedures. In children with an unsuccessful procedure that requires a repeat procedure fluoroscopy could be an important concern and the cumulative radiation dose should be reduced as much as possible. Therefore, the decreased total fluoroscopy time could be determinant to use the magnetic approach in children with VT.

Limitations

In this study, no randomization was performed for direct comparison of magnetic and manual catheter ablation therapy. We used our prospective registry for the evaluation of the acute and long-term outcomes of repeat ablation procedures. Our data demonstrate the use of MNS in this specific patient population, but randomized trials are required to evaluate the true value of the magnetic system.

Today, enhanced MNSs are available (EPOCH, Stereotaxis) that might allow faster and more effective catheter ablation. Furthermore, for this study no deflectable sheath was used

during MNS procedures, which might have influenced procedural success. Novel developments on the field of remote magnetic navigation and the use of steerable sheaths could lead to improved outcomes of catheter ablation. However, further clinical evaluation is necessary to reveal the true value of this system.

Furthermore, a higher percentage of AT and fewer AVNRT were included in the MNS group as compared with MAN. This mix of difference in arrhythmia complexity could have influenced the acute success and recurrence rates. Since subgroup analyses for AT and AVNRT in this study would not lead to valuable clinical recommendations, more research is necessary in this field of arrhythmias.

CONCLUSION

Our data suggest that the use of MNS leads to similar acute and long-term success as manual ablation, independent of what technique has been used during the initial procedure. Overall, MNS is comparable with MAN in acute success of repeat catheter ablation and may reduce recurrences on the long term. Therefore, it may be considered as an alternative technique although it has the potential to prolong procedure times.

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CHAPTER 4

Remote magnetic navigation in atrial fibrillation

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ABSTRACT

Atrial fibrillation (AF) is of profound public health importance and is largely a disease of aging and is responsible for increased morbidity- and mortality-related healthcare expenditures. Catheter ablation to isolate the pulmonary veins has become the therapy of choice for treatment of drug-refractory AF. Procedures can be very challenging and multiple difficulties must be overcome in order to achieve a successful outcome. The magnetic navigation system (MNS) has advantages in catheter maneuverability, stability and reproducibility. Due to the catheter design safety and efficacy of AF, ablation has increased. New developments are being made to allow fully remote ablation procedures in combination with the MNS. However, new technologies are still necessary to improve MNS ablation for AF.

INTRODUCTION

Atrial fibrillation (AF) is of profound public health importance with a lifetime risk between 22 and 26% by 80 years of age.[1,2] AF is largely a disease of aging and is responsible for increased morbidity- and mortality-related healthcare expenditures owing to the aging population of Western society.[3] With this increasing prevalence of AF in the general population, novel strategies need to be applied for treatment of this arrhythmia.

Catheter ablation to isolate the pulmonary veins (PVs) has become the therapy of choice for treatment of drug-refractory, symptomatic paroxysmal AF. Radiofrequency (RF) catheter ablation targets arrhythmogenic substrates by delivering high amounts of energy to the cardiac tissue, preventing electrical conduction and thus eliminating the arrhythmia. RF catheter ablation is considered to be an effective treatment and is recommended as a second-line treatment according to the latest guidelines.[4]

Recently, several strategies have been developed to increase the effectiveness of AF ablation.[5-8] These techniques are mostly based on a variety of methods to obtain PV isolation (PVI). This strategy includes creation of block lines to inhibit electrical conduction between the left atrium (LA) and the PVs. However, for treatment of persistent AF where PVI alone is not sufficient, extensive linear or complex fractionated atrial electrogram ablation in the LA is performed as well. Both of these approaches require precision and stability of the ablation catheter.

Rationale for robotics: efficacy & safety

Accurate mapping and ablation of the area of interest can be complex. Even for experienced operators, procedures can be very challenging and multiple difficulties must be overcome in order to achieve a successful outcome without unnecessary adverse events.[9-11] Crucial requirements for successful AF ablation are catheter maneuverability to access target regions, catheter stability in difficult anatomical situations and reproducibility of the catheter location.[12-14]

Issues regarding catheter control are often encountered using manual ablation catheters. Manual catheters are limited in their freedom of movement by their predefined curve. In certain anatomic situations, this will make maneuvering within the heart extremely difficult, and on occasion, anatomic regions of interest cannot be reached at all.

Considering the importance of contact force during catheter ablation, manual approaches have some constraints. Operators are not always able to make an adequate estimation on the contact force, which is applied during ablation, thus causing different forces to be applied between target areas in the PVs and LA. Some results suggest that higher forces are applied on the right septal inferior position, where the lowest force during ablation was applied at the left anterior inferior ridge and in the right septal superior position.[15] For the mitral isthmus, providing sufficient contact force can be difficult due to the continuous movements of the valve. Since good contact force is related to effective ablation lesions, lower forces will result in fewer transmural lesions.[16] These inadequate ablation lines will be predominant sites of reconduction or occurrence of new macroreentrant arrhythmias.[10]

In addition to issues of maneuverability, manipulation of a stiff manual catheter can have a high risk of complications. When moving the catheter, high contact forces are often applied and can be at risk of perforating the atrial wall.[15] Although tamponade is a complication with an overall incidence of 1–1.5%, it is the most commonly reported major complication.[17-19] However, AF ablation is the most commonly performed electrophysiological procedure and the complication rate definitely needs to decline.

Magnetic navigation for the ablation of AF: safety, efficacy & efficiency

Novel techniques are continually being developed to increase safety and efficacy of AF ablation procedures. The magnetic navigation system (MNS; Niobe II, Stereotaxis Inc., MO, USA) is a remote catheter control technology that can provide advantages to prevent complications and improve lesion formation. The MNS consists of two external magnets located on either side of the patient that generate a magnetic field (0.08 or 0.1 T) within the patient. An atraumatic magnetically enabled catheter (Biosense Webster Inc., CA, USA or Biotronik, Berlin, Germany) incorporates four magnets in the distal segment that allow the catheter to be manipulated remotely by directional magnetic fields. The operator can alter

the vector of the magnetic field and the catheter tip will align to this vector, allowing the operator to navigate the distal tip of the catheter. The MNS allows storage of magnetic vectors for repeated access while the magnetic catheter is navigated automatically. Advancement and retraction of the catheter are controlled separately by a joystick-controlled motor drive (Cardiodrive, Stereotaxis Inc.). Images from 3D mapping systems, real-time fluoroscopy and CT scans can be fully integrated, thus facilitating fully remote-controlled mapping and ablation procedures.

One of the most important features of the MNS is the decreased use of fluoroscopy for both the patient and operator.[20-22] The magnetic ablation catheter can be safely manipulated with no risk of causing perforations. An integrated 3D mapping system (CARTO RMT, Biosense Webster Inc.) can be used for localization of the catheter. Manipulation of the catheter does not need continuous fluoroscopy and it is generally used only to confirm tip localization prior to application. Despite longer ablation times using MNS, fluoroscopy time is considerably shorter compared with manual ablation. Differences of up to 29 min of fluoroscopy have been described.[21] Moreover, fluoroscopy time for magnetic-guided AF ablation decreases over time, once more MNS procedures are executed.[23]

Catheter ablation as a treatment for AF is often associated with a substantial risk of major complications.[17,24] Safety of this procedure has been increased considerably by the introduction of MNS. To date, this issue has been evaluated and MNS appears to improve the safety of AF ablation procedures.[25,26] However, it should be taken into account that these studies included a limited number of patients and are retrospective in nature. In order to really understand the effect on safety using MNS, randomized trials need to be executed. Early reports on MNS in AF using non-irrigated ablation catheters describe char formation at the catheter tip after LA ablation.[5,25] Some patients had thrombus formation and experienced embolic events.[27]

Introduction of the first-generation irrigated MNS catheters (Navistar RMT Thermocool, Biosense Webster Inc.) improved catheter performance, although some cases of charring were reported.[27] Once the second-generation irrigated magnetic catheters were available,

this problem was solved, and no tip charring and related embolic events occurred (Table 1).[28]

In reports evaluating MNS in AF ablation, tamponades are described as a complication of the procedure.[23] However, these traumas were subacute and probably related to prolonged ablation and not to acute perforation with the MNS-guided catheter tip. Recently, some data have suggested that MNS is related to changes in esophageal temperatures causing acute esophageal injury. These esophageal lesions all demonstrated complete remission within 14 days and were comparable for MNS and conventional approaches.[29] This same group evaluated the Sensei™ robotic system (Hansen Medical, CA, USA) and noted a significantly higher incidence of thermal esophageal injury compared with conventional procedures. Overall no major complications directly related to MNS have been reported (Table 1). Access site hematoma is reported as a complication of MNS, although this is comparable with manual procedures.[20]

Several groups have evaluated the use of MNS in AF ablation and report advantageous capabilities regarding tissue contact, positional stability, catheter maneuverability and procedural safety.[12,20,25,27,30] The ablation catheter can easily be navigated within the atrium and is not restricted by any predefined curve. Because of the flexible distal portion of the catheter that aligns to the magnetic vector, there are no restrictions for navigating the catheter, and complex anatomical areas can be reached. These improved navigating capabilities may result in better circumferential lesions of the PVs and linear lesions in the LA.

After the introduction of the irrigated MNS ablation catheters, several studies evaluated the efficacy of MNS in paroxysmal AF. After summarizing the available data, the authors concluded that good acute success rates were achieved using MNS, and this was sustained over time (Table 2). After the procedures were completed, PVI was reached in 96% of patients. During a mean follow-up period of 11.6 months, 76.3% of the patients remained free of recurrence. As previous studies showed before, these results using MNS are comparable with the conventional technique.[23,31] Previous studies were all nonrandomized and therefore randomized prospective trials are necessary to compare efficacy between MNS and manual AF ablation.

Table 1
Paroxysmal atrial fibrillation ablation safety summary data

Study (year)	Paroxysmal patients (*n*)	Complication definition or notation in text	Complication rate (%)	Ref.
Augello *et al*. (2009)	20	Cardiac or vascular complications	0	[39]
Pappone *et al*. (2011)	81	Adverse events causing either: temporary or permanent change in health status requiring intervention; or persistent hemodynamic compromise or vascular compromise requiring intervention	0	[30]
Chun *et al*. (2010)	18	No intra- or post-procedural complications were noted	0	[27]
Arya *et al*. (2011)	35	One patient in the MNS group experienced a femoral vascular complication after the procedure	2.9	[22]
Miyazaki *et al*. (2010)	30	Access site hematoma was observed in two patients	6.7	[28]
Sorgente *et al*. (2010)	24	Left femoral artery pseudoaneurysm	†	[31]
Solheim *et al*. (2011)	15	Procedure-related complications, such as cardiac tamponade, atrioesophageal fistula, PV stenosis, TIA or major bleeding	0	[34]
Lüthje *et al*. (2011)‡	34	One patient experienced cardiac tamponade requiring puncture and one patient had a transient ischemic attack	5.9	[23]
Choi *et al*. (2011)	24	Cardiac tamponade, stroke or TIA	0	[26]
Summary§	281 (223 with complication data)		1.3	

†Aggregate data are presented. Unable to determine this value for paroxysmal atrial fibrillation ablation patients.
‡Publication did not stratify complication data by paroxysmal/persistent. Personal communication with the authors was required. Cardiac tamponades were noted to have occurred subacutely.
§Summary line reports overall percentages or simple weighted averages.
MNS, Magnetic navigation system; PV, Pulmonary vein; TIA, Transient ischemic attack.

The MNS allows better perpendicular alignment of the catheter tip that, which improves energy delivery. Because of the constant magnetic vector, optimal stability is obtained and the location of the ablation catheter will not change during an application. In complex anatomical locations, such as the mitral valve and the trabeculated myocardium, this enhanced wall contact and stability will lead to better energy delivery.[32,33]

In addition, longer total RF current application duration has been described as well.[22,34] To realize equally effective ablation lesions, more RF current needs to be delivered as compared

with the conventional approach. In prior studies, it was suggested that the MNS was not sufficiently effective in making ablation lines.[5,35] This statement was based on using a 4 or 8-mm non-irrigated MNS ablation catheter. However, these results were partially confirmed based on longer RF application times while using an irrigated MNS catheter.[23] Data suggest that MNS requires a longer total application time than manual procedures and is therefore less effective at creating linear lesions; however, the long-term outcome is equivalent.[22,23]

Table 2
Paroxysmal atrial fibrillation ablation effectiveness summary data

Study (year)	Paroxysmal patients (*n*)	Acute success definition	Acute success (%)	Follow-up time (months)	Chronic success definition	Chronic success (%)	Ref.
Augello *et al*. (2009)	20	PVI (Lasso)	100	12	Stable sinus rhythm without AAD therapy	90	[39]
Pappone *et al*. (2011)	81	PVI (Lasso)	100	15.3	Freedom from AT/AF (48-h Holter, daily event monitor) without AAD therapy	76.2	[30]
Chun *et al*. (2010)	18	PVI (Lasso)	†	13.9	Freedom from AF recurrence without AAD therapy	†	[27]
Arya *et al*. (2011)	35	PVI (Lasso in 10 patients, RMT in 25 patients)	†	6	Freedom from AF (7-day Holter)	65.7	[22]
Miyazaki *et al*. (2010)	30	PVI (Lasso)	95	12	Freedom from AT/AF (48-h Holter) without AAD therapy	69	[28]
Sorgente *et al*. (2010)	24	PVI (Lasso)	100	11.8	Freedom from AT/AF (Holter) without AAD therapy	†	[31]
Solheim *et al*. (2011)	15	PVI (Lasso in 2 patients, RMT in 13 patients)	100	12.2	Freedom from AT/AF (Holter) without re-do procedure for AF	†	[34]
Lüthje *et al*. (2011)‡	34	PVI (RMT)	91	12	Freedom from any AT/AF (7-day Holter)	66	[23]
Choi *et al*. (2011)	24	PVI (Lasso)	79	3	Freedom from AF (ECG)	87	[26]
Summary§	281		96 (194 patients)	11.6		76.3 (190 patients)	

†Aggregate data are presented. Unable to determine this value for paroxysmal atrial fibrillation ablation patients.
‡Aggregate data are presented. Personal communication with the authors was required.
§Summary line reports overall percentages or simple weighted averages.
AAD, antiarrhythmic drug; AF, atrial fibrillation; AT, atrial tachycardia; PVI, pulmonary vein isolation.

The MNS catheter remains stable despite complex atrial anatomy or cardiorespiratory movement. In contrast to manual catheters, which can be anchored in the tissue by applying torque to the catheter, the MNS catheter has a lower but constant contact force and results in less tissue deformation caused by the applied magnetic force. The contact force applied by the Stereotaxis MNS system on the endocardial surface is approximately 10–15 g. This value is substantially lower than when using conventional ablation catheters.[15] However, the increased contact force does not result in less effective lesions. The magnetic stability of the catheter provides constant wall contact of the catheter tip with less variation in contact forces, whereas conventional techniques show intermittent or variable contact forces. Lesion formation is thought to be a function of contact force and applied energy. However, it has been shown that stability combined with lower contact force can produce efficacious lesions.[36] This decreased variation of contact force will create more transmural and larger volume lesions at comparable forces. In order to create similar lesions using conventional manual catheters higher, forces are required.[37] This means that for a given force, MNS has better energy delivery as compared with manual catheters. However, despite these observations, MNS-guided AF ablation is related to longer total application times. Most likely there are still difficult regions where the MNS cannot provide sufficient contact force, resulting in lower energy delivery. These regions are exactly the same regions that are the most difficult using manual ablation catheters too. The significant difference is that until now with MNS, the authors have had no options to adjust and improve the contact force and increase lesion size. In these cases, there are three options: use longer application times, since the authors know that the RF lesion does not stop growing after 30 s;[38] higher power output; or switch to a manually controlled ablation catheter.

Although the use of MNS is very intuitive with a steep learning curve, it is related to longer procedure times for AF.[20,21] Initially, this was thought to be explained by the learning curve of the new technology. However, even recent data suggest that procedure times are 35–60 min longer using MNS.[21,22] Lüthje et al. observed no learning curve for procedure duration. In addition, ablation times, defined as time from the first to the last ablation point, are described as being increased related to MNS.[23] This could be explained by a slower navigation speed of the LA and other chambers using MNS compared with experienced manual navigators. The separate movements of changing the magnetic vector, movements

of the two magnets and subsequently catheter movement, will increase the time spent on navigating the catheter and thus the procedure and ablation time.

While evaluating this technology, the authors realized that there are some limitations related to the system as compared with conventional catheter ablation. First, the use of the magnetic system might create a less efficient workflow. When a circular mapping catheter is used in the PVs, the operator needs to leave the control room in order to manually manipulate this mapping catheter. Given that manipulation of the catheter needs to be performed several times, it could be more time consuming than during a manual ablation procedure. Besides, manipulating the magnetic ablation catheter could be slower as compared with manually controlled catheters resulting in longer procedure times. Altering the alignment of the catheter tip is separated from the back and forward movements, which are performed by a separate device, and providing the desirable vector by the magnets takes some time as well. Furthermore, in order to make use of the MNS, it requires expensive hardware and specially designed ablation catheters are needed for the procedures.

Novel developments: a step further toward fully remote solutions

Recently, new developments have been made to make the ablation procedure fully remote controlled. Optimal outcomes of AF ablation with the MNS require manual manipulations of the circular mapping catheter. Although some groups perform catheter ablation of AF without the use of a circular mapping catheter, it can be used to evaluate complete PVI at the end of the ablation procedure. Until recently, it was not possible to navigate the circular mapping catheter from the remote MNS workstation and could only be done manually.

Recently, the Vdrive^{TM} system (Stereotaxis Inc.) has been introduced to permit remote manipulation of specialized diagnostic catheters. The operator in the remote workstation utilizes a remote controller to manipulate the catheter movements. The catheter can be advanced, retracted, rotated and deflected. The loop size of the circular mapping catheter can be modified as well. The Vdrive can be used for navigation between PVs, mapping of the chambers and identifying gaps with segmental isolation.

The early initial experience of this in 94 patients demonstrated that the use of the Vdrive is feasible and safe for the ablation of atrial arrhythmias. In the first unpublished clinical series evaluating Vdrive, 100% of the patients achieved the clinical end point of complete pulmonary isolation. In only 3.2% of the patients, manual crossover was required, in all cases to assess the right inferior PV. As this was the first model of the Vdrive, further developments are needed to further improve the catheter manipulation. The Vdrive is a very promising tool for making AF ablation fully remote and appears to be useful to reduce procedure times. However, more research is necessary to assess the true value of this system.

Expert commentary & five-year view

To understand completely about the recent developments and to define the course, the authors carry out studies into further improvements and should understand the basic principles of robots and robotics. Introduction of robots in catheter ablation would make sense only if these machines will address the most important challenges in clinical cardiac electrophysiology. These challenges include the following: inefficient workflow; enormous interoperator differences; serious safety issues; and suboptimal efficacy. Furthermore, since the robot is defined as an artificial agent that can do tasks on its own, a step further from the level of manipulators to the introduction of robots should be taken.

For a better understanding, consider an analogy from other innovative fields such as automobile manufacturing. If one examines how the cars have changed from the 1960s until now, the element that has changed the least has been speed. Although the promise of the flying car has not yet materialized, many significant changes have occurred with the simple goal of making the driver's life easier. Most importantly, however, is the fact that overall automobile safety has improved enormously. This factor relates directly to the need for changing the culture of medical engineering. As patient awareness increases exponentially due to the explosion of information available on the internet and through social media, the demand for a safer system will be much more obvious.

This comparison to the automobile industry raises a very logical question: What are the main obstacles for developing true cardiac robots? Obviously, the above-mentioned targets were

not defined clearly at the beginning. The whole system has been often used more as a toy rather than a real tool, despite the fact that some aspect of safety (especially the dramatic reduction in fluoroscopy exposure and the almost 0 cardiac perforation level) were very attractive from the very beginning.

In addition, it seems that after the early enthusiasm a certain level of concern has developed. This may be due to the idea that the project of further developing robotic technology was not well thought out. One example is the introduction of some automatic features such as automated LA mapping too far before the achievement of fully remote solutions. The authors believe that the next step should definitely have been the development of fully remote workflow prior to the introduction of automated features.

On this road, a significant improvement is the new EpochTM solutions, which will be commercially available very soon. Utilizing an additional robotic arm for remote manipulation of diagnostic catheters and sheaths will be available, as well as a significant improvement in the speed of the magnet response time. These steps should be mandatory before the automation is included, since in reality an efficient catheter ablation procedure for atrial fibrillation includes an almost synchronous and instant movement of more than one catheter in the LA.

Another development that should take place soon is the better control of RF energy delivery. In an ideal situation, a contact force sensor should be included in the next generation of magnetic catheters, and visualization of the RF lesions is desirable.

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CHAPTER 5

Clinical outcome of ablation for long-standing persistent atrial fibrillation with or without defragmentation

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ABSTRACT

Objective

To assess the outcome and associated risks of atrial defragmentation for the treatment of long-standing persistent atrial fibrillation (LSP-AF).

Methods

Thirty-seven consecutive patients (60.4 ± 7.3 years; 28 male) suffering from LSP-AF who underwent pulmonary vein isolation (PVI) and linear ablation were compared. All patients were treated with the Stereotaxis magnetic navigation system (MNS). Two groups were distinguished: patients with (n = 20) and without (n = 17) defragmentation. The primary endpoint of the study was freedom of AF after 12 months. Secondary endpoints were AF termination, procedure time, fluoroscopy time and procedural complications. Complications were divided into two groups: major (infarction, stroke, major bleeding and tamponade) and minor (fever, pericarditis and inguinal haematoma).

Results

No difference was seen in freedom of AF between the defragmentation and the non-defragmentation group (56.2 % vs. 40.0 %, P = 0.344). Procedure times in the defragmentation group were longer; no differences in fluoroscopy times were observed. No major complications occurred. A higher number of minor complications occurred in the defragmentation group (45.0 % vs. 5.9 %, P = 0.009). Mean hospital stay was comparable (4.7 ± 2.2 vs. 3.4 ± 0.8 days, P = 0.06).

Conclusion

Our study suggests that complete defragmentation using MNS is associated with a higher number of minor complications and longer procedure times and thus compromises efficiency without improving efficacy.

INTRODUCTION

Currently, catheter ablation in patients with paroxysmal atrial fibrillation (AF) in which the pulmonary veins (PVs) are electrically isolated is a well-accepted treatment and has proven to be successful.[1-3] However, the efficacy of PV isolation (PVI) alone in long-standing persistent AF (LSP-AF) is poor.[4] Whereas the single procedure drug-free success rate of PVI in paroxysmal AF ranges between 57 and 80 %,[5-8] in contrast PVI in LSP-AF offers rather low success rates (21–22 %).[9-11] Additional ablation lines and other techniques have been proposed to increase the success rate of LSP-AF ablation, one of these being atrial defragmentation.[12] During this procedure electrogram-based ablation is performed. Treatment targeting specific areas in the atrial substrate, showing complex fractionated atrial electrograms (CFAEs), has also been proposed.[13] Although successful termination of AF by using this technique alone has been reported, others have not replicated the encouraging results of this study.[14] The benefit of PVI and additional linear ablation in the treatment of LSP-AF has been shown in several studies.[4,12,15] It remains unclear if a combination of PVI and CFAE ablation significantly increases the success rate of LSP-AF ablation as opposed to PVI and linear ablation.[4,16]

The aim of this study was to assess whether complete defragmentation is a useful additional technique in order to achieve a satisfactory clinical outcome in the treatment of LSP-AF.

METHODS

This study was a retrospective data analysis. Data from 37 consecutive patients (age 60.4 ± 7.3 years; 28 male) diagnosed with LSP-AF were compared. Before all procedures a transoesophageal echo was performed to exclude left atrial (LA) thrombus. Twenty-six patients underwent radiofrequency catheter ablation for AF at the Erasmus Medical Center in Rotterdam, the Netherlands, and 11 patients were treated at the Onze Lieve Vrouwe Gasthuis in Amsterdam, the Netherlands. However, the same team of electrophysiologists performed all the procedures at two different locations using identical equipment and

procedure strategies. During the procedure, activated clotting time (ACT) levels were monitored and were required to be between 275 and 350 s. Patients were divided into two groups: LA ablation (PVI and linear ablation) with and without defragmentation. Data on outcome and post-procedural complications were collected. The primary endpoint of the study was freedom of AF after 12 months. Secondary endpoints were the following: acute AF termination, procedure time, fluoroscopy time and (post) procedural complications. Complications were divided into two categories: major and minor. Major complications were defined as: acute myocardial infarction, stroke, major bleeding and tamponade. Minor complications included: fever, pericarditis and inguinal haematoma.

Study population

Only patients with LSP-AF, defined as AF being persistent for 12 months or longer, were included (Table 1).[17] Exclusion criteria for this study were: fever or infection, renal failure (on dialysis or at risk of requiring dialysis, serum creatinine >200 µmol/l), a malignancy needing therapy or a life expectancy shorter than the duration of the study. Additional exclusion criteria were intracardiac thrombus, severe cerebrovascular disease (neurological deficit of cerebrovascular cause that persists beyond 24 h), active gastrointestinal bleeding, bleeding or clotting disorders or inability to receive heparin and intractable heart failure (NYHA class IV).

Table 1
Patient demographics and procedural parameters

	Defragmentation	**No Defragmentation**	***P* value**
Number of patients (*n*)	20	17	
Age (years)	59.2 ± 7.7	61.8 ± 6.8	0.28
Male sex (*n*), (%)	13 (65.0%)	15 (88.2%)	0.10
Years of AF (y)	5.7 ± 6.1	5.6 ± 4.4	0.95
Repeat procedures (*n*), (%)	6 (30.0%)	2 (11.8%)	0.17
Class III antiarrhythmics (*n*), (%)	13 (65.0%)	15 (88.2%)	0.10
Mean LA diameter (mm)	47.4 ± 5.5	45.1 ± 4.9	0.21
Left ventricular ejection fraction (%)	47.8 ± 13.9	52.3 ± 13.1	0.66
Mean procedure time (min)	332.5 ± 78.3	261.1 ± 96.6	0.02
Mean fluoroscopy time (min)	58.3 ± 25.8	49.6 ± 20.8	0.33

Lastly, patients with an allergy to contrast, patients with uncontrolled diabetes (fasting blood glucose ≥10.0 mmol/l), pregnant patients or women of child-bearing potential not using a highly effective method of contraception and patients who were unable to attend

the outpatients clinic were excluded from the study. The institutional ethics committee approved the study protocol and written informed consent was obtained from all patients.

Follow-up

All patients were followed up for 12 months. They attended outpatient appointments after 3, 6 and 12 months. An ECG was obtained at every visit. Before the procedure, a standard echo and a transoesophageal echo were performed. Data from the transthoracic echo was used to measure the left ventricular ejection fraction. Three months before and 12 months after the procedure, patients were fitted with a 24-hour ambulatory ECG device. The first month before and the third month after the procedure, patients received a transtelephonic cardiac event monitor, which they wore for 1 week. Every day patients submitted their ECG and were instructed to send extra recordings if they experienced any symptoms. After the first 3 months an assessment was made regarding the use for antiarrhythmic drugs (AADs). At 6 and 12 months after the procedure the need for anticoagulants was reassessed (Table 2).

Table 2
Patient follow-up timeline

Before/after PVI	Time	Activity (ECG on every visit)
Before	3 months	24-hour Holter registration
	1 month	Transtelephonic cardiac event monitor
	1 day	Standard echo, transoesophageal echo, standard blood work
After	3 months	Clinical visit, event recorder, AAD check up
	6 months	Clinical visit, assessment anticoagulants
	12 months	Assessment anticoagulants, 24-hour Holter registration

AAD, antiarrhythmic drugs.

Treatment arms

PVI with defragmentation

All patients were treated with the Niobe Stereotaxis, Magnetic Navigation System (MNS) (Stereotaxis Inc., St. Louis MO, USA). The use of this system has been extensively described in previous reports.[18,19] Every patient was treated under general anaesthesia because of the long procedure times and rather extensive and potentially painful ablation. Invasive arterial blood pressure monitoring was mandatory throughout the procedure. Pre-ablation 3D images (CT or MRI) were not routinely used as it was not considered essential for the procedures.

Both groins were prepared for puncture. Intracardiac echocardiography guided transseptal puncture was performed. Two 8.5 F SL1 (or SL0) sheaths were introduced into the left atrium. A decapolar catheter was placed into the coronary sinus. A Lasso catheter (Biosense Webster Inc., Diamond Bar, CA, USA) was inserted into the left atrium via one transseptal sheath. Using the second transseptal sheath a magnetic irrigated-tip mapping and ablation catheter (RMT Navistar, Biosense Webster Inc., Diamond Bar, CA, USA) was inserted in the left atrium.

The left atrium was extensively mapped (density: min 350 equally distributed points) using the MNS system. All PVs were mapped as separate chambers. Special attention was paid to the accurate definition of the PV ostia. The ablation sequence adhered to the following: First all PVs were isolated. Then electrogram-based ablation (i.e. defragmentation) in the left atrium and the coronary sinus was performed at all sites that displayed any of the following electrogram features: CFAEs, sites with a significant electrogram offset between distal and proximal recording bipoles of the mapping catheter suggesting a local re-entrant wavefront and regions with a cycle length (CL) shorter than the mean LA appendage CL. Specific CFAE maps using dedicated software were not performed.

Endpoint of ablation was in the transformation of fractionated electrograms into discrete electrograms and slowing of the mean atrial CL compared with LA appendage CL or the elimination of the electrograms in each region. If AF still persisted, linear ablation was performed: First a roof line, then a mitral line and lastly a posteroinferior line. The right atrium and superior vena cava were targeted for ablation if suspected to be a source perpetuating AF (lesser prolongation of CL in the right atrium, resulting in left-right fibrillatory CL gradient) and only after all LA ablation steps. Endpoint was the elimination or significant reduction (>75 %) of the local electrograms along the ablation lines. After restoration of sinus rhythm, bidirectional block was assessed at every line using differential pacing methods. Arrhythmia induction was not part of this protocol. In case of conversion to a regular atrial tachycardia, this was targeted for ablation in the same session.

Power settings were conservatively and individually adjusted (note: these settings are valid only for ablation using the MNS). In all regions 25 W, 48°, and 30 s with an irrigation rate of

17 ml was used as initial setup. The bipolar and unipolar local electrograms were carefully and continuously monitored during and after every ablation application. If the local electrical activity persisted, the following adjustments were made: posterior wall: max 35 W, anterior wall: max 40 W, carina, or other ridge-like structures: max 45 W. At difficult regions ablation time was extended to 45 s. Thirty minutes after the last application all PVs were revisited to confirm electrical isolation.

PVI without defragmentation

The same sequence as aforementioned was used, with the exception that after PVI and additional line ablation defragmentation was not performed.

Statistical analysis

The Kolmogorov-Smirnov test was used to assess the normality of distribution. Descriptive statistics was presented as mean ± SD for continuous variables if normally distributed. Continuous data were compared with the Student's t test or Mann-Whitney U test, where appropriate. Categorical data were presented as percentages and compared with the Fisher's exact test. Statistical analysis was performed with PASW version 18 (IBM Corp., Somers, NY). Statistical significance was defined as $P < 0.05$ (two-tailed).

RESULTS

Patient population

A total of 37 patients were included. The defragmentation group had 20 patients and 17 patients were included in the non-defragmentation group. No differences in age, gender, years of AF, number of repeat procedure and use of class III antiarrhythmics were noted (Tables 1 and 3). For the repeat procedures, a mean number of 1.75 ± 1.75 [range 0–4] PVs needed to be reisolated. The mean LA diameter of the whole population was 46.4 ± 5.3 mm. No difference in mean LA diameter was seen between the two groups ($P = 0.214$, Table 1). Furthermore, there was no difference in left ventricular ejection fraction between the treatment arms (Table 1). The mean number of electrical cardioversions in the whole population was 3.6 ± 3.0. No differences were seen between the defragmentation and the non-defragmentation group (3.2 ± 2.1 vs. 4.0 ± 3.7; $p = 0.404$, respectively).

Table 3
Use of antiarrhythmics before and after procedure

	Defragmentation	No Defragmentation	All
Before			
Amiodarone (*n*), %	10 (50%)	13 (76.5%)	23 (62.2%)
Sotalol (*n*), %	5 (25.0%)	6 (35.3%)	11 (29.7%)
After			
Amiodarone (*n*), %	12 (63.2%)	12 (70.6%)	24 (66.7%)
Sotalol (*n*), %	4 (21.1%)	3 (17.6%)	7 (19.4%)

Ablation data

Procedure times in the defragmentation group were longer and the use of fluoroscopy was comparable between both groups (Table 1). The mean number of applications for the total group was 134.2 ± 69.6. A significant difference in the mean number of applications was seen between the defragmentation group and the non-defragmentation group (161.9 ± 74.1 vs. 96.5 ± 41.4, P = 0.014). Mean radiofrequency application time from the whole group was 3438 ± 1664 s. No difference in mean application time was reported between the defragmentation group and the non-defragmentation group (3947 ± 1782 vs. 2837 ± 1350 s, P = 0.105). Furthermore, no differences were observed between the two groups in acute AF termination (70.0 % vs. 76.5 %: P = 0.474).

Complications

No major complications occurred in any of the patients. A significantly higher occurrence of minor complications was seen in the defragmentation group (45.0 % vs. 5.9 %, P = 0.009) (Fig. 1). No difference in type of minor complications was seen. Patients who experienced complications received a significantly higher number of radiofrequency (RF) applications (173.7 ± 69.9 vs. 109.6 ± 58.8, P = 0.019). Of all patients, 8.1 % (n = 3) had inguinal haematoma, 8.1 % (n =3) had mild pericardial effusion, 5.4 % (n = 2) had fever and 2.7 % (n = 1) had pericardial effusion and fever. In the defragmentation group, 10.0 % (n = 2) had inguinal haematoma, 15.0 % (n = 3) had mild pericardial effusion, 10.0 % (n = 2) had fever and 5.0 % (n = 1) had mild pericardial effusion and fever. In the non-defragmentation group 1 (5.9 %) patient had inguinal haematoma. There was no difference in mean hospital stay between the defragmentation group and the non-defragmentation group (4.7 ± 2.2 vs. 3.4 ± 0.8, P = 0.06) (Fig. 2).

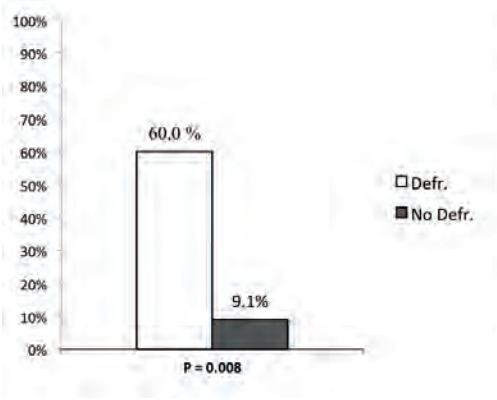

Figure 1: Percentage of minor complications for both the defragmentation and non-defragmentation group.

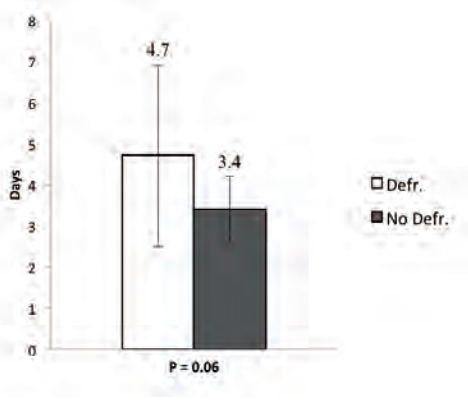

Figure 2: Average hospital stay presented with standard deviation for patients in the defragmentation and non-defragmentation group.

Follow-up

For all three moments in time during follow-up (3, 6 and 12 months) no difference was observed in freedom of AF between the two groups (Fig. 3). After 3 months, 40.0 % of the patients in the defragmentation group were still in sinus rhythm, whereas in the non-defragmentation group this was 47.1 % (P = 0.611). At 6 months, the number of patients in sinus rhythm was 50.0 % vs. 35.3 % (P = 0.653). After completion of 12 months of follow-up 56.2 % of the patients from the defragmentation group were in sinus rhythm and 40.0 % of the patients in the non-defragmentation group (P = 0.344). During follow-up the use of AADs was comparable for the two groups (70.0 % vs.76.5 % ,P = 0.474) (Table 3). In 13.5 % (n = 5) of the patients a repeat procedure was performed during follow. During electrophysiology (EP) study one patient had reconduction in both the left inferior and right superior PV, another in the right superior PV, another in the left superior PV, one patient had reconduction of all PVs and in one patient all PVs were isolated and additional defragmentation needed to be performed only. During follow-up, 24.3 % of the total population experienced atrial tachycardia. This was not statistically different when compared among the defragmentation and non- defragmentation group (11.8 % vs. 35.0 %, P = 0.103).

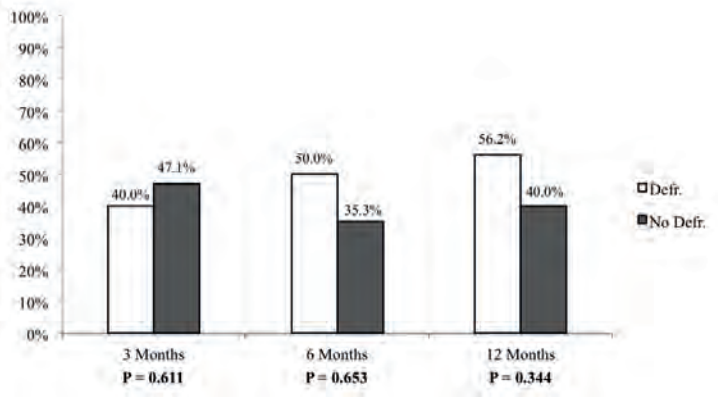

Figure 3: The number of patients in sinus rhythm during follow-up. Data from three moments in time are presented (3, 6 and 12 months).

DISCUSSION

This is the first study to evaluate the use of complete defragmentation using magnetic navigation in addition to conventional PVI and linear ablation. The major finding is that defragmentation for the ablation of LSP-AF after PVI and linear ablation is associated with a higher number of minor complications and more time-consuming procedures. After 12 months of follow-up no additional effect was observed for defragmentation therapy regarding freedom of AF. Therefore, the use of additional defragmentation for LSP-AF compromises procedural efficiency without improving efficacy.

Freedom of atrial fibrillation

Achieving satisfactory success rates for ablation of LSP-AF is very challenging. As demonstrated by Brooks et al.[4], a great variety of techniques remain available for the ablation of LSP- AF, including: PVI, pulmonary vein antrum isolation (PVAI) and different kinds of combinations of these treatments with ablation lines and defragmentation or CFAE ablation. Several other studies have evaluated the effect of the implementation of CFAE ablation for LSP-AF.[14,20,21] The single-procedure, drug-free success rates from CFAE ablation alone range from 24 % to 33 % at approximately 1 year. However, no previous study has been performed on the use of subsequential PVI, linear ablation and defragmentation for LSP-AF and therefore makes it difficult to compare our results with previous findings.

Our study suggests that 56.2 % of the patients who had defragmentation are in sinus rhythm after 12 months of follow-up. However, most patients in the defragmentation and non-defragmentation group were on antiarrhythmic drugs during this period. Nevertheless, these patients suffered from severe drug-refractory AF prior to the ablation procedure. This may also explain the incremental increase in percentage of patients who were in sinus rhythm at 3, 6 and 12 months, respectively, after defragmentation therapy. In patients who underwent PVI and linear ablation without additional defragmentation, 40 % were free from AF. Since the difference between these groups did not meet statistical significance, it can be concluded that defragmentation therapy in addition to PVI and linear ablation does not improve outcome of LSP-AF.

Reconduction

One of the largest limitations of ablation for LSP-AF is the lack of durability of the venous electrical isolation.[22] Prior studies demonstrated that the majority of patients had recovered venous conduction, which was established during the repeat procedure.[14,23,24] This finding can be supported by our findings that a significant number of patients who experienced recurrence had PV reconduction during EP study. Willems et al. found PV reconduction in approximately 75 % of patients after the first procedure.[25] For some patients with LSP-AF the PVs are an important trigger and durable lesions may improve outcome for these patients. Therefore, we cannot conclude that defragmentation therapy had no beneficial effect for patients with LSP-AF at all, since we are not yet able to perform ablations where durability of the PVI and linear ablations can be ensured over time. In this study a limited number of repeat procedures were performed and therefore we cannot draw conclusions about the specific cause of low success rates. Possibilities are reconduction after venous isolation, linear ablation, and insufficient defragmentation therapy. However, the single procedure success rate after 12 months is not improved by performing defragmentation in LSP-AF patients.

Amount of defragmentation

Until today, the ideal amount of defragmentation for the treatment of LSP-AF remains unknown and is highly operator dependent. Our study demonstrates that additional defragmentation after linear ablation and PVI has no favourable effect on the outcome. A

possible explanation for the ineffectiveness of defragmentation could be the amount of additional application time. Our results demonstrate that patients who underwent defragmentation received a significantly higher number of RF applications (on average 65 additional lesions). However, as the mean application time tends to be higher in the defragmentation group with approximately 1000 s of RF ablation, no statistically significant difference was found regarding total RF application time. The question rises as to whether more additional defragmentation would lead to an improved outcome. In other studies evaluating the effect of defragmentation in LSP-AF patients the average amount of additional RF application time was 15–33 min with a total application time of 54–64 min.[14,26] Our study achieved comparable results regarding ablation data with 18.5 min additional defragmentation and a total ablation time of 66 min.

Complications

Although we did not see a higher rate of major complications associated with defragmentation, as was the case in the study by Elayi and co-workers,[27] we observed a higher number of minor complications. Pericarditis due to extensive ablation remains a common complication.[28,29] Our results demonstrated that patients who experienced any complications received significantly more RF applications (almost 70 more applications). This increased number of RF applications (>200) is in some patients responsible for the occurrence of reactive pericarditis leading to mild pericardial effusion and fever. Most of the patients, however, recover spontaneously and are treated conservatively.[29] Considering these complications and the fact that mean hospital stay and more importantly freedom of AF did not differ significantly according to our data could suggest that a certain restraint regarding the use of defragmentation may be indicated.

Clinical impact

From the findings of this study, the question arises whether additional defragmentation may not be beneficial for all LSP- AF patients and should not be performed routinely, but for selected patients who did not benefit from PVI and linear ablation. In these individual patients the risk of persisting AF should be balanced against the risk associated with the procedure. However, as previously stated by Tilz et al.[30], our study suggests that the additional risk of complication is not justifiable for an initial treatment with defragmentation.

When looking at the longer procedure times associated with defragmentation in our study (with a mean difference of almost 2 hours), one can conclude that ablation procedures could be much more efficient without this additional treatment and therefore less burdensome. This supports the findings concluded by Tilz et al.[30] This might also influence the cost-efficacy of LSP-AF ablation procedures.

Limitations

In this study a limited number of patients were included and analyzed. However, despite this limited number of patients the absence of significant differences between the characteristics suggests homogeneity between the two groups and contributes to the validity of the conclusions drawn from these results. Furthermore, patient characteristics from our study population were in line with those from other studies.[4,14,27] To really elucidate the effect of additional defragmentation in addition to conventional PVI and linear ablation randomized trials with a higher number of patients are necessary.

An important issue regarding follow-up which was raised by Tilz et al.[30] remains whether observed AF recurrence rates merely depend on the length of follow-up. Like most studies about LSP-AF ablation, our follow-up lasted for 1 year and therefore does not offer further insight into this matter.[14,27] However, longer follow-up would provide more detailed information on the treatment effect and the outcomes in the long term. In this study, patients were being treated with an antiarrhythmic drug during follow-up. Although the use of these drugs was comparable between the two groups, it might have influenced the outcomes during follow-up.

CONCLUSION

The lack of difference in freedom of AF and mean hospital stay between the two groups and the higher occurrence of minor complications in the defragmentation group suggests there is no strong ground to deliver complete defragmentation therapy in addition to PVI and linear ablation for patients suffering from LSP-AF.

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CHAPTER 6

Safety and feasibility of single-catheter ablation using remote magnetic navigation for treatment of slow-fast atrioventricular nodal reentrant tachycardia compared to conventional ablation strategies

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ABSTRACT

Objective

Ablation of atrioventricular nodal re-entrant tachycardia (AVNRT) is a highly effective procedure both with radiofrequency (RF) and cryoenergy (CE). Conventionally, it requires several diagnostic catheters and hospital admission. This study assessed the safety and efficacy of a highly simplified approach using the magnetic navigation system (MNS) compared to CE and manual RF ablation (MAN).

Methods and Results

In the MNS group a single magnetic-guided quadripolar catheter was inserted through the internal jugular vein to perform ablation. In the CE group cryomapping preceded ablation and for MAN procedures conventional ablation was performed. The following parameters were analyzed: success- and recurrence rate, procedure-, fluoroscopy- and total application time. In total 69 eligible patients were treated with MNS (n = 26), CE (n = 25) and MAN (n = 16). The success rates were 100 %, 100 % and 94 %, respectively (P = ns). The mean procedural time was 83 ± 25 min for MNS, 117 ± 47 min for CE and 117 ± 55 min for MAN (P < 0.01). Total radiation time was significantly lower for MNS [0.0 min (IQR 0.0 - 0.0)] compared to CE [15.1 min (IQR 9.1 - 23.8), P < 0.001] and MAN [17.5 min (IQR 7.0 - 31.3), P < 0.001]. The total application time was comparable for both RF groups: 357 ± 315 s (MNS) vs. 204 ± 177 s (MAN) (P = 0.14). No major adverse events occurred. After 3 months follow-up similar PR intervals were recorded for all patients. During a follow-up of 26 ± 5 months recurrence rates were 3.8 %, 4.0 % and 6.3 %, respectively, for each group.

Conclusion

The MNS-guided single-catheter approach is a feasible and safe technique for the treatment of patients with typical AVNRT.

INTRODUCTION

Catheter ablation is the preferred therapy for atrioventricular nodal re-entrant tachycardia (AVNRT), the most common regular supraventricular tachycardia.[1] Although it is a highly effective treatment modality with success rates varying between 95 and 99%,[2,3] conventionally it still requires the insertion of multiple diagnostic catheters into the heart for both RF and cryoablation procedures.[4] Theoretically, multiple catheters augment the risk of complications such as venous thrombosis and perforation of the myocardium. Furthermore, procedures become more expensive using multiple catheters. Venous catheterization using the femoral vein is associated with haematomas, arteriovenous (AV) fistulas, pain, vagal reactions, and temporary immobilization.[5,6] Therefore, this procedure is typically performed in the setting of an overnight hospital stay. In order to simplify the procedure, we developed an alternative approach involving just a single catheter for the diagnosis and treatment of AVNRT. The magnetic navigation system (MNS) consists of two external magnets, which can manipulate the catheter by altering the magnetic vector. The flexible and non-traumatic design of magnetic-guided catheters might allow an easy, single-catheter procedure, approaching the heart from the upper limb or central vein, as this catheter can be manoeuvred to all sites of interest.

We compared the safety and efficacy of this approach (MNS) to the use of conventional cryoablation (CE) and standard manual RF (MAN) ablation. During CE and MAN procedures multiple diagnostic catheters were used.[7] To date, several studies have been conducted demonstrating the feasibility of the MNS for treatment of AVNRT.[8-10] However, this is the first study evaluating the feasibility and advantages of the MNS using a single-catheter approach compared to conventional approaches.[10,11]

METHODS

Patient selection

Prospectively, 100 consecutive patients with recurrent narrow QRS-complex tachycardias were screened. Twelve-lead ECG criteria were as follows: (1) a documented narrow QRS

tachycardia on the surface ECG (2) with retrograde P waves in the inferior leads (3) no further than 100 milliseconds after the ending of the QRS complex. In total 69 patients with a 12-lead ECG suggestive for AVNRT were selected and analyzed (Figure 1). The mean age was 48.5 ± 15.2 years and 30.4% were males. Patients were enrolled for ablation using either MNS, CE or MAN. Investigators were not involved in the decision as to whether a patient was scheduled in the MNS-equipped laboratory or the MAN- and CE-equipped laboratory. Our department disposes of two operating rooms, one equipped with MNS and one to perform MAN and CE procedures. Therefore, the assignment of the patients into the three study arms was dependent on the availability of the labs. Between the MNS group and the CE and MAN group an equal distribution was found for age (P = 0.15 and P = 0.11, respectively) and gender (P = 0.54 and P = 0.49, respectively) (Table 1). Furthermore, an equal proportion of underlying heart diseases was found between MNS and CE (P = 0.48) and MAN (P = 0.64). The ablation procedures were performed by the same group of electrophysiologists experienced with both manual and MNS techniques.

Electrophysiology study

Written informed consent for the ablation procedure was obtained from all patients. All included patients agreed with a single-catheter MNS procedure, performed as an outpatient treatment, or the cryoablation and manual RF ablation as a conventional treatment. Resting 12-lead ECG, and laboratory tests, a chest x-ray image and a two-dimensional echocardiogram were acquired from all patients within the month prior to the procedure. All antiarrhythmic drugs (AAD) were discontinued for the duration of five half-lives prior to the procedure. The procedures were performed during a fasting state using local anaesthesia.

MNS procedures

Magnetic-guided ablation procedures were performed using the Stereotaxis Niobe Magnetic Navigation System (Stereotaxis, Inc., Saint Louis, MO, USA) in an electrophysiology lab equipped with a Siemens Axiom Artis (Siemens, Erlangen, Germany) fluoroscopy system. A combined field strength of 0.08 T was used. A single magnetic navigation quadripolar catheter (Celcius RMT 4 mm, Biosense-Webster, Diamond Bar, CA, USA) was introduced through the internal jugular vein. This catheter was remotely manoeuvred using a computer-controlled workstation (Navigant, Stereotaxis, Inc., St. Louis, MO, USA) to allow changes of

the magnetic field orientation and navigate the ablation catheter (Figure 2). The principles and use of the MNS have been extensively described before.[12] Initially, the catheter was introduced into the right atrium (Figure 3). Using magnetic vectors to manoeuvre towards the lateral wall, a right atrial lateral position was achieved. At this position the atrial signal amplitude should be large, and the stimulation threshold low. Subsequently, the His position was reached. The catheter was placed into this His region providing ventricular capture on the distal electrode pairs with wide-paced QRS duration, while on the proximal pole a clear atrial signal was still visible. The position of the His bundle was tagged on the MNS in LAO (left anterior oblique) and RAO (right anterior oblique) views, through the fluoroscopic annotation option. A yellow marker was continuously displayed on the fluoroscopy screen indicating the His bundle in all incidences. Subsequently, the coronary sinus was cannulated using the navigation system. All the magnetic vectors of the above-mentioned anatomical locations were stored in the system. This allowed quick re-navigation to a selected position using this target navigation option. Images of these positions were stored in two radiological views: RAO 30° and LAO 30°.

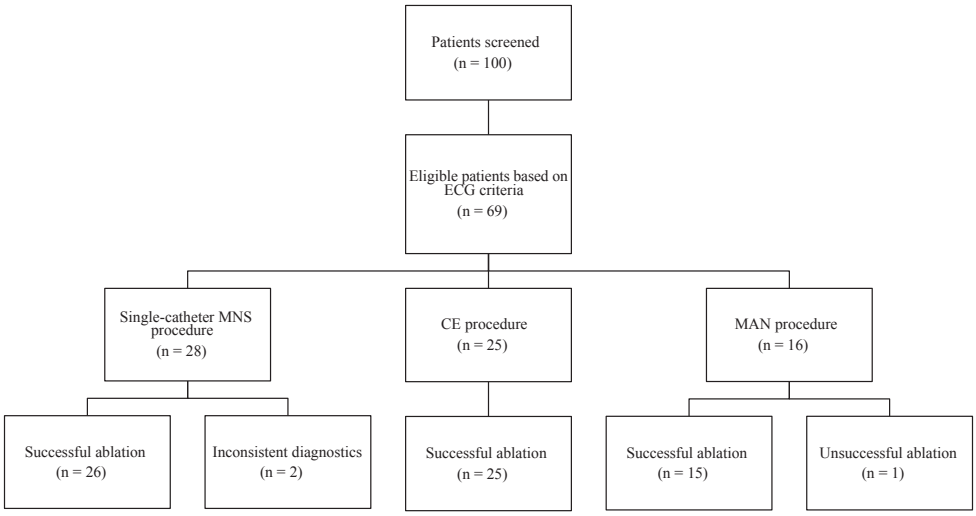

Figure 1: Flow chart illustrating study design and patient enrollment.

Table 1
Patient characteristics

	MNS	CE	*P* value	MAN	*P* value
Number of patients (*n*)	26	25		16	
Sex (male) (*n*)	8 (31%)	7 (28%)	0.54	4 (25%)	0.49
Age (years)	45 ± 10	51 ± 19	0.15	51 ± 15	0.11
Weight (kg)	79 ± 18	74 ± 15	0.27	69 ± 12	0.22
Length (m)	1.71 ± 0.10	1.64 ± 0.37	0.38	1.70 ± 0.10	0.83
Previous RF ablation (*n*)	0 (0%)	0 (0%)	NA	0 (0%)	NA
Underlying heart disease/hypertension (*n*)	3 (12%)	4 (16%)	0.48	2 (13%)	0.64
Duration of symptoms (months)	132 (IQR 57 – 240)	60.0 (IQR 24 – 216)	0.07	66 (IQR 12 – 120)	0.02
Symptoms/week (*n*)	0.50 (IQR 0.25 – 3.0)	1.0 (IQR 0.38 – 3.0)	0.30	1.0 (IQR 1.0 – 2.0)	0.11
AAD use after ablation (*n*)	3 (12%)	2 (8%)	0.52	2 (13%)	0.64
Number of AAD before ablation (*n*)	1.0 (IQR 1.0 – 1.0)	1.0 (IQR 0.5 – 1.0)	0.12	1.0 (IQR 0.25 – 1.0)	0.32
Number of AAD after ablation (*n*)	0.0 (IQR 0.0 – 1.0)	0.0 (IQR 0.0 – 0.5)	0.82	0.0 (IQR 0.0 – 0.0)	0.52

Data are presented as mean ± standard deviation (SD) or median with interquartile range (IQR).
AAD, antiarrhythmic drugs; CE, cryoenergy; MAN, manual RF ablation; MNS, magnetic navigation system; NA, not applicable; RF, radiofrequency.

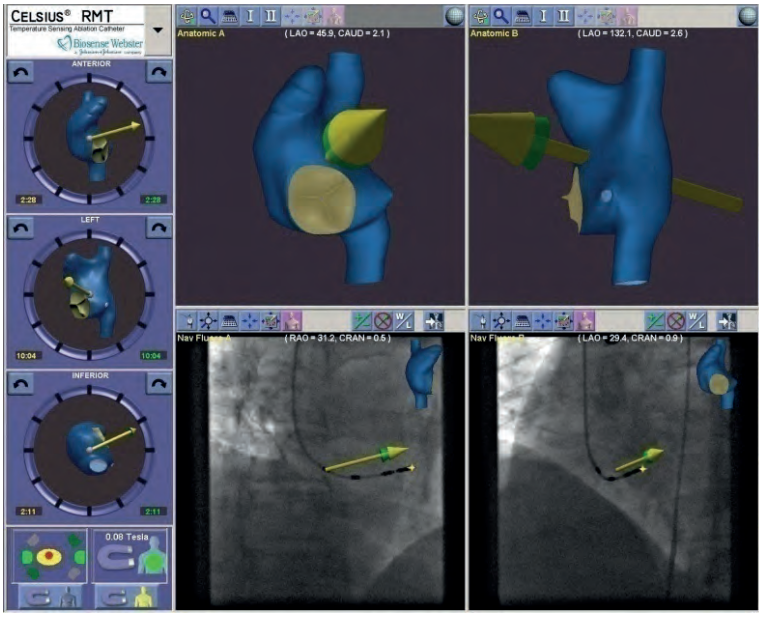

Figure 2: Part of the interface of the MNS, displaying vector navigation and the ability to store magnetic vectors. A cast of the right atrium is displayed at the top of the screen in LAO 45 degrees (*A*) and 130 degrees (*B*), and the yellow arrow indicates the direction of the imposed vector on the catheter tip in the RAO (*C*) and LAO 30 degrees (*D*) views. The green arrow indicates the actual direction of the catheter tip. The yellow marker at the tip of the catheter is annotates at the His position.

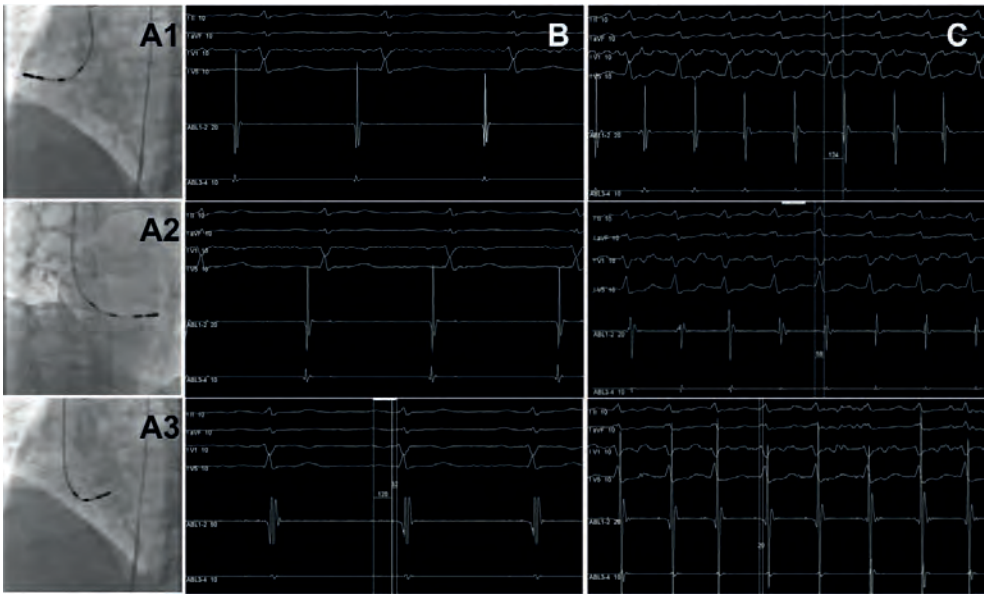

Figure 3: Fluoroscopic views of the single catheter in the high right atrium (LAO 30 degrees) (*A1*), coronary sinus (RAO 30 degrees) (*A2*) and His position (LAO 30 degrees) (*A3*). Corresponding electrograms during sinus rhythm (*B*) and during ongoing tachycardia (*C*) are shown as well.

Mapping

MNS – Mapping

After registration of the important anatomical locations, programmed stimulation was performed. Decremental conduction, anterograde and retrograde effective refractory periods (ERP) of the AV node, and Wenckebach point were determined using incremental atrial and right-ventricular (RV) programmed stimulation and extra stimulus testing. RV and parahisian stimulation, using the distal electrode pair from the catheter at the His position, and recordings of an atrial signal on the proximal electrode pair were performed to exclude the presence of retrograde conducting parahisian accessory pathways. During pacing from the right atrium an A-QRS jump was searched. Diagnosis of a dual AV nodal pathway was made on the basis of standard diagnostic criteria modified according to the single-catheter approach.[13] Subsequently, induction of a sustained tachycardia was performed. During ongoing tachycardia the catheter was re-navigated using the stored magnetic vectors to the

His position, into the proximal and distal part of the CS, and VA measurements were recorded (Figure 3). A VA time of less than 90 ms at all of these locations was a requirement.

Based on the findings of the electrophysiology study the diagnosis of AVNRT was made. If the ventricular and atrial signals appeared almost simultaneously and the shortest VA time was measured at the His position, diagnosis of a typical slow-fast AVNRT with an anterior exit point was made.[13] If sustained tachycardia could not be induced, isoproterenol and - if necessary - atropine were infused to facilitate tachycardia. If any of the above- mentioned tests were not consistent with the diagnosis of AVNRT, the procedure was converted into a standard electrophysiology study by inserting diagnostic catheters in the standard locations in the heart, and ablation was performed according to the identified diagnosis.

MAN – Mapping

Procedures in the manual group were performed in an electrophysiology lab equipped with a Siemens Megalix (Siemens, Erlangen, Germany) fluoroscopy system. In the CE and MAN group a standard electrophysiological study was performed. One bipolar catheter, one decapolar and one quadripolar catheter was inserted into the right femoral vein and advanced to the right ventricular apex, coronary sinus and His bundle, respectively. Detailed measurements were taken and CE or MAN ablation was performed if the diagnosis of dual AV nodal pathways (AH-jump) and AVNRT was made based on standard diagnostic criteria.[14]

CE procedures

Cryomapping and ablation was performed using a 4-mm tip Freezor 3 catheter and a CCT2 CryoConsole (Cryocath Technologies, Montreal, Canada). Initially, ice mapping was performed by cooling to –30°C for a maximum of 60 s 14.

Ablation

RF catheter ablation in the MNS and MAN group was performed in a temperature-controlled mode (maximum temperature 55°C, maximum duration 60 seconds, maximum 40 W) with the use of a Stockert RF generator (Stockert GmbH, Freiburg, Germany). For MAN procedures ablation was performed using an Alcath Gold Full- Circle RF catheter (Biotronik Inc., Berlin, Germany). The target was the slow pathway guided by a combination of

intracardiac electrogram criteria and anatomical landmarks.[15] During MNS procedures the target position was labeled using a hollow white dot on the fluoroscopic images in both RAO and LAO radiological planes, with also a full white dot on the His bundle as a reference (Figure 4). When changing the angle of the fluoroscopy, these markings on the fluoroscopy screen moved concordantly. The fluoroscopy image was set at LAO 30°, and the navigation started at the His position. The magnetic vector was changed in the same plane inferior from the His, providing safe distance from the His bundle. Movement of the catheter was continuously monitored and recorded. During the MAN and CE procedures catheter positioning was done manually. When an optimal balance of a small fractionated A and large V signals were seen and a stable catheter position was attained (Figure 4), RF energy was applied starting at a low energy level during MNS and MAN procedures. Each application was started with the power set at 10 W and, if AV conduction was preserved, the power was progressively increased to 40 W until a maximum of 55°C was reached or junctional rhythm appeared. For CE procedures, if a potential successful site was identified after cryomapping, cryoablation was performed till –75°C for at least 240 s. Fluoroscopy was used throughout each application.

For the 3 groups, the end point of the procedure was non-inducibility of AVNRT. Inducibility of AVNRT was tested after each application, and if non-inducible, repeated after a 30-min waiting period.

Data collection and analysis

Direct post-procedural success rates were analyzed. Acute success was assessed according to the criteria described before. Procedural parameters such as procedure time, physician radiation time and patient radiation time and dose were analyzed as well. Procedure time was measured from the moment of puncturing the jugular vein or groin in the electrophysiology lab until the removal of the sheath, including the 30-min waiting period. Furthermore, the number of applications and the total ablation duration was recorded in all patients. All complications (including haematoma, tamponade, high-degree AV block and death) were registered and analyzed. For all patients the PR-interval and heart rate were measured before the procedure, and one day and 3 months after the ablation.

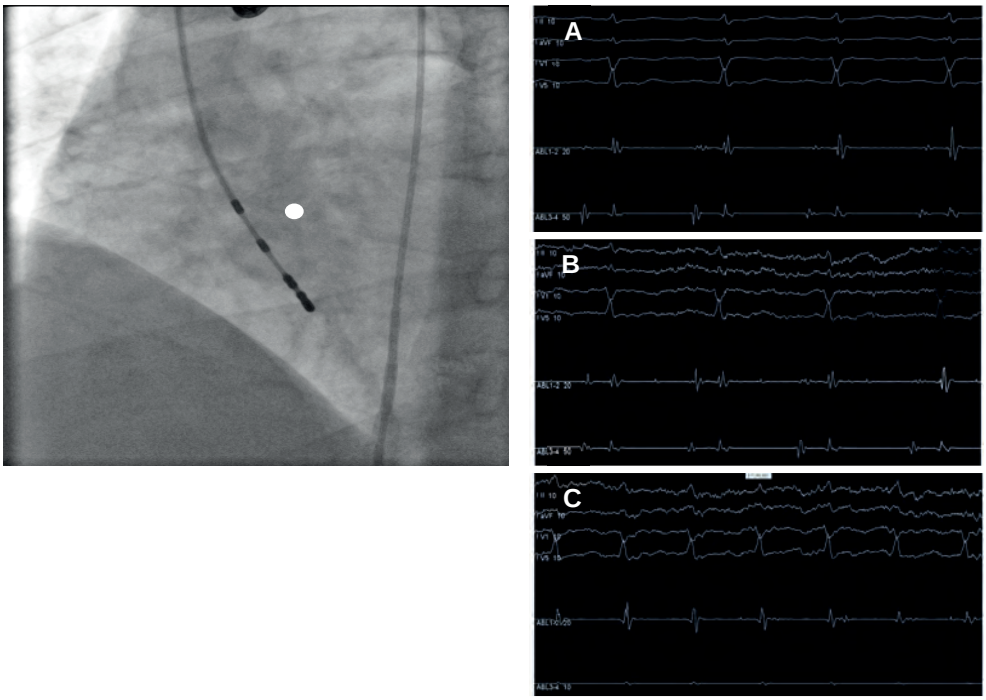

Figure 4: Fluoroscopic view (*A*) of the ablation spot (LAO view) with labeling of the His bundle by a white dot. The electrocardiograms are recorded during sinus rhythm (*B*), during a radiofrequency application (*C*) and during junctional rhythm (*D*).

Follow-up

Immediately after ablation all patients received a 24-hour Holter registration. Patients treated with MNS were discharged on the same day of the procedure. The day after the procedure all patients were seen at the outpatient clinic of the Department of Cardiology, Erasmus MC, and an electrocardiogram and transthoracic echocardiographic examination was performed. Three months after the procedure all patients received again a 24-hour Holter monitor. Furthermore, examinations at the outpatient clinic were performed and patients were asked about recurrent palpitations. In case of long-standing palpitations during follow-up, an additional 24-hour Holter registration was performed to obtain ECG recordings at the time of complaints. In total, patients underwent a mean follow-up of 26 ± 5 months.

Statistical analysis

Normality of distribution was determined by using the Kolmogorov-Smirnov test. Continuous variables were expressed as mean ± SD, if normally distributed, and compared with the Student's t test for independent samples. In case of non-normal distribution of data, medians and interquartile ranges (IQR) were reported and the Mann-Whitney U test was used for data comparison. Categorical data were expressed as percentages and compared with the Chi-square test or Fisher's exact test when appropriate. Statistical analysis was performed using SPSS 15.0 (SPSS Inc., Chicago, IL, USA). Statistical significance was defined as $P < 0.05$ (two-tailed).

RESULTS

Patient data

Out of 100 patients who were screened, 69 were found to be eligible based on documented ECG criteria. Two of the 28 patients enrolled for the single-catheter MNS approach were excluded due to inconsistent diagnostic results. Finally, 26 patients were ablated with MNS, 25 patients were treated using CE, and 16 patients underwent MAN ablation (Figure 1, Table 1). None of the included patients underwent previous ablation procedures. Compared to the MNS group, patients in the MAN group had significantly less duration of symptoms [132 months, IQR (57 – 240 months) vs. 66 months, IQR (12 – 120 months), P = 0.02]. Between the MNS and MAN group an equal duration of symptoms was found [60.0 months, IQR (24 – 216 months), P = 0.07]. The number of symptoms per week was comparable for MNS [0.50, IQR (0.25 – 3.0)], CE [1.0, IQR (0.38 – 3.0), P = 0.30) and MAN [1.0, IQR (1.0 – 2.0), P = 0.11]. The median number of total AAD used before the procedure was 1.0 (IQR 1.0 – 1.0) and decreased to 0.0 (IQR 0.0-0.0) for the overall group after the procedure (P < 0.001). The number of patients who continued AAD after the procedure was comparable for MNS (n = 3) and CE (n = 2, P = 0.52) or MAN (n = 2, P = 0.64).

Procedure and ablation data

A right-sided jugular venous access was achieved in all but 3 patients, in whom the left subclavian vein was used. Details of the electrophysiology procedures are shown in Table 2.

In all patients a typical slow-fast AVNRT could be induced. The mean procedural time was significantly shorter for the MNS group (83 ± 25 min) than for the CE (117 ± 47 min, P < 0.01) and the MAN group (117 ± 55 min, P < 0.01). The physician radiation time for MNS procedures [0.0 min (IQR 0.0 – 0.0 min)] was significantly lower compared to the CE [15.1 min (IQR 9.1 – 23.8 min), P < 0.001] and MAN procedures [17.5 min (IQR 7.0 – 31.3 min), P < 0.001]. Patient radiation time was also shorter for MNS [6.8 min (IQR 4.4 – 16.1 min)] than for CE (15.1 min (IQR 9.1 – 23.8 min), P < 0.01] and MAN [17.5 min (IQR 7.0 – 31.3 min), P = 0.02]. The patient radiation dose was comparable between the groups (Table 2). The median application number in the MNS, CE and MAN group was 8.5 [IQR 4 – 15], 2 [IQR (1 – 2), P < 0.001] and 3.5 [IQR (1 – 6), P < 0.01], respectively. The mean duration of RF applications was comparable for the MNS and MAN group (357 ± 315 vs. 204 ± 177, P = 0.14).

Table 2
Electrophysiology study and ablation results

	MNS	**CE**	***P* value**	**MAN**	***P* value**
Anterograde jump ≥ 50ms (*n*)	15 (58%)	16 (64%)	0.43	12 (75%)	0.21
Slow-fast AVNRT (*n*)	26 (100%)	25 (100%)	NA	16 (100%)	NA
CL tachycardia (ms)	339 ± 51	343 ± 58	0.78	333 ± 65	0.74
Application number (*n*)	8.5 (IQR 4 – 15)	2 (IQR 1 – 2)	< 0.001	3 (IQR 1 – 6)	< 0.01
Application duration (s)	357 ± 315	605 ± 322	0.01	204 ± 177	0.14
Occurrence of junctional rhythm (*n*)	26 (100%)	0 (0%)	< 0.001	16 (100%)	NA
Residual jump after ablation (*n*)	1 (4%)	3 (12%)	0.29	1 (6%)	0.62
Non-inducibility (*n*)	26 (100%)	25 (100%)	NA	15 (94%)	0.38
Procedure time (min)	83 ± 25	117 ± 47	< 0.01	117 ± 55	< 0.01
Patient radiation time (min)	6.8 (IQR 4.4 – 16.1)	15.1 (IQR 9.1 – 23.8)	< 0.01	17.5 (IQR 7.0 – 31.3)	0.02
Patient radiation dose (μGym2)	695 (IQR 441 – 1515)	999 (IQR 482 – 1797)	0.37	742 (IQR 312 – 1532)	0.80
Physician radiation time (min)	0.0 (IQR 0.0 – 0.0)	15.1 (IQR 9.1 – 23.8)	< 0.001	17.5 (IQR 7.0 – 31.3)	< 0.001

Data are presented as mean ± SD or median with interquartile range (IQR).
CE, cryoenergy; CL, cycle length; MAN, manual RF ablation; MNS, magnetic navigation system; NA, not applicable.

RF delivery was interrupted in two MNS patients because of the appearance of a first-degree AV block and in one patient due to a second-degree AV block. The conduction disturbances spontaneously resolved within 6 ± 5 minutes. A transient third-degree AV block was seen in two patients during cryomapping and spontaneously resolved after 8 seconds and 10

minutes, respectively. Transient AV block was seen in two patients during RF applications in the MAN group. After interrupting the application, normal AV conduction returned. In one MAN patient ablation of the AVNRT was unsuccessful. In all other patients successful ablation was achieved.

Heart rate and PR intervals

The PR interval and heart rate of all patients before and 24 hours after the procedure are presented in Table 3. No differences were observed between the MNS, CE and MAN group for both heart rate and PR. Three months after the procedure the heart rates and PR intervals were also comparable between the MNS, CE and MAN group (Table 3). None of the patients had a PR interval > 200 ms or significant arrhythmias during 24 hour Holter registrations after three months follow-up.

Table 3
Heart rate and PR intervals (at baseline, 24 hours after the procedure and 3 months after the procedure)

	MNS	CE	*P* value	MAN	*P* value
Heart rate at baseline (bpm)	75 ± 12	70 ± 14	0.21	72 ± 11	0.53
PR at baseline (ms)	149 ± 25	143 ± 33	0.44	165 ± 21	0.10
Heart rate after 24 hour (bpm)	75 ± 13	71 ± 13	0.23	70 ± 10	0.28
PR after 24 hour (ms)	148 ± 25	149 ± 24	0.90	155 ± 17	0.43
Heart rate after 3 months (bpm)	75 ± 12	78 ± 13	0.41	74 ± 10	0.78
PR after 3 months (ms)	152 ± 26	142 ± 24	0.24	155 ± 20	0.70

Data are presented as mean ± SD.
CE: cryoenergy, MAN: manual RF ablation, MNS: magnetic navigation system, RF: radiofrequency.

Complications

During the procedures no major adverse events occurred. One patient had a haematoma localized in the neck, which spontaneously resolved after a few weeks.

Follow-up data

After a mean follow-up of 26 ± 5 months no further documented bradycardia or conduction disturbance was reported. After initial successful AVNRT ablation 25 patients from the MNS group (96 %), 24 patients from the CE group (96 %, P = 0.745) and 14 patients from the MAN group (93 %, P = 0.321) remained asymptomatic. The patient treated with MNS had a recurrent documented small complex tachycardia more than three months after the index

procedure, which was thought to be AVNRT. However, the symptoms were no longer disabling and further treatment was not required. The two other patients (one from the CE and one from the MAN group) underwent a repeat procedure.

DISCUSSION

The major finding of this study is that RF ablation with a single-catheter approach using MNS for treatment of AVNRT is a feasible technique. Furthermore, the use of MNS is associated with shorter procedures and less radiation exposure for both patient and physician as compared to conventional techniques.

MNS in AVNRT

Although ablation treatment modalities for AVNRT are highly effective with success rates up to 95%, a conventional procedure requires the insertion of several diagnostic catheters into the heart.[15] These procedures were initially associated with a significant radiation exposure for both patient and investigator,[16] but in recent times radiation exposure dropped significantly.[17] This report supports the idea of using the different advantages of the advanced MNS technology to simplify RF ablation. Furthermore, it allows faster procedures and reduces radiation exposure in patients with AVNRT.[8,11]

Safety

In experienced hands the incidence of inadvertent high-degree heart block, using either RF- or cryoenergy, is low.[18,19] Compared to an extremely safe technique such as cryoablation, the single-catheter approach did not result in inadvertent heart blocks as well. If an AV block temporarily occurred during an application, the ablation was interrupted and normal conduction was restored in all patients.

To enhance safety, the position of the His bundle was tagged on the MNS in LAO and RAO views and by means of the fluoroscopic annotation option. This feature makes the presence of a His catheter redundant, however, this can be performed with other navigation or mapping systems as well. Catheter stability, enhanced navigation capabilities and tagging of the His on fluoroscopy all contribute to the safety of this procedure. During this study slow

pathway potentials were not searched, but tagging of the slow pathway region would have been possible as well. Even though we observed two transient first-degree and one transient second-degree AV block, no permanent heart block remained after the procedure. During long-term follow-up, where a large variation of arrhythmias may be discovered after AVNRT ablation, no conduction disturbances were observed.[20]

Advantages of the MNS in the Koch's triangle

The soft and flexible tip of the magnetic navigation catheter permits easy manipulation and manoeuvrability.[21,22] The possibility of perforating the myocardial wall with the extremely floppy catheter tip is very unlikely and has not been reported to date.[10,21,23,24] Precise target or vector navigation can be achieved with accuracy up to 1 mm or 1 degree. As long as the magnetic field is applied, the catheter will remain at the desired location, irrespective of deep breaths or during accelerated junctional rhythm. This characteristic of the MNS is particularly important if mapping and ablating needs to be performed in small regions such as the triangle of Koch and in direct proximity of the compact AV node and His bundle. Additionally, different locations can be stored in the MNS workstation and exact re-navigation is accomplished by reapplying these vectors.[25] This feature of the MNS allows making the diagnosis of AVNRT quickly and with the use of a single catheter, which can be re-navigated to the right atrial lateral position, His position and into the CS ostium. In this study the overall procedure time was reduced by 52% to an average of 83 minutes in comparison to previous reported results and with 29% to conventional RF in this study.[12] The decrease in overall procedure time is mainly due to the possibility of immediate and precise re-navigation to pre-stored positions facilitating diagnostics and therapy.

Patient radiation exposure was significantly reduced with the use of MNS compared to both conventional groups, as has been demonstrated by previous results as well.[12] In comparison to the CE group, the overall procedure time and patient radiation exposure were also significantly reduced. The decrease in radiation exposure is supported by recent papers.[26,27]

Advantages of an upper limb or jugular access

The use of the jugular venous access literally allows patients to walk in and out of the electrophysiology lab. In combination with the aforementioned advantages this permits to

treat many more patients with AVNRT in the same electrophysiology lab when compared to the conventional approach. With the jugular access all patients can be discharged on the same day of the procedure. By using Doppler-echo techniques, it might have been possible to avoid the subclavian punctures as well, making the overall advantage more clear.

Limitations

A possible limitation of the current single-catheter approach was the inconsistency in diagnostic findings in two patients, in whom a correct diagnosis could not be made with a single catheter. Furthermore, monitoring of the VA conduction from the surface electrocardiograms is very difficult and could have contributed to the short-lasting AV block.

CONCLUSION

In conclusion, the use of the MNS is safe and offers further advantages for ablation of the slow pathway since procedural times are shortened compared to CE and MAN catheter navigation. Furthermore, physician's radiation exposure is virtually zero and radiation exposure to the patient is significantly decreased. The present study demonstrated that in the large majority of patients with typical AVNRT, a safe and fast outpatient procedure could be executed with the use of a single remotely controlled catheter.

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CHAPTER 7

Empiric slow pathway ablation in non-inducible supraventricular tachycardia

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ABSTRACT

Background

The data supporting the practice of empiric slow pathway ablation (ESPA) in patients with documented supraventricular tachycardia (SVT) who are non-inducible at electrophysiology study (EPS) is limited. The aim of this study is to assess the efficacy of ESPA in adults.

Methods

A multi-center cohort study of patients who had ESPA between January 2008 and October 2013 was performed. Patients were identified by screening sequential SVT ablation procedures.

Results

Forty-three (5%) out of 859 SVT ablation procedures were identified as ESPA. The median age was 53 (IQR: 24) years; 63% were female. All patients had pre-EPS documentation of SVT (either strip or ECG). In 23 (53.5%) cases, pre-EPS ECG showed short RP tachycardia. Thirty-two (74.4%) patients had dual atrioventricular nodal physiology (DAVNP) plus echo beats. Junctional rhythm (JR) as procedural endpoint was noted in 39 (90.7%) patients. In 18 (41.9%) patients, the abolishment of DAVNP was achieved. No complications were encountered. A median follow-up of 17 months (range: 6 to 31 months) revealed 83.7% (36 of 43) success rate, defined as the absence of pre-procedural symptoms and any documented sustained arrhythmia. As compared to patients with recurrence (n = 7), patients with no recurrence (n = 36) had significantly higher prevalence of clinical short RP tachycardia (61.1% vs. 14.3%, p = 0.038), and EPS finding of DAVNP plus echo beats (80.6% vs. 42.9%, p = 0.034).

Conclusions

ESPA is a reasonable approach in patients with documented SVT, in particular in short RP tachycardia, who are not inducible at EPS. Larger studies are required to assess this practice.

INTRODUCTION

Catheter ablation has become a well-established, first-line therapy for atrioventricular nodal reentrant tachycardia (AVNRT), the most common clinical reentrant supraventricular tachycardia (SVT).[1,2] Some patients have documentation of SVT (either strip or ECG) suggestive of AVNRT but fail to demonstrate the induction of AVNRT during the electrophysiology study (EPS). Empiric slow pathway ablation (ESPA) as a plausible option in these patients, even in the absence of proven AVNRT, can be considered.[1,3]

The practice of ESPA is common (~ 5–10% of SVT cases).[3,4] However, unlike pediatric population,[5,6] there is a very limited data to support and guide this practice in adults. Very few studies have reported on the efficacy of ESPA[4,7,8], with little input on predictors of success. Currently, there is a significant variability in the practice of ESPA among operators.[3] Factors like operator's experience and perception of complication rate and outcomes have shown to influence the operators' tendency to ablate slow pathway empirically.[3]

The aim of this study is to assess the clinical efficacy of ESPA in adults. Furthermore, we aimed to evaluate clinical characteristics and peri-procedural measures that could help operators to guide their ESPA practice.

METHODS

All patients who had any catheter ablation procedure for SVT at Sunnybrook Health Sciences Centre (Canada) and Erasmus University Medical Center (Netherlands) between January 2008 and October 2013 were identified by reviewing procedure and clinic notes. Ethics approval was obtained from the institutional review board. The following inclusion criteria were applied 1) age > 18 years old; 2) pre-EPS documentation of SVT (either strip or ECG); 3) radiofrequency (RF) ESPA was performed and defined as slow pathway ablation/modification in the absence of three or more beats of inducible SVT at the time of EPS and 4) clinical follow-up available for at least 6 months post-procedure.

Pre-EPS documentation of SVT (either strip or ECG) was further grouped into short RP tachycardia and non-short RP tachycardia. Short RP tachycardia was defined as R-P interval of less than 70 ms during the tachycardia and non-short RP tachycardia included long RP tachycardia, or ECGs/strips of limited diagnostic value. The interpretation of each strip/ECG as short RP versus non-short RP tachycardia was performed by two operators and sometimes by a third operator to solve disagreements.

We retrieved data related to 1) baseline clinical/demographic characteristics; 2) intraprocedural data related to EPS endpoints (dual atrioventricular nodal physiology (DAVNP) only or DAVNP plus echo beats), ablation endpoints (junctional rhythm (JR) only or JR plus abolishment of DAVNP); 3) complications; and 4) follow-up data based on symptoms or documentation of any sustained arrhythmia with extended monitoring.

Electrophysiology study

Whenever possible all antiarrhythmic drugs were discontinued for 5 half-lives prior to the EPS. Only limited sedation protocols were used. A comprehensive EPS was performed. Ventricular and atrial programmed electrical stimulation (including sensed triggered atrial stimuli), with up to two extrastimuli was performed with at least two driving cycle lengths (at minimum cardiac pacing cycle length of 400 msec and 600 msec, respectively), as well as burst atrial and ventricular pacing. Isoproterenol infusion was administered in all patients resulting in at least 20% increase in baseline sinus cycle. Pacing protocol was performed during isoproterenol infusion and washout. Dual AV node physiology was defined as the prolongation of the AH interval during atrial pacing or extrastimulus or the HA interval during ventricular pacing or extrastimulus for > 50 ms with a 10-ms decrease of the coupling interval.[8,9] Ablation endpoint varied among operators as some ended the procedure with only a 60–90 s of JR transitioning into sinus rhythm, while others repeated applications until the abolishment of DAVNP (abolishment of DAVNP was defined as eliminating DAVNP with ablation as confirmed by EPS post-ablation). All operators delivered a power of 50 W during RF ablation, using non-irrigated catheter.

Follow-up

Patients were followed up initially in 2–3 months after the procedure with extended

monitoring including holters (typically 72 h to week) and in case of symptoms with external loop recorders (2–4 weeks). Routine follow-up was conducted at variable frequency based on clinical need and to cover twice typical baseline symptoms frequency at least (i.e. in patents with quarterly symptoms at least 6 months etc.). Moreover, patients with recurrence of symptoms had more rigorous monitoring and follow-ups to document recurrence of tachycardia using multiple extended monitors.

Statistical analysis

Continuous variables were expressed as median and interquartile range (IQR), and categorical variables as number and percentages. The distributions of the continuous variables across the study groups were tested with the Shapiro–Wilks test. Continuous data were analyzed using Mann–Whitney U test. Categorical data were compared using chi-square or Fisher's exact tests, where appropriate. The probability of freedom from recurrence following the procedure was estimated using the Kaplan–Meier method. Differences in the probabilities were assessed using the log-rank test. Cox's proportional hazards regression analysis was used to evaluate predictors of recurrence. A 2-tailed p value < 0.05 was considered statistically significant. All statistical analyses were performed using the IBM SPSS software (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.).

RESULTS

Forty-three (5%) out of 859 SVT ablation procedures were identified as cases of ESPA. The median age of patients was 53 (IQR: 24) years, 63% were female; none had structural heart disease. Pre-EPS documentation of SVT in 23 (53.5%) cases demonstrated short RP tachycardia. Frequency of pre-procedural episodes ranged between daily to quarterly.

During diagnostic EPS, none of the patients had explicit signs of an accessory pathway. Thirty-two (74.4%) patients had DAVNP plus echo beats, 9 (20.9%) patients had DAVNP only, and 2 (4.7%) patients had no DAVNP. All patients underwent ablation of the slow pathway

area with radiofrequency application. JR as procedural endpoint was noted in 39 (90.7%) patients. In 18 (41.9%) patients, the abolishment of DAVNP was also achieved. No complications were encountered.

A median follow-up of 17 months (range: 6 to 31 months) revealed 83.7% (36 of 43) success rate, defined as the absence of pre-procedural symptoms and any documented sustained arrhythmia during follow-up (Table 1).

Table 1
Baseline characteristics of the study group (*n* = 43)

Age (year)	53 (24)
Female gender	27 (62.8%)
Clinical tachycardia	
Short RP tachycardia	23 (53.5%)
Non-short RP tachycardia	20 (46.5%)
Modality	
Radiofrequency	40 (93.0%)
Stereotaxis	3 (7.0%)
Electrophysiological endpoint	
DAVNP + echo beat	32 (74.4%)
DAVNP only	9 (20.9%)
None of above	2 (4.7%)
Ablation endpoint	
Junctional rhythm + abolishment of DAVNP	18 (41.9%)
Junctional rhythm only	21 (48.8%)
None of above	4 (9.3%)
Follow-up duration (month)	17 (14)
No recurrence	36 (83.7%)

Continuous variables are presented as median and interquartile range, and categorical variables as number and percentages. DAVNP indicates dual atrioventricular nodal physiology.

All recurrences (n = 7) occurred within 2 months after the procedure. As compared to patients with recurrence (n = 7), patients with no recurrence (n = 36) had significantly higher prevalence of clinical short RP tachycardia (61.1% vs. 14.3%, p = 0.038), and EPS finding of DAVNP plus echo beats (80.6% vs. 42.9%, p = 0.034). Groups were similar with respect to other baseline characteristics (Table 2).

Patients with pre-EPS documentation of short RP tachycardia had significantly higher 2-year probability of freedom from recurrence (95.7% vs. 70%, log-rank p = 0.023) (Fig. 1). In patients with baseline DAVNP, the presence of echo beats at EPS was associated with a

higher 2-year probability of freedom from recurrence (90.6% vs. 55.6%, log-rank p = 0.023) (Fig. 2). Baseline absence of both DAVNP plus echo beats on EPS was the only predictor of recurrence in Cox proportional hazards model (HR: 4.53, 95%CI 1.013 to 20.23; p = 0.048). In 21 cases, operators achieved 60–90 s of JR as a procedural endpoint without abolishment of DAVNP. JR alone versus JR plus abolishment of DAVNP as ablation endpoints had no influence on long-term success (p = 0.27).

Table 2
Baseline characteristics of the patients with and without recurrence

	Recurrence		
	No (*n* = 36)	**Yes (*n* = 7)**	***P* value**
Age (year)	40 (37)	55 (24)	0.339
Female gender	21 (58.3%)	6 (85.7%)	0.229
Clinical tachycardia			
Short RP tachycardia	22 (61.1%)	1 (14.3%)	0.038
Non-short RP tachycardia	14 (38.9%)	6 (85.7%)	
Modality			
Radiofrequency	34 (94.4%)	6 (85.7%)	0.421
Stereotaxis	2 (5.6%)	1 (14.3%)	
Electrophysiological endpoint			
DAVNP + echo beat	29 (80.6%)	3 (42.9%)	0.034
DAVNP only	5 (13.9%)	4 (57.1%)	
None of above	2 (5.6%)	0 (0.0%)	
Ablation endpoint			
JR + abolishment of DAVNP	17 (47.2%)	1 (14.3%)	0.270
JR only	16 (44.4%)	5 (71.4%)	
None of above	3 (8.3%)	1 (14.3%)	

Continuous variables are presented as median and interquartile range, and categorical variables as number and percentages. DAVNP indicates dual atrioventricular nodal physiology; JR, junctional rhythm.

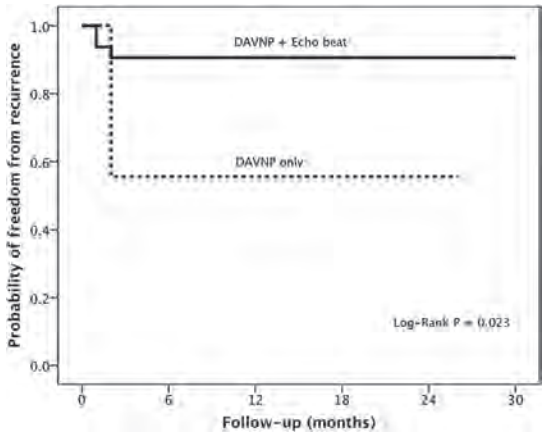

Figure 2: Kaplan-Meier survival curve for freedom from tachycardia recurrence in DAVNP plus echo beat versus DAVNP only. DAVNP indicates dual atrioventricular nodal physiology.

DISCUSSION

This study demonstrates that ESPA is effective in eliminating SVT recurrence in patients with documented tachycardia which is noninducible at the time of EPS. Furthermore, the pre-EPS documentation of short RP tachycardia, and/or EPS finding of DAVNP plus echo beats were predictive of long-term clinical success.

Bogun and colleagues[7], in the pioneering clinical series of seven patients have shown that slow pathway ablation is clinically useful in patients with documented but noninducible SVT who have evidence of dual AV node pathways. More so, they suggested to consider reclassifying the presence of dual AV node pathways in patients with spontaneous but noninducible SVT as a class I indication for slow pathway ablation. The efficacy of ESPA was further confirmed by Lin and colleagues[8], where none of the 16 patients enrolled in their study with empiric slow pathway catheter ablation had recurrence of SVT. Wang and colleagues[4], showed similar results with ESPA in 49 patients. The willingness of operators to offer ESPA in patients with documented SVT and DAVNP is discordant to this limited literature. In a survey assessing the practice of ESPA[3], we found that only 2 among 41 Canadian operators (5%) would perform ESPA in the presence of DAVNP without echo beat and 13 operators (32%) would perform ESPA if only a single echo beat was present at the time of EPS. All prior studies in small sample size support ESPA and have shown the utility of baseline identification of DAVNP but fail to comment on the utility of pre-procedural ECG characteristics of tachycardia or the usefulness of JR during the procedure. This study confirms the efficacy of ESPA. Furthermore, it demonstrates that the pre-procedure ECG/documentation of SVT, in particular short RP tachycardia, has a powerful role in predicting long-term clinical success of ESPA. As well as in those with DAVNP, the presence of echo beats at time of EPS would be associated with a higher probability of freedom from recurrence of SVT. In the absence of inducible SVT, some operators may hesitate to ablate the slow pathway empirically given the absence of a clear procedural endpoint with the infrequent risk of complete AV block.[10,11] Interestingly, in this study some operators decided to achieve sustained JR as procedural endpoint without abolishment of the DAVNP as a recognized reliable marker of success.[12,13] The results did not show significant difference on

long-term success between JR alone versus JR plus abolishment of DAVNP as ablation endpoints. Operators do not need the greater effort and therefore the greater risk in trying to achieve abolishment of DAVNP.

Our results have shown that in 14 patients with non-short RP tachycardia, 5 patients with DAVNP only (without echo beats) and 2 patients without DAVNP, ESPA was effective in eliminating SVT recurrence. This might be related to the fact that eliminating the slow pathway in these cases has modified the tachycardia substrate, such as atrial tachycardia frequently originating from the coronary sinus ostium area[14], or atypical AVNRT. In other occasions, sluggish antegrade slow-pathway conduction or intermittent suppression of DAVNP due to sedation or other transient factors during EPS may mask DAVNP. The inducibility of AVNRT during EPS is sometimes complex and requires a perfect balance between the slow and fast pathway conductions. Ablating the slow pathway in highly symptomatic patients with documented SVT that is noninducible at the time of EPS, could be sometimes the only option even in the absence of clear pre-EPS short RP tachycardia or baseline DAVNP at EPS.

Limitations

The retrospective nature of our study and the lack of a control group limit our conclusions. Although our findings represent a small sample size of 43 patients, these patients were pooled from 859 sequential SVT ablation procedures. Nevertheless, the results should be further confirmed by larger studies or by randomly applied strategy in noninducible SVTs. We have excluded ablation procedures using cryoablation, as JR is not observed during cryoablation delivery. We aimed to assess different ablation endpoints using the same source of energy (RF) with more consistent ablation outcomes among all cases. In the absence of JR with cryoablation more definitive endpoint should be achieved such as abolishment of DAVNP. The practice of cryoablation in ESPA should be assessed separately as the only source of energy delivered to better evaluate the ablation endpoints. We could not perform this assessment separately in our study, as the number of cryoablation procedures was very small to produce reasonable conclusions.

CONCLUSIONS

ESPA is a reasonable approach in patients with documented SVT, in particular in documented short RP tachycardia, who are not inducible at EPS. In patients with DAVNP, the presence of echo beats at EPS is associated with a higher probability of freedom from recurrence of SVT. The surrogate procedural endpoint of junctional rhythm could be a sufficient endpoint in these cases without the need of abolishing the DAVNP. Larger studies are required to assess this practice.

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CHAPTER 8

Safety and efficacy of the remote magnetic navigation for ablation of ventricular tachycardias - a systematic review

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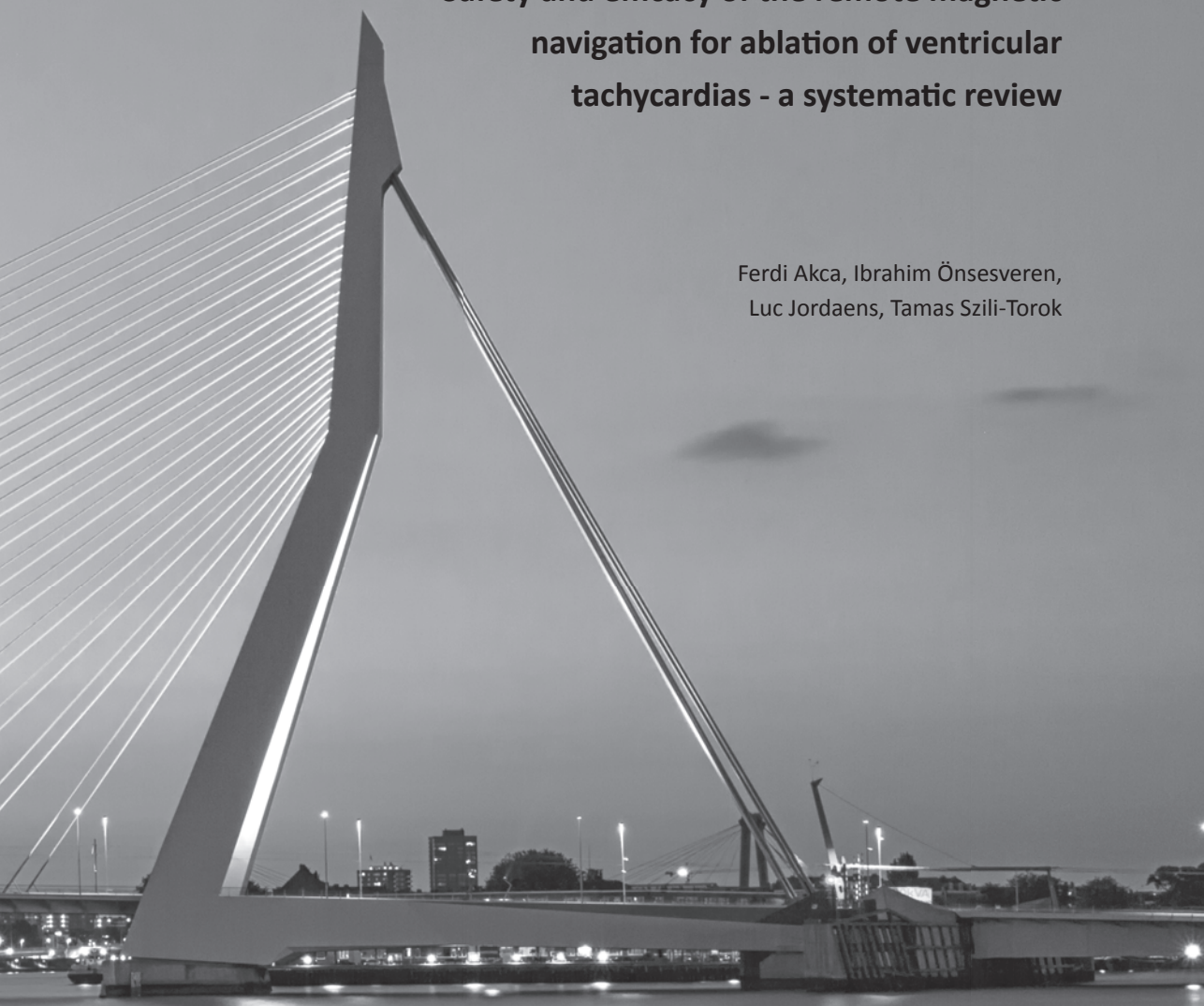

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ABSTRACT

Objective

Remote magnetic navigation (RMN) is considered to be a solution for mapping and ablation of several arrhythmias. In this systematic review we aimed to assess the safety and efficacy of RMN in ablation of ventricular tachycardia (VT).

Methods

The National Library of Medicine's PubMed database was searched for articles containing any of a predetermined set of search terms that were published prior to November 1, 2011. Quality of evidence was rated using the GRADE system.

Results

The database search resulted in 11 relevant articles evaluating the usefulness of RMN. Three groups of VTs were studied: VT in patients with ischemic cardiomyopathy (ICMP), non-ischemic cardiomyopathy (NICMP) and structurally normal hearts (SNH). The use of RMN in patients with ICMP has been associated with success rates ranging from 71 to 80 %. RMN has been shown to be a feasible and effective method for ablation of VT in NICMP and SNH patients. Success rates between 50 % and 100 % have been reported in NICMP populations. Rates ranging from 86 % to 100 % have been reported for SNH patients. The lowest rates of arrhythmia recurrence are reported for SNH patients (0–17 %). In ICMP and NICMP, recurrence rates of 0–30 % and 14–50 %, respectively, have been reported. One patient experienced total heart block, and one patient experienced a thromboembolic event after RMN catheter ablation procedures.

Conclusion

RMN has been shown to be an effective and safe method for ablation of VT in various patient populations with low recurrence and complication rates. However, more comparative and randomized studies are necessary, and therefore the true value of RMN for VT ablation remains still unknown.

INTRODUCTION

Treatment of ventricular tachycardia (VT) has gone through great improvements in recent years.[1-3] When drug therapy is not effective, catheter ablation of VT can be an effective alternative that has been shown to eliminate ventricular tachycardias with high efficacy.[4,5] Different approaches can be used depending on the arrhythmia's origin: left endocardial, right endocardial and epicardial approach.[6] Accurate mapping of the area of interest can be difficult to achieve due to complex anatomical structures or structural heart diseases. Remote magnetic navigation (RMN) is considered to be an effective tool for mapping and ablation of arrhythmias that has the potential to overcome some of these challenges.[6,7] It is a navigation system, which provides good catheter stability during mapping and ablation procedures.[8-10] While the capabilities of manual navigation are limited by the fixed curves of manual catheters, the magnetic catheters have a flexible catheter design enabling them to access otherwise difficult anatomy.[11] The RMN-guided ablation catheter is manipulated by two external magnetic fields situated on either side of the patient. The catheter tip aligns with the magnetic vector produced by the system, allowing the operator to navigate the catheter from its distal tip. Additionally, the RMN system allows the operator to store and reapply specific magnetic vectors in order to facilitate repeated access to difficult anatomy.[12] Some data suggest that utilizing an atraumatic catheter design results in less cardiac perforations.[13,14] Previous research has shown that RMN may allow the operator to reduce fluoroscopy time.[14-16] RMN has been reported as a feasible tool for ablation of several types of arrhythmias, including AV nodal and AV reentrant tachycardias and atrial fibrillation.[17-21] VT can occur in patients with or without structural heart disease (SHD). SHD can be a result of either ischemic cardiomyopathy (ICMP) or non-ischemic cardiomyopathy (NICMP).[22] Scar-related VT (SRVT) could have several causes such as myocardial infarction (MI), dilated cardiomyopathy (DCMP), arrhythmogenic RV cardiomyopathy (ARVC) and hypertrophic cardiomyopathy (HCMP).[6] Idiopathic VT originated in most cases from the outflow tract regions or the fascicles of the left ventricle in patients with structurally normal hearts (SNH).[23] VTs originating from the left ventricular outflow tract (LVOT) and VT originating from above the pulmonary and aortic valve are recognized more often than before.[24-26]

This systematic review aims to provide an overview of the safety and efficacy of RMN in VT ablation.

METHODS

Our aim was to identify all articles that discuss the use of RMN for VT ablation procedures. The National Library of Medicine's PubMed database was searched until November 1, 2011. The following predetermined set of search terms was applied:

"Tachycardia, Ventricular"[Mesh] AND "Magnetics" [Mesh] AND Catheter Ablation"[Mesh] OR "Ventricular"[All Fields] AND "Magnetic"[All Fields] AND "Remote"[All Fields] AND "Ablation"[All Fields].

The reference list of each returned article was examined for additional studies that may have been missed in the PubMed database search. All studies discussing use of RMN for VT ablation in human were included.

GRADE system

All data from the included articles were analyzed according to the internationally developed GRADE system in order to define the quality of the evidence.[27] The overall quality of the evidence was rated into four categories (high, moderate, low, very low) using the criteria of GRADE. From the studies that met the inclusion criteria, four factors were considered in appraising the overall strength of the evidence according the GRADE system: study design, study quality, consistency of evidence and directness of evidence.

Data extracting process

Two authors independently reviewed the eligible articles and extracted the following data: VT type, RMN catheter type, acute success rate, manual crossover rate, follow-up time, follow-up recurrence rate and procedural complications. The authors then cross-checked their results to ensure accuracy. If the authors did not reach complete agreement, the results were discussed and a consensus opinion was reached.

Table 1 - Data from included publications

Publication	GRADE score	RMN catheter type	Number of VT ablation procedures / VT type			Acute succes				Manual crossover	Follow-up (months)	Recurrence				Complications
			ICMP	NICMP	SNH	ICMP	NICMP	SNH	Overall			ICMP	NICMP	SNH	Overall	
Di Biase *et al.* 2010 (USA)	Low	Irrigated	33	14	63	-	-	-	86% (95/110)	14% (15/110)	11.8	30% (10/33)	14% (2/14)	8% (5/63)	15% (17/110)	Total heartblock (*n* = 1)
Di Biase *et al.* 2009 (USA)	Low	Non-irrigated	44 SR		21	36% (16/44)		86% (18/21)	52% (34/65)	SR: 64% (28/44) SNH: 14% (3/21)	12	-	-	-	40%	Groin hematoma (*n* = 2)
Arya *et al.* 2010 (GER)	Low	Irrigated	30	-	-	80% (24/30)	-	-	-	0%	7.8	25% (6/24)	-	-	-	No
Aryana *et al.* 2007 (USA)	Low	Non-irrigated	17	ARVC (*n*=3) HCM (*n*=2) DCM (*n*=3) CS (*n*=2)	-	71% (12/17)	ARVC: 100% (3/3) DCM: 50% (1/2) CS: 50% (1/2)	-	-	92% (22/24)	7	27% (3/11)	CS: 50% (1/2)	-	-	Right ulnar nerve palsy (*n* = 1) DVT (*n* = 1)
Konstantinidou *et al.* 2011 (GER)	Very low	Non-irrigated	-	-	13	-	-	92% (12/13)	-	0%	8.4	-	-	17% (2/12)	-	No
Thornton and Jordaens 2006 (NL)	Very low	Non-irrigated	-	-	7	-	-	100% (7/7)	-	0%	12	-	-	14% (1/7)	-	No
Haghjoo *et al.* 2009 (GER)	Very low	Irrigated	5	-	-	80% (4/5)	-	-	-	0%	4.2	0%	-	-	-	No
Thornton *et al.* 2006 (NL)	Very low	Non-irrigated	-	-	1	-	-	100% (1/1)	-	0%	12	-	-	0%	-	No
De Torres *et al.* 2008 (NL)	Very low	Non-irrigated	-	-	1	-	-	100% (1/1)	-	0%	12	-	-	0%	-	No
Schwagten *et al.* 2009 (NL)	Very low	Non-irrigated	-	-	3	-	-	100% (3/3)	-	0%	6	-	-	0%	-	No
Burkhardt *et al.* 2006 (USA)	Very low	Non-irrigated	-	-	1	-	-	100% (1/1)	-	0%	1 day	-	-	-	-	No

Abbreviations of Table 1
ARVC, arrhythmogenic RV cardiomyopathy; CS, cardiac sarcoidosis; DCM, dilated cardiomyopathy; DVT, deep venous thrombosis; HCM, hypertrophic cardiomyopathy; LVOT, left ventricular outflow tract; NICMP, non-ischemic cardiomyopathy; RV, right ventricle; RVOT, right ventricular outflow tract; SNH, structural normal heart; SR, scar-related.

Outcome measurement

The studies on RMN-guided VT ablation were compared with respect to all extracted data.

RESULTS

Our PubMed search returned in 22 results based on the predefined search method. Eleven of the returned articles did not evaluate the use of RMN in VT and were consequently excluded.[21,28–37] In all, data from 11 articles—seven clinical trials, three case reports and one case series—were assessed.[6,7,11,20,22,38–43] After quality assessment according to the GRADE system, four studies were considered as low evidence and seven as very low evidence (Table 1). Three main VT subtypes were studied: VT in ICMP, NICMP and SNH. Additionally, studies on SRVT in patients with ICMP, NICMP or both are analyzed.

In Table 1 an overview of the extracted data is presented. As the article by De Torres et al. did not report a recurrence rate, we contacted the authors in order to obtain the missing data.[42]

Overall success rate

Overall success rates ranged from 52% to 86% for studies assessing VT ablation in ICMP, NICMP and SNH. Two studies reported crossover to manual irrigated tip catheters in 14% and 48% of procedures, respectively.[22,38] Thirty-four of 65 ablation procedures (52%) by Di Biase et al. (2009) utilized only non-irrigated tip RMN ablation catheters. The remaining procedures required the use of manual ablation catheters in order to achieve procedural success. Di Biase et al. (2010) report manual crossover in 15 cases (14%).

Ischemic cardiomyopathy

For ablation of VT in ICMP, success rates ranging from 71% to 80% were achieved.[6,20,39] Arya et al. and Haghjoo et al. report success rates of 80% using the irrigated RMN ablation

catheter. In both studies 20% of the cases resulted in partial success, defined as inducibility of non-clinical VT following the ablation procedure.[20,39] Manual crossover was never necessary to achieve procedural success in these studies. Aryana et al. report a 71% success rate for VT ablation in patients with ICMP.[6]

Di Biase et al. report an acute success rate of 36% for SRVT ablation.[38] This study combines the ICMP and NICMP populations into a single cohort. In 64% of the procedures the non-irrigated tip RMN ablation catheter was unable to achieve acute success, so the procedure was crossed-over to manual technique.

Non-ischemic cardiomyopathy

Aryana et al. evaluated the use of RMN for VT ablation in patients with NICMP and report an acute success rate of 50% in patients with cardiac sarcoidosis after two VT ablation procedures.[6] In patients with ARVC and DCMP acute success was achieved in 100% and 50% of procedures, respectively. Because of lack of VT inducibility, successful catheter ablation could not be performed in HCMP population.

Structurally normal heart

Success rates for RMN ablation in patients with SNH vary from 86% to 100%.[7,11,38,40–43] Di Biase et al. report manual crossover in 14% of cases. Thornton et al., Konstantinidou et al., De Torres et al., Schwagten et al. and Burkhardt et al. completed all cases without crossover to manual catheters.

Recurrence rates

Following acutely successful ablation procedures, 0–30% of ICMP patients experienced recurrence.[6,20,22,39] Recurrence rates ranging from 14% to 50% are reported for the NICMP population.[6,22] Recurrence rates ranged from 0% to 17% for patients with SNH after VT ablation procedures.[11,22,40–43] Thornton et al. note one patient (14%) who experienced non-sustained VT after an acutely successful catheter ablation procedure. Because this patient had sustained VT prior to ablation, the procedure was considered as partial success.[40]

Di Biase et al. reported an overall recurrence rate of 40% in a mixed sample of patients treated with 4 mm RMN, 8 mm RMN and manual catheters. The same group reported an overall recurrence rate of 15% in 2010. For the RMN subgroup, VT recurrence was 14% and 27% for patients that were crossed over to manual technique.[22]

Complications

Four complications were associated with VT ablation procedures. Di Biase et al. noted heart block in one patient with a right bundle branch block (RBBB).[22] Two additional patients developed groin hematomas.[38] Another study reports an uncomplicated bilateral lower-extremity deep venous thrombosis in one patient.[6] This thromboembolic complication occurred during left-sided ablation with a non-irrigated tip catheter, so the risk of similar events is likely to be reduced by using irrigated tip RMN ablation catheters.[44] Aryana et al. report a case of right ulnar nerve palsy after an epicardial RV mapping procedure. It is unclear whether the palsy is caused by an embolic stroke or was a result of long immobilization under general anesthesia.[6]

Crossover to manual ablation

In this systematic review the use of RMN in ablation of VT has been investigated. Several groups report use of RMN ablation to treat patients with ICMP, but these results are quite varied.[6,20,38,39] Three groups reported favorable success rates between 71% and 80%. Two of 15 ablation procedures (13%) by Aryana et al. utilized only non-irrigated tip RMN ablation catheters. The remaining procedures required the use of manual irrigated tip ablation catheters in order to achieve acute procedural success. Di Biase et al., however, achieved a rate of only 36% for SRVT ablation procedures. This low success rate may not accurately reflect the potential of RMN as the study employs only non-irrigated RMN catheters and showed a low threshold for manual crossover.[38] The most recent trial by Di Biase et al. (2010) with irrigation demonstrated a considerable lower crossover rate of 14%. Previous research has shown that catheter irrigation improves ablation efficacy and decreases the risk of thrombotic events.[44] However, very scarce data are available on SRVT using an irrigated ablation catheter.

Idiopathic VT

RMN is most effective when used in patients with SNH and is successful in 86% to 100% of these procedures.[7,11,38,40– 43] The usefulness of RMN in ablation of idiopathic VTs has been investigated by several groups. Although they evaluate RMN in a relatively small sample of patients, these studies demonstrate the feasibility of RMN for successful ablation of RVOT, LVOT, left fascicular and aortic cusp VT. Still, more evidence is needed to assess the efficacy and safety of RMN in different subtypes of idiopathic VT.

Future studies or areas of investigation

This review showed successful results in patients with ARVC, DCMP and sarcoidosis.[6] However, these groups included a minimal number of patients, and more research is needed in this patient population. Therefore, we call for more research on the use of RMN in ablation of VT in NICMP.

The safety and efficacy of RMN in ablation of VT is evaluated in multiple studies. Schwagten et al. report on the superior capabilities of RMN in VT ablation.[45] A higher rate of acute success (97% vs. 81%, P = 0.03) and lower rate of arrhythmia recurrence (14% vs. 50%, P < 0.01) were achieved in RMN procedures compared to manual catheter ablation.

The use of RMN compared to manual procedures has been evaluated for multiple arrhythmias, including VT.[13] Bauernfeind et al. evaluated the safety and long-term efficacy of RMN in a large number of patients. These data showed that the use of RMN reduced the occurrence of major complications (0.34 vs. 3.2%, P = 0.01) without compromising efficacy compared to manual ablation. Further, RMN was significantly more successful for VTs (93 vs. 72%, P < 0.05). In this population both SNH and SRVT were studied; however, the superiority of RMN in SNH VT was largely responsible for the difference. Di Biase et al. (2010) stated that procedure times were longer using RMN, although with decreased use of fluoroscopy. To achieve similar results, a statistically greater number of RF lesions needed to be applied in RMN group. However, Bauernfeind et al. report both decreased procedure times and fluoroscopy times using RMN. This could be explained by the steep learning curve for the RMN system. This demonstrates that new methods are needed to increase efficacy of

ablation compared to conventional manual techniques. However, no randomized studies have been executed to prove superiority.

Limitations of the study

In this review we evaluated the safety and efficacy of RMN in VT ablation. Several studies show advantages of RMN for VT ablation, although this is based on low quality evidence according to the GRADE system. High quality randomized studies are needed for more consistent evidence to assess the efficacy and safety of RMN in ablation of VT.

CONCLUSION

The available data on RMN suggests that it is an effective and safe method for ablation of VT with relatively low recurrence and complication rates. RMN has been used to achieve successful outcomes in various patient populations and VT subtypes. SNH VT appears to have the best outcome using RMN in comparison to ICMP and NICMP VT. In case of NICMP extremely limited data are available for the effectiveness of RMN. Although these are promising results, more comparative and randomized studies are necessary to assess superiority. The true value of RMN for VT ablation remains still unknown.

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CHAPTER 9

Catheter ablation of ventricular tachycardias using remote magnetic navigation: a consecutive case-control study

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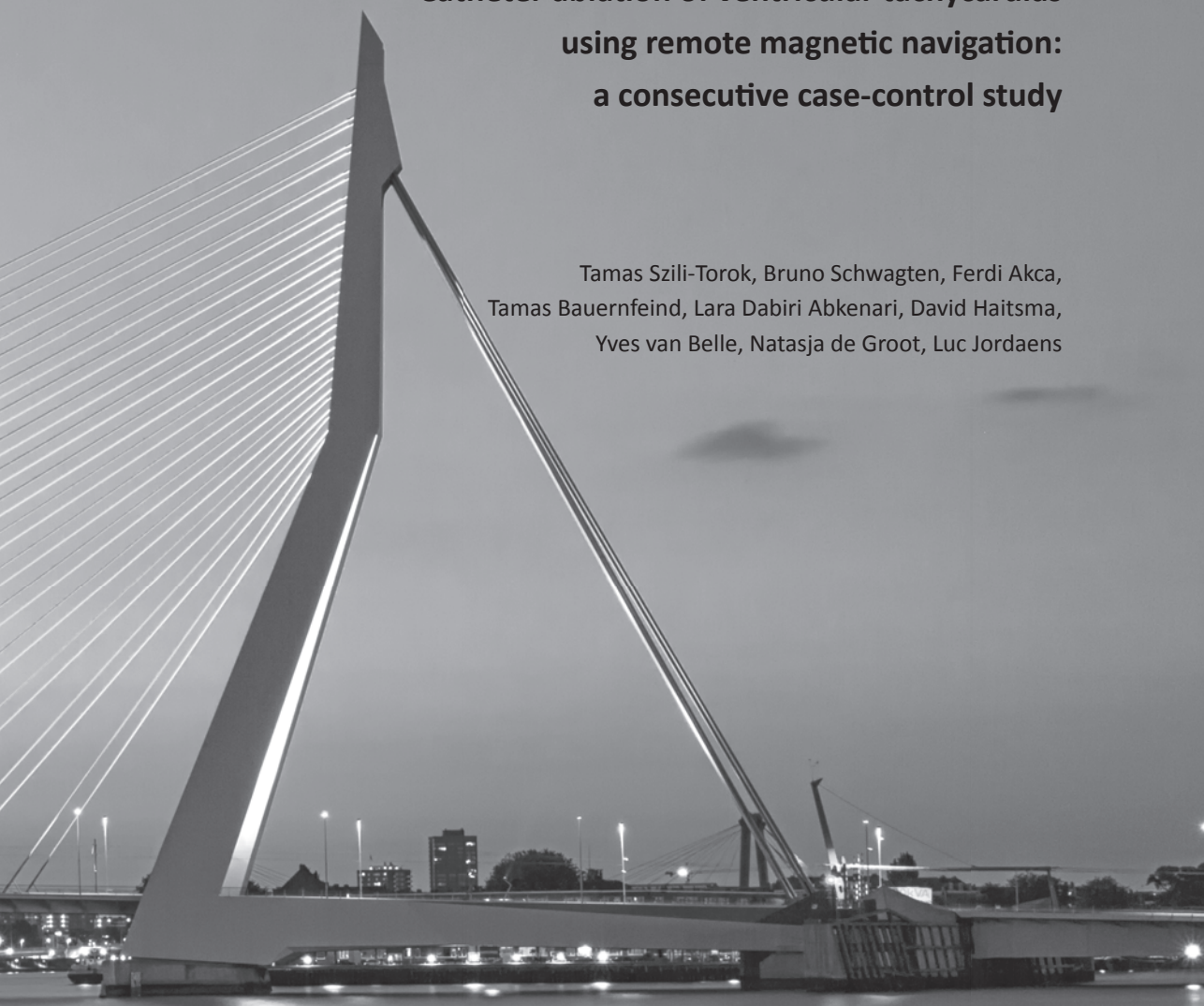

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ABSTRACT

Background

This study aimed to compare acute and late outcomes of VT ablation using the magnetic navigation system (MNS) to manual techniques (MAN) in patients with (SHD) and without (NSHD) structural heart disease.

Methods

Ablation data of 113 consecutive patients (43 SHD, 70 NSHD) with ventricular tachycardia treated with catheter ablation at our center were analyzed. Success rate, complications, procedure, fluoroscopy, and ablation times, and recurrence rates were systematically recorded for all patients.

Results

A total of 72 patients were included in the MNS group and 41 patients were included in the MAN group. Patient age, gender, and right ventricular and left ventricular VT were equally distributed. Acute success was achieved in 59 patients in the MNS group (82%) versus 27 (66%) patients in the MAN group (P = 0.046). Overall procedural time (177 ± 79 vs. 232 ± 99 minutes, P < 0.01) and mean patient fluoroscopy time (27 ± 19 vs. 56 ± 32 minutes, P < 0.001) were all significantly lower using MNS. In NSHD pts, higher acute success was achieved with MNS (83,7% vs. 61.9%, P = 0.049), with shorter procedure times (151 ± 57 vs. 210 ± 96, P = 0.011), whereas in SHD-VT these were not significantly different. No major complications occurred in the MNS group (0%) versus 1 cardiac tamponade and 1 significantly damaged ICD lead in the MAN group (4.9%, NS). After follow-up (20 ± 11 vs. 20 ± 10 months, NS), VT recurred in 14 pts (23.7%) in the MNS group versus 12 pts (44.4%) in the MAN group (P = 0.047).

Conclusion

The use of MNS offers advantages for ablation of NSHD-VT, while it offers similar efficacy for SHD-VT.

INTRODUCTION

Catheter ablation was introduced in clinical electrophysiology in the 1980s.[1,2] In the past decades, it has become well established as first-line therapy for many types of arrhythmias, including ventricular tachycardia (VT).[3] Further technological developments such as electroanatomical mapping, integration of cardiac imaging, and improved catheter design have been implemented to improve the consistency of the procedural outcome.[4-6] Until recently, all of the above mentioned techniques were based on manual navigation of catheters within the heart. The innovation of the remote magnetic navigation system (MNS) has offered important theoretical advantages in safety due to the atraumatic catheter design and less physical stress and radiation exposure for the physician.[6-9] Higher efficacy is also expected due to the unrestricted and reproducible catheter movement as well as improved catheter stability.[7,10,11]

The objective of this prospective study was to evaluate the acute and long-term efficacy of MNS for ventricular tachycardia when compared to conventional manual ablation in the hands of the same operators at a single center. We hypothesized that the superior navigation capabilities of MNS tip delivery would lead to a superior and more consistent outcome with an improvement in procedural safety when compared to conventional methods.

METHODS

Patients

A total of 113 consecutive VT patients were included in this case series (consecutive VT patients from January 1, 2008 until August 31, 2010). A total of 72 patients were included in the MNS group and 41 patients were included in the MAN group. Patient age, gender, etiology, and right ventricular (RV) and left ventricular (LV) VT were equally distributed between the 2 groups (P = NS, Table 1).

At our center, we have 2 separate electrophysiology laboratories: one equipped with the MNS system and one without an MNS system. A responsible person assigns individual patients to 1 of the 2 laboratories without input from the investigators. Though this study was clearly not randomized, our internal policy does afford some of the scientific benefits of a formal randomization, as is evident by the homogeneity of the 2 groups. The reason for the lower number of manual ablations is that the electrophysiology laboratory where the manual ablations were performed serves as a device lab, too, while in the magnetic room only ablations are performed.

Electrophysiology studies — ablation strategy

The procedures were performed over the entire study duration by the same senior electrophysiologist group with the assistance of 4 fellows, trained for both manual catheter navigation and for remote MNS ablation. All catheter procedures were performed in accordance with institutionally approved local medical treatment protocols of the Erasmus MC, Thoraxcenter, Rotterdam. Prior written, informed consent for the ablation procedure was obtained from all patients. Resting 12-lead ECG, laboratory tests, an X-ray thorax image, and a 2-dimensional echocardiography were acquired from all patients within 48 hours of the procedure.

Standard peri-procedural medication protocols were followed in all patients. For planned procedures, patients were instructed to stop taking antiarrhythmic drugs for a period of at least 4 half lives prior to undergoing the procedure (except amiodarone). In cases of emergency VT ablation, medication remained unchanged. The procedures were performed during a fasting state, using local or general anaesthesia. Market-approved diagnostic and ablation catheters were used as clinically indicated at the discretion of the operator. Investigators were not involved in the decision as to whether a patient was placed in our MNS laboratory or our MAN laboratory.

The left heart was accessed via retrograde aortic route or transseptal puncture based on the operator's preference. Generally, left-sided ventricular arrhythmias were performed via retrograde approach (MNS 32/37, 87%; MAN 21/25, 84%; P = NS, Table 1). The use of a 3-dimensional mapping system was mandatory in both groups for all patients. Intracardiac

echocardiography (ICE) was used to guide transseptal punctures in all patients where applicable.

For patients with SHD, the procedure started with induction of VT and was followed by detailed mapping of the ventricle in order to localize of the myocardial scars as potential targets for catheter ablation. Programmed stimulation was performed using up to triple extrastimuli pacing from the right ventricular apex, right ventricular outflow tract or left ventricle. Twelve-lead ECG recordings were obtained for all inducible arrhythmias. If only VF or polymorphic VT was inducible, the procedure was continued with electroanatomical substrate mapping using either the CARTO RMT (Biosense Webster, Inc., Diamond Bar, CA, USA) or the EnSite NavX system (St. Jude Medical, Inc., St. Paul, MN, USA). Bipolar contact electrograms were recorded and used to create a 3-dimensional map of the chamber based on the voltage amplitude. After creating a substrate map an extensive scar ablation (scar homogenization) was performed in all regions where scar tissue was identified. Scar was defined as a low voltage area under 1.5 mV. However, in order to minimize myocardial damage all lesions were made at the ≤1.0 mV border. In case of a hemodynamically stable VT the operators were allowed to tackle the VT by creating an activation map and identifying either the exit points or the critical isthmus of the tachycardia. In the MNS group 82.6% of the tachycardias were terminated during hemodynamically stable VT compared to 80.0% in the MAN group (P = NS). However, even after successful treatment of the clinical VT, eventual scar homogenization was always performed. For patients with idiopathic VTs, standard ablation and mapping techniques were applied based on the operator's choice. In principle, during hemodynamically stable VTs an activation map was created during the VT, usually followed by pace mapping (the site with a paced 12-lead QRS morphology identical to an inducible monomorphic VT was assumed to be the exit site or the site of origin of that particular VT) for confirmation. In patients where the VT was hemodynamically untolerable or was nonsustained, pace mapping was used as the primary technique to identify the origin and/or exit of the tachycardia. If that was possible the VT was ablated during ongoing tachycardia in this group. There were no differences between treatment strategies in the MNS and manual ablation groups.

Crossover from the magnetic navigation catheter to manual navigation catheter was allowed at the discretion of the investigator. Any crossover was counted as an acute failure for the MNS group. Crossover from the MAN to the MNS group was not possible due to the fact that the MAN procedures were performed in another EP laboratory which was not equipped with MNS.

The endpoints of procedural success were defined as follows: if the VT was inducible, noninducibility was the endpoint; if only ventricular extrasystoles (VES) were present, then the complete abolishment of VES as assessed by 24 hours telemetry was required for acute success. The presence of pacemaker (PM) or implantable cardioverter defibrillator (ICD) was not considered as a contraindication for MNS guided ablations, which is consistent with the product labeling for the MNS. There was a statistically greater percentage of implantable devices in the MAN group (22/41, 53.7%) when compared to the MNS group (22/72, 30.6%, P = 0.013, Table 1).

MNS-guided ablations

The procedures were performed in the MNS group using the Stereotaxis Niobe Magnetic Navigation System (Stereotaxis, Inc., Saint Louis, MO, USA) in an EP lab equipped with a Siemens Axiom Artis (Siemens, Erlangen, Germany) fluoroscopy system. All patients were treated with the NaviStar RMT ThermoCool catheter (Biosense Webster, Inc., Diamond Bar, CA, USA). Electroanatomical mapping was performed using the CARTO RMT (Biosense Webster, Inc., Diamond Bar, CA, USA) system.

Manual-guided ablations

The procedures in the MAN group took place in an EP lab equipped with a Siemens Megalix (Siemens, Erlangen, Germany) fluoroscopy system. Electroanatomical mapping was performed using the EnSite NavX system (St. Jude Medical, Inc.). The following ablation catheters were used: Biosense Webster B, D and F curve Celsius Thermocool, St. Jude Cool Path Duo.

Data collection and analysis

The following parameters were analyzed for both the MNS group and the MAN group: acute success rate, fluoroscopy time, procedure time, total RF time, RF applications, and complications. Acute success rate was assessed according to the terms mentioned above. Fluoroscopy time was recorded from the fluoroscopy system in each room. Procedure time was defined as the interval between subcutaneous injection of lidocaine to the groin and removal of catheters from the patient's body including a 30-minute waiting time for every case. Any adverse event recognized by the operator during the procedure by the attending cardiologist prior to hospital discharge or by the general physician during follow-up was investigated by a trained electrophysiologist and was considered as a complication if the event could be related to the procedure. Major complications were defined as pericardial effusion or/and tamponade, permanent AV block, PM/ ICD damage requiring device or electrode replacement, stroke, major bleeding, or death. Minor complications were defined as minor bleeding (groin hematomas), transient ischemic attack and temporary AV block.

Subgroup analyses were performed for patients with and without structural heart disease (SHD and NSHD) and for right-sided versus left-sided ablations.

Follow-up

Follow-up visits were scheduled for all patients at the outpatient clinic of our department 3 months following the procedure and for every 3 months thereafter. For patients treated for idiopathic VT, 24-hour Holter recordings were scheduled during these clinic visits, while for scar-related VT patients the ICD interrogations served as primary source for documentation of recurrent arrhythmias. Programming of the ICD for patients with primary prevention is performed using a 2-zone configuration (VT: above 170 bpm, VF: above 207 bpm). ATP is only programmed in the VT zone. ICD shock and antitachycardia pacing (ATP) is reported as an event as well.

Statistics

All patient data were analyzed using SPSS 15.0 (SPSS Inc., Chicago, IL, USA). Patient demographic and baseline characteristics were presented as mean ± SD. The 2-tailed Student's *t*-test was used for comparing continuous unpaired samples, assuming unequal

variances. For categorical variables, the $\chi 2$ test or Fisher's exact test was performed. A 2-sided P value < 0.05 was considered to be statistically significant.

RESULTS

Overall

The 2 groups were statistically homogeneous when comparing age, gender distribution, number of pediatrics, hospital stay, and RV/LV distribution (Table 1). Acute success was greater in the MNS group when compared to the MAN group (81.9% vs. 65.9%, P = 0.046). After unsuccessful endocardial ablation an epicardial approach was considered necessary in 31% and 29% of the MNS and MAN procedures, respectively (NS). In MNS patients the postprocedural amiodarone use was significantly lower than in the MAN group (9.7% vs. 34.1%, P < 0.01). Overall, the ablation procedures were shorter and fluoroscopy time was reduced in the MNS group: 177 ± 79 versus 232 ± 99 minutes (P < 0.01) and 27 ± 19 versus 56 ± 31 minutes (P < 0.001), respectively. Between MNS and MAN there was no difference in number of applications (17.8 ± 21.5 vs. 24.4 ± 24.0, P = NS), although in the MNS group there was significantly reduced total ablation time (816 ± 902 vs. 1330 ± 1289 seconds, P = 0.024).

NSHD-VT

The success rate in the NSHD-VT subgroup was higher in MNS group (83.7% vs. 61.9%, P = 0.049). In this group the occurrence of left and right-sided VTS was equal (Table 1). In 1 patient an endo-epicardial approach was required. MNS procedures in the NSHD-VT group were shorter (151 ± 57 vs. 210 ± 96 minutes, P = 0.011) and less fluoroscopy was utilized (19.7 ± 11.2 vs. 42.3 ± 20.3 minutes, P < 0.001). The number of RF applications and total ablation times were not significantly different (10.2 ± 8.1 vs. 12.4 ± 9.3, P = NS; 494 ± 402 vs. 652 ± 541 seconds, P = NS, respectively). In the subgroup no difference in ICD implantation is noticed between MNS and MAN pts (Table 1). In this group 6 patients were diagnosed with papillary muscle and one interfascicular VT. In this subgroup the mean number of RF applications was significantly higher compared to the other NSHD-VT procedures (21.50 ± 12.9 vs. 10.5 ± 9.5, P = 0.011).

Table 1
Comparison of ablation results between the MNS and MAN groups

	MNS–Number	MNS–Percentage	MAN–Number	MAN–Percentage	*P* value
Total patients (*n* = 113)	72 patients		41 patients		
Patient age (years)	51 ± 15		49 ± 17		NS
Sex (male)	49	68.1%	33	80.5%	NS
Pediatric	2	2.8%	2	4.9%	NS
Hospital stay (days)	4.7		7.1		NS
NSHD-VT	3.5 ± 2.9		4.4 ± 4.5		NS
SHD-VT	7.4 ± 9.0		9.9 ± 12.1		NS
ASA	40	55.6%	21	51.2%	NS
Acenocoumarol	3	4.2%	5	12.2%	NS
Amiodarone	7	9.7%	14	34.1%	<0.01
Beta-blocker	16	22.2%	14	34.1%	NS
RV/LV distribution					
RV:	35	48.6%	16	39.0%	NS
LV:	37	51.4%	25	61.0%	
VT Etiology					
NSHD:	49	68.1%	21	51.2%	0.046
SHD:	23	31.9%	20	48.8%	
Retrograde approach LV	32/37	86.5%	21/25	84.0%	NS
Overall acute success	59	81.9%	27	65.9%	0.046
NSHD-VT	41/49	83.7%	13/21	61.9%	0.049
SHD-VT	18/23	78.3%	14/20	70.0%	NS
Procedural time (minutes)	177 ± 79		232 ± 99		<0.01
NSHD-VT	151 ± 57		210 ± 96		0.011
SHD-VT	237 ± 91		250 ± 101		NS
Number of RF applications	17.8 ± 21.5		24.4 ± 24.0		NS
NSHD-VT	10.2 ± 8.1		12.4 ± 9.3		NS
SHD-VT	33.3 ± 30.8		34.0 ± 27.8		NS
Application time (seconds)	816 ± 902		1330 ± 1289		0.024
NSHD-VT	494 ± 402		652 ± 541		NS
SHD-VT	1540 ± 1254		1636 ± 1412		NS
Fluoroscopy time (min)	26.9 ± 19.3		55.9 ± 31.5		<0.001
NSHD-VT	19.7 ± 11.2		42.3 ± 20.3		<0.001
SHD-VT	42.5 ± 23.7		68.9 ± 35.1		<0.01
Major complications	0	0%	2	4.9%	NS
Follow-up (months)	20 ± 11		20 ± 10		NS
Recurrence	14	23.7%	12	44.4%	0.047
NSHD-VT	7	17.1%	4	30.8%	NS
SHD-VT	7	38.9%	8	57.1%	NS
Freedom of AAD	56	77.8%	24	58.5%	0.027
NSHD-VT	45/49	91.8%	17/21	81.0%	NS
SHD-VT	11/23	47.8%	7/20	35.0%	NS
ICD	22	30.6%	22	53.7%	0.013
NSHD-VT	5	10.2%	4	19.0%	NS
SHD-VT	17	73.9%	18	90.0%	NS
ATP	0.94±2.19 [0–9]		1.18±2.21 [0–8]		NS
NSHD-VT	0.50±1.00 [0–2]		0.50±1.00 [0–2]		NS
SHD-VT	1.08±2.47 [0–9]		1.38±2.47 [0–8]		NS
ICD shock	0.41±0.87 [0–3]		0.88±2.03 [0–7]		NS
NSHD-VT	0.75±0.96 [0–2]		0.50±1.00 [0–2]		NS
SHD-VT	0.31±0.85 [0–3]		1.00±2.27 [0–7]		NS

NSHD, nonstructural heart disease; RV, right ventricle; LV, left ventricle; SHD, structural heart disease; VT, ventricular tachycardia; RF, radiofrequency; AAD, antiarrhythmic drugs; ICD, implantable cardioverter defibrillator; ATP, antitachycardia pacing.

SHD-VT

In the VT subgroup with SHD acute success between the MNS and MAN groups was not different (78.3% vs. 70.0%, P = NS). Between ischemic and nonischemic VTs no differences were observed in success rates (Table 2). In the MNS group less fluoroscopy was used compared to the MAN group (42.5 ± 23.7 vs. 68.9 ± 35.1 minutes, P < 0.01). No statistical differences were found between MNS and MAN in procedural time (237 ± 91 vs. 250 ± 101 minutes, P = NS), RF applications (33.3 ± 30.8 vs. 34.0 ± 27.8, P = NS) and ablation time (1540 ± 1254 vs. 1636 ± 1412 minutes, P = NS). There was no statistical significant difference in patients having ICDs between both groups (Table 1).

Crossovers

In 2 MNS procedures the operator switched to a manual ablation catheter. During one operation the arterial sheath was dislocated resulting in inguinal bleeding (minor bleeding). In another patient the VT focus was closely located to the His bundle and for safety reasons cryoablation was applied.

Complications

There were no major complications in the MNS group (0%). In the MAN group, 1 patient suffered a cardiac tamponade that ultimately led to the patient's demise, and 1 patient suffered a significantly damaged ICD lead, thus yielding a major complication rate of 4.9% (Fig. 1). However, this group includes a too-limited amount of patients to correctly deduce any conclusion about complication. These complication rates were not significantly different between the two groups. In MNS and MAN occurrence of groin hematomas was similar (6% vs. 7%, P = NS). In 2 patients in the MNS group, the ICD switched to magnet mode (asynchronous pacing). Neither of these patients was PM dependent; therefore, temporary programming allowed electroanatomical mapping without further problems. Of interest, both of these patients had an implant that was abdominally placed. No long-term effect on ICD or PM function was observed in any patient, including these 2 magnet mode switched patients.

No other complications were recorded in both groups.

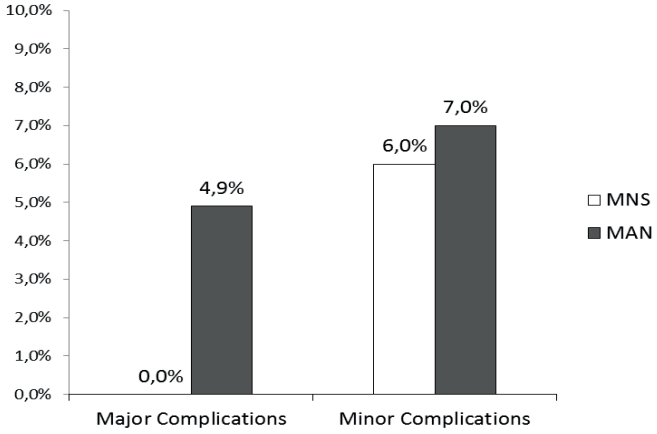

Figure 1: Comparison of major and minor complications.

Follow-up

Patient follow-up was obtained at a mean of 20 ± 11 months in the MNS group and 20 ± 10 months in the MAN group (P = NS). For the overall MNS group, 14 of 72 patients had a recurrence of their arrhythmia (23.7%) compared to 12 of 41 patients in the MAN group (44.4%). This difference was statistically significant (P = 0.047, Table 1). Overall freedom of antiarrhythmic drugs was higher in MNS compared to MAN (77.8% vs. 58.5%, P = 0.027). For the NSHD and SHD subgroups, no statistical differences were found for recurrence: 17.1% vs. 30.8% (P = NS) and 38.9% vs. 57.1% (P = NS), respectively. During follow-up, fewer recurrences were observed in NIHD patients from the SHD subgroup (Table 2). No differences were found in ATP therapy and ICD shocks between the overall groups and the VT subgroups (Table 2). Furthermore, postprocedural use of amiodarone in the MNS group was significantly lower than in the MAN group (9.7% vs. 34.1%, P = 0.002).

Table 2
Comparison of acute success and recurrence rates between all subgroups within MNS and MAN main groups

Total Pts: *n* = 113	**MNS Acute Success**	**MAN Acute Success**	***P* value**	**MNS Recurrence**	**MAN Recurrence**	***P* value**
NSHD-VT						
RV	26/30 (86.7%)	8/13 (61.5%)	NS	5/26 (19.2%)	2/8 (25%)	NS
LV	15/19 (78.9%)	5/8 (62.5%)	NS	2/15 (13.3%)	2/5 (40%)	NS
SHD-VT						
IHD	15/16 (93.8%)	8/12 (66.7%)	NS	7/15 (46.7%)	3/8 (37.5%)	NS
NIHD	3/7 (42.9%)	6/8 (75%)	NS	0/3 (0%)	5/6 (83.3%)	0.048

NSHD, nonstructural heart disease; RV, right ventricle; LV, left ventricle; SHD, structural heart disease; VT, ventricular tachycardia; IHD, ischemic heart disease; NIHD, nonischemic heart disease.

DISCUSSION

This is the first study that directly compares the efficacy and safety of VT ablation between remote magnetic and manual navigation involving statistically equivalent, large-scale patient groups and including both idiopathic and scar-related VT patients. The major finding of this study is that MNS was found to have a higher rate of acute success for catheter ablation of NSHD-VT, while for patients with SHD the success rate was equal. Furthermore, this advantage remained apparent during the follow-up, as fewer recurrences occurred in the MNS group compared to the MAN group.

Rationale of MNS for VT ablation

The success of catheter ablation procedures depends on accurate substrate location, followed by optimal delivery of energy provided by good tissue contact.[12] Manual navigation of catheters in the human ventricles has limitations. Some regions are difficult to reach, and compromised catheter positioning may result in insufficient lesion formation.[7,10,12] Catheter movement in some positions is accompanied by the risk of major complications, including pericardial effusion or tamponade.[13] Although several predefined catheter curves were introduced to help appropriate lesion delivery, there are no optimal curves available for all subtypes of group of patients such patients with small hearts, patients with complex congenital heart defects, or for patients with extremely dilated hearts.[14] The introduction and utilization of MNS was aimed to surmount these difficulties. It provides improvement of safety by the flexible catheter design, and no pericardial effusion or tamponade was reported related to catheter navigation using MNS.[6,15-19] MNS also provides better navigation capability, which is not limited by preformed or evolved catheter curves.[11,14,20]

In this study an epicardial approach has been applied in 1 patient using MNS. Although this is a very limited number, our impression is that it is indeed a feasible technique for epicardial ablation. However, epicardial mapping itself is rather straightforward and therefore we do not see significant advantages of MNS for this particular VT, except the reduced fluoroscopy time. Di Biase and colleagues published their results on 36 patients undergoing epicardial ablation and demonstrated that MNS guided epicardial ablation is associated with slightly longer procedure and RF ablation times, and reduced fluoroscopy time.[15]

In addition, nonfluoroscopic imaging and software-based automated functions such as automapping and stored magnetic vectors may allow for reductions in fluoroscopy time to both operator and patient.[21] Stored magnetic vectors also make it possible to renavigate to spots previously defined and stored during the procedure.[11] Promising initial results have been published concerning these capabilities of the MNS.[6,15,17-19]

Differences in mapping capabilities have also been noted between the MNS and conventional methodology. Latcu and colleagues reported on 20 patients with suspected arrhythmogenic right ventricular dysplasia who underwent RV mapping with both MNS and MAN techniques. In this series, they reported higher RV volumes and surface areas and fewer, more defined low voltage areas and concluded that MNS maps were more accurate than MAN maps.[22]

Other authors have shown a reduction in ventricular extrasystolies (VES) when using MNS for outflow tract tachycardias. Konstantinidou and colleagues recently published a series of 13 RVOT tachycardia patients who were treated with the MNS and concluded that the MNS was associated with a very low incidence of catheter-induced VES.[23] Our own group published a series of 3 cases with minimal ventricular extrasystolies and precise ablation in right ventricular outflow tract tachycardia ablation.[7]

Ablation of VT: tip delivery versus therapy delivery

This is the first larger-scale case–control study to prove some advantages of MNS for ablation of VT when compared to manual navigation. This is demonstrated in patients with NSHD-VT most of the analyzed parameters, including acute success rate, procedure, and fluoroscopy times, and recurrence rate. There are multiple reasons to explain this finding. The MNS guided catheter retains its maneuverability even in difficult positions, such as those encountered in cusp-related VT and papillary muscle originated VT, where the capabilities of manual navigation are seriously limited by the multiple curves of the catheter.[7] However, the above mentioned report demonstrates that for papillary muscle and interfascicular VTs the number of RF applications is higher compared to other NSHD-VTs. The MNS controls the tip of the catheter without the need for a predefined curve, which means that the unavoidable curves of the catheter do not hinder the positioning of the tip, and

good contact can be achieved. This consistent contact results in appropriate lesion formation.[10]

VT ablation in patients with and without structural heart disease

Reports until now focused more on feasibility rather than assessment of efficacy of MNS.[24-27] Our data showed an increase in acute success in the MNS when compared to the MAN group, mainly in NSHD-VT. The majority of the patients in this study had NSHD this results in that and the overall success rate is significantly better using MNS. In our study, this acute difference leads to an improvement in recurrence rates in patients treated with remote magnetic navigation when compared to patients treated with manual methods. The acute success rate for NSHD-VT presented in this study is lower than generally reported. However, the NSHD population was a mixture of groups including very difficult papillary muscle VTs and complex LVOT VTs.

Limitations of the study

This study is not a randomized, prospective trial, and the follow-up interval was relatively short. To address this limitation, we included consecutive patients in both groups and did not exclude any patient from our study cohort. Also, at our center, patients are placed into either our MNS laboratory or our MAN laboratory by a responsible person who is not involved in clinical decision-making. This process effectively allows us to practically compare 2 disparate treatment groups without major bias, as is confirmed by the homogeneity between our 2 study groups. However, since the study has a nonrandomized nature, unknown biases may have entered into determing which room a particular patient had their procedure performed in. Furthermore, this study includes all consecutive VT patients from our hospital regardless the etiology of the tachycardias. This resulted in an obvious difference in the follow-up method. For the ICD subgroup, the ICD follow-up provides extreme accuracy; however, device follow-up was not available for the idiopathic group, where Holter ECG monitoring served as a primary source for the follow-up.

CONCLUSION

In conclusion, our data strongly suggest that the MNS offers significant advantages mainly for the ablation of NSHD- VT when compared to conventional methods. Prospective, randomized studies should be conducted to confirm the conclusions from our retrospective case–control study.

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CHAPTER 10

Acute and long-term outcomes of catheter ablation using remote magnetic navigation in patients with congenital heart disease

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ABSTRACT

Aim

The aim of the present study was to assess the feasibility, safety, and long-term results of remote magnetic navigation in arrhythmias associated with complex congenital heart disease (CHD). The improved outcomes for CHD resulted in an increased number of complex arrhythmias requiring distinctive ablation techniques.

Methods

Thirty-six patients with CHD (age 35 ± 19 years, 21 male) were divided into 3 complexity groups and underwent 43 radiofrequency catheter ablation procedures using the magnetic navigation system (including 7 redo ablations) in combination with the CARTO RMT system.

Results

A total of 59 tachyarrhythmias were identified. Most patients had surgical scar-related tachycardia (25 focal, including 4 microreentrant atrial tachycardia, and 27 macroreentrant atrial tachycardia). Four accessory pathways and three ventricular tachycardias were diagnosed and treated. In 31 patients, ablation was successful, with an end point of noninducibility (86%). The success rate for CHD complexity of type I, II, and III was 50%, 88%, and 89%, respectively. The mean procedure and fluoroscopy time was 216 ± 101 minutes and 40 ± 34 minutes, respectively. The number of radiofrequency applications was 42 ± 47. No major complications related to the procedures occurred. Of the patients, 67% remained free of recurrence during a mean follow-up of 26 ± 4 months. Recurrence developed in 0%, 16%, and 45% of patients with CHD type I, II, and III, respectively.

Conclusion

In conclusion, the magnetic navigation system is feasible to treat arrhythmias with reasonable success rates and good long-term outcomes in adult patients with CHD. The use of the magnetic navigation system offers advantages in complex anatomic situations.

INTRODUCTION

Catheter ablation became first-line therapy for several forms of arrhythmias in the 1990s, with reports of successful ablations in patients with congenital heart disease (CHD).[1,2] However, catheter ablation of patients with CHD still presents a challenge for the electrophysiologist. The cardiac anatomy is usually very different from that of the normal population (often children with small hearts, anatomic abnormalities, surgical reconstructions), making navigation difficult and resulting in a greater risk of complications.[3] The differential diagnosis of the relevant arrhythmia is often more challenging in patients with CHD, a crucial point in the planning of an adequate and successful ablation strategy. The magnetic navigation system (MNS) has advantages that could help to overcome these mentioned difficulties, including improved safety owing to the atraumatic catheter design, less restricted and reproducible catheter movement, and improved catheter stability.[4–8] Despite these advantages of the MNS, the long-term results in adults with CHD are sparse. Our purpose was to evaluate the acute and long-term safety and efficacy of the MNS for the ablation of arrhythmias in patients with CHD.

METHODS

Patients

A total of 36 consecutive patients with CHD (age 35 ± 19 years, 21 male) with symptomatic, drug-refractory tachyarrhythmias underwent ablation from March 2007 to April 2011 and were included in the present study. Incessant drug-refractory arrhythmias were seen in 31% of the patients. The patients were divided into 3 categories of complexity according to the American College of Cardiology/ American Heart Association 2008 guidelines: grade I for simple CHD, grade II for CHD of moderate complexity; and grade III for CHD of great complexity.[1] Of the 36 patients, 29 had undergone previous heart surgery.

Electrophysiology studies – ablations

All patients provided written informed consent for the ablation procedure. A 12-lead electrocardiogram at rest, laboratory tests, radiographic thorax image, and 2-dimensional

echocardiogram were acquired from all patients within the month before and 48 hours after the procedure. A transesophageal echocardiogram was performed, if considered necessary. The procedures were performed during a fasting state, using local or general anesthesia. In general, patients were instructed to stop taking antiarrhythmic drugs for a period of at least 4 half lives before undergoing the procedure. Exceptions were made for amiodarone use and for patients with ongoing tachycardias even with antiarrhythmic drugs or requiring urgent catheter ablation procedures.

The ablation procedures were executed by the same group of our senior electrophysiologist and were performed in all patients using MNS (Stereotaxis Niobe II, Stereotaxis, St. Louis, Missouri) implemented in an electrophysiology laboratory equipped with a Siemens Axiom Artis (Siemens, Erlangen, Germany) fluoroscopy system. The principles and use of the MNS have been previously reported.[9,10] The Niobe II MNS consists of 2 permanent magnets situated on both sides of the patient. The system uses a computer-controlled workstation (Navigant, Sterotaxis, St. Louis, Missouri) to allow changes in the magnetic field orientation to navigate the ablation catheter. A combined field strength of 0.08 or 0.1 T was used. The following ablation catheters were used: Celsius RMT (4 mm; Biosense Webster, Diamond Bar, California) and NaviStar RMT ThermoCool and Navistar RMT DS (8 mm). Electroanatomic mapping was performed in all patients using the CARTO RMT (Biosense Webster, Diamond Bar, California) system.

Atrial tachycardias (ATs) were classified as centrifugal AT (CAT), including a focal and microreentrant mechanism or macroreentrant atrial tachycardia (MRAT). These classifications were made using atrial activation maps. A micro-reentrant mechanism was diagnosed according to the entrainability combined with a centrifugal activation pattern. For both centrifugal and macroreentrant atrial tachycardia, the end points of procedural success were defined as termination of the tachycardia and noninducibility. For circus movement tachycardia, it was the elimination of accessory pathway conduction, and for ventricular tachycardia, it was noninducibility. If multiple sustained arrhythmias could be induced in the same patient, each was ablated consecutively. The ablation strategies were tailored to the type of arrhythmia. For CAT, the radiofrequency applications were applied at the site of the

earliest activation. In the case of MRAT, linear ablation was performed to interrupt the reentrant circuit (Figure 1).

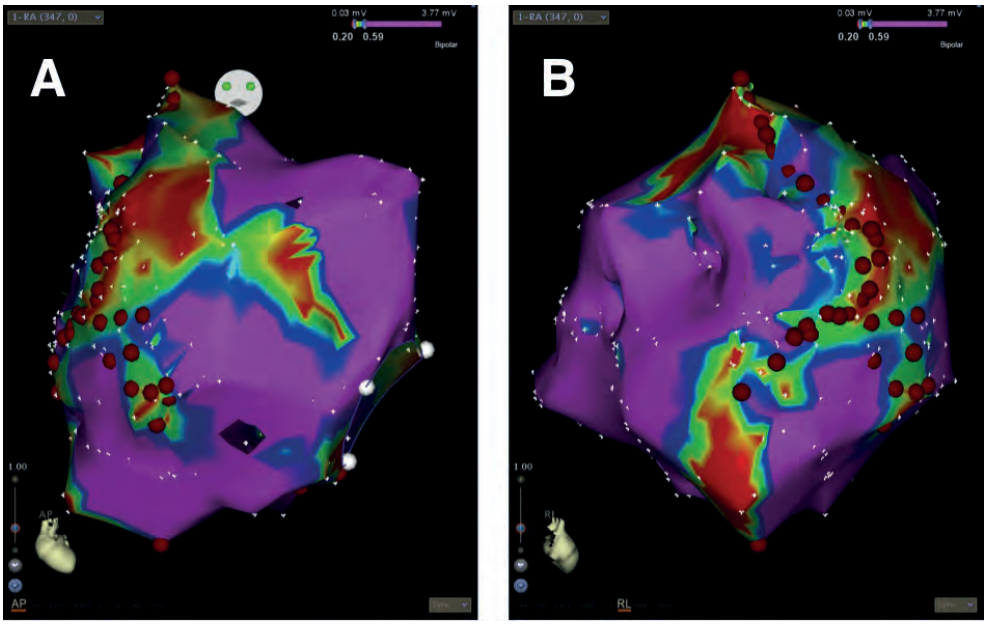

Figure 1: CARTO bipolar voltage maps of the right atrium after surgical correction of Ebstein's anomaly. Healthy myocardium is marked purple (>0.59 mV). The remaining atrial myocardium is marked as scar tissue with potentials of 0.20 to 0.59 mV. Successful scar modification was performed. (*A*) Anteroposterior view and (*B*) right-to-left view.

Data collection and analysis

The following parameters were analyzed: acute success rate, number of baffle or transseptal punctures, fluoroscopy time, procedure time, number of radiofrequency applications, total radiofrequency application duration, recurrence during follow-up, and complications. The acute success rate was assessed according to the terms reported. The fluoroscopy and procedure times (beginning at subcutaneous injection of lidocaine to the groin and ending when the catheters were removed) were recorded in the clinical procedure log and included a 30-minute waiting time. Any adverse event during the procedure, before hospital discharge, or reported by the general physician during follow-up was investigated by a trained electrophysiologist and was considered as a complication if the event could be

related to the procedure. Complications were categorized as major (pericardial effusion or/and tamponade, permanent atrioventricular block, stroke, major bleeding or death) or minor (minor bleeding, transient ischemic attack and temporary atrioventricular block).

Follow-up

Follow-up visits were scheduled for all patients at the outpatient clinic of the cardiology department (Erasmus Medical Center) 3 months after the procedure and every 3 months thereafter. After 1 year, the patients were followed up by their referring congenital or pediatric cardiologist.

Statistics

The parameters obtained from the registry were analyzed using SPSS, version 15.0 (SPSS, Chicago, Illinois). The patient demographic and baseline characteristics were presented as the mean ± SD. Cumulative Kaplan-Meier survival curves were constructed for recurrence-free survival, and a log-rank test was performed.

RESULTS

The baseline patient characteristics are listed in Table 1. The underlying disease of all 36 patients is listed in Table 2. Of the 36 patients, 29 had undergone previous heart surgery (Table 3). A total of 59 arrhythmias were identified during the 43 procedures.

Patients with previous heart surgery

In the 29 patients who had undergone surgical repair, 90% of the arrhythmias proved to be AT (45% CAT and 55% MRAT). Nine patients had 13 CATs, and 21 MRATs were seen in 17 patients. Three patients had both, with a total of 10 arrhythmias. Of the 17 patients with MRAT, 4 had 2 reentry circuits. Five patients had typical atrial flutter; the rest of the 19 MRATs were atypical atrial flutter mechanisms related to the surgical incisions. In the patient group with a history of surgical repair, 2 patients had circus movement tachycardia (1 left- and 1 right-sided accessory pathway) and 3 patients had ventricular tachycardia. In these postoperative patients, 45 arrhythmias could be ablated successfully (92%). One CAT, 2

MRATs, and 1 circus movement tachycardia using a left-sided accessory pathway could not be terminated by ablation, and electrical cardioversion was performed, resulting in a sinus rhythm. For 1 MRAT, the most critical part of the circuit could not be reached endocardially and was therefore not successful.

Patients without previous heart surgery

In the 7 patients with CHD without previous heart surgery 10 arrhythmias were identified. Eighty percent of these arrhythmias were AT (63% CAT and 38% MRAT). Three CATs were diagnosed in 3 patients, and 2 MRATs were seen in 2 patients. One patient had both CAT and MRAT, and 3 arrhythmias were identified. In 2 patients, circus movement tachycardia with right-sided accessory pathways was identified. In the 7 patients with CHD and without surgery, 5 of the arrhythmias could be ablated (50%). However, 2 CATs and 3 MRATs could not be terminated, and electrical cardioversion was performed. Two figure-of-8 MRATs could not be ablated owing to the presence of a percutaneous atrial septal defect closure device.

Arrhythmias and success rates: CHD complexity grades

Of those with complexity score I, 25% had undergone previous surgery. A total of 6 arrhythmias were identified, including 3 CATs and 2 MRATs. Two CATs and one MRAT could be ablated successfully, for an overall success rate of 50%.

Of those with complexity score II, 73% of these patients had undergone earlier surgery. A total of 24 tachycardias were targeted, including 10 CATs and 10 MRATs. The acute success rate for CAT was 100% and 80% for MRAT.

Of those with complexity score III, all the patients had a history of surgery. There were 29 inducible tachycardias: 12 CATs and 15 MRATs. Of the CATs and MRATs, 92% and 87% reached the end point of noninducibilty after the ablation procedure, respectively.

Table 1
Patient baseline characteristics (n = 36)

Characteristic	Value
Age (years)	
Mean ± SD	35 ± 19
Range	2 – 77
Gender	
Male	21
Female	15
Congenital heart disease complexity	
Grade I	4 (11%)
Grade II	15 (42%)
Grade III	17 (47%)
Amiodarone prescription	8 (22%)
Sotalol prescription	14 (39%)
β Blocker prescription	8 (22%)
Digoxin prescription	1 (3%)
Verapamil prescription	3 (8%)
Heart surgery (number of operations)	1.7 ± 0.8

Table 2
Distribution of congenital heart defects, including age at ablation

Main diagnosis (*n* = 36)	Patients (*n*)	Age at Ablation (years)
Aortic valve stenosis	1 (3%)	31 ± 0
Atrial septal defect	4 (11%)	56 ± 9
Sinus venosus defect	2 (6%)	54 ± 18
Atrioventricular septal defect	2 (6%)	14 ± 1
Double outlet right ventricle	1 (3%)	42 ± 0
Ebstein anomaly	6 (17%)	31 ± 18
Patent ductus arteriosus	1 (3%)	77 ± 0
Pulmonary valve stenosis	2 (6%)	28 ± 6
Transposition of the great arteries	10 (28%)	25 ± 13
Tetralogy of Fallot	2 (6%)	59 ± 6
Tricuspid artresia	4 (11%)	24 ± 5
Ventricular septal defect	1 (3%)	42 ± 0

Table 3
Distribution of previous heart surgeries, including age at surgery and ablation

Main Operation (*n* = 29)	Patients (*n*)	Age at Surgery (years)	Age at Ablation (years)
Atrial septal defect closure	3 (10%)	40 ± 27	55 ± 9
Atrioventricular septal defect closure	2 (7%)	3 ± 2	14 ± 1
Fontan procedure	7 (24%)	4 ± 3	23 ± 8
Mustard-Senning procedure	8 (28%)	7 ± 10	29 ± 14
Pulmonary valvulotomy	2 (7%)	1 ± 0	28 ± 7
Tetralogy of Fallot correction	3 (10%)	12 ± 7	53 ± 11
Tricuspid valve surgery	3 (10%)	6 ± 1	42 ± 8
Ventricular septal defect closure	1 (3%)	7 ± 0	42 ± 0

Overall success

Ablation was successful in 31 patients (86%), with an end point of noninducibility. The success rate was 88% (22 of 25) for CAT, 81% (22 of 27) for MRAT, 100% (3 of 3) for circus movement tachycardia using a right-sided accessory pathway, and 100% (3 of 3) for ventricular tachycardia. The circus movement tachycardia with a left-sided accessory pathway could not be terminated by radiofrequency ablation. The overall acute success rate for patients with CHD complexity type I, II, and III was 50%, 88%, and 89%, respectively.

Procedural data

Biatrial mapping was necessary in 15 of the 43 procedures, with a retrograde approach in most cases. A transseptal puncture was needed in 3 patients, and 1 baffle puncture was performed. Crossover to manual cryoablation was necessary in 3 procedures for successful ablation (septal CAT, right posterior accessory pathway, and typical flutter). In 1 patient, crossover to manual cryoablation was tried but did not result in successful ablation. The mean fluoroscopy and procedure time was 40 ± 34 minutes and 216 ± 101 minutes, respectively. The mean number of radiofrequency applications was 42 ± 47, and the mean radiofrequency application duration was 1,217 ± 1,035 seconds.

Complications

No major complications were related to the procedures. Three minor complications were all groin hematomas.

Redo procedures

Redo procedures were performed in 19% of all patients. Of these, 57% were in CHD grade III, 43% in grade II, and 0% in grade I. In 3 of these patients, the initial targeted arrhythmia was induced (1 CAT, 1 MRAT, and 1 typical flutter), and in 4 patients, a different arrhythmia was identified.

Follow-up

Of the 36 patients, 22 (61%) remained free of recurrence during a mean follow-up of 26 ± 14 months (Figure 2). All patients with recurrence presented within the first 6 months after procedure. After redo procedures, 24 patients (67%) did not experience any recurrence.

During follow-up, recurrence occurred mostly in patients with type III CHD complexity (45%): transposition of the great arteries (56%), tricuspid valve atresia (33%), and double outlet of the right ventricle (11%). In type II complexity, 16% had recurrence (P = 0.075): Ebstein anomaly (67%) and sinus venosus defect (33%). After successful ablation, none of the patients with type CHD I experienced a recurrence during the follow-up period (Figure 3).

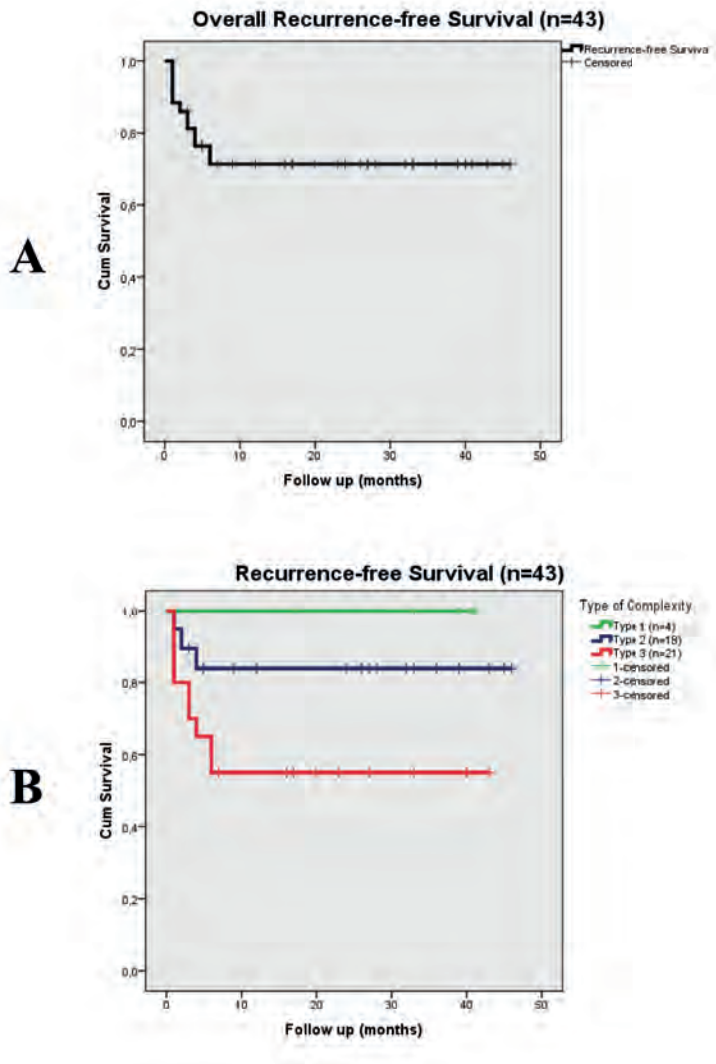

Figure 2: Kaplan-Meier curves demonstrate overall recurrence-free survival (*A*) and recurrence-free survival for each type of CHD complexity (*B*) after catheter ablation, including redo procedures.

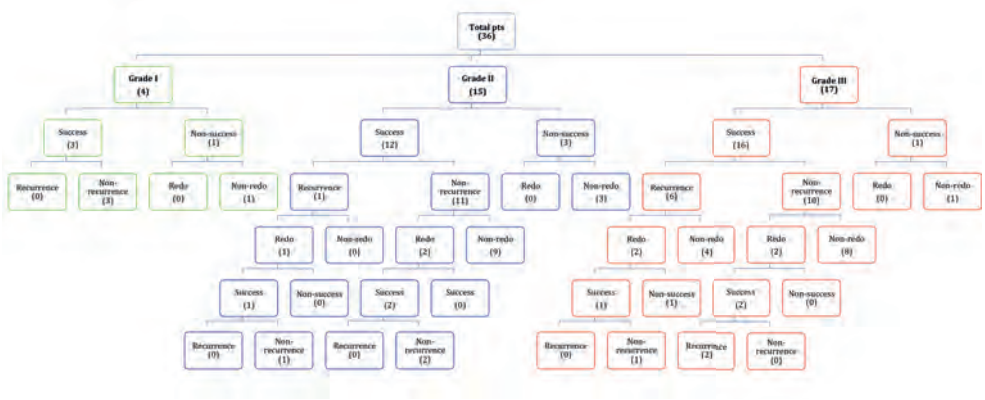

Figure 3: Overview of success, recurrence, and redo procedures for grade I, II, and III CHD complexity.

DISCUSSION

This is one of the first studies assessing the acute and long-term outcomes of catheter ablation using MNS in adult patients with CHD. Our data suggest that MNS is safe and effective and provides reasonable acute success rates and good outcomes during relatively long-term follow-up in this specific group of patients.

Acute and long-term paradox

The present study has shown that in patients with the lowest CHD complexity score, fewer procedures achieved acute success compared to those in the more complex groups. However, during follow-up, it seems that recurrence in complexity group I is lower than that in groups II and III. In the group without previous heart surgery, 1 patient with complexity score I and 1 with complexity score II had a percutaneous implanted atrial septal defect closure device. Owing to the presence of these closure devices, the catheter could not reach the critical part to terminate the tachycardia. This partially explains the lower acute success rate in CHD complexity group I. During follow-up, complexity group III experienced the most recurrences, followed by groups II and I. As our data suggest, most recurrences were related to newly developed arrhythmias. This has also been demonstrated in previous research.[11]

Arrhythmias in CHD and rationale of using MNS

The improvement in surgical techniques for young patients with CHD resulted in significant life prolongation. As these patients reach adulthood, they become high susceptible to late complications associated with the reparative surgery.[12] This includes cardiac arrhythmias originating from either the myocardial substrate owing to the abnormal physiology or the presence of surgical scars.[3] Catheter ablation might be a curative treatment of most ATs in patients with CHD.[13] However, most of the arrhythmias in patients with CHD are different forms of AT: MRATs or CATs, including focal and microreentrant mechanisms.[14,15] This can be attributed to the various substrates present in these patients such as atrial scars formed by surgical sutures and myocardial abnormalities secondary to chronic chamber dilation or increased wall stress.[16,17] Targeting the complex arrhythmias could be very difficult, and different ablation strategies are needed to treat these patients. Frequently, multiple tachycardias can be induced during the electrophysiologic study.[18] Because the anatomy of the heart is different from the normal cardiac anatomy, it can be difficult to localize and reach the origin of the tachycardia. Therefore, a very dense electroanatomic map of the site of interest is essential.[18] However, this could lead to longer ablation procedures and, especially, increased use of fluoroscopy. These challenges need to be considered when choosing the optimal ablation strategy.

The MNS offers several advantages and might overcome these difficulties. Owing to the structural cardiac abnormalities, some regions are difficult to reach, which can result in inadequate lesion formation using a manual ablation catheter.[19] Although multiple catheters with predefined curves has been introduced, no ablation catheter is optimal for treating patients with CHD. The movements of the MNS catheter are not restricted by the curves of the catheter, and the improved navigation capabilities allow enhanced energy delivery.[20] The MNS also provides good catheter stability with constant tissue contact.[7] Because of the flexible and atraumatic catheter design, the risk of perforation is reduced and no pericardial effusion or tamponade has been reported using the MNS.[4,21,22] The pulmonary venous atrium can be reached retrogradely using an arterial approach with less need for transseptal or transbaffle puncture. In patients with CHD and an abnormal anatomy and, often, a history of cardiac surgery, the MNS has specific advantages concerning safety. The MNS decreases

the fluoroscopy time, and this is particularly essential in CHD owing to the number of pediatric patients and the need for redo procedures.

Previous experiences

Several groups have evaluated the usefulness of the MNS system in patients with CHD. Schwagten et al[3] reported the initial MNS experience of our group in 12 patients with CHD and achieved comparable acute success results. Furthermore, no major complications were observed related to the procedures. Wu et al[23] confirmed these findings in their study of MNS mapping of MRATs after the Mustard or Senning procedure. Their results reflected the preciseness and safety of the MNS and a possible reduction in the fluoroscopy time was suggested by the investigators. This hypothesis proved to be valid in the subsequent study by Wu et al,[23] in which a significant reduction of fluoroscopy time was realized during mapping of ATs in postoperative patients with CHD using MNS.[20]

These previous studies evaluated the advantages of MNS in treating patients with CHD; however, the follow-up period was relatively short and the long-term effect of MNS was not assessed. Our study evaluated the efficacy and safety during a long follow-up period. These data support that the acute benefits of MNS were sustained over time and good long-term results can be achieved.

Limitations of the study

In the present study, we did not perform randomization to compare magnetic and manual catheter ablation therapy. We used our prospective registry to evaluate the acute and long-term efficacy and safety of MNS in patients with CHD. The present single-center experience without a comparator has, at best, shown the feasibility of MNS in this specific group of patients. Our data suggest promising results, but randomized trials are needed to prove superiority. A very limited number of patients were included in CHD group I. In this group, more patients are necessary to reveal the true value of MNS compared to the other CHD groups. Therefore, larger, randomized registries are needed for all new catheter ablation methods and devices.

CONCLUSION

This report reflects the advantages of MNS for catheter ablation in complex anatomy without compromising outcome data. It demonstrated to be safe without occurrence of major complications. MNS is a feasible method to treat complex arrhythmias in CHD patients with high success rates that sustains well on the long term.

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CHAPTER 11

The presence of extensive atrial scars hinders the differential diagnosis of focal or macroreentrant atrial tachycardias in patients with complex congenital heart disease

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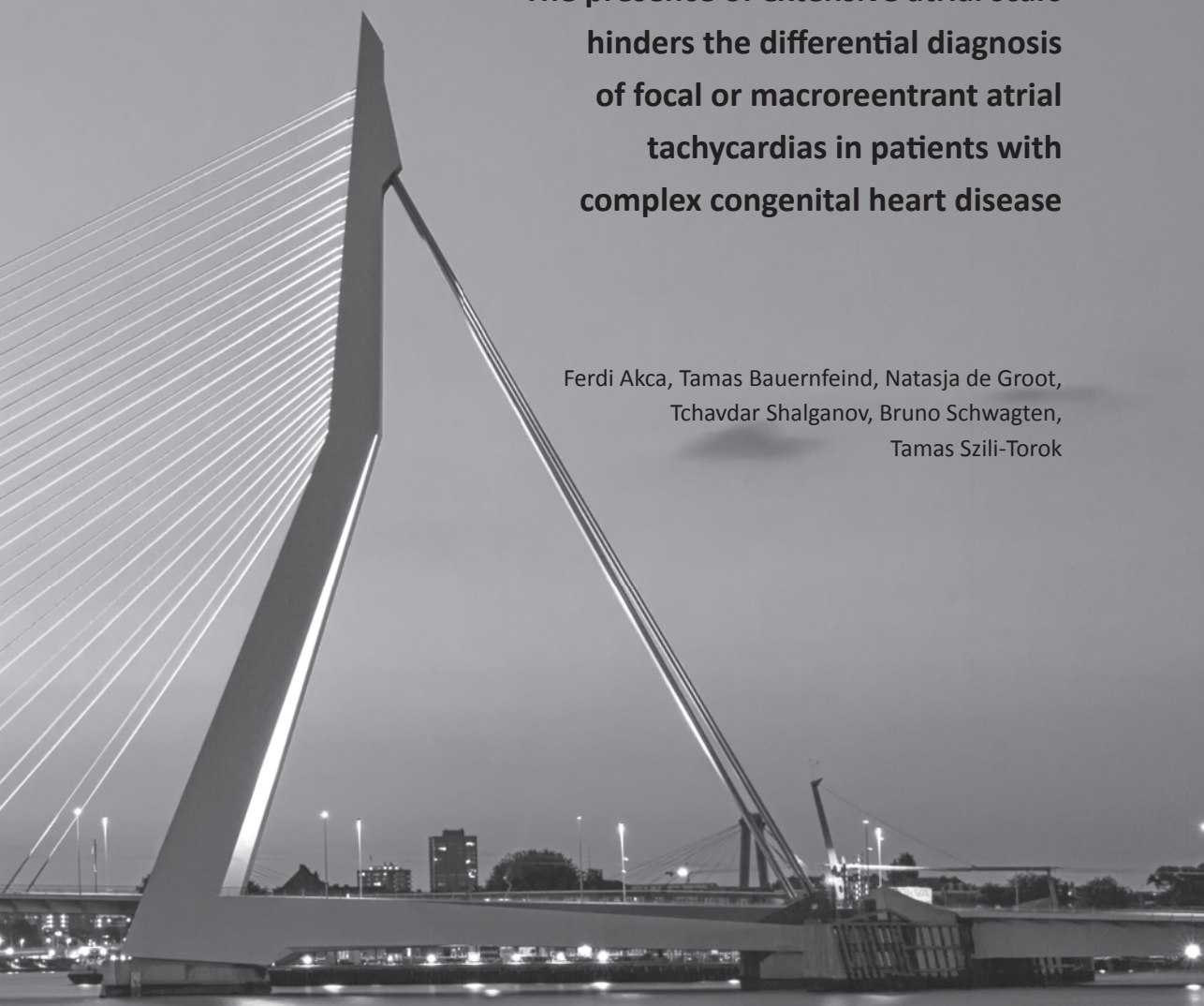

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ABSTRACT

Aims

Atrial tachycardias (ATs) frequently develop in patients with congenital heart defects (CHDs). This study aimed to evaluate the effects of extensive atrial scar formation on the total atrial activation time (TAAT) and its relation to the tachycardia cycle length (CL) to classify AT.

Methods and Results

Seventy-one patients were included and divided into two groups: patients without CHD (Group I, 35 patients) and with CHD (Group II, 36 patients). All patients underwent CARTO electroanatomical activation mapping. Two subgroups were created: centrifugal (CAT) or macroreentrant AT (MRAT). Total atrial activation time, CL, and mean bipolar signal amplitude (BiSA) were analyzed. In Group I, 18 patients (51.4%) had CAT and 17 (48.6%) MRAT. The mean BiSA for Group I was 1.30 ± 0.32 mV. Total atrial activation time/CL ratios were different between CAT and MRAT (28.4 ± 16.9 vs. 66.6 ± 14.3%, $P < 0.001$). In Group II, 18 patients (50%) had CAT and 18 patients (50%) MRAT. The mean BiSA was 0.94 ± 0.50 mV and was not different for CAT and MRAT subgroups (1.04 ± 0.64 vs. 0.85 ± 0.29, $P = 0.243$). Total atrial activation time/CL ratios were comparable between CAT and MRAT patients (69.0 ± 40.4 vs. 83.6 ± 8.3%, $P = 0.243$). A significant lower BiSA was found for CAT with TAAT/CL ratios above 40% (0.62 ± 0.11 vs. 1.90 ± 0.18 mV, $P < 0.001$). A strong negative correlation was identified between the BiSA and the TAAT/CL ratio in patients with CAT in Group II (– 0.742; $P < 0.001$).

Conclusion

Low mean BiSA values in CHD patients are associated with altered impulse propagation, making TAAT- and CL-based diagnostic tools inaccurate. Further diagnostic tests are needed to determine the correct mechanism of ATs.

INTRODUCTION

To establish the effective ablation strategy for atrial tachycardias (ATs), the identification of the underlying mechanism is crucial. The surface electrocardiogram (ECG) of the tachycardia does not always provide good accuracy in predicting the site of origin and the mechanism, and can even be misleading.[1,2] Several diagnostic approaches were developed to differentiate the origin and mechanism of atrial arrhythmias.[3–5] The total atrial activation time (TAAT) and its relation to the tachycardia cycle length (CL) plays an important role in the differential diagnosis of the underlying mechanism.[3,6] In case of a centrifugal AT (CAT) with a radial spread of the impulse across the atria, the TAAT is comparably low and results in a low TAAT/CL ratio. However, a high TAAT/CL ratio is very suggestive for a macroreentrant AT (MRAT), since the TAAT lasts nearly the entire time of the CL. A TAAT/CL ratio below 40% implies a centrifugal mechanism, whereas a ratio above 40% is indicative for MRAT.[3] In patients with structural normal hearts, these distinctive and simple parameters allow to differentiate between focal and macroreentrant mechanisms.[3,6,7]

However, arrhythmias associated with congenital heart defects (CHDs) present major diagnostic and therapeutic challenges for the treating physicians.[4,8–11] In these patients, arrhythmias may be related to suture lines, surgical scars, or myocardial abnormalities secondary to chronic chamber dilatation or increased wall stress.[8,9,12,13] These conditions significantly influence wave front propagation in atrial tissue. Theoretically, the more extensive the atrial scars, the more they influence wave front propagation. The extension of low-voltage regions (indicating damaged myocardial tissue with altered conductive properties) in the atrial wall can be assessed by electroanatomical mapping, represented by low bipolar signal amplitude (BiSA) values.[10,14,15] Theoretically, extensive atrial scars and low BiSA could lead to difficulties in the differential diagnosis and thwarts identification of the underlying mechanism of the arrhythmia using the TAAT/CL ratio. Therefore, the TAAT/CL ratio might be an unreliable parameter to guide AT ablation procedures for CHD patients and could be one of the contributing factors for the lower efficacy of AT catheter ablation.

The primary aim of our study was to assess the effect of extensive atrial scar on atrial electrophysiological characteristics, and to investigate possible pitfalls of the conventional

differential diagnosis of AT in CHD patients. Our hypothesis was that due to the extensive scarring the atrial conductive properties are changed in such a way that current cut-off values for the TAAT/CL ratio are inaccurate to differentiate between CAT and MRAT in CHD patients.

METHODS

Patients

Seventy-one patients were included into this retrospective study. Patients were divided into two groups: 35 patients without CHD were included in Group I (age 44.2 ± 17.7 years, 15 male) and 36 patients with CHD in Group II (age 36.3 ± 16.2 years, 19 male). Patient demographics and type of surgical correction for Group II patients are presented in Table 1.

Electrophysiology studies

Written informed consent was obtained from all patients prior to electrophysiology study (EPS). Resting 12-lead ECG, laboratory test, a chest X-ray, and a two-dimensional echocardiography were acquired from all patients within 1 month before and within 48 h following the procedure. The mean left atrial dimension from CHD patients was 49.5 ± 12.5 mm. A transoesophageal echocardiogram was performed if considered necessary. The procedures were performed during a fasting state, using local or general anaesthesia. In general, patients were instructed to stop taking antiarrhythmic drugs for a period of at least four half-lives prior to undergoing the procedure. Exceptions were made for amiodarone use or patients with ongoing tachycardias even under antiarrhythmic drugs.

Mapping

Market-approved diagnostic and ablation catheters were used as clinically required at the discretion of the investigator and the availability of the catheters. The left heart, if needed, was accessed via transseptal puncture guided by intracardiac echocardiography or by retrograde aortic approach. All patients underwent CARTO (Biosense Webster) electroanatomical activation mapping during the tachycardia and eventual ablation.

Whenever needed, both atria were mapped before ablation. Twenty-six patients in Group I (74.3%) and 29 patients in Group II (80.6%) (P = ns) were mapped and ablated using the Stereotaxis Niobe II RMT system (Stereotaxis Inc.). Since the aim of this study was to evaluate the effect of extensive atrial scar in CHD patients on electrophysiological characteristics, patients after successful ablation were included into the study. On this basis the successful ablation justified the proposed mechanism and a correct diagnosis of the underlying mechanism was made based on accurate tachycardia mapping. Both procedural and fluoroscopy times were recorded as well.

Atrial tachycardias were defined as tachycardias not involving extra-atrial tissue and were independent of the atrioventricular (AV) conduction. Therefore, AV nodal reentrant and AV reentrant tachycardias were not included. During EPS, ATs were classified as CAT, including focal and microreentrant mechanisms, or MRAT. These classifications were made using atrial activation maps acquired by electroanatomical mapping. For CAT, the activation started in a single small area and showed clearly an area of earliest endocardial activation with radial spread. A microreentrant mechanism was diagnosed based on entrainability combined with a centrifugal activation pattern. During MRATs activation was recorded in multiple time points throughout the cardiac cycle and electroanatomical mapping showed circus movement of the activation front. For both CAT and MRAT, the endpoints of procedural success were defined as termination of the tachycardia and non-inducibility using programmed atrial stimulation up to three extrasystoles. Despite different underlying mechanisms, both focal and microreentrant ATs were classified as CAT since the ablation strategy (except for entrainment) and the effect on TAAT time are identical.

The following electrophysiological parameters were measured and analyzed: TAAT, CL, and mean BiSA. Deliberate care was taken by performing electroanatomical mapping: each map consisted of at least 60 points well dispersed on the walls of the mapped heart chamber. Total atrial activation time was defined as the time interval between the first and the last atrial activation signal. The BiSA values were extracted from the CARTO bipolar voltage maps and a mean BiSA value was calculated for each patient. In both groups, patients were divided into two subgroups based on the mechanism of the diagnosed arrhythmia: CAT and MRAT subgroups.

Power calculation

According to previous results, we assumed that the TAAT/CL ratio for CAT in non-CHD patients would be 20%.[3] We hypothesized that in CHD patients the ratio would be at least 40%. A power analysis revealed that a minimum of five patients per group were required to assure at least 90% power for detecting the anticipated between-group differences in TAAT/CL ratio for the diagnosis of CAT.

Statistics

Normality of distribution was determined by using the Kolmogorov– Smirnov test. Continuous variables were expressed as mean ± SD, if normally distributed, and compared with the two-tailed Student's *t*-test for independent samples assuming unequal variances. In case of non-normal distribution of data, medians and interquartile ranges (IQRs) were reported. Categorical data were expressed as percentages and compared with the X^2 test or Fisher's exact test when appropriate. Pearson's bivariate correlation analysis was used to identify possible correlations between BiSA scores and TAAT/CL ratios. Statistical analysis was performed using SPSS 15.0 (SPSS Inc.). Statistical significance was defined as $P < 0.05$ (two-tailed).

RESULTS

Patient data

The two groups were matched for sex and age. The baseline characteristics of the patients are presented in Table 1. Type of CHD and reconstructive surgery of Group II patients are shown as well (Table 1).

Ablation data and electrophysiological parameters

The distribution of CAT and MRAT was equal for both groups (Table 1). In Group II, procedures were longer (198 ± 51 vs. 118 ± 32min, $P < 0.001$) and more fluoroscopy (47 ± 13 vs. 23 ± 10min, $P < 0.001$) was used. Furthermore, total ablation time was longer in Group II as well (2074 ± 1470 vs. 1387 ± 652 s, $P < 0.001$). In Table 2, procedural parameters of Groups I and II are displayed for both CAT and MRAT patients. For Group I patients, the TAAT/CL ratio was significantly lower for CAT patients (28.4 ± 16.9%) compared with MRAT

patients (66.6 ± 14.3%, P < 0.001). In Group II, this difference could not be demonstrated and TAAT/CL ratios were comparable for both CAT and MRAT patients (69.0 ± 40.4 vs. 83.6 ± 8.3%, P = 0.243).

Table 1
Demographic data

	Group I (no CHD)	Group II (CHD)	*P* value
Number of patients (*n*)	35	36	
Sex (male)	15 (42.9%)	19 (52.8%)	0.275
CAT (*n*)	18 (51.4%)	18 (50.0%)	0.547
MRAT (*n*)	17 (48.6%)	18 (50.0%)	0.547
Age at ablation (years)	44.2 ± 17.7	36.3 ± 16.2	0.054
Age at CHD correction (years)		2.0 (IQR [1.0 – 8.5])	
Fontan procedure (*n*)		9 (25.0%)	
Mustard-Senning procedure (*n*)		7 (19.4%)	
Ductus Botalli closure (*n*)		3 (8.3%)	
Tricuspid valve replacement (*n*)		5 (13.9%)	
Blalock-Hanlon procedure (*n*)		3 (8.3%)	
ASD closure (*n*)		8 (22.2%)	
Jatene-procedure (*n*)		1 (2.8%)	

ASD, atrial septal defect; CAT, centrifugal atrial tachycardia; CHD, congenital heart defect; MRAT, macroreentrant atrial tachycardia.

Table 2
Procedural parameters

	Group I (no CHD)			Group II (CHD)		
	CAT	MRAT	*P* value	CAT	MRAT	*P* value
Number of patients (*n*)	18 (51.4%)	17 (48.6%)		18 (50%)	18 (50%)	
Mean BiSA (mV)	1.30 ± 0.32			0.94 ± 0.50		0.001
Mean BiSA (mV)	1.28 ± 0.38	1.31 ± 0.25	0.790	1.04 ± 0.64	0.85 ± 0.29	0.243
TAAT (ms)	106 ± 57	184 ± 67	<0.001	252 ± 148	215 ± 37	0.556
CL (ms)	400 ± 119	270 ± 51	<0.001	370 ± 83	304 ± 70	0.015
TAAT/CL ratio (%)	28.4 ± 16.9	66.6 ± 14.3	<0.001	69.0 ± 40.4	83.6 ± 8.3	0.243

BiSA, bipolar signal amplitude; CAT, centrifugal atrial tachycardia; CHD, congenital heart defect; CL, cycle length; MRAT, macroreentrant atrial tachycardia; TAAT, total atrial activation time.

Association between mean bipolar signal amplitude and total atrial activation time/cycle length

Significant negative correlation between BISA and TAAT/CL ratio were found for the overall population (r^2 = – 0.608, P < 0.001) and for CAT patients (overall: r^2 = – 0.688, P < 0.001; Group I: r^2 = – 0.546, P = 0.019; Group II: r^2 = – 0.742, P < 0.001) (Figure 1). Contrarily, no correlation was found in the MRAT patients (Group I: r^2 = 0.094, P = 0.719; Group II: r^2 = – 0.450, P = 0.061).

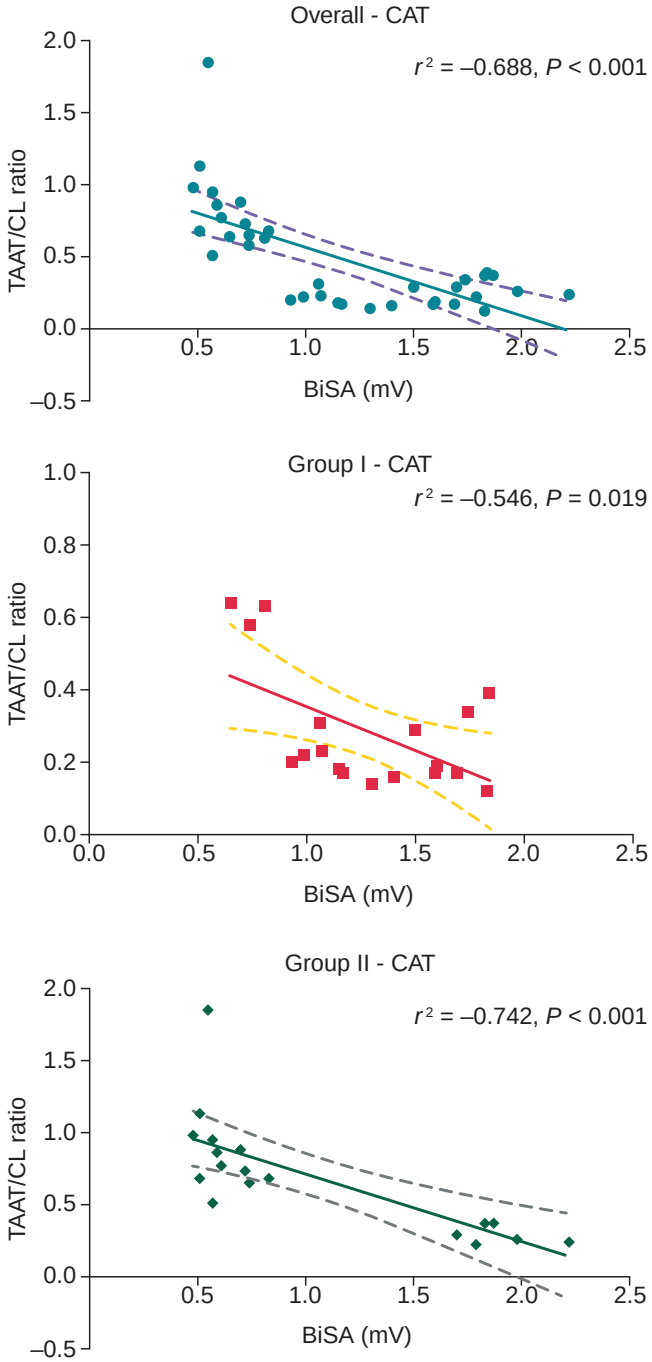

Figure 1: Distribution of CAT and MRAT in Group I and II. The relationship between the TAAT/CL ratio and mean BiSA value for CAT patients from the overall group, Group I and Group II. The linear regression line (continuous) with a 95% confidence band (dotted) is presented.

When evaluating the diagnostic performance of the TAAT/CL ratio using the current standard cutoff (40%), we found that 67% of the CAT patients had TAAT/CL > 40% and would be diagnosed as MRAT. Patients with CAT and TAAT/CL ratio > 40% showed a significant lower mean BiSA as compared to those with TAAT/CL < 40% (0.62 ± 0.11 vs. 1.90 ± 0.18 mV, P < 0.001) (Table 3). A cut-off value for mean BiSA was established using a confidence interval of 99% (mean ± 2.5 SD) in Group II CAT patients to predict TAAT/CL ratios below 40%: 0.62 + 0.28 = 0.90 mV (Figure 2).

Furthermore, significant difference was observed between CHD patients based on their complexity of heart surgery: patients with Fontan-, Mustard–Senning-, and Blalock–Hanlon procedures had lower BiSA values compared with patients after tricuspid valve replacement, atrial septal defect (ASD) closure, and Jatene procedure (0.62 ± 0.11 vs. 1.89 ± 0.18 mV, P < 0.001).

Table 3
CAT patients in Group II (CHD) (*n* = 18)

	TAAT/CL < 40%	**TAAT/CL > 40%**	***P* value**
Number of patients (*n*)	6 (33.3%)	12 (66.7%)	
TAAT (ms)	110 ± 25	287 ± 119	0.002
CL (ms)	383 ± 73	328 ± 83	0.145
TAAT/CL ratio (%)	29.2 ± 6.5	85.7 ± 22.4	<0.001
Mean BiSA (mV)	1.90 ± 0.18	0.62 ± 0.11	<0.001

BiSA, bipolar signal amplitude; CAT, centrifugal atrial tachycardia; CHD, congenital heart defect; CL, cycle length; TAAT, total atrial activation time.

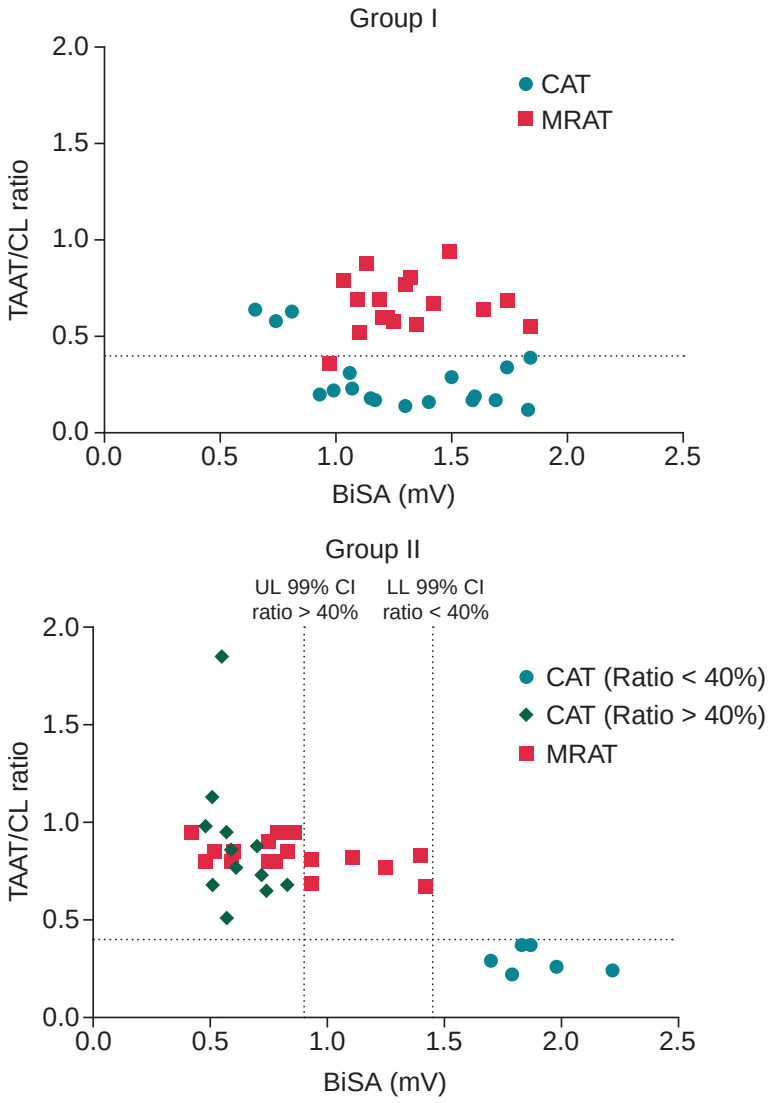

Figure 2: Distribution of CAT and MRAT in Group II. The relationship between the TAAT/CL ratio and mean BiSA value for CAT and MRAT patients is presented. The dotted horizontal line represents the theoretical cut-off value for the TAAT/CL ratio (40%) to distinguish CAT from MRAT. For all CATs in Group II with a lower mean BiSA than the upper limit of the 99% confidence interval (CI, 0.90 mV), the TAAT/CL ratio was > 40%.

DISCUSSION

Diagnosis and catheter ablation of ATs emerging in patients with CHD is a major challenge for the electrophysiologist.[7,12,14] The major finding of this study is the explanation of how the extent of atrial conduction disturbances in CHD patients influences conventional diagnostic parameters like TAAT, CL, and TAAT/CL ratio causing differential diagnostic challenges. Our study clearly demonstrates that mean BiSA values should be integrated into the diagnostics, whereas low mean BiSA values represent extensive scars, resulting in the significant alteration of impulse propagation. A strong negative correlation was found between mean BiSA and TAAT/CL ratio for CAT patients. Therefore, in case of low mean BiSA values, the TAAT/CL ratio provides inaccurate information to correctly distinguish CAT from MRAT. For these CHD patients additional diagnostic tools (e.g. very extensive electroanatomical mapping) are required to determine the correct underlying mechanism of the arrhythmia.

Mechanisms of atrial tachycardias

Concerning wave front propagation ATs belong either to the centrifugal origin tachycardias (including microreentrant and focal mechanisms) or to macroreentrant circuit-based ATs.[16] In the case of CAT, the focal impulse spread centrifugally to all directions in the myocardium, reaching every part of the wall in the shortest possible time. In these patients, electroanatomical mapping clearly showed an area of earliest endocardial activation with radial spread.[3,16] On the contrary, macroreentrant tachycardias have a defined circuit with a slow conducting area, activating the atrial wall parallel to the activation of the whole circuit.[3,5]

Algorithms for identification of tachycardia mechanisms

Although non-fluoroscopic imaging and electroanatomical mapping underwent major development in the last decade, and new navigational methods became invented and implemented; the differential diagnosis of atrial arrhythmias still needs careful evaluation, as correct definition of the underlying mechanism is an indispensable element of successful ablative treatment.[17,18] The adequate ablation strategy for CAT and MRAT has distinct differences: ablation of the earliest activation point for CAT, while creating a line between two non-conduction zones, crossing the activation circuit for the ablation of MRAT.

Parameters like TAAT, CL, TAAT/CL ratio are very useful and uncomplicated tools to differentiate between focal and macroreentrant mechanisms.[3,6,7] In case of CAT, the TAAT is comparably low because of the radial spread of the impulse, resulting in a low TAAT/CL ratio. However, in case of a MRAT, the TAAT takes almost the whole time of the CL, resulting in a high TAAT/CL ratio. According to the literature, a TAAT/CL ratio below 40% strongly suggests a focal activation pattern, a ratio above 40% macroreentrant tachycardia.[3] In our set of patients, the same correlation could be confirmed with marked significance for patients without CHD.

Patients with congenital heart defect

The improvement of surgical techniques resulted in significant life prolongation of many young patients with CHD. However, as these patients reach adulthood, their risk for late complications associated with surgery is also increased, including the high incidence of cardiac arrhythmias that arise from either the myocardial substrate created by abnormal physiology or the presence of surgical scars.[17] These arrhythmias contribute considerably to the morbidity of this special group of patients.[11] Catheter ablation may be a curative treatment for most ATs in patients with CHD, however, identification of the proper underlying mechanism is a major challenge.[12,15]

Total atrial activation time/cycle length ratio in patients with congenital heart defect

The treatment of patients with CHD usually involves heart surgery with varying complexity. Atrial scar formation depends on the type of CHD, the performed surgical method, and the progression of the disease on the long-term. As the presence of atrial scar influences the wave front propagation, the applicability of the TAAT/CL ratio becomes questionable. Although the activation may spread virtually in all directions in the atrial wall in case of focal impulse formation, the scars hinder or block the activation pathways, leading to lengthening of the TAAT without significantly affecting the CL itself.[10] However, in case of the macroreentrant mechanism, both the CL and the TAAT are affected by the scar burden; furthermore, the ratio of TAAT/CL has a comparably high value without any scar as well. As our study demonstrates, 66.7% of the CHD patients with CAT had a TAAT/ CL ratio >40%, who would otherwise be classified as MRAT. These conditions in patients with CHD lead to possible failure of the TAAT/CL ratio to differentiate between CAT and MRAT in CHD patients.

The importance of bipolar signal amplitudes

Complexity of CHDs and their surgical corrections also have great variations, ranging from relatively simple ASD closures to Senning or Mustard operations. Several reports concerning evaluation of atrial scars on electroanatomical maps, represented by mean BiSA values are usually below 0.1 – 0.2 mV.[14]

In this study, we assessed the mean BiSA values to represent the extension of atrial scars, which was indeed lower in the group with CHD than the group without CHD. Furthermore, patients with complex CHD and extensive surgical treatment (Fontan-, Mustard – Senning-, and Blalock–Hanlon procedures) had lower mean BiSA than patients with less serious CHD and less extensive reconstructive surgery (tricuspid valve replacement, ASD closure, and Jatene procedure).

Correlation of mean bipolar signal amplitude and total atrial activation time/cycle length ratio

We emphasized that the feasibility of the TAAT/CL ratio depends on the extension of atrial scars. This hypothesis was supported by our data, whereas a strong negative correlation was revealed between the TAAT/CL ratios and the BiSA values in CAT patients with CHD. Based on this observation, we compared the TAAT/CL ratios and BiSA values in the CAT patients of Group II by dividing them based on the TAAT/CL ratio of 40%. We found that the feasibility of these diagnostic parameters are related to the mean BiSA values, since a 99% confidence interval of a correct diagnosis can be established if the mean BiSA value is above 0.90 mV.

Limitations

In this study, the mean BiSA was determined as a parameter for the healthiness of the atrial myocardium and represents the extension of atrial scars. However, in a patient with a relatively small area of dense atrial scar (e.g. < 0.1 mV), the mean BiSA could be similar compared with a patient with a large area of mild scarring (e.g. < 1.5 mV). In the patients included in this study, with complex CHD after corrective surgery, the amount of scarring would be generally high and extends across large areas of the atrium. We observed that CHD patients after complex reparative surgery had lower mean BiSA values compared with less invasive surgery, suggesting a more diffuse area of atrial scarring. However, the total area of

scar would provide contributing information to understand the effect of scarring on atrial conduction, TAAT, and tachycardia CL. Therefore, further studies on total atrial scarring and conduction disturbances in CHD patients are required. Preferably, this could be performed using magnetic resonance imaging to measure atrial scar burden.

CONCLUSION

In conclusion, low mean BiSA values in CHD patients are associated with altered impulse propagation, making TAAT- and CL-based diagnostic tools inaccurate. To allow correct differentiation between CAT and MRAT in CHD patients, a mean BiSA of at least 0.90 mV is required. In case of low mean BiSA values, further diagnostic tests are needed to determine the correct mechanism of the atrial tachycardia.

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PART II

CONTACT FORCE SENSING

CHAPTER 12

A prospective study on safety of catheter ablation procedures: contact force guided ablation could reduce the risk of cardiac perforation

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ABSTRACT

Background

Contact force (CF) sensing catheters provide advantages with regard to safety and efficacy. This study aimed to evaluate if CF catheters reduce cardiac perforations and other major complications and offer equal safety compared to the magnetic navigation system (MNS).

Methods

Data from 1.517 ablation procedures from our prospective registry was analyzed. Ablations were performed using either CF guided catheters (CF group, n = 248), non-CF catheters (NCF group, n = 813), or MNS (n = 456). Four subgroups were analyzed: atrial fibrillation (AF, n = 557), supraventricular tachycardia (SVT, n = 715), ventricular tachycardia (VT, n = 190) and patients with congenital heart defects (CHD, n = 55). The primary endpoint of this study was incidence of cardiac perforation. Secondary endpoints were major and minor complications within 30 days of the procedure.

Results

Complications occurred in 11.3% (n = 172) of the procedures. In 2.8% (n = 43) a major complication occurred, 0.9% (n = 13) had a perforation, 8.5% (n = 129) had a minor complication and 2 patients died (0.1%). No cardiac perforation occurred in the CF group, which was significantly different from NCF procedures (0.0% vs. 1.6%; relative risk 0.76, 95% CI 0.74–0.79, P = 0.031) and equal to MNS (0.0%). This was also observed in the AF subgroup (0.0% vs. 3.3%; RR 0.67, 95% CI 0.63–0.72, P = 0.021), and the occurrence of major complications was lower for CF versus NCF procedures (2.1% vs. 7.8%, P = 0.010).

Conclusions

CF-guided catheter ablation is superior to NCF with regard to procedural safety and avoidance of cardiac perforation. This difference is due to a reduction of cardiac perforation and major complications in the AF subgroup.

INTRODUCTION

Several reports have been published concerning the safety of conventional catheter ablation procedures.[1-6] In experienced academic centers major complication rates vary between 1% and 6%, depending on the type of procedure. With an increasing eligible population suffering from arrhythmias, the safety of procedures is crucial to determine which patients should be considered for ablation. Most procedures are performed electively for patients suffering from a non-life-threatening condition. To make the ablation procedure worthwhile the risk of a major complication should be as low as possible. Since the reported complication rates are certainly not negligible new developments are necessary to further minimize complications.

In 2002, the magnetic navigation system (MNS) was introduced and developed to perform remote-controlled ablation procedures.[7] The use of this system has been well investigated and has been proven to enhance procedural safety.[8-11] Due to the specific catheter design no catheter-related cardiac perforations have been reported and MNS is ahead with regard to procedural safety. However, the use of MNS is associated with longer procedure times and higher procedural expense.[11,12] Since the cath lab needs to be rebuilt, not all EP centers are able to use the MNS system. Therefore, there is a demand for a system that provides the same level of safety as MNS with a more efficient workflow and lower costs.

Recently, contact force (CF) sensing catheters are available for use during catheter ablation procedures. Several advantages of this catheter are described and focus mainly on lesion size, procedural efficacy and benefits during electrophysiology (EP) study.[13-17] When assessing the advantages, CF catheters could become the standard for ablation procedures. However, no prospective high-volume study has been performed on the safety of CF catheters. The aim of this study was to evaluate if CF catheters could reduce cardiac perforations and other major complications during ablation procedures and offer equal safety compared to MNS. Our hypothesis was that procedures using CF catheters improve safety and offer comparable major complication rates as MNS and lower complications than conventional ablation procedures.

METHODS

Patient Groups

In this prospective safety registry, patients who underwent catheter ablation at our center were included from January 2008 until November 2013. Data from 1.517 ablation procedures was analyzed. Ablations were performed using either CF guided catheters (CF group, n = 248), non-CF catheters (NCF group, n = 813), or MNS (n = 456). Patients were classified into four subgroups: atrial fibrillation (AF, n = 557), supraventricular tachycardia (SVT, n = 715), ventricular tachycardia (VT, n = 190) and patients with congenital heart defects (CHD, n = 55). In the SVT subgroup patients were included with atrial flutter (AFl, n = 217), atrial tachycardia (AT, n = 82), atrioventricular nodal reentrant tachycardia (AVNRT, n = 186), atrioventricular reentrant tachycardia (AVRT, n = 189), and atrioventricular nodal ablation (AVN, n = 41). Patient demographics and distribution of arrhythmias are presented in Table 1. The procedures were performed by a group of senior electrophysiologists with the assistance of an EP fellow who had been trained to perform both manual and magnetically guided ablation. Written informed consent for the ablation procedure was obtained from all patients. The study was approved by the institutional review board and ethical committee.

Outcomes

The primary endpoint of this study was incidence of cardiac perforation. Secondary endpoints were classified as major and minor complications and duration of hospital stay. Major complications included: in-hospital death, major bleeding requiring surgical intervention, arteriovenous (AV) fistula requiring vascular surgery, device lead dislodgement, severe hemoptysis, phrenic nerve lesion, thrombo-embolic event, and permanent AV block. Minor complications included: hemodynamically stable pericardial effusion, inguinal/subclavian hematoma, temporary AV block, bundle branch block, and temporary ST elevation. Procedure-related complications that occurred during 30 days of follow-up were also included in the analysis.

Complications were registered directly after the ablation procedure, before discharge and during follow-up. All data from this safety registry was stored electronically. After all

ablation procedures a written report was composed including all acute complications. Before discharge a mandatory written checklist was filled in, in which complications were registered. Patients were provided with our contact information and were instructed to contact our department in case of a complication. Furthermore, all rehospitalizations within 30 days were analyzed.

The following procedural parameters were retrospectively analyzed and compared between the patient groups: procedural approach (antegrade, transseptal, retrograde), VT localization, VT etiology, number of radiofrequency (RF) applications, RF application time, fluoroscopy time, procedure time, average CF, minimum CF and maximum CF, and total and average force-time integral (function of CF and application time). Patients who underwent ablation using cryo-energy (n = 424) were included in the study, however procedural parameters were excluded from analyses since these could not be compared directly to parameters from RF procedures (e.g. RF application number and duration).

Ablation procedures

For the CF group three types of CF catheters were used: Tacticath (n = 92; Endosense SA, Geneva, Switzerland), Tacticath Quartz (n = 97), and Thermocool Smarttouch (n = 59; Biosense Webster, CA, USA). MNS procedures were performed using the Stereotaxis Niobe II (Stereotaxis, Inc., St Louis, MO, USA) implemented in an EP lab equipped with a Siemens Axiom Artis (Siemens, Erlangen, Germany) fluoroscopy system. Detailed descriptions of the CF and MNS systems have been reported before.[7,18] Ablations for SVT in the CF group were performed in non-irrigated ablation mode and the catheter was used for CF guidance during mapping and ablation. Preceding RF application the saline irrigation flow rate was set at 1 ml/min, resulting in non-irrigated applications. The ablation catheters were used as clinically required at the discretion of the operator. The left heart could be accessed via the retrograde aortic route (n = 199) or transseptal puncture (TSP, n = 615) based on the operator's preference. Intracardiac echocardiography (ICE) was used to guide TSPs. Epicardial ablation was necessary in 19 patients (1.3%).

If preferred by the operator, crossover to another ablation catheter was possible from CF to NCF group (n = 1, 0.1%) or MNS to NCF group (n = 4, 0.3%). Patients were classified to the

group according to the catheter that was crossed over to during the procedure. It was not possible to switch from NCF or MNS catheters to a CF catheter, since CF catheters were not yet available at the time these patients were enrolled. Crossover from either NCF or CF to MNS could not occur since NCF procedures were performed in an operation room which was not equipped with the MNS system.

Statistics

Previously published data demonstrated that cardiac perforation occurs in up to 2.5% of all conventional catheter ablation procedures.[3,5,6] This study aimed to evaluate whether CF procedures could reduce the risk of cardiac perforation and equal MNS procedures with a statistical power of 80% and a bilateral type I error of 0.1. It was estimated that at least 242 patients per treatment group were required to reach the primary endpoint of the study.

Normality of distribution was determined by using the Kolmogorov Smirnov test. Continuous variables were expressed as mean ± SD, if normally distributed, and compared with the two-tailed Student's T-test for independent samples assuming unequal variances. In the case of non-normal distribution of data, medians and interquartile ranges (IQRs) were reported and the Mann-Whitney U test was used for data comparison. Categorical data was expressed in percentages and compared with the chi-square test or Fisher's exact test when appropriate (univariate analysis) and logistic regression (multivariate analysis). All potential risk factors for the occurrence of major complications (univariate analysis, $P < 0.1$) underwent multivariate analysis using a logistic regression model to determine independent risk factors. To decrease the potential confounding effect of the learning effect, the cohort was divided into quartiles according to the procedural date to adjust for experience over time and entered into the logistic regression model as well. Statistical analysis was performed using SPSS 15.0 (SPSS Inc.). Statistical significance was defined as $P < 0.05$ (two-tailed).

RESULTS

From the total 1.517 ablation procedures complications occurred in 11.3% (n = 172). In 2.8% (n = 43) a major complication occurred, 0.9% (n = 13) had a perforation, 8.5% (n = 129) had a

minor complication and 2 patients died (0.1%) (Table 1). Twenty-four patients were rehospitalized within 30 days due to a complication (1.6% of all procedures) and were mostly due to vascular complications (58.3%; 10 inguinal hematomas, 2 AV fistulas, 2 major bleedings). No cardiac perforation was observed in the CF group, which was significantly lower compared to the NCF group where thirteen patients had an event (0.0% vs. 1.6%; relative risk 0.76, 95% CI 0.74 – 0.79, p = 0.031). In the MNS group no cardiac perforation was observed as well. The distribution of major and minor complications between the subgroups is presented in Figure 1 and 2.

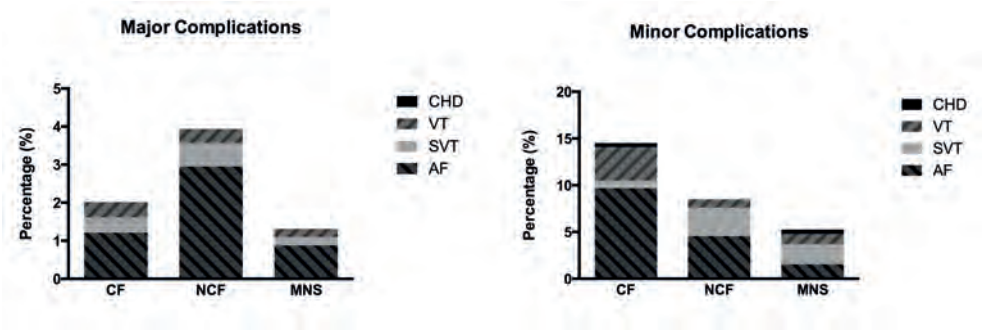

Figure 1: Presentation of major and minor complications – Presentation of major and minor complications for the CF, NCF and MNS groups. The amount of complications for the subgroups is illustrated. AF, atrial fibrillation; CHD, congenital heart defect; SVT, supraventricular tachycardia; VT, ventricular tachycardia.

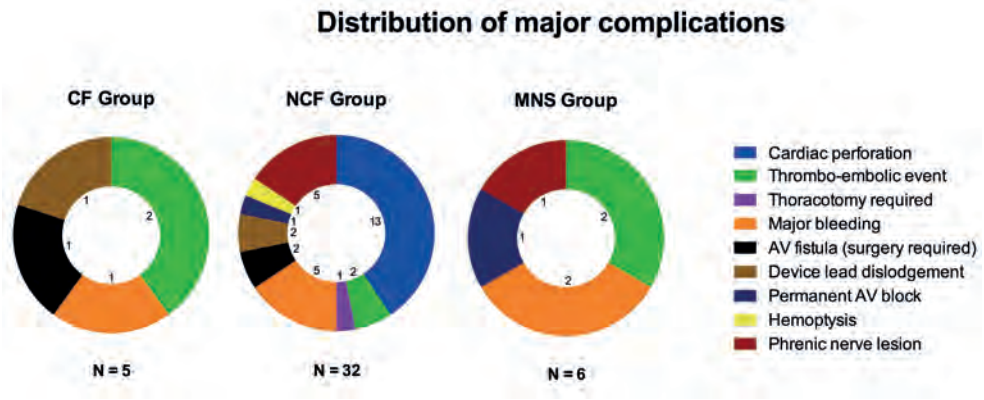

Figure 2: Distribution of major complications – Distribution of major complications for the CF, NCF and MNS groups separately. The frequency of each complication is illustrated in the presented circle.

Table 1 - Categorical variables: patient demographics, procedural parameters and complications. The NCF and MNS groups are both compared to the CF group. Data are presented as percentage.

	Overall		CF		NCF		*P* value	MNS		*P* value
	n =	%	*n* =	%	*n* =	%		*n* =	%	
Number of patients	1517		248		813			456		
Gender (male)	931	61.4	146	58.9	508	62.5	0.171	277	60.7	0.342
Pediatrics	105	6.9	9	3.6	45	5.5	0.151	51	11.2	< 0.001
AF	557	36.7	143	57.7	306	37.6	< 0.001	108	23.7	< 0.001
SVT	715	47.1	57	23.0	430	52.9	< 0.001	228	50.0	< 0.001
AFl	217	14.3	19	7.7	138	17.0	< 0.001	60	13.2	0.017
AT	82	5.4	19	7.7	17	2.1	< 0.001	46	10.1	0.178
AVNRT	186	12.3	5	2.0	148	18.2	< 0.001	33	7.2	0.002
AVRT	189	12.5	11	4.4	98	12.1	< 0.001	80	17.5	< 0.001
AVN	41	2.7	3	1.2	29	3.6	0.037	9	2.0	0.339
VT	190	12.5	41	16.5	66	8.1	< 0.001	83	18.2	0.328
VT side										
Right sided	84	44.2	21	51.2	24	36.4	0.095	39	47.0	0.400
Left sided	91	47.9	16	39.0	38	57.6	0.048	37	44.6	0.347
Epicardial	15	7.9	4	9.8	4	6.1	0.364	7	8.4	0.523
VT type										
Idiopathic	114	60.0	22	53.7	35	53.0	0.554	57	68.7	0.076
Ischemic	57	30.0	13	31.7	24	36.4	0.390	20	24.1	0.245
NICMP	19	10.0	6	14.6	7	10.6	0.370	6	7.2	0.161
CHD	55	3.6	7	2.8	11	1.4	0.103	37	8.1	0.003
Cryo-energy	424	27.9	0	0.0	424	52.2	< 0.001	0	0.0	NA
Approach										
Antegrade	689	45.4	77	31.0	390	48.0	< 0.001	222	48.7	< 0.001
Transseptal	614	40.5	150	60.5	337	41.5	< 0.001	127	27.9	< 0.001
Retrograde	195	12.9	17	6.9	81	10.0	0.085	97	21.3	< 0.001
Epicardial	19	1.3	4	1.6	5	0.6	0.136	10	2.2	0.414
Overall complications	172	11.3	41	16.5	101	12.4	0.062	30	6.6	< 0.001
Rehospitalizations	24	1.6	8	3.2	13	1.6	0.224	3	0.7	0.225
Major complications	43	2.8	5	2.0	32	3.9	0.102	6	1.3	0.337
Cardiac perforation	13	0.9	0	0.0	13	1.6	0.031	0	0.0	NA
Minor complications	129	8.5	36	14.5	69	8.5	0.005	24	5.3	< 0.001
Death	2	0.1	0	0.0	2	0.2	0.587	0	0.0	NA

Abbreviations of Table 1
AF, atrial fibrillation; AFl, atrial flutter; AT, atrial tachycardia; AVN, atrioventricular node; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; CF, contact force; CHD, congenital heart defect; MNS, magnetic navigation system; NA, not applicable; NCF, non-contact force; NICMP, non-ischemic cardiomyopathy; SVT, supraventricular tachycardia; VT, ventricular tachycardia.

Cardiac perforation was the most frequent major complication (n = 13) and the incidence was similar for all quartiles of experience (p = 0.333). Eight patients had major bleeding (18.6%), 9 patients had a phrenic nerve lesion (14.0%), 9 patients had a thrombo-embolic event (14.0%), 3 patients had damage to the lead of an implanted device (7.0%), 3 patients had AV fistula that required vascular surgery (7.0%), 2 patients had permanent AV block (4.7%), one patient had severe hemoptysis (2.3%), and one patient required a thoracotomy due to the remnance of a foreign body in the right atrium (2.3%). The most frequently occurring minor complication was inguinal hematoma (n = 65, 50.4%).

Analyses of subgroups

Subgroup analysis demonstrated that CF procedures were associated with less major complications and cardiac perforation during AF ablation compared to NCF (2.1% vs. 7.8%, p = 0.010 and 0.0% vs. 3.3%, p = 0.021; respectively). For AF ablation the occurrence of major complications was comparable to CF and MNS (3.7%, p = 0.349). Compared to the CF group, an equal rate of minor complications was observed for NCF procedures (16.8% vs. 12.1%, p = 0.115) and less minor complications occurred in the MNS group (6.5%, p = 0.010).

For the SVT subgroup equal rates of major complications were observed for CF, NCF and MNS procedures (1.8% vs. 1.2%, p = 0.528; 0.4%, p = 0.361; respectively). The number of cardiac perforations (0.0% vs. 0.2%, p = 0.883; 0.0%, p = NA; respectively) and minor complications (3.5% vs. 5.8%, p = 0.366; 4.4%, p = 0.557; respectively) was also equal for the three study groups.

During VT ablation in the CF, NCF and MNS group an equal rate of major complications (2.4% vs. 4.5%, p = 0.503; 1.2%, p = 0.554; respectively) and cardiac perforations (0.0% vs. 3.0%, p = 0.378; 0.0%, p = NA; respectively) occurred.

In the CHD subgroup no major complication occurred during the time of our study.

Procedural parameters

Data on intracardiac CF and procedural parameters are presented in Table 2 for the total overall CF group. For CF guided AF procedures the average force per RF application was 9.6 ± 4.3 g, the maximum force was 28.4 ± 14.5 g and the FTI was 300 ± 156 gs (Figures 4 and 5). In the CF group more fluoroscopy was used for AF and SVT ablations compared to NCF procedures (Table 2). Compared to MNS procedures more fluoroscopy was used for SVT and VT procedures in the CF group (Figure 3).

Table 2
Continuous variables: patient demographics and procedural parameters. Data are presented as mean ± SD or median with interquartile range between square brackets.

	CF	NCF	*P* value	MNS	*P* value
Age (years)	55.7 ± 15.1	51.7 ± 16.6	0.001	48.4 ± 18.3	< 0.001
Application number (*n*)					
AF	43.8 ± 24.9	76.7 ± 28.4	< 0.001	92.1 ± 53.6	< 0.001
SVT	13.5 [4.0 – 36.3]	7.0 [3.0 – 15.0]	0.001	10.0 [4.0 – 25.0]	0.186
VT	8.0 [5.0 – 22.0]	12.0 [6.0 – 26.3]	0.443	8.0 [4.0 – 20.0]	0.699
CHD	47.4 ± 28.7	71.0 ± 107	0.584	34.9 ± 35.1	0.384
Application time (s)					
AF	1499 ± 841	2287 ± 508	< 0.001	2280 [1511 – 3075]	< 0.001
SVT	524 [220 – 1217]	260 [120 – 780]	0.012	398 [130 – 861]	0.217
VT	472 [179 – 993]	644 [315 – 1540]	0.088	400 [190 – 1110]	0.995
CHD	2133 ± 2003	2573 ± 2887	0.785	1178 ± 1008	0.066
Fluoroscopy time (min)					
AF	57.5 ± 20.1	45.7 ± 24.2	< 0.001	58.1 ± 18.7	0.806
SVT	37.4 ± 24.6	22.6 [12.5 – 40.0]	0.008	20.3 [13.2 – 37.2]	0.008
VT	38.6 ± 19.6	49.6 ± 30.4	0.104	20.4 [10.9 – 29.4]	0.001
CHD	28.0 ± 19.0	34.0 ± 20.2	0.651	31.9 ± 28.1	0.791
Procedure time (min)					
AF	191 ± 56	194 ± 72	0.702	273 ± 87	< 0.001
SVT	156 ± 78	120 [90 – 150]	0.075	140 [100 – 190]	0.769
VT	196 ± 61	207 ± 93	0.658	153 [120 – 240]	0.242
CHD	171 ± 106	188 ± 32	0.850	200 ± 88	0.552
Hospital stay (days)	3.0 [3.0 – 4.0]	3.0 [2.0 – 4.0]	0.468	3.0 [2.0 – 3.0]	0.371
Average CF (g)	9.0 [6.0 – 12.0]				
Min CF (g)	2.0 [1.0 – 4.0]				
Max CF (g)	25.2 ± 14.0				
Total FTI (gs)	8217 [4024 – 14500]				
Average FTI (gs)	286 [197 – 427]				

AF, atrial fibrillation; CF, contact force; CHD, congenital heart defect; FTI, force–time integral; MNS, magnetic navigation system; NCF, non-contact force; SVT, supraventricular tachycardia; VT, ventricular tachycardia.

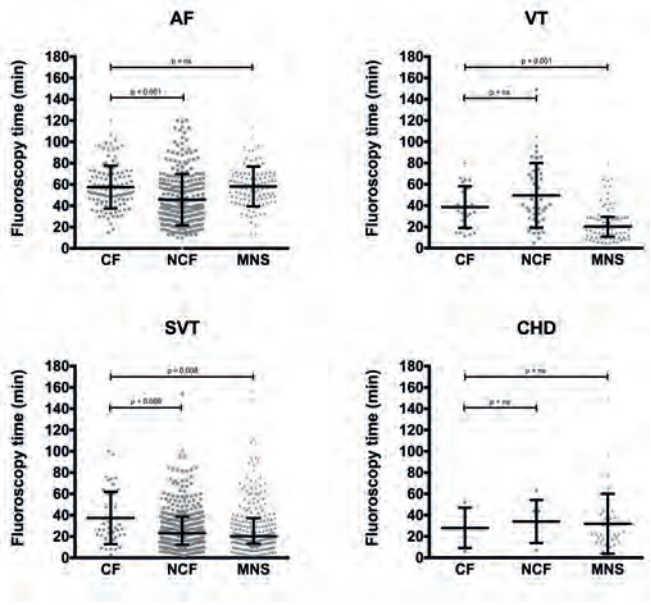

Figure 3: Procedural fluoroscopy times for each group. Mean ± SD values are presented as well. For NCF and MNS procedures for SVT ablation and for MNS VT procedures median values with IQR's are illustrated. *P* values are presented for comparison between the groups.

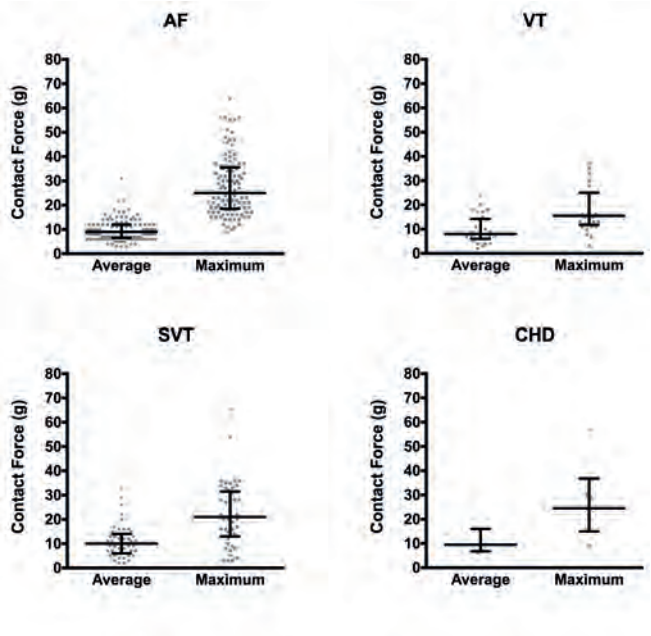

Figure 4: Presentation of used contact forces during ablation. The average and maximum CF values are presented for all subgroups during CF procedures. Median values with IQR's are illustrated.

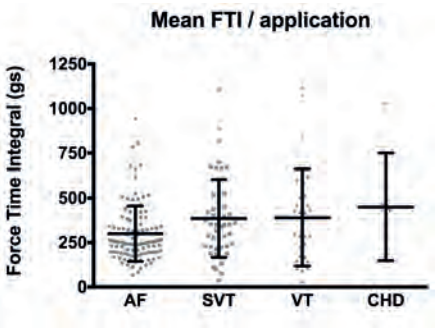

Figure 5: Mean force time integral (FTI) per application. The mean FTI per application is presented for the arrhythmia subgroups in the CF group.

Table 3
Univariate analysis for predictors of major complications

	Major complication ***n*** **= 43**	**None** ***n*** **= 1.474**	***P*** **value**
Age (years)	57.0 ± 13.7	51.2 ± 17.1	0.030
Age > 50 years	72.1%	60.3%	0.079
CF procedure	11.6%	16.5%	0.270
NCF procedure	74.4%	53.0%	0.004
MNS procedure	14.0%	30.5%	0.011
Gender (male)	53.5%	61.6%	0.179
Pediatrics	2.3%	7.1%	0.188
AF	72.1%	35.7%	<0.001
SVT	16.3%	48.0%	<0.001
AFl	7.0%	14.5%	0.115
AT	2.3%	5.5%	0.313
AVNRT	0.0%	12.6%	0.003
AVRT	7.0%	12.6%	0.196
AVN	0.0%	2.8%	0.303
VT	11.6%	12.6%	0.544
VT side			
Right sided	20.0%	47.1%	0.233
Left sided	40.0%	49.2%	0.520
Epicardial	40.0%	3.7%	0.018
VT type			
Idiopathic	60.0%	59.8%	0.681
Ischemic	20.0%	29.6%	0.540
NICMP	20.0%	10.6%	0.440
CHD	0.0%	3.7%	0.200
Cryo-energy ablation	44.2%	27.5%	0.015
Approach			
Antegrade	11.6%	46.6%	<0.001
Transseptal	79.1%	39.4%	<0.001
Retrograde	4.7%	13.4%	0.064
Epicardial	4.7%	0.6%	0.037

AF, atrial fibrillation; AFl, atrial flutter; AT, atrial tachycardia; AVN, atrioventricular node; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; CF, contact force; CHD, congenital heart defect; MNS, magnetic navigation system; NA, not applicable; NCF, non-contact force; NICMP, non-ischemic cardiomyopathy; SVT, supraventricular tachycardia; VT, ventricular tachycardia.

Univariate and multivariate analyses

Univariate analysis for predictors of major complications revealed that major complications occurred more often in older patients (57.0 ± 13.7 vs. 51.2 ± 17.1, p = 0.030), NCF procedures (p = 0.004), AF ablation (p < 0.001), cryo-energy ablation (p = 0.015), transseptal approach (p < 0.001) and epicardial approach (p = 0.037) (Table 3). Multivariate analysis has been performed using the following parameters: age > 50 years, NCF procedure, AF ablation, transseptal approach and epicardial approach, the use of cryo-energy and procedural experience. NCF procedures (odds ratio, 4.0; 95% confidence interval, 1.6 – 9.9; p = 0.003), transseptal approach (odds ratio, 7.2; 95% confidence interval, 1.8 – 29.6; p = 0.006) and epicardial approach (odds ratio, 42.2; 95% confidence interval, 9.0 – 197.7; p < 0.001) were independent predictors for major complications during catheter ablation. Procedural experience did not independently contribute to a reduction of major complications (odds ratio, 1.2; 95% confidence interval, 0.8 – 1.7, p = 0.45).

DISCUSSION

Main findings

This is the first study that systematically assessed the safety of CF ablation procedures in a large cohort of patients and compared this to manual and magnetically guided procedures. During this study major complications occurred in 2.8% of the procedures with a cardiac perforation rate of 0.9%. The 30-day rehospitalization rate due to a complication was 1.6%. The major findings of this study were that (1) CF catheters could reduce the risk of cardiac perforation compared to conventional ablation catheters, (2) the lower cardiac perforation rate of the CF group was due to a reduction of complications in the AF subgroup, (3) CF procedures had an equal amount of other major procedure-related complications, (4) during AF and SVT ablations more fluoroscopy was required for CF procedures compared to NCF procedures, (5) independent predictors for major complications were NCF catheters, transseptal approach and epicardial approach, and (6) CF ablation offers equal safety compared to MNS procedures.

Complication rate

In the overall study population major complications occurred in 2.8% of the procedures. This is comparable to the results of Bohnen et al. where an overall complication rate of 3.8% was reported. The updated worldwide survey from Cappato et al. and other groups report complication rates for AF procedures around 5%.[1,2,19,20] We report a major complication rate for AF ablation of 5.6%. This higher amount of complications could be attributed to our broader definition of major complications compared to other studies.

Risk factors for major complications

The association between transseptal approach and higher risk of procedural complications was earlier demonstrated.[21] Some centers use intra-cardiac echocardiography which proved to enhance safety in transseptal ablation procedures.[22] However, when only fluoroscopy is used to guide transseptal punctures a higher risk of cardiac perforation is described, irrespective of the technique used (transseptal needle or RF energy needle).[22,23] Not only the transseptal puncture itself, but also the greater anticoagulation and number of left sided applications play a role in causing tamponade after cardiac perforation. Furthermore, our study demonstrated that epicardial ablation is associated with more complications compared to endocardial procedures. Other groups also describe the risk of serious adverse events during epicardial ablation.[24,25]

Bohnen et al. found that the serum creatinine level was an independent predictor for major complications in the overall population with AF, SVT and VT procedures.[3] Other studies demonstrated that for AF procedures age > 70 years, female gender, presence of coronary artery disease and congestive heart failure were predictors for major complications.[2,19,20] However, none of these studies evaluated the association between complications and catheter type. Our results demonstrated that CF and MNS ablation catheters, compared to conventional catheters, could reduce the risk of procedure-related major complications for AF ablation. Apparently, the lack of objective CF feedback during manipulation and ablation increases the risk of exceeding the critical CF limit and causing complications. The continuous display of intracardiac forces using the CF catheter and the design of the MNS result in less cardiac perforation.

Importance of CF sensing

The value of continuous CF monitoring during ablation procedures has been described in previous studies. It is well known that CF is an important determinant of lesion formation to create transmural lesions and reduce arrhythmia recurrence.[15,18,26,27] Even in the hands of experienced operators a significant proportion of applications do not result in appropriate lesions using tactile feedback and fluoroscopy, both endo- and epicardially.[17] Furthermore, more reliable electroanatomical maps could be created during VT ablation using CF sensing.[13] However, previous research focused mainly on the electrophysiological advantages of CF-guided catheter ablation. In animal models different advantages regarding safety have been described, such as prediction of steam pops, thrombus formation and the relation between CF and complications during epicardial ablation.[18,28] Our study contributes to the current knowledge of procedural safety using CF catheters for the treatment of different arrhythmias in humans. Whereas low CF may result in inappropriate lesion formation, high CF carries the risk of major complications (e.g. cardiac perforation, steam pop). Unintentionally very high CF's could be applied during catheter manipulation using conventional catheters.[29] Perforation of the atrial wall in a swine model can occur when using only a CF of 77 g. This is reduced by 23% when RF energy is applied.[30] The use of CF catheters allows continuous force feedback and the occurrence of high CF's can be avoided. Our data demonstrate that the maximum force in the CF group did not exceed 70 g in all groups (Figure 4). Furthermore, our study proved that additional CF data during ablation could reduce cardiac perforation rates and allow safer procedures compared to manual ablation. This was mainly due to a reduction of cardiac perforation in the AF subgroup. We confirmed that during AF ablation cardiac perforation is a common complication, probably due to extensive catheter manipulation, transseptal puncture, and thickness of the atrial wall.[1] The increased risk of complications and the higher number of procedures explain the higher occurrence of major complications in the AF subgroup compared to other subgroups.

Fluoroscopy

Fluoroscopy use is also an important parameter concerning procedural safety, both for patient and physician. Our data shows that more fluoroscopy was used during AF and SVT ablations for CF procedures compared to NCF procedures. Since our institution is an academic and tertiary referral center where high complex patients are treated, a large

variation in fluoroscopy times was seen. Kerst et al. demonstrated that the use of CF catheters could facilitate a decrease in fluoroscopy and provide even zero-fluoroscopy procedures.[14] However, during the procedures anatomical positions of the catheter tip were checked before every application. The higher amount of fluoroscopy in the CF group could be explained by the possibility that the operators were not instantly used to the new system and both CF-guidance as well as fluoroscopy were used. When the operators get used to the system and rely more on CF information, less fluoroscopy could be used during catheter manipulation. However, further studies are required to evaluate this issue.

Clinical implications

The MNS offers improved procedural safety with an enhanced catheter design that eliminates the risk of cardiac perforation. In order to use the MNS system specific structural changes to the operation room are necessary such as a specially stabilized floor for the magnets. For complex procedures MNS has more useful advantages such as superior catheter maneuverability and accurate mapping. Besides the logistical issues, procedural costs could be a reason for concern as well.[31] Economic considerations are becoming more important in current clinical decision-making processes. However, the use of CF sensing catheters offers equal procedural safety without the need to purchase expensive equipment. The CF system could easily be implemented in more EP centers for everyday use to improve patient safety.

Study limitations

This study has been conducted in a non-randomized, single center setting. In this study a multivariate analysis has been performed to adjust for differences between the study groups. However, statistical analyses could never compensate entirely for clinical differences at baseline and a randomized study must be conducted to eliminate all possible confounders on the effect of CF-guidance on procedural safety. Preferably this should be executed in a multicenter setting, including comparison of clinical outcomes. In this paper we present our own experiences with CF catheters on procedural safety, but the experience of other international centers is currently unknown. To evaluate the overall effect of CF-guided procedures on patients' safety other centers should publish their experience or participate in a multicenter study.

For this study the minimal required number of patients to achieve sufficient power was calculated. With the included number of patients we were able to detect differences in complication rates between the groups. To specifically study the differences for each arrhythmia subgroup and approach (e.g. epicardial ablation) higher numbers of patients were required for each group. With this study we could provide answers to the question whether CF-guided catheter ablation could reduce cardiac perforation and major complications for the overall representative patient population. However, to investigate the effect for every arrhythmia subgroup further research is required. This is especially the case for the CHD subgroup. Although we are a tertiary referral center with more complex procedures a relatively low number of CHD patients were included. For this patient population a multicenter registry could provide more data to make reliable conclusions about the effect of CF-guided procedures.

Furthermore, the occurrence of pulmonary vein (PV) stenosis was not routinely assessed and only on indication when patients presented with symptoms. Therefore, there may be an underreporting of the number of PV stenosis. Arentz et al. demonstrated that 28% of patients who underwent ablation for AF had PV stenosis at the two year follow-up.[32] However, at our institution ostial and PV antrum ablations were performed which is associated with a lower occurrence of PV stenosis.[32]

CONCLUSION

Ablation using CF-guidance is superior to NCF ablation with regards to procedural safety and avoidance of cardiac perforation. CF ablation offers the same level of safety when compared to MNS procedures. The lower cardiac perforation rate of the CF group was due to a reduction of complications in the AF subgroup.

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CHAPTER 13

The first human experience of a contact force sensing catheter for epicardial ablation of ventricular tachycardia

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ABSTRACT

Contact force (CF) is one of the major determinants for sufficient lesion formation. CF-guided procedures are associated with enhanced lesion formation and procedural success. We report our initial experience in epicardial ventricular tachycardia (VT) ablation with a force-sensing catheter using a new approach with an angioplasty balloon. Two patients with arrhythmogenic right ventricular cardiomyopathy who underwent prior unsuccessful endocardial ablation were treated with epicardial VT ablation. CF data were used to titrate force, power and ablation time.

INTRODUCTION

An epicardial approach for ablation of ventricular tachycardia (VT) is often required, since the substrate cannot always be reached entirely from the endocardium.[1–3] Particularly in patients diagnosed with arrhythmogenic right ventricular dysplasia (ARVC) an epicardial ablation approach is frequently inevitable.[4] Radiofrequency (RF) catheter ablation in the epicardial space is substantially different from endocardial ablation. First of all, there is the absence of circulating blood in the epicardium and therefore lack of convective cooling during ablation, the catheter orientation is usually different, and the varying presence of epicardial adipose tissue interferes with lesion formation.[5,6] These factors all have significant influence on RF lesion formation and should be taken into account during epicardial VT ablation. A European study demonstrated that the overall success rate of epicardial ablation for different aetiologies is 71.6 %.[7] However, during follow-up a significant proportion of 31.4 % experienced recurrence of the tachycardia. In the past, several techniques were developed to improve energy delivery in the epicardial space. Cooled-tip ablation proved to be superior to standard ablation and bipolar ablation resulted in more effective energy delivery than unipolar ablation.[8,9] In order to further increase the efficacy of epicardial ablation, CF-sensing catheters may play a role.

Contact force (CF) is a very important determinant of lesion formation.[10,11] Since effective lesion formation in the epicardium can be challenging, we hypothesized that the use of a CF-sensing catheter might contribute to efficacy and safety during epicardial RF ablation. The aim of this paper is to report our initial experience and demonstrate the CF-guided epicardial approach and its feasibility for epicardial VT ablation. This report describes two patients with ARVC who had undergone prior unsuccessful endocardial ablation and were referred for epicardial ablation of VT.

METHODS

Before the procedure, the patients were informed about the epicardial approach and written informed consent was obtained from both patients prior to the procedure. The

procedures were performed under general anaesthesia with a cardiothoracic surgical team on standby during the entire intervention. After the procedure a pericardial drain (PeriVac pericardial tray) remained in place for 8–12 h if no significant bleeding or fluid drainage occurred.

Epicardial access

Percutaneous epicardial access was obtained from a subxyphoid level. This was performed with a Tuohy needle (18G, length 15 cm) and a 9 Fr, 24 cm Arrow flex sheath. The pericardial puncture was fluoroscopy guided with the X-ray C arm at 90° latero-lateral projection. Continuous, intermittent small amounts of iodine-based contrast were injected, until the typical layering of the epicardial space was seen (Fig. 1a).[12] A guide wire (Cordis Exchange wire 35”) was introduced via the needle. Afterwards the soft flexible vascular sheath (9 Fr) was inserted using the Seldinger technique to manipulate the ablation catheter in the pericardium (Fig. 1b).

CF-sensing catheter

An open irrigated-tip RF catheter with CF sensing technology (TactiCath®, Endosense SA, Geneva, Switzerland) was used. This catheter integrates a CF sensor at the distal part of an RF open-irrigated catheter between the second and third electrode.[13] The force sensor has a deformable body and makes use of infrared laser light and three optical fibers (diameter of 0.125 mm) to detect deformations, which are related to the amount of force applied to the catheter tip.[10] The sensor is able to measure the lateral and axial forces distinctly. The system displays both magnitude and angle of the CF vector with intervals of 100 ms on a separate screen during the ablation procedure. The amount of CF is expressed in grams, and the integrated software calculates a Force-Time Integral™ (FTI, function of force and time, expressed in g).[11]

Mapping and ablation

Both groins were prepared for percutaneous punctures. The chest and abdomen around the xyphoid process were prepared and isolated. A 6 Fr sheath was inserted to gain right femoral venous access for standard diagnostic EP catheters. A quadripolar electrode was placed into the right ventricular (RV) apex to serve as a reference for the electroanatomical mapping

system (EAM). Three-dimensional EAM was performed using the NavX™ Velocity system (St Jude, St Paul, MN, USA). Endocardial and epicardial bipolar voltage maps were made. Scar tissue was defined as local bipolar electrograms <0.5 mV. Low voltages associated with high-frequency late components were considered as scar area and this was used to create a voltage map. A selective coronary angiogram was performed before power delivery to the epicardial tissue in order to evaluate the proximity to the coronary arteries.

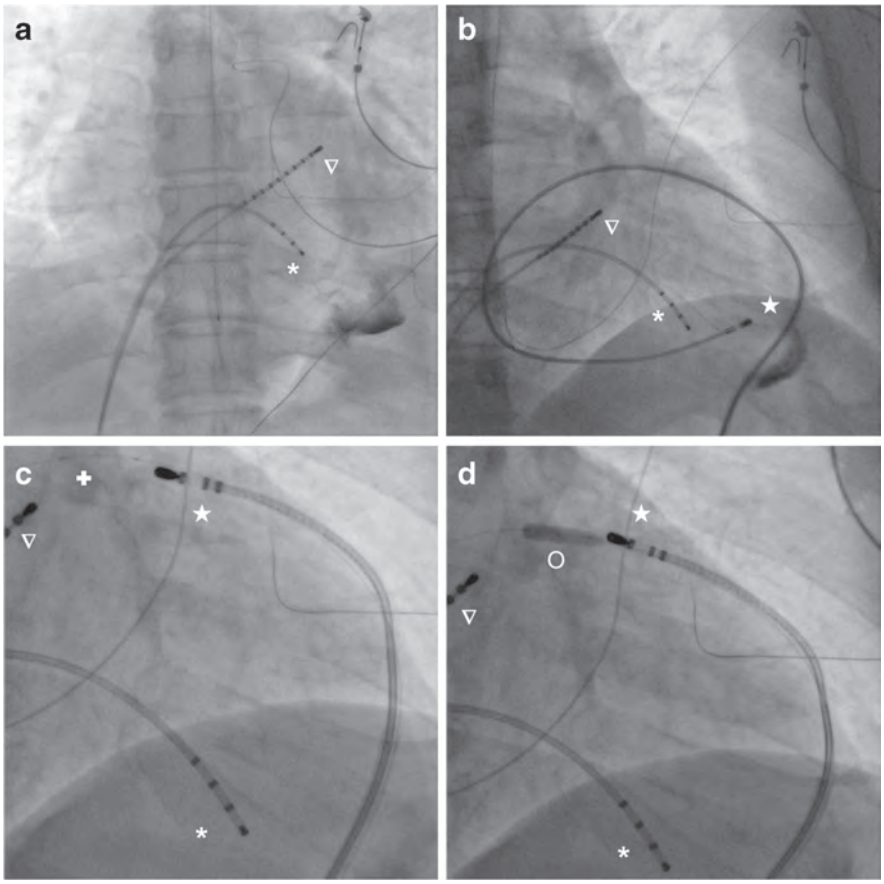

Figure 1: Fluoroscopic recordings during the ablation procedure - *a*: Catheter placed in the right ventricle and coronary sinus with contrast fluid visible in the pericardial space. *b*: Through the soft flexible vascular sheath, the CF sensing ablation catheter is inserted into the pericardium. *c*: Introduction of an additional catheter through the same sheath from the CF catheter. *d*: Introduction of the angioplasty balloon in the pericardial space. * Quadripolar catheter into the RV apex. ▽ Diagnostic catheter placed in the coronary sinus. ★ CF sensing ablation catheter. **+** Additional catheter into the pericardium. O Angioplasty balloon advanced into the pericardium.

Calibration of CF catheter

For precise CF measurement, calibration in a no-contact position is required. This was achieved by introduction of an additional catheter together with an angioplasty balloon (5x15 mm compliant Trek coronary dilatation catheter™, Abbott Vascular, Santa Clara, USA) through the same sheath (Fig. 1c). The CF catheter is 7 F sheath compatible, making simultaneous introduction of the two catheters possible in the 9 F sheath. The balloon was inflated at 10 Atm just beyond the tip of the catheter in the pericardium (Fig. 1d). Calibration was performed in a single position where the inflated balloon and the ablation catheter tip could be adjacent in a linear fashion. During inflation, the calibration was carried out and the balloon was removed for the rest of the procedure. Dynamic CF data were used to guide the manipulation of the catheter for mapping and RF delivery epicardially.

CASE PRESENTATION

Case 1

A 67-year-old man diagnosed with ARVC and a preserved systolic left ventricular function presented with multiple episodes of very symptomatic non-sustained VT, which was refractory to medical therapy (Fig. 2). The VTs had a typical morphology indicating an origin from the right outflow region. The patient had a single chamber defibrillator. Endocardial ablation had been attempted twice (1 year and 3 years previously) and failed to eliminate the substrate of the VTs. An epicardial origin was suspected on the basis of mapping during the endocardial procedure.

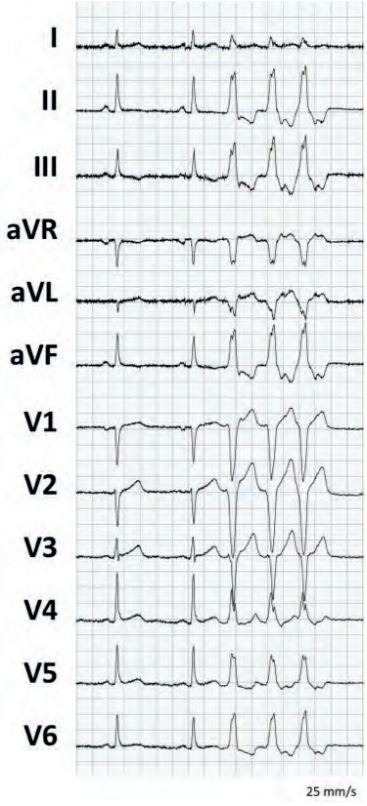

Figure 2: 12-lead ECG displaying non-sustained VT with a left bundle branch block morphology and inferior axis, suggestive for RVOT origin.

During mapping, extensive anterior right ventricular outflow tract (RVOT) epicardial scarring was identified. Other RV regions had no low bipolar voltages. Scar homogenisation was performed endocardially as well as in the adjacent epicardial sites. This led to complete diminution of the premature ventricular contractions, and non-inducibility of VTs during a 30-min waiting period.

The CF remained under 25 g throughout the whole epicardial mapping procedure. In some regions it was very challenging to increase the contact force above 2 g. A total number of 6 RF applications (power: 30–45 W, time: 60 s, irrigation flow >17 mL/min) were applied epicardially. The average force during the ablations was 9 g, with an average FTI of 418 g. In total 33 min of fluoroscopy were used. No audible steam pop was observed during applications. No complications occurred.

After 1 year of follow-up the patient was free from symptoms and ICD interrogation detected no more ventricular arrhythmias. No antiarrhythmic drugs were used during follow-up.

Case 2

A 48-year-old man, previously a top level sporter, was referred because of incessant VT. Sinus rhythm was obtained by electrical cardioversion. Interestingly enough he had previously undergone RF ablation for idiopathic RVOT tachycardia. The first episode had occurred 16 years ago. He was initially treated with beta-blocker therapy, and remained asymptomatic for 16 years without medication until he presented with haemodynamically stable VTs. After further investigations he was diagnosed with ARVC. This clinical VT was basically different than the one described 16 years ago.

During the procedure two distinct VTs (cycle length 370 ms and 330 ms) with left bundle branch block morphology, left axis and initial slurring in the QRS complex were reproducibly induced by programmed ventricular stimulation. Epicardial mapping identified their origin in the apical region of the right ventricle, where dense scar bordered healthy tissue. A linear epicardial line of ablation was drawn from the border of the scar to the healthy tissue (Fig.

3a). The VT terminated during the third ablation point (Fig. 3b). The tachycardia was no longer inducible after ablation, even after a 30-min waiting period.

The average CF was 6 g, and remained under 17 g during the entire mapping procedure. A total number of 14 RF applications (power: 30–45 W, time: 60 s, irrigation flow: 20 ml/min) were applied epicardially. The average FTI was 150 g per ablation point (maximum 476 g). In total 34 min of fluoroscopy were used. No audible steam pop was observed during the applications. No complications occurred. The patient remains free of symptoms at 6 months of follow-up.

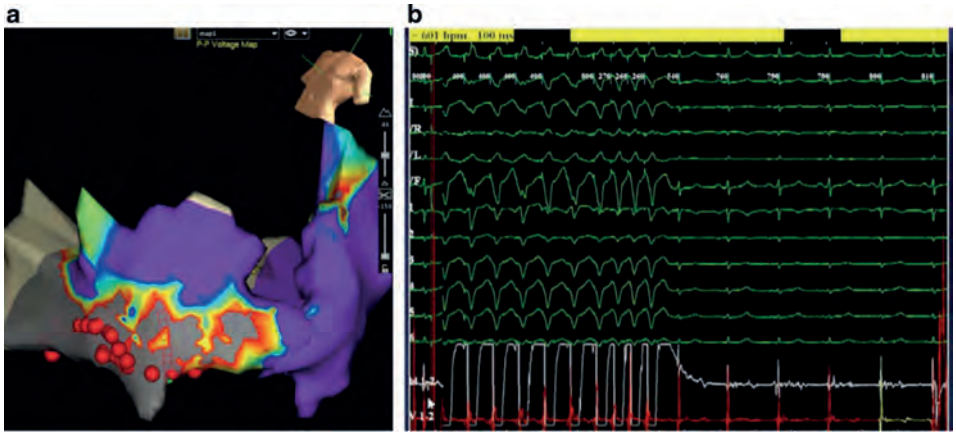

Figure 3: *a*: Electroanatomical map from Case 2 after ablation. Sites where RF applications were applied are indicated by red dots. Ablation was performed along the borders of the scar region (marked by grey coloration). *b*: Intra-cardiac electrograms at the successful ablation site showing late potentials (fragmented potentials occurring after the end of surface QRS complex) recorded by the ablation catheter. During ablation termination of the tachycardia occurred.

DISCUSSION

Importance of contact force

Previous research demonstrated that CF is a major determinant for lesion formation and has a greater effect on lesion size than RF output power.[10] CF appears to be associated with FTI, lesion size, and procedural success.[10,11,14] Research on pulmonary vein isolation for atrial

fibrillation (AF) revealed that the rate of recurrence was associated with the percentage of ablations with very low CFs (<10 g) and predicts recurrence at 12 months. All AF patients who were treated with an average CF of <10 g experienced recurrences, whereas 80 % of the patients treated with a CF of >20 g experienced no AF recurrences.[15] These data demonstrate that proper catheter-tissue contact is crucial to establish appropriate lesions and avoid conduction recovery.[13,15,16] Previously only surrogate information regarding CF was available during ablation procedures such as tactile feedback, movement of the catheter tip on fluoroscopy, ST elevation in the unipolar electrogram and impedance monitoring.[17,18] However, these criteria seemed to be inadequate for estimating real-time CF.[17,18] Kuck et al.[14] demonstrated that tactile feedback during mapping and ablation is not a reliable parameter and dangerous forces could be applied during catheter manipulation. Furthermore, Kumar et al.[18] found that impedance fall with ablation only has modest predictive value for CF and FTI, and could not accurately differentiate between low and high CFs. Currently, catheters are available that provide direct and continuous feedback regarding CF. The use of this type of catheter has been associated with a decrease in the number of RF applications, which does not result in lesion formation because of insufficient CF.[5]

Another important issue during catheter ablation is intermittent CF due to the continuous movements of the heart and respiratory movements. This may occur if the catheter is not in constant contact with the myocardium. This leads to impaired energy delivery and subsequently inferior lesion formation.[15] Reddy et al. showed a strong correlation between low CF and intermittent catheter-tissue contact. Continuous CF feedback allows the operator to adapt the CF during applications, therefore improving lesion quality. However, in some regions it is difficult to achieve a good and stable catheter position with sufficient CF, as we experienced as well during our ablation procedures. Shah et al.[11] demonstrated that FTI is strongly and linearly correlated with lesion depth and volume. Therefore, the operator could compensate low CF by varying RF power and duration of an application.

Specific concerns during epicardial ablation

Circumstances for catheter ablation on the epicardium are substantially different from endocardial ablation. The absence of a heat sink effect (no circulating blood) results in larger lesions on the epicardium, even though the FTI is twice as low compared with endocardial

applications.[5] In the endocardium a CF <10 g or FTI <500 g would lead to non-identifiable lesions on the myocardium. The results from Sacher et al. demonstrate that this was not the case for the epicardium. Wong et al.[6] report that for each doubling of tissue contact between 5 g and 40 g of CF, there is a corresponding doubling in absolute lesion formation and point out the advantage of CF sensing during the ablation. Nevertheless, on the epicardium sufficient lesion formation will occur at lower CF and power output than endocardially. Furthermore, the parallel catheter orientation with lower axial CF compared with endocardial ablation creates more broad and shallow lesions.[19] Using an epicardial approach, complete transmural lesions could be created in the right ventricle (because of the thinner myocardium).[6] However, for ablation at sites with a thicker myocardial wall a combined endo-epicardial approach could be necessary to achieve transmural lesions.

During ablation, an obstacle for the energy transmission to the epicardium is often the presence of epicardial fat. The low electrical and thermal conductive properties reduce the transmission of energy to the underlying tissue. When ablating at sites with a thick layer of adipose tissue, a high CF is required to achieve at least minimal lesion formation.[6] At sites with epicardial fat of >5 mm, epicardial lesion depth was 1–2 mm when high CF ablation was performed. For ablation at these specific sites, the CF-sensing catheter might have benefits in order to create clinically significant lesions. However, further clinical studies are needed to investigate this issue.

Calibration of catheter

During endocardial procedures the CF reference (‘no electrode-tissue contact’) is set when the catheter is floating in the heart chamber and can be verified during the procedure. Calibration is thus a crucial part of reliably, or at least relatively, measuring contact force. We describe the first cases in which a non-contact reference in the epicardium was achieved by using an inflated angioplasty balloon (visually beyond the borders of the catheter tip) in an attempt to minimize tissue contact. In this setting the non-contact and subsequent measurements were not considered as absolute values but as an indication of relative force, as the ‘zero’ is set by the operator. In the animal study by Wong et al.[6] normal saline was introduced into the pericardial space to allow catheter floating and therefore zero calibration of CF. However, we assume that the advantages of the angioplasty balloon might

be the otherwise compromising haemodynamics. The infusion of saline into the pericardial space could cause tamponade symptoms. This is especially important in patients with a decreased left ventricular function. However, more clinical experience is necessary to evaluate the use of different epicardial calibration methods.

Safety

Epicardial approach as a first-line treatment of VT has been increasingly used (35.8 %).[7] Sacher et al.[20] performed a multi-center study on epicardial VT ablation and demonstrated that major complications could occur during and after the procedure. Although recent techniques are developed to minimize these complications as much as possible, careful evaluation is necessary for the correct approach to ablation, which has been described previously.[21-23]

As this paper describes the importance of good CF during ablation for appropriate lesion formation, high CF values could have serious implications regarding procedural safety. Excessive CF values may result in complications such as myocardial perforation, steam pop, cavitation, thrombus formation, oesophageal injury, lung lesions and coronary artery and phrenic nerve damage.[5,13,24] It is important that the vector of force is pointing towards the myocardium to prevent pulmonary lesions.[5] As it has been reported that CF information at the epicardial side may not be as useful as endocardially, the CF-sensing catheter could contribute to visualising the vector of the force and therefore energy delivery. Furthermore, Wong et al.[6] described the impact of applied CF and phrenic nerve (PN) injury. Although it is an uncommon complication during epicardial ablation, their results demonstrated that PN injury occurs with increasing, directly applied CF. At 5 or 10 g of CF, PN injury appeared to be unlikely, but was practically universal when 20 g of force was applied.

CONCLUSION

We report the first epicardial CF-guided VT ablation in humans with the use of an angioplasty balloon for CF calibration. The information provided on CF could be useful to create more accurate electroanatomical maps, produce better transmural lesions and avoid inefficient ablation points. Although our limited initial experience was successful and safe, more clinical evidence is required to demonstrate the efficacy and safety of CF-guided epicardial VT ablation.

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CHAPTER 14

Safety and clinical outcome of catheter ablation of ventricular arrhythmias using contact force sensing

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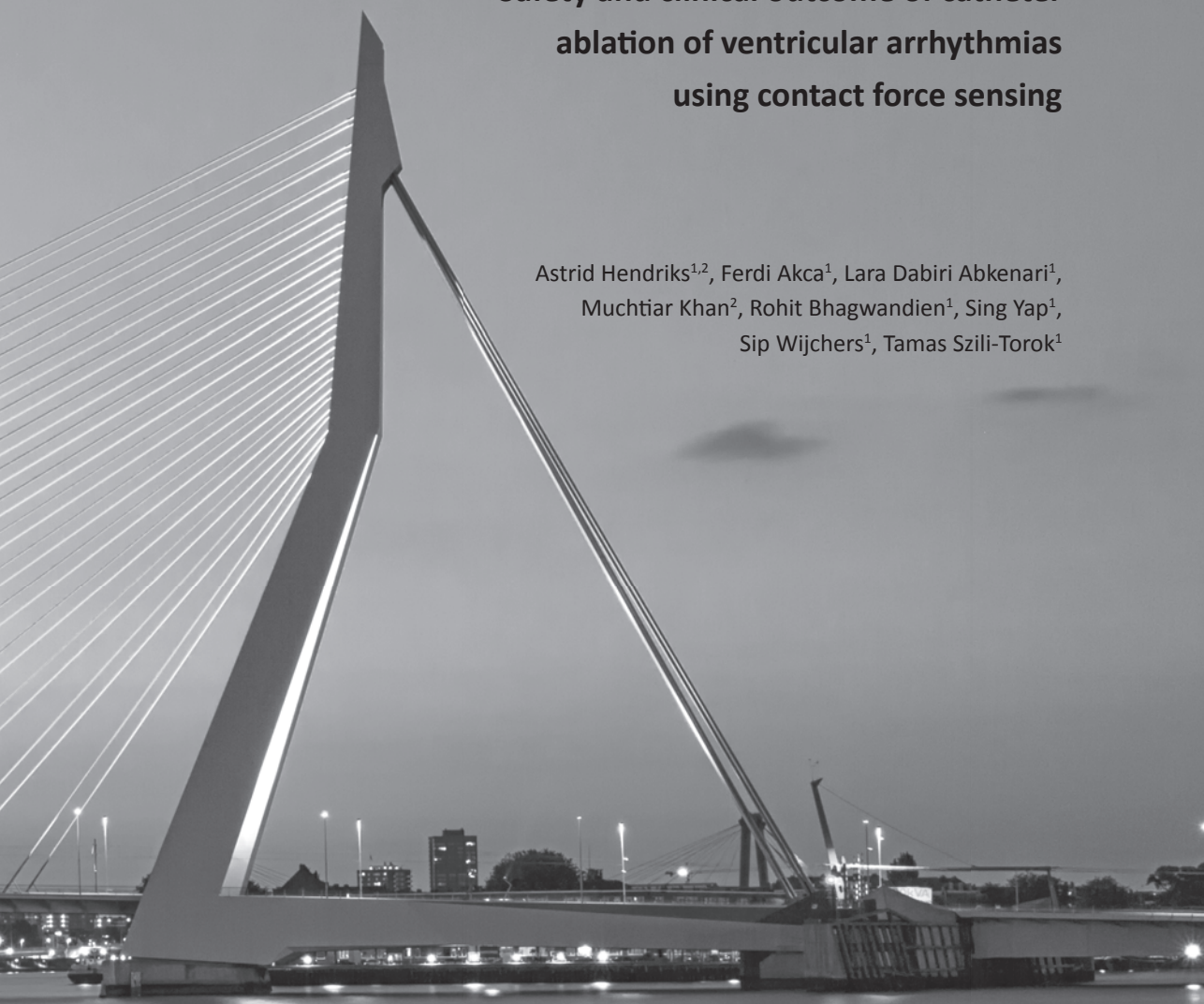

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ABSTRACT

Background

Poor catheter-to-myocardial contact can lead to ineffective ablation lesions and suboptimal outcome. Contact force (CF) sensing catheters in ventricular tachycardia (VT) ablation has not been studied for their long-term efficacy. The aim of this study was to compare CF ablation to manual ablation (MAN) and to remote magnetic navigation (RMN) ablation for safety and efficacy in acute and long-term outcome.

Methods

A total of 249 consecutive patients who underwent VT ablation were included in this single center cohort study from January 2007 until March 2014. The primary endpoints were procedural success, acute major complications and VT recurrences at follow-up. The median follow-up period was 25 [IQR 14 -35] months.

Results

Acute success was achieved in 191 out of 249 procedures (75.9%). Acute success in manual ablation, CF ablation and RMN ablation was 70.1% and 72.3% and 85.2% respectively (P = 0.038). Overall there were 3.2% major complications and there was a trend towards less major complications (P = 0.055) in the RMN and MAN group. Thirty six percent of the patients with an initially successful procedure had a recurrence during follow-up (CF 41.2%, MAN 37.5%, RMN 32.0%, P = NS).

Conclusion

The use of CF sensing catheters does not improve procedural outcome or safety profile in comparison to non-CF sensing ablation in ventricular arrhythmias. RMN non-CF sensing ablation has the highest procedural success rate. Future studies are necessary to investigate the role of CF in VT ablation and to define the optimal force.

INTRODUCTION

Catheter ablation of ventricular tachycardia (VT) has become standard therapy.[1-3] Meanwhile there is a persistent demand for novel technologies to reduce complications and to improve success rate. Poor catheter-to-myocardial contact can lead to ineffective lesions and suboptimal outcome. Information on contact force has shown to be an important determinant in the success of atrial radiofrequency ablations.[4,5] It has been suggested that contact force improves ablation results in radiofrequency application in the ventricle and is related to improved safety and acute efficiency in VT ablation in vitro in a small cohort.[6-8] There is no data on the improvement of long-term clinical outcome with contact force feedback.

Magnetic navigation in VT ablation has shown to be superior to manual ablation, especially in non structural heart disease.[9,10] There has not been a direct comparison of visual and tactile feedback for VT ablation.

The aim of this study is to compare contact force to manual ablation and to remote magnetic navigation (RMN) ablation for safety and efficiency in acute and long-term outcome. Our primary hypothesis was that contact force improves safety compared to manual ablation, and may improve efficacy.

METHODS

Study population

A total of 249 consecutive patients undergoing ablation for ventricular arrhythmia – VT and ventricular extrasystole (VES) – were included in this cohort from January 2007 until March 2014. There were 109 patients in the manual navigation (MAN) group, 88 in the remote magnetic navigation (RMN) and 52 in the contact force (CF) group. Structural heart disease (ischemic and non-ischemic) and non-structural heart disease were studied as well.

Data collection

All data was collected prospectively with the exception of the contact force data which was collected later. The study was approved by the MEC (MEC-2014-214).

Electrophysiology study and ablation procedure

All catheter ablation procedures were performed in accordance with institutionally approved local medical treatment protocols of the Erasmus MC, Thoraxcenter, Rotterdam. Written informed consent for the procedure was obtained from all patients. Within 48 hours to the procedure a resting 12 lead ECG, laboratory tests and X-ray thorax image were acquired. Thrombus in the left ventricle was excluded by the use of a 2 dimensional echocardiography. Antiarrhythmic drugs were discontinued for at least 4 halve lives prior to the procedure with the exception of amiodarone. In case of an emergency VT procedure antiarrhythmic drugs were not ceased. The procedures were performed under local or general anaesthesia.

The choice of access (transaortic or transseptal) to the left ventricle was left up to the preference of the operator. The transaortic route was most often used (87%). In the CF group a transseptal puncture is more frequently applied compared to MAN and RMN (P = 0.03). A transseptal puncture was always guided by intracardiac echocardiography (ICE). Epicardial access was obtained by subxiphoid puncture in a total of 10 patients (2.5%).

Three dimensional electroanatomical maps (CARTO Navistar or EnSite NavX), including activation and voltage maps, were obtained in sinus rhythm and if present, during hemodynamically stable VT. In the presence of a hemodynamically stable VT, exit points and critical isthmus were identified and targeted. Pace mapping was used mainly in hemodynamically unstable or non-sustained VT. In patients with structural heart disease electroanatomical substrate mapping took place. We used established peak-to-peak bipolar voltage criteria for scar, scar-border and healthy tissue (≤ 0.5mV, 0.5 – 1.5mV and ≥ 1.5 mV respectively). In the presence of a scar homogenization was the primary approach.

Crossover from RMN to manual ablation and CF to MAN was allowed at the discretion of the

operator. Crossover from manual catheter navigation to RMN ablation was not possible due to logistical reasons. Crossover was considered as an acute failure.

Ablation with force sensing catheters

The procedures were performed using EnSite NavX 3D (St. Jude Medical Inc., St. Paul, MN) mapping or CARTO system (Biosense Webster, Inc., Diamond Bar, California). The following contact force ablation catheters were used: Thermocool Smart Touch catheter (Biosense Webster, Diamond Bar, California), and EndosenseTacticath SA (St. Jude Medical Inc., St. Paul, MN). Contact between the catheter and the myocardium for each mapping point was measured in average and maximum force and expressed in grams (g). The area under the real time force is measured as force time integral expressed in gram seconds (gs).

Data collection and analysis

We analysed the following parameters: acute procedural success, complications and recurrences on follow-up. Acute success is defined as non-inducibilty of the clinical ventricular arrhythmia. Additional procedural data was also compared including the number of applications, application time, fluoroscopy time, procedural time and contact force information (average and maximum force, total force-time-integral). The length of the procedure was defined as the time from placement of the sheaths until removal of catheter. Force time integral (FTI) is the area under the curve of CF for the duration of RF delivery.[11]

Follow-up

Duration of follow-up ranges from 6 months to 54 months. Adverse events were collected up to 30 days after the procedure. All patients were seen for a regular follow up visit at 3 months after the ablation. For idiopathic VT or VES, a 24-hour electrocardiogram (holter) recording was scheduled for the 3 months follow-up visit and thereafter when symptomatic.

Recurrence rates

Recurrence was defined as any VT documented during follow-up. When available, the morphology and the cycle length of the arrhythmia were studied. Medical charts from emergency room visits, discharge letters, ICD interrogation, electrocardiograms and holter recordings were studied. Time to recurrence from index procedure, quantity of ICD therapy

[shock and/ or antitachycardia pacing (ATP)] were analyzed. In case of an ablation of VES, recurrence is defined as VES on holter recording < 95% reduction compared to pre-ablation beats per 24h, with a morphology identical to the ablated VES.

Adverse events

An adverse event is considered a complication if the event could be related to the procedure up to 30 days after the index procedure. If an adverse event occurred before the end of the procedure it was accounted an acute complication. Complications were defined as minor and major. Minor complications included: groin hematomas, AV fistula, pericardial effusion not requiring intervention, transient ischemic attack and temporary AV block. The following were valued to be major complications: pericardial effusion requiring intervention, persistent AV-block, stroke, arterial venous fistula requiring surgery and major bleeding. We also specifically studied ablation related complications which excluded complications related to the vascular access.

Statistical analysis

All patient data were analyzed using SPSS 15.0 (SPSS INC., Chicago, IL, USA). Normality of distribution was determined by the Kolmogorov-Smirnov test. If normally distributed continuous variables for independent samples were analyzed with the Student *t*-test. They were expressed as mean ± SD. In case of non-normal distribution of data, medians and interquartile ranges (IQR) were reported and the Mann-Whitney U test was used for data comparison. Categorical data were expressed as percentages and compared with the Chi-square test. Analysis between group means were performed with the ANOVA test. Event-free survival rates were determined using the Kaplan-Meier method and differences were evaluated by the log-rank test. A two sided p-value of < 0.05 (two tailed) is considered significant. A multivariate analysis was performed for all univariate baseline variables with a difference in prevalence between the groups of $P < 0.1$.

RESULTS

Demographics

The majority of all patients (72.7%) was male, and the average age was 53.4 ± 16.7 years (Table 1). More than halve of the ablations were left sided and 33.3% of all ablations were scar related. VES was in 35.3% of all cases the indication for ablation. More than one-third of the subjects had an arrhythmia originating from one of the outflow tracts (OT). Ten epicardial ablations were performed, 70% planned after failed endocardial ablation and 30% took place during the same procedure when encountering an epicardial exit. For epicardial VT ablation, VES was the indication in 4 cases, OT arrhythmia in 3 cases and ARVC in 4 cases. There were 2 epicardial VT ablations in a structurally abnormal heart of which one was ischemic in origin.

Table 1
Baseline characteristics presented for the overall group; and CF, MAN and RMN groups

	Overall	**CF**	**MAN**	**RMN**	***P* value**
Total (*n)*	249	47	114	88	
Male (%)	181 (73%)	28 (60%)	90 (79%)	63 (72%)	0.04
Age (y)	53.4 ± 16.7	56.8 ± 16.4	52.4 ± 17.4	52.7 ± 15.8	0.69
Pediatric (*n, %*)	12 (5%)	2 (4%)	7 (6%)	3 (3%)	0.65
VES (*n, %*)	88 (35%)	23 (49%)	33 (29%)	32 (36%)	0.05
Repeat procedure (*n, %*)	55 (22%)	14 (30%)	13 (11%)	28 (32%)	0.001
OT (*n, %*)	88 (35%)	27 (58%)	25 (22%)	36 (41%)	0.001
Fascicular (*n, %*)	24 (10%)	1 (2%)	12 (11%)	11 (13%)	0.14
Epicardial (*n, %*)	10 (3%)	5 (11%)	1 (1%)	4 (5%)	0.16
Left sided (*n, %*)	135 (54%)	21 (45%)	70 (61%)	44 (50%)	0.09
Transaortic route (*n, %*)	116 (86%)	2 (10%)	60 (86%)	40 (91%)	0.03
Transseptal puncture (*n, %*)	13 (10%)	16 (76%)	9 (13%)	2 (5%)	0.03
Ischemic SHD (*n, %*)	83 (33%)	15 (32%)	48 (42%)	20 (23%)	0.02
Non-SHD (*n, %*)	128 (51%)	20 (43%)	47 (41%)	61 (69%)	< 0.001
Non-ischemic SHD (*n, %*)	38 (15%)	12 (26%)	19 (17%)	7 (8%)	0.02
ICD (*n, %*)	108 (43%)	19 (40%)	63 (55%)	26 (30%)	0.001
FU time [IQR] (months)	25 [14 – 35]	19 [13 – 26]	25 [17 – 37]	29 [15 – 39]	< 0.001
OAC (*%*)	20%	17%	26%	15%	0.20
B-blockers (*%*)	54%	62%	55%	47%	0.24
Class I AAD (*%*)	14%	21%	12%	13%	0.27
Class III AAD (*%*)	40%	46%	47%	27%	0.01

AAD, antiarrhythmic drugs; FU, follow up; ICD, implantable cardioverter defibrillator; OAC, oral anticoagulation; OT, outflow tract; VES, ventricular extrasystole; SHD, structural heart disease.

We observed significantly more OT ablations in de CF group compared to the MAN group (P = 0.001). In comparison to the MAN population, the RMN and CF groups contained a higher number of repeat ablation procedures (P = 0.001). In the CF group non-ischemic

cardiomyopathy was more frequent the underlying substrate of VT compared to the RMN group (P = 0.022). VT without structural heart disease was more common in the RMN group (P < 0.001). There were more patients with an ischemic substrate in the MAN group (P = 0.015) and subsequently more ICD carriers (P = 0.001). Age, paediatric population, epicardial and VES ablations and medication at baseline – with the exception of class III antiarrhythmics – was equally distributed among the different groups.

Procedural outcome

Acute success was obtained in 75.9% of all procedures, there was a significant difference between the groups (P = 0.038). The difference was observed only in patients without structural heart disease (P = 0.010). The best procedural outcome was seen in the RMN group, which was 85.2%. There were no significant differences between manual and CF group, respectively 70.1 and 72.3% (Figure 1).

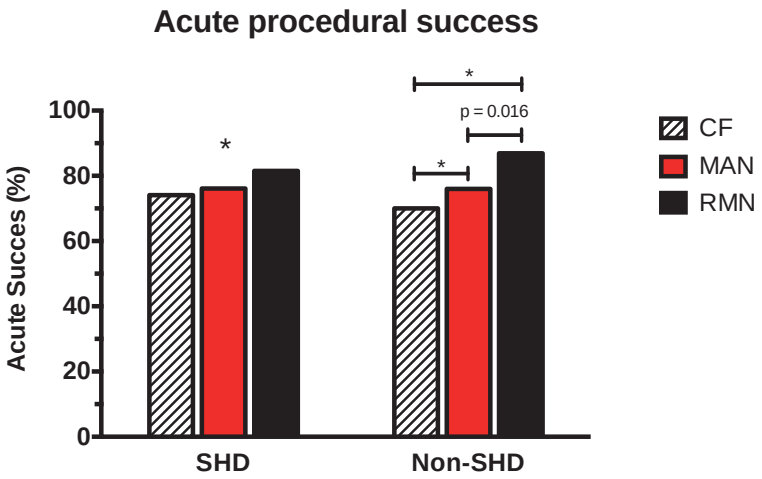

Figure 1: *Acute procedural success presented in percentages in the different groups for structural heart disease and non-structural heart disease. * P* = not significant.

Crossover occurred in two cases in the RMN group and in 5 cases in de CF group. One reason for switching to a manual catheter in a RMN procedure was safety, for the exit site of the VT was in the proximity of the conductions system. In the three CF patients who had a crossover, the reason was anatomical location for ablation (posterior fascicle, anterior crux

and side branch of the coronary sinus). Other reasons were ineffective ablation, damage to the catheter and in one patient RF energy was not tolerated. In 3 out of 6 CF ablations conversion of procedural technique changed the outcome of the procedure.

Complications

Major complications occurred in 3.2% of all procedures, and 0.5% of the major complications were acute. There were no significant differences between groups. We did observe a trend in more complications in the CF group (P = 0.062). Three out of 4 complications were due to the vascular access site and were not related to the contact force catheter itself. Major complications that occurred were arterial venous fistula requiring surgery and major bleeding. One patient in the manual group who underwent an endocardial ablation, had a pericardiocentesis for tamponade. One patient in the CF group died (not shown) within 48 hours of the procedure of refractory heart failure. In this patient the procedure was performed under left ventricular assist device (LVAD), which had been indicated for cardiogenic shock. The VT ablation was unsuccessful.

Recurrences

The median patient follow-up was 25 months [IQR 14-35] (Table 1). Thirty six percent of the patients with an initially successful procedure had a recurrence of ventricular arrhythmia on follow-up. The number of patients having a recurrence did not differ between CF and the other two approaches (Table 2). CF was not significantly superior or inferior in subgroups with structural heart disease or without structural heart disease. Median time to recurrence was 3.5 months [IQR 1.5 - 9.5] ranging from 1 day to 38 months. Time to therapy and number of therapy did not differ between groups (Figure 2).

Epicardial ablation

Eight of in total 10 epicardial ablations (not shown) had acute success. Acute success was achieved in 5 out of 5 procedures from the CF group, 2 out of 4 in the RMN group and in the 1 manual ablation. In total 2 complications occurred. One patient from the CF group suffered from a reactive pericarditis and in 1 patient from the RMN group had pericardial effusion that did not require intervention. There was 1 recurrence out of 10 procedures (10%), this concerned a CF procedure.

Table 2
Acute success, complications and recurrences for the CF, MAN and RMN groups

	Overall	CF	MAN	RMN	*P* value
Acute success	189 (76%)	34 (72%)	80 (70%)	75 (85%)	0.04
Structural heart disease	93 (77%)	20 (74%)	51 (76%)	22 (82%)	0.79
Non-structural heart disease	96 (75%)	14 (70%)	29 (76%)	53 (87%)	0.01
Complications	27 (11%)	9 (19%)	13 (11%)	5 (6%)	0.06
Major	8 (3%)	4 (9%)	3 (3%)	1 (1%)	0.06
Major acute	1 (1%)	1 (2%)	0 (0%)	0 (0%)	0.57
Major catheter ablation related	4 (2%)	1 (2%)	2 (2%)	1 (1%)	0.31
Major vascular access related	4 (2%)	3 (6%)	1 (1%)	0 (0%)	0.31
Minor	19 (8%)	5 (11%)	10 (9%)	4 (5%)	0.37
Recurrences	68 (36%)	14 (41%)	30 (38%)	24 (32%)	0.56
Structural heart disease	43 (46%)	10 (50%)	22 (43%)	11 (50%)	0.89
Non-structural heart disease	25 (26%)	4 (29%)	8 (28%)	13 (43%)	0.92
Time to recurrence (months) [IQR]	3.5 [1.5 – 9.5]	3.5 [1.5 – 5.5]	3 [0.5 – 6.5]	3.5 [1.5 – 13.5]	0.75

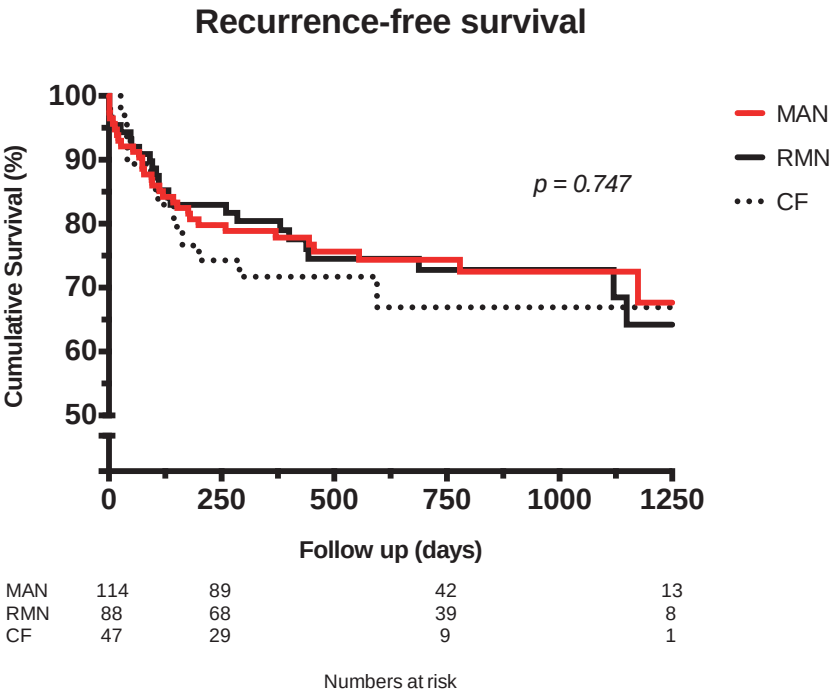

Figure 2: Kaplan-Meier curve illustrating the recurrence-free survival for the CF, RMN and MAN groups.

Multivariate analyses

The two groups were statistically heterogeneous for baseline variables. Multivariate analysis of baseline variables for outcome, acute success or recurrence did not identify significant differences.

Procedural related factors

Duration of the procedure was on average 180 [IQR 120 – 220] minutes and was not significantly shorter by using CF. The number of applications and total ablation time in CF were similar to those in the MAN and RMN group (Table 3). The median average procedural force in the CF group was 7.5 g [IQR 5 – 12.5], with a maximum of 16 g. Seven patients had mean ablation forces of 5 g or less. In 5 patients the maximum force was more than 25 g [IQR 12 – 25]. Among the CF study cases average force time integral (FTI) was 3759 gs [IQR 1493 – 10434]. In epicardial procedures the median average force was 6 g [IQR 5.5 – 12] and the maximum force 15 g [IQR 13 – 15.5]. The median total FTI in the epicardial group was 2105 gs [564 – 7012]. There was no significant difference between epicardial ablation compared to all CF ablations in procedural force, average en maximum and FTI.

Table 3
Procedural data for the CF, MAN and RMN groups. Data are presented as median with interquartile range.

	Overall	CF	MAN	RMN	*P* value
Procedural time (min)	180 [120 – 220]	180 [106 – 210]	185 [131 – 220]	150 [120 – 230]	0.39
Application number (*n*)	11.0 [5.0 – 23.3]	12.0 [5.8 – 18.3]	12.0 [6.0 – 33.0]	8.0 [4.0 – 20.8]	0.52
Application time (s)	480 [252 – 1140]	472 [229 – 760]	634 [278 – 1739]	407 [190 – 1095]	0.95

DISCUSSION

This is the first study that investigates the long-term clinical outcome in VT ablation using contact force catheters. In this VT cohort study contact force did not improve results in manual ablation in terms of complications, acute success and recurrence on follow-up. Magnetic navigation was superior in acute success and reduction of major complications.

Main findings

A wide range of acute success of VT ablation has been reported, varying from 41 - 99%.[12-16] One of the first prospective multicenter studies is reported in 2000.[15] Over time there has been a remarkable evolution of mapping and ablation techniques, also the indication for VT ablation has become wider. These are factors that possibly affect procedural success. In the present study patients were included as early as 2007 up to 2014 and calculated an average acute success rate of 75.9%. Other studies over the last years have reported a long-term

efficacy of VT ablation ranging from 27 – 49% during a follow-up of 8 – 48 months, comparable to the 36% recurrence rate in our cohort. Our group has previously shown a positive outcome on remote magnetic navigation VT ablation in structural heart disease.[9] With the current data contact force shows not to be superior to remote magnetic navigation or manual ablation.

Rationale for CF in VT ablation

The TOCCATA study was one of the first AF studies that showed clinical benefit of CF on clinical outcome.[4] Recently two clinical studies from Mizuno[7] and Titz[8] et al. studied CF in VT ablation and found that continuous information on contact force resulted in less inefficient or excessive lesion formation. The two studies however were limited in their number of cases (17 and 10, respectively) and lacked proof of clinical outcome. Our observations, did not confirm the extrapolated theoretical improvement of lesion formation into an improved long-term outcome or a better safety profile.

In general catheter force related complications in VT ablation such as perforation and tamponade are rare.[14,17] In comparison to the atria the ventricles and especially the left ventricle is a thick muscle in which perforation does not occur without excessive force.

Secondly, the lack of an integrated feedback loop in contact force ablation may be critical in the current results. An optimal endocardial lesion in an animal model needed a total force of 30-40 gram[6], substantially higher than the average and even maximum force in the present study. Despite being informed, the operator might not know how to interpret and integrate the given information. In the animal study of Sacher et al.[6] a dramatic decrease was observed in the number of RF applications that do not result in adequate lesion formation with the addition of CF information. An in vivo study of Mizino et al.[7] calculated the best cut-off value for contact force in ventricular ablation is at least 8 grams when compared to other parameters of lesion formation. Although CF sensing may be useful to prevent exertion of excess force on the myocardium, there is no consensus how CF sensing may be useful to guide the formation of effective lesions in VT ablation.

Remote magnetic navigation versus contact force

The average contact force in the current study is relatively low. However we also know that RMN does not provide high force.[18] Therefore it is unlikely to be the reason for the relatively low success. To note contact force has primarily been used as a safety tool not an efficacy tool. A possible explanation for the higher acute success in RMN guided VT ablation is enhanced maneuverability.[19,20] It has the ability to reach anatomical structures which are otherwise difficult to access. Also improved catheter stability in RMN is an important advantage.[21]

Force behavior during ventricular tachycardia

Low CF during ablation in atrial fibrillation has proven to be associated with a higher recurrence rate.[4,22] In contrast to the ablation of atrial arrhythmias the excursion of the ventricle during a VT ablation especially during tachycardia itself might lead to less stable catheter position. An unstable catheter position results in intermittent impaired energy delivery and subsequent inappropriate lesion formation. This might explain how the use of CF in atrial arrhythmia is well established, the benefit is not yet clear for VT ablations. Ideally catheter force sensing in the future can be integrated in robotic navigation as both entities could magnify the benefit of CF.[23]

Epicardial ablation and contact force

Our study shows an 80% acute success rate of epicardial ablation with only one recurrence. In current literature the success rate ranges from 70-100%.[24,25] The reported recurrence rate is 19 - 33%. Most epicardial procedures in this study were repeat procedures where a primary endocardial strategy has failed to succeed. By selecting the more complicated cases we have possibly introduced a bias. Nevertheless if successful, by approaching the arrhythmogenic substrate both endo- and epicardial long-term outcome is secured. The rate of major complications in epicardial ablation as described by Tung *et al*.[26] and Sacher *et al*.[27] is higher compared to our study. The present study was not powered to compare contact force in epicardial ablation to other methods.

Previous reports on contact force in epicardial VT ablation are only case reports.[28] A pathology study from Sacher *et al*.[6] has stated epicardial ablation to be associated with

larger lesions because of the absence of a heat sink effect of the circulating blood. They found a contact force less then 10 grams was enough to create a lesion. In our cohort study the average and maximum force was similar for endo- and epicardial ablation.

Limitations of the study

Although this study was able to provide data on follow-up from a substantial number of patients who underwent VT ablation, it was performed in a non-randomised fashion. The group studied was heterogeneous; also the indication for ablation varied from VES, idiopathic VT to scar related VT. Baseline characteristics significantly differed between groups but correcting for inequalities did not result in a different outcome. However to eliminate all possible bias randomised trials are required. For follow-up ICD interrogation was performed, that was available in a little less than half of the study population, thereby providing excellent accuracy for recurrence detection. In the other patients holter ECG and clinical events were used. The shortest duration of follow-up was 6 months. Follow-up was shorter in CF group, even so this did not result in less recurrences in the CF group.

CONCLUSION

This study shows remote magnetic navigation to be superior to CF in VT ablation in terms of acute success. The contact force sensing catheter did not improve the safety or alter outcome of VT ablation. There is insufficient knowledge how to use CF in VT ablation, for which we encourage more research.

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14

PART III

LESION FORMATION

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CHAPTER 15

Radiofrequency ablation at low irrigation flow rates using a novel 12-hole gold open-irrigation catheter

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ABSTRACT

Background

High irrigation rates during radiofrequency (RF) ablation may cause fluid overload and limit lesion size. This in vivo animal study assessed the safety and efficacy of RF ablation at low irrigation rates using a novel 12-hole gold catheter.

Methods

A total of 103 lesions, created on the thigh of five mongrel dogs, were analyzed. Lesions were created using a 12-hole irrigated gold-tip (Au) and a six-hole irrigated platinum–iridium (PtIr) catheter (both 7F/3.5-mm electrode; BIOTRONIK SE & CO, KG, Berlin, Germany) in parallel and perpendicular orientation. RF current was delivered for 60 seconds at 30 W using 8 mL/min and 15 mL/min irrigation. Electrode temperature, steam pops, lesion dimensions, and coagulum formation were recorded.

Results

Electrode temperatures were lower for Au compared to PtIr in parallel (8 mL/min: 38.1 ± 1.7°C vs 48.0 ± 4.8°C, $P < 0.0001$; 15 mL/min: 36.0 ± 1.5°C vs 46.9 ± 5.4°C, $P < 0.0001$) and perpendicular position (15 mL/min: 35.5 ± 1.2°C vs 38.4 ± 2.5°C, $P = 0.003$). The number of steam pops between Au and PtIr was comparable for parallel (8 mL/min: 14% vs 27%, $P = 0.65$; 15 mL/min: 14% vs 43%, $P = 0.21$) and perpendicular orientation (8 mL/min: 25% vs 17%, $P = 1.00$; 15 mL/min: 18% vs 0%, $P = 0.48$). Au created larger volumes than PtIr at 8 mL/min irrigation (861 ± 251 mm^3 vs 504 ± 212 mm^3, $P = 0.004$); however, for 15 mL/min, volumes were comparable (624 ± 269 mm^3 vs 768 ± 466 mm^3, $P = 0.46$). No coagulum formation was observed for any of the catheters on the surface and catheter tip.

Conclusion

RF ablation at low flow rate using a novel 12-hole irrigation Au catheter is safe and results in larger lesions than with a PtIr electrode.

INTRODUCTION

The introduction of irrigated-tip radiofrequency (RF) catheters increased efficacy of catheter ablation procedures.[1] It has theoretical advantages over nonirrigated-tip catheters and higher success rates have been demonstrated for many arrhythmias.[2-5] Several catheter designs are currently available with either a gold (Au)-tip electrode or a platinum–iridium (PtIr)-tip electrode. The irrigated Au-tip electrode has been well evaluated and allows for improved energy delivery at lower catheter-tip temperatures compared to irrigated PtIr-tip catheters.[6, 7]

Saline infusion during RF applications allows more energy delivery resulting in increased lesion volume and less coagulum formation.[8] Although high irrigation rates during RF catheter ablation ensures safety, it can be disadvantageous for patients with impaired left ventricular function. Amounts of 1,500–2,000 mL of saline infusion are not uncommon and due to fluid overload occurrence of heart failure or pulmonary edema during the procedure have been reported.[4,9]

The aim of this study was to evaluate the safety and efficacy of a novel 12-hole Au open-irrigation catheter for RF ablation at low irrigation flow rates. Our primary hypothesis was that a reduction in the irrigation flow rate for the Au-tip catheter as compared to typical flow rates for the standard ablation catheter does not compromise safety concerning thrombotic events and ablation effectiveness.

METHODS

Endpoints of the study

To test our hypothesis, the primary endpoint to assess this objective was the presence of coagulum on the tissue surface at the lesion location after completion of an RF application. In addition to this primary endpoint, a number of secondary endpoints were addressed, aimed at a comparison of additional safety characteristics and collection of data with respect

to the ablation performance of the novel 12-hole Au open-irrigation catheter and the six-hole PtIr ablation catheter. The following secondary endpoints were included: formation of coagulum and/or thrombus on the ablation electrode as a result of RF ablation, occurrence of steam pops, lesion dimensions, temperature of the catheter tip and electrode-tissue interface, delivered RF power during RF ablation, and impedance during RF ablation.

Description of the model

In this study a canine thigh muscle model has been used. This model was developed and first described by Nakagawa et al.[10] This study has been conducted according to good laboratory practice regulations at a certified laboratory. Five mongrel dogs were anesthetized with sodium pentobarbital (25 mg/kg) and either mechanically ventilated with room air or allowed to breathe spontaneously. General anesthesia was maintained with additional doses of sodium pentobarbital. The arterial pressure was continuously monitored by means of a right carotid artery cannulation. A skin incision was made and the skin edges were raised to create a cradle. The cradle was filled with blood (controlled 37°C, activated clotting time >350 seconds), which is exchanged at a rate of 250 mL/min, to mimic cardiac circulation. The ablation electrode was positioned in perpendicular or parallel orientation with respect to the muscle surface and held at a constant contact force of 10 g by use of a custom-made balance. Temperatures were measured by a fluoroptic temperature probe (Luxtron model STB, LumaSense Technologies, Santa Clara, CA, USA) immediately below the surface and as close as possible to the ablation catheter, as an approximation of the electrode–tissue interface temperature. All the temperatures were logged electronically. In addition, the data from the RF generator, including the programmed and actually delivered RF power, impedance, and electrode temperature, were electronically recorded (Fig. 1).

Ablation catheters

RF ablations were carried out using the AlCath Flux eXtra Gold catheter (BIOTRONIK SE &CO, KG, Berlin, Germany) as the test item and the AlCath Flux Full Circle Pt/Ir catheter (BIOTRONIK) as the reference item. Both catheters are 7F in diameter and have a 3.5-mm ablation tip electrode. The AlCath Flux eXtra Gold ablation catheter has a gold ablation electrode with a novel configuration of 12 irrigation holes (Fig. 2). The AlCath Flux Full Circle catheter has a platinum-iridium electrode with six irrigation holes.

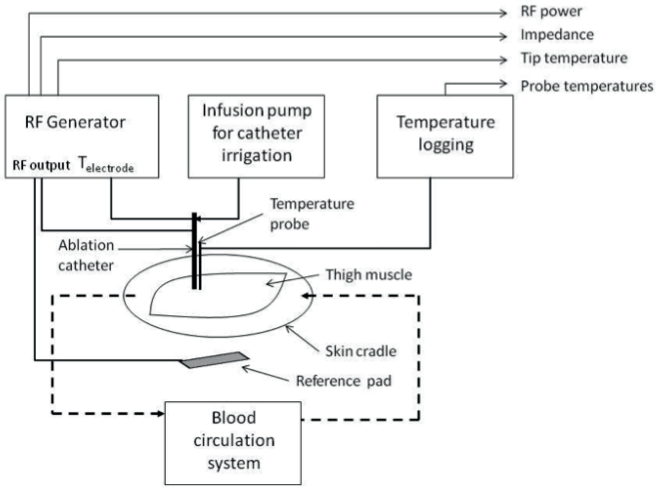

Figure 1: Schematic representation of the experimental setup. The reference pad is attached to the contralateral thigh.

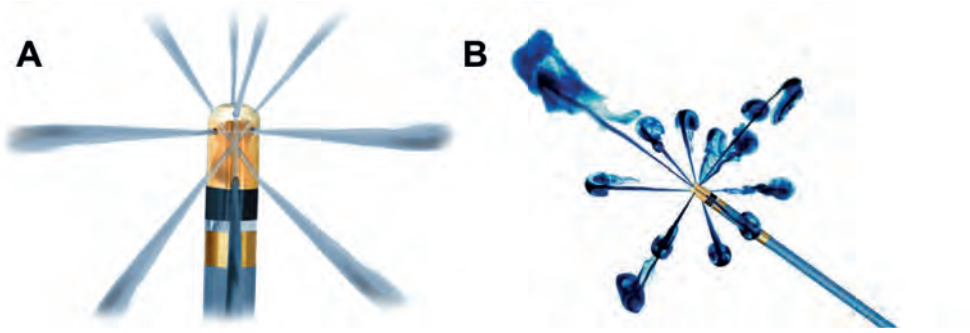

Figure 2: Image of the novel 12-hole Au open-irrigation catheter displaying the new design (panel A) that allows cooling in all directions of the catheter (panel B).

Ablation Protocol

Lesions were created with the ablation catheter oriented parallel and perpendicular to the muscle surface, an RF power of 30 W, and 8 mL/min and 15 mL/min irrigation flow rates. The ablation catheter was irrigated through the catheter lumen with heparinized (2 U/mL) normal saline at room temperature (20–22°C). Ablation settings (RF power, irrigation flow rate) and conditions (catheter type and electrode orientation) were applied in random order to avoid bias using the randomization function in an Excel® spreadsheet (v2010, Microsoft

Corp., Redmond, WA, USA). The randomization was carried out according to the following procedure: randomization of the electrode orientation (perpendicular or parallel), for each orientation the type of catheter was randomized, and for each combination of catheter type and electrode orientation the irrigation flow rate was randomized. For each lesion, RF energy was delivered for 60 seconds or until the first steam pop. The occurrence of steam pops was recorded and after each RF application, the muscle surface and the ablation electrode were visually inspected for the presence of thrombus and coagulum formation. Furthermore, the cradle was emptied and inspected for the presence of coagulum on the surface. The location of each lesion was documented to establish a cross-reference between the applied experimental settings and subsequent lesion processing and determination of lesion dimensions.

Tissue Staining and Conservation

Two hours after completion of the RF ablations at the left and right thigh muscle, 30 mL of 2% triphenyl tetrazolium chloride was administered intravenously as a staining, allowing identification of necrotic tissue and revealing the extent of the lesion (Fig. 3). After sacrificing the dog, the muscles were excised and fixated in formalin. Thigh muscle dimensions were determined before fixation to be able to correct for tissue shrinkage due to fixation. Following fixation, the lesions were sectioned and the lesion dimensions were determined as described by Lewalter et al.[11]

Lesion Dimensions

For each created lesion the following dimensions were determined: lesion depth (A), maximum lesion diameter (B), lesion depth at maximum diameter (C), and lesion diameter at surface (D). The lesion volume (Vlesion) was calculated using the following formula[12]:

$$\mathrm{V_{lesion}} = (1/6) * \pi * (\mathrm{A} * \mathrm{B}^2 + \mathrm{C} * \mathrm{D}^2/2).$$

Muscle dimensions before and after fixation by formalin, allowing for correction with respect to tissue shrinkage, were not obtained for all experiments. Therefore, uncorrected results, directly obtained from fixated muscle tissue, were used to calculate mean lesion

dimensions. For those experiments in which shrinkage due to fixation could be determined, muscle shrinkage was most frequently less than 5%.

Statistics

Continuous variables were expressed as mean ± standard deviation (SD) and compared with the Student's t-test for independent samples. Categorical data were expressed as percentages and compared with the χ2 test or Fisher's exact test when appropriate. Statistical analysis was performed using SPSS 15.0 (IBM Corp., Armonk, NY, USA). A P value of 0.05 was considered as statistically significant.

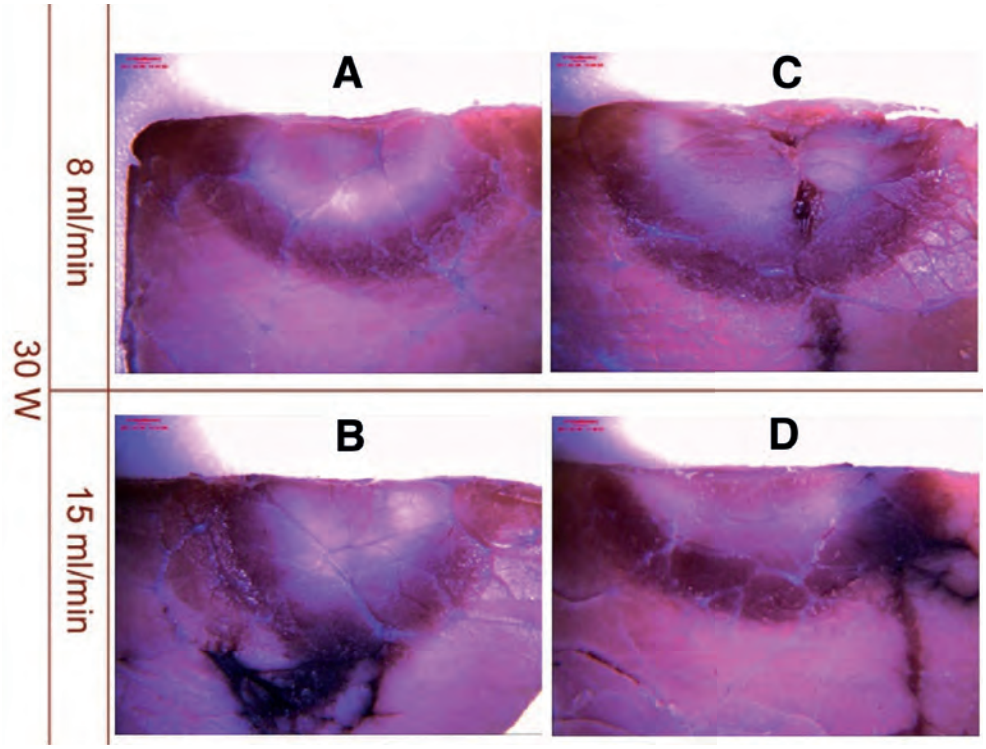

Figure 3: Macroscopic image of the fixated lesion tissues. Lesions were created using 30 W and either 8 mL/min or 15 mL/min irrigation. Lesions (*A*) and (*B*) represent lesions with a parallel catheter position, lesions (*C*) and (*D*) were created with perpendicular catheter orientation.

RESULTS

Lesion Overview

In total 106 lesions were created in five mongrel dog models. Three lesions were excluded from the analysis due to movement of the ablation catheter (n = 1) and inappropriate irrigation (n = 2). Data from the remaining 103 RF applications (51 Au and 52 PtIr electrodes) and resulting lesions were analyzed for the primary and secondary endpoints.

Primary Endpoint Analysis: Incidence of Coagulum on Tissue Surface

No coagulum formation on the tissue surface was observed for any of the 103 RF applications included in the analysis. Due to the absence of any coagulum formation for both catheters, the observed rate of coagulum formation was 0% for the Au-tip catheter as well as for the PtIr-tip catheter.

Secondary Endpoint Analysis: Incidence of Steam Pops

The occurrence of steam pops during RF application is summarized in Table 1. As indicated in Table 1, no significant difference was observed in the incidence of steam pops between both catheter types. With the electrode in parallel orientation, the Au electrode showed comparable number of steam pops as the PtIr electrode for both 8 mL/min (14% vs 27%, P = 0.65) and 15 mL/min irrigation (14% vs 43%, P = 0.21). Results were identical for lesions created in perpendicular orientation and no difference was found regarding steam pops for 8 mL/min (25% vs 17%, P = 1) and 15 mL/min irrigation flow rates (18% vs 0%, P = 0.48).

Delivered RF Power, Impedance, and Dynamic Temperature Profiles

For all ablations the protocol required the target RF power to be programmed to 30 W. The actually delivered RF power as recorded by the RF generator reached the target power within 2 seconds after RF onset and RF power was maintained at this level throughout the entire RF application for all ablations. The mean power output for all lesions during ablation was 29.5 ± 0.05 W. The mean impedance for the Au electrode was 90.1 ± 12.8 Ω and for the PtIr electrode 87.6 ± 10.4 Ω. The impedance drop during ablation was comparable for the Au and PtIr electrodes in both parallel (at 8 mL/min: 11.0 ± 4.2 Ω vs 11.0 ± 4.5 Ω, P = 1; at 15

mL/min: 11.5 ± 3.9 Ω vs 10.1 ± 3.9 Ω, P = 0.331) and perpendicular orientation (at 8 mL/min: 14.7 ± 10.5 Ω vs 12.7 ± 5.0 Ω, P = 0.578; at 15 mL/min: 12.5 ± 3.1 Ω vs 9.9 ± 4.3 Ω, P = 0.115).

Table 1
Incidence of steam pops

Orientation	Flow rate (mL/min)	Catheter	*N*	Steam pops	*P* value (Au vs. PtIr)
Parallel	8	Au	14	2 (14%)	0.65
		PtIr	15	4 (27%)	
	15	Au	14	2 (14%)	0.21
		PtIr	14	6 (43%)	
Perpendicular	8	Au	12	3 (25%)	1
		PtIr	12	2 (17%)	
	15	Au	11	2 (18%)	0.48
		PtIr	11	0 (0%)	

Au = 12-hole gold irrigation catheter; PtIr = six-hole platinum-iridium irrigation catheter.

Table 2 presents the mean temperatures during RF application for each combination of electrode orientation, irrigation flow rate, and type of ablation catheter. Except for the perpendicular orientation and an irrigation flow rate of 8 mL/min, the Au-tip ablation catheter was associated with a significantly lower electrode temperature than the PtIr-tip catheter. This observation was done for the peak temperature reached during ablation, as well as for the averaged temperature. Temperatures also tended to be lower for the Au electrode in perpendicular orientation and a flow rate of 8 mL/min, but differences did not reach statistical significance. The tissue-interface temperature for the Au-tip catheter was comparable to the PtIr-tip catheter for parallel (at 8 mL/min: 51.5 ± 21.4°C vs 50.7 ± 19.4°C, P = 0.923; at 15 mL/min: 47.7 ± 14.1°C vs 54.2 ± 16.7°C, P = 0.266) and perpendicular orientations (at 8 mL/min: 55.0 ± 16.2°C vs 54.8 ± 15.8°C, P = 0.974; at 15 mL/min 59.2 ± 27.3°C vs 53.9 ± 21.0°C, P = 0.607) independent of irrigation flow rates. Figure 4 shows the electrode temperature curves for different catheter positions and irrigation flow rates.

Secondary Endpoint Analysis: Coagulum Formation on Electrode

For none of the 103 RF ablations included in the analysis, coagulum was observed on the electrode after RF application. As a result, the rate of coagulum formation is 0% for both the Au catheter and the PtIr catheter.

Table 2
Electrode temperatures during radiofrequency applications

Orientation	Flow rate (mL/min)	Catheter	*N*	Peak temperature during ablation		Averaged temperature during ablation	
				(°C) ± SD	*P* value	(°C) ± SD	*P* value
Parallel	8	Au	14	39.39 ± 1.88	<0.0001	38.07 ± 1.65	<0.0001
		PtIr	15	53.77 ± 8.07		48.02 ± 4.81	
	15	Au	14	37.34 ± 2.51	<0.0001	35.96 ± 1.50	<0.0001
		PtIr	14	50.15 ± 6.49		46.93 ± 5.43	
Perpendicular	8	Au	12	42.11 ± 8.92	0.21	39.89 ± 5.81	0.15
		PtIr	12	46.69 ± 8.41		43.82 ± 6.96	
	15	Au	11	36.68 ± 1.00	0.005	35.55 ± 1.22	0.004
		PtIr	11	40.99 ± 4.32		38.41 ± 2.50	

Au = 12-hole gold irrigation catheter; PtIr = six-hole platinum-iridium irrigation catheter; SD = standard deviation.

Secondary Endpoint Analysis: Lesion Dimensions

Mean values for lesion dimensions including only lesions created without steam pop are presented in Table 3 and Figure 5. The use of a 12-hole Au catheter was associated with greater lesion volumes as compared to PtIr catheters in parallel position at a flow rate of 8 mL/min (861 ± 251 mm^3 vs 504 ± 212 mm^3, P = 0.004). For perpendicular catheter orientations at 8 mL/min irrigation, the Au catheter produced larger lesions; however, this did not meet statistical significance (908 ± 285 mm^3 vs 629 ± 280 mm^3, P = 0.07). At a 15 mL/min flow rate, lesion volumes were comparable for Au and PtIr in both parallel and perpendicular position (624 ± 269 mm^3 vs 768 ± 466 mm^3, P = 0.46; 949 ± 284 mm^3 vs 805 ± 226 mm^3, P = 0.29, respectively).

For lesions created in parallel orientation using the PtIr electrode, the amount of irrigation (8 mL/min or 15 mL/min) did not influence the lesion volumes (504 ± 212 mm^3 vs 768 ± 466 mm^3, P = 0.157). The same results were achieved for PtIr electrode in a perpendicular orientation (629 ± 280 mm^3 vs 805 ± 226 mm^3, P = 0.255). For the Au electrode, lesions with 8 mL/min or 15 mL/min irrigation in parallel orientation (861 ± 251 mm^3 vs 624 ± 269 mm^3, P = 0.072) and perpendicular orientation (908 ± 285 mm^3 vs 949 ± 284 mm^3, P = 0.791) had comparable volumes as well.

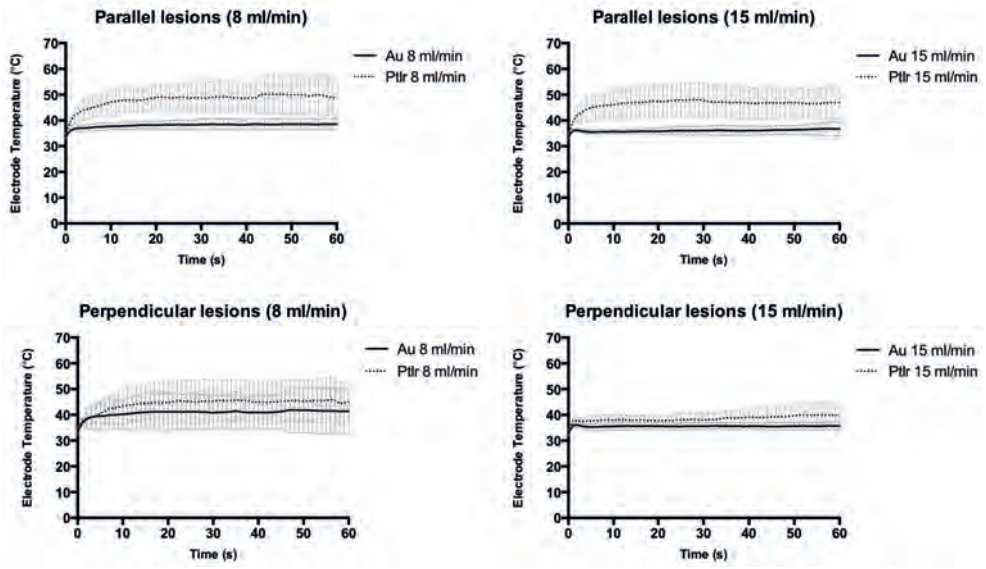

Figure 4: Integrated mean electrode temperature curves in function of time for Au- and PtIr-tip catheters. Different curves are plotted for catheter orientation (parallel or perpendicular) and amount of saline infusion (8 mL/min or 15 mL/min). the curves are plotted in mean ± standard deviation (SD) values for both catheters.

Table 3
Mean lesion dimensions ± standard deviation (SD) (ablations with steam pops excluded)

Orientation	Flow rate (mL/min)	Catheter	No histo*	*N*	Depth (mm)	Max. diameter (mm)	Volume (mm^3)	*P* value (volume)
Parallel	8	Au	2	10	9.30 ± 1.96	12.75 ± 1.78	861 ± 251	0.004
		PtIr	2	9	7.72 ± 1.48	10.28 ± 1.70	504 ± 212	
	15	Au	4	8	7.63 ± 1.62	11.44 ± 2.67	624 ± 269	0.46
		PtIr	0	8	8.50 ± 2.17	11.88 ± 3.06	768 ± 466	
Perpendicular	8	Au	2	7	8.43 ± 0.93	13.64 ± 1.95	908 ± 285	0.07
		PtIr	1	9	7.61 ± 1.96	11.78 ± 2.69	629 ± 280	
	15	Au	2	7	9.93 ± 1.57	12.93 ± 1.86	949 ± 284	0.29
		PtIr	2	9	8.83 ± 1.37	12.67 ± 1.64	805 ± 226	

* Lesions for which no histology data (lesion dimensions) were available because the lesion was not identifiable in the muscle preparation (after exclusion of steam pop lesions).
Au = 12-hole gold irrigation catheter; PtIr = six-hole platinum-iridium irrigation catheter.

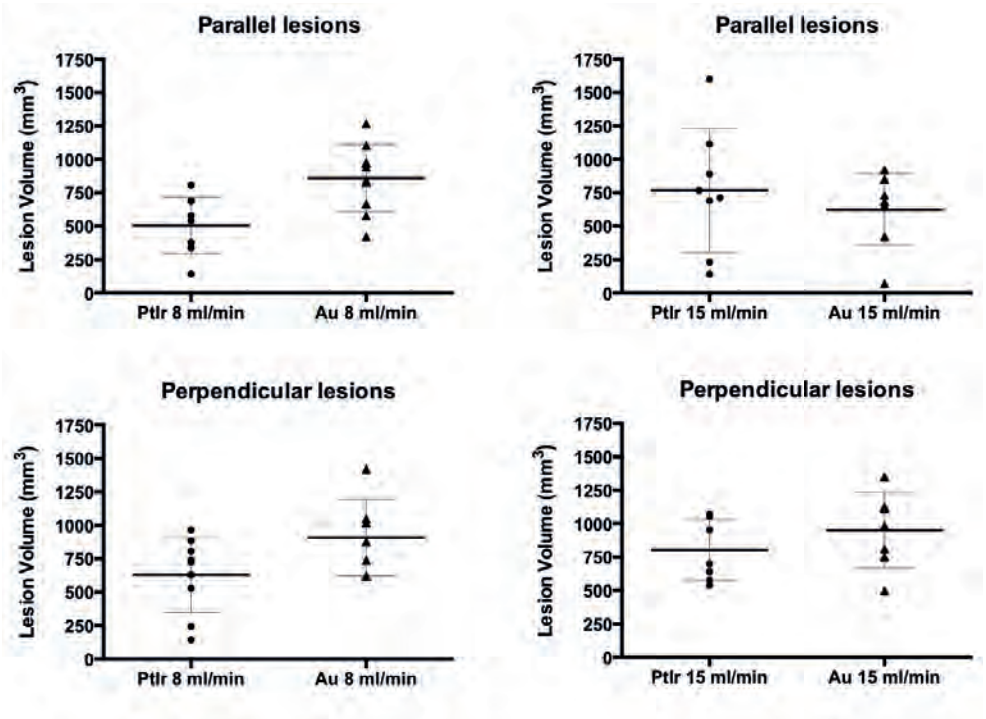

Figure 5: Lesion volumes for different catheter orientations and amount of saline insufion. Each symbol represents one lesion. Values are plotted in mean ± standard deviation for both catheters.

DISCUSSION

In this study we assessed the safety and efficacy of a novel 12-hole Au open-irrigation catheter for RF ablation at low irrigation flow rates compared to a six-hole PtIr ablation catheter at standard irrigation flow rates. The primary endpoint was the presence of coagulum on the tissue surface at the lesion location after completion of an RF application. The major finding of this study is that the Au electrode is comparable to the PtIr electrode since no coagulum was observed on the tissue interface after any of the RF application for both catheters. As a result, our data are in support of the hypothesis that using the Au electrode with 12 irrigation holes, RF ablation at low flow rates is safe and results in larger lesions than using a PtIr electrode.

Coagulum Formation

Coagulum formation on the tissue as a result of RF application was studied by Matsudaira et al.,[13] using temperature-controlled RF application in canine thigh muscle model, similar to the model used during this study. Experiments were performed with the electrode oriented perpendicularly to the muscle and application of a 10-g contact force. For a 4-mm nonirrigated ablation electrode, without blood flow in the cradle, and a target electrode temperature of 75°C, coagulum was found in 90% of the RF applications. At an electrode temperature of 65°C and no blood flow, coagulum formation was not observed. The authors suggest that "thrombus" formation is temperature related, possibly due to denaturation of blood proteins. As they also measured the electrode–tissue interface, they conclude that coagulation occurs at interface temperatures well below 100°C. Electrode temperatures measured during the study were generally lower than reported by Matsudaira et al., which may explain the complete absence of coagulum formation in these experiments. Other aspects that may have prevented coagulation include a higher blood circulation in the cradle (250 mL/min vs 150 mL/min) and a possible "washing" effect from the irrigation flow.

Occurrence of Steam Pops

Steam pops occurred in 21 (19.8%) of the 106 ablations performed in these experiments. In 12 occasions, the electrode temperature averaged over the ablation at which a steam pop occurred exceeded the mean electrode temperature for the corresponding setting (electrode type, orientation, and flow rate). Although the averaged electrode temperature during ablation was usually below 50°C, peak values frequently reached temperatures up to 80°C. It cannot be excluded that coagulum formation occurred in these cases, as the destructive process of a steam pop may have destroyed the histological evidence. Furthermore, in this thigh muscle setting the applied force with the ablation catheter is very stable and provides a much better constant wall contact than within the human heart due to heart beating and respiratory movements.

No significant differences were found between the Au and PtIr electrodes with respect to the incidence of steam pops. The mean lesion volume in parallel orientation using 8 mL/min irrigation was significantly larger with the Au electrode compared to the PtIr electrode. In perpendicular orientation at an irrigation flow rate of 8 mL/min, the lesions tended to be

larger using the Au electrode as well, but this difference was not statistically significant. However, it appears to be that the differences in the conductive properties of the metal and the novel catheter design are more pronounced using lower irrigation flow rates. Furthermore, the mean electrode temperatures during ablation were consistently lower for the Au catheter. The temperature differences were significant for all settings except for a perpendicular electrode orientation and a flow rate of 8 mL/min.

Limitations

The results of this study demonstrate the feasibility of using a novel 12-hole Au-irrigated tip catheter at reduced irrigation rates. However, these results could be a result of the natural conductive properties of gold instead of the novel catheter design. In order to really elucidate the effect of the novel irrigation system, further comparative studies are required using a six-hole Au-tip catheter.

In this study, ablation was performed using 30 W power for a duration of 60 seconds. The study was designed in a way to acquire sufficient data per ablation setting to draw valid and accurate conclusions. It remains unclear if coagulum formation would occur using 40 W or 50 W during different time periods. Therefore, more data are required to answer the question whether RF ablation at low irrigation flow rates is safe using high-power settings. Furthermore, during this study we aimed to compare a novel 12-hole irrigated-tip catheter with an industry standard catheter. Currently the six-hole-irrigated tip is no longer the industry standard catheter. Therefore, this study cannot be extended to apply to newer PtIr catheter designs.

These data are acquired using an animal model. Although this model mimics the conditions in the human heart as much as possible, the contact force and stability will influence the ablation results. In clinical situations the stiffness of the catheter may result in different ablation results than acquired during this study in an experimental setup. During these experiments, lesions were created with a fixed contact force where catheter stiffness did not influence the results. Therefore, further clinical investigation is needed to reveal the true value of this new 12-hole Au irrigated-tip catheter in everyday practice.

CONCLUSION

In conclusion, the data obtained during this study demonstrate that the novel 12-hole Au tip ablation catheter allows reduction of the irrigation flow rate compared to the PtIr catheter without compromising safety. Compared to the six-hole PtIr-tip catheter, the Au electrode achieves similar ablation effectiveness at lower electrode temperatures. For patients with an impaired left ventricular function in which fluid overload is a matter of concern this novel Au tip catheter could be valuable.

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CHAPTER 16

High-volume lesions using a new second-generation open irrigation radiofrequency catheter are associated with the development of inhomogeneous lesions

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ABSTRACT

Background

After catheter ablation there is often a discrepancy between acute and chronic success rates. We aimed to evaluate major determinants for lesion quality and understand different manifestations of lesion structures.

Methods and Results

In a canine thigh muscle model radiofrequency (RF) current was delivered for 60 seconds at 30 W (n = 39) or 50 W (n = 18) with 15-g contact force. A second-generation 12-hole gold open irrigation catheter (SGIT) and a first-generation six-hole platinum-iridium catheter (FGIT; Biotronik, Berlin, Germany) were used. Electrode and tissue temperatures (at the surface and 3.5-mm and 7-mm depth) were recorded and lesion dimensions were measured. Lesions with steam pops were excluded. Histological examination was performed to evaluate homogeneity of the lesions. Inhomogeneity was defined as a visual multiband lesion pattern indicating different histological characteristics. In total 57 lesions were created. Seventeen lesions were excluded (steam pops) and 40 lesions were analyzed. A total number of 11 homogeneous and 29 inhomogeneous lesions were identified. Using the SGIT catheter 16.7% of the lesions was homogeneous and 83.3% inhomogeneous; for FGIT it was 43.8% and 56.2% (P = 0.065), respectively. Homogeneous lesions had lower volumes as compared to inhomogeneous lesions (514.0 ± 198.8 vs 914.8 ± 399.1 mm^3, P = 0.003). Multiple logistic regression analysis indicated that the SGIT catheter is a significant predictor for inhomogeneous lesions (odds ratio 6.5, 95% confidence interval 1.1–38.8; P = 0.040) independent from power setting and flow rate.

Conclusions

The development of inhomogeneous lesions after acute RF ablation is associated with higher lesion volumes and the use of the second-generation irrigation gold-tip catheter.

INTRODUCTION

The use of irrigated-tip radiofrequency (RF) catheters is a well-established therapeutic option that is implemented in everyday catheter ablation procedures.[1] It has been demonstrated that it increases efficacy of catheter ablation procedures and allows for increased energy delivery and higher lesion volumes.[2] Several catheter designs are currently available using either a gold (Au)-tip or a platinum iridium (PtIr)-tip electrode. Multiple studies have compared these irrigated-tip RF catheters and evaluated several parameters such as catheter temperatures and lesion volumes.[3-5] The irrigated Au-tip electrode has been well evaluated, which allows for improved energy delivery at lower catheter-tip temperatures as compared to irrigated PtIr-tip catheters.[6,7] However, about the new-generation 12-holes RF irrigation catheter only limited data are available.[8] Previous studies on open irrigation RF ablation catheters focused on created lesion volumes by using the same formula, which was the basis of the comparison.[9] For multipolar ablation catheters even lesion continuity was studied,[10] but prior studies never meticulously evaluated the structure of the lesions.

Energy delivery of the ablation catheter is dependent on multiple factors such as contact force, irrigation flow rate, power output, ablation time, ablated tissue characteristics, catheter tip orientation, and the type of metal from which the catheter tip is manufactured.[11] These individual factors influence the efficacy of energy delivery to the tissue and therefore contribute to lesion formation and lesion quality. Different conducting properties of the ablation catheter and different amounts of absorbed energy by the tissue might lead to different macroscopic and microscopic manifestations of the lesion (coagulation necrosis and reactive degeneration with interstitial edema). This could effect chronic lesion development. Our aim was to assess which characteristics can play a role as major determinants for lesion quality and to understand the different manifestations of lesion structures. Furthermore, we aimed to evaluate whether the use of a first-generation (FGIT) and second-generation (SGIT) irrigated-tip RF catheter has effect on the development of lesion size and structures. Our primary hypothesis was that the use of different irrigation

catheters (first- and second-generation) would result in different lesion sizes and macroscopic and microscopic lesion characteristics.

METHODS

Description of the Model

In this study, a canine thigh muscle model has been used. This model was developed and first described by Nakagawa and colleagues.[12] This study has been conducted according to good laboratory practice regulations in a certified laboratory. Three mongrel dogs were anesthetized with sodium pentobarbital (25 mg/kg) and either mechanically ventilated with room air or allowed to breathe spontaneously. General anesthesia is maintained with additional doses of sodium pentobarbital. The arterial pressure is continuously monitored by means of a right carotid artery cannulation. A skin incision was made and the skin edges were raised to create a cradle. The cradle was filled with blood (controlled 37°C, activated clotting time > 350 seconds), which is exchanged at a rate of 250 mL/min, to mimic cardiac circulation. The ablation electrode was positioned in perpendicular or parallel orientation with respect to the muscle surface and held at a constant contact force of 15 g by use of a custom-made balance. This amount of contact force was applied, since this value represents the average amount of contact force that is applied mostly by operators during pulmonary vein isolation (PVI) and is therefore a clinically relevant value.[13]

Temperatures were measured by fluoroptic temperature probes (Luxtron model STB, Santa Clara, CA, USA) immediately below the surface and as close as possible to the ablation catheter, as an approximation of the electrode-tissue interface temperature, and at 3.5 mm and 7 mm below the muscle surface. All the temperatures were logged electronically and the maximum and mean temperatures were recorded. Additionally, the data from the RF generator, including the programmed and actually delivered RF power, impedance, and electrode temperature, were electronically recorded (Fig. 1, Chapter 15).

Ablation Catheters

RF ablations were carried out using either the (SGIT) AlCath Flux eXtra Gold catheter (Biotronik, Berlin, Germany) or the (FGIT) AlCath Flux Full Circle Pt/Ir catheter (Biotronik). Both catheters are 7F in diameter and have a 3.5-mm ablation-tip electrode. The SGIT ablation catheter has an Au ablation electrode with a novel configuration of 12 irrigation holes (Fig. 2). The FGIT catheter has a platinum-iridium electrode with six irrigation holes.

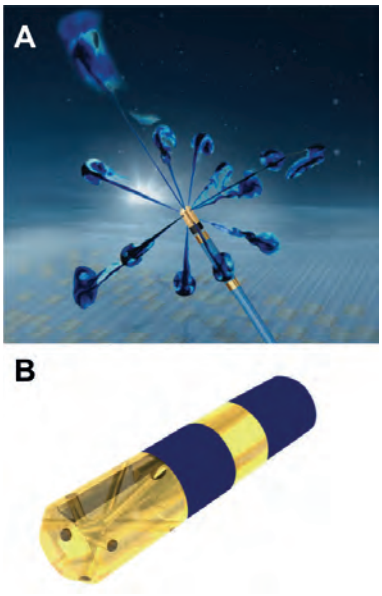

Figure 2: Catheter design. Image of the novel 12-hole Au open-irrigation catheter displaying the irrigation directions (*A*) and the new catheter design (*B*).

Ablation Protocol

Lesions were created with the ablation catheter oriented parallel and perpendicular to the muscle surface; an RF power of 30 W and 50 W; and 8 mL/min, 15 mL/min, and 30 mL/min irrigation flow rates. The ablation catheters were irrigated through the catheter lumen with heparinized (2 U/mL) normal saline at room temperature (20–22°C). Ablation settings (RF power, irrigation flow rate) and conditions (catheter type and electrode orientation) were applied in random order to avoid bias using the randomization function in an Excel® spreadsheet (v2010 Microsoft Corp., Redmond, WA, USA). The randomization was carried out according to the following procedure: randomization of the power output and the electrode orientation (perpendicular or parallel); for each orientation the type of catheter was randomized, and for each combination of catheter type and electrode orientation the irrigation flow rate was randomized. For each lesion, RF energy was delivered for 60 seconds or until the first steam pop. The occurrence of steam pops was recorded and these lesions were excluded from histological assessment since it could affect lesion dimensions and macro- and microscopic characteristics of the tissue.

Tissue Staining and Conservation

Two hours after completion of the RF ablations at the left and right thigh muscle, 30 mL of 2% triphenyl tetrazolium chloride was administered intravenously as a staining allowing macroscopic visualization of necrotic tissue and revealing the extent of the lesion (Fig. 3). After sacrificing the dog, thigh muscle dimensions were determined before fixation to correct tissue shrinkage due to fixation. Following formaldehyde fixation, the lesions were sliced into 1- to 2-mm-thin slices and the lesion dimensions were determined as described by Lewalter and colleagues.[14] Afterwards, the muscle slices were embedded into paraffin and sections were prepared and stained according to the phosphotungstic acid-hematoxylin (PTAH) method to demonstrate muscle structure. This allowed microscopic evaluation of the lesions (Figs. 4 and 5).

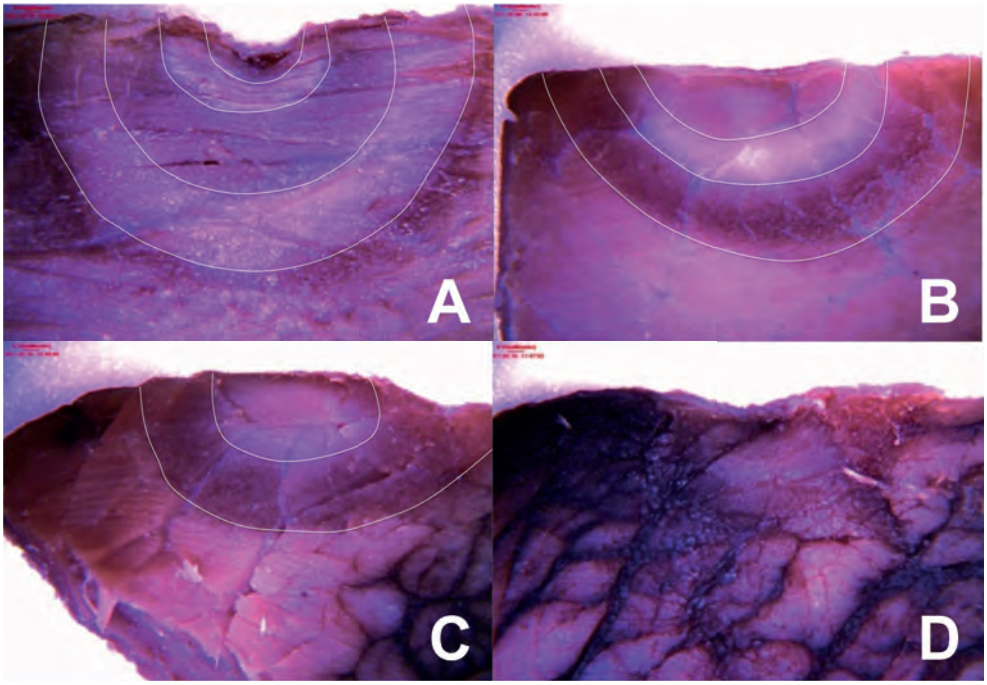

Figure 3: Macroscopic image of the fixated lesion tissues. Lesion *A* illustrates a lesion with four macroscopic bands, lesion *B* demonstrates three bands, lesion *C* has two macroscopic bands, and during creation of lesion *D* steam pop occurred.

Lesion Dimensions

For each created lesion, the following dimensions were determined histologically: lesion depth (A), maximum lesion diameter (B), lesion depth at maximum diameter (C), and lesion diameter at surface (D). The lesion volume (Vlesion) was calculated using the following formula[9]:

$$V_{lesion} = (1/6) \times \pi \times \left(A \times B^2 + C \times D^2/2\right).$$

Muscle dimensions before and after fixation by formalin, allowing for correction with respect to tissue shrinkage, were not obtained for all experiments. Therefore, uncorrected results, directly obtained from fixated muscle tissue, were used to calculate mean lesion dimensions. For those experiments in which shrinkage due to fixation could be determined, muscle shrinkage was most frequently less than 5%.

Lesion Quality Assessment

After staining the tissue, macroscopic and histological examination of the lesions were performed. The macroscopic examination allowed evaluation of the homogeneity of the RF lesions. This was determined by assessing the number of different colored bands that were visible in the lesion, indicating different histological characteristics (Figs. 4 and 5). These macroscopic classifications were confirmed histologically. A homogenous lesion was defined as an RF lesion in which a maximum of two different colored bands were observed. Inhomogeneous lesions were lesions with a pattern of more than two visual bands. Two authors (F.A. and T.S.T.) independently classified the lesions according to the amount of visible bands. In case of a discrepant classification, this lesion was re-evaluated to gain a consensus opinion. Between the homogenous and inhomogeneous lesions analyses were performed to determine in what extend catheter type, irrigation flow rate, catheter orientation, and power settings are responsible for the different lesion formation.

Statistics

Normality of distribution was determined by using the Kolmogorov-Smirnov test. Continuous variables were expressed as mean ± standard deviation, if normally distributed, and compared with the Student's t-test for independent samples. In case of nonnormal distribution of data, medians and interquartile ranges (IQRs) were reported and the Mann-

Whitney U test was used for data comparison. Categorical data were expressed as percentages and compared with the $\chi 2$ test or Fisher's exact test when appropriate. Univariate analyses were performed for all variables and odds ratios (ORs) and 95% confidence intervals (95% CIs) were determined. All variables with $P < 0.150$ in the univariate analysis (due to the limited sample size) were entered into a multivariate logistic regression model. ORs, 95% CIs, and P-values were calculated. Because of the observational nature of the study, power calculation to prove statistical significant differences has not been performed. Statistical analysis was performed using SPSS 15.0 (IBM Corp., Armonk, NY, USA). Statistical significance was defined as $P < 0.05$ (two-tailed).

RESULTS

Lesion Overview

Using the mongrel dog model, 57 lesions were created. Seventeen out of 57 lesions were not further analyzed due to the occurrence of steam pops. In 23.5% of the cases the steam pop occurred using the SGIT catheter and in 76.5% the FGIT catheter was used (OR 0.2, 95% CI 0.1–0.7; P = 0.012). No differences were found between the SGIT and FGIT catheter for power and flow rate setting (50.0 ± 0.0 vs 43.9 ± 9.6 W, P = 0.230; 15.0 ± 0.0 vs 16.9 ± 8.1 mL/min, P = 0.660, respectively). In total, 40 lesions were further analyzed in this study.

Homogeneous and Inhomogeneous Lesions

Eleven lesions (27.5%) were classified as a homogenous lesion and 29 lesions (72.5%) had an inhomogeneous aspect. In total, one lesion had a single visual band (2.5%), 10 lesions had two bands (25.0%), 26 lesions had three bands (65.0%), and three lesions had four bands (7.5%). In Table I the distribution of catheter type, orientation, power output, and flow rate is displayed between the homogeneous and inhomogeneous group. For all these variables, an equal distribution was observed between the two groups (Table I). Using the SGIT catheter 16.7% of the lesions was homogeneous and 83.3% was inhomogeneous (OR 0.3, 95% CI 0.1–1.1; P = 0.065). The FGIT catheter created in 43.8% homogeneous lesions and in 56.2% inhomogeneous lesions were formed (OR 3.9, 95% CI 0.9–16.7; P = 0.065). The

median number of colored bands in the homogeneous group was 2 (IQR [2–2]) and 3 (IQR [3–3]) bands were evident in the inhomogeneous group ($P < 0.001$).

Histological Tissue Assessment

Histological evaluation demonstrated clearly a central area of the lesions, which stains light pinkish using PTAH staining and illustrates coagulation necrosis (Fig. 5). Between the central area and the intact muscle, there is a reactive zone, with mild damaged muscle tissue, hypercontraction, interstitial edema, and slightly decreased staining. Intact muscle tissue stained blue-purple and was visible either at the border of the lesion or between the central coagulation necrosis and reactive zone (Fig. 4).

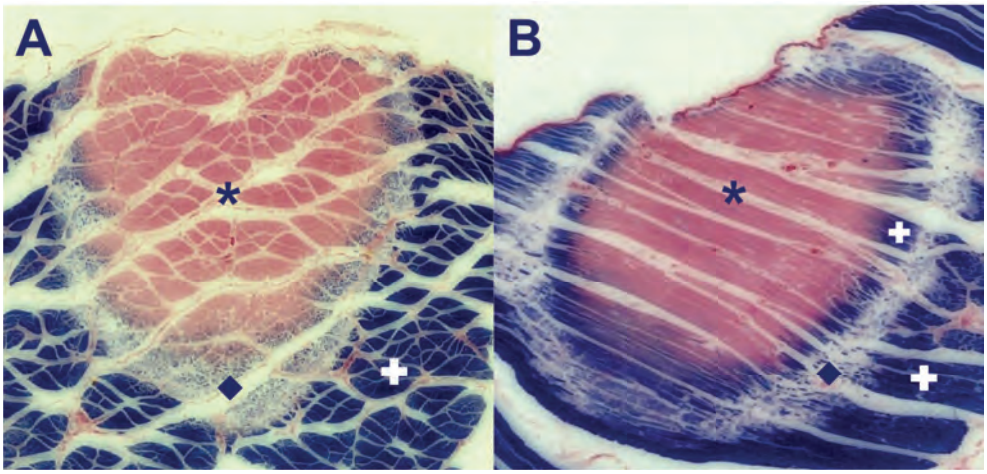

Figure 4: Two histological phosphotungstic acid-hematoxylin (PTAH)-stained pictures of the lesions illustrating different microscopic bands. (A) Overview of a lesion with two lesion bands. (*B*) Overview of a lesion with three lesion bands. * Central coagulation necrosis; ♦ Reactive zone with hypercontraction, interstitial edema and degenerative reaction of the muscle cells. + Intact muscle.

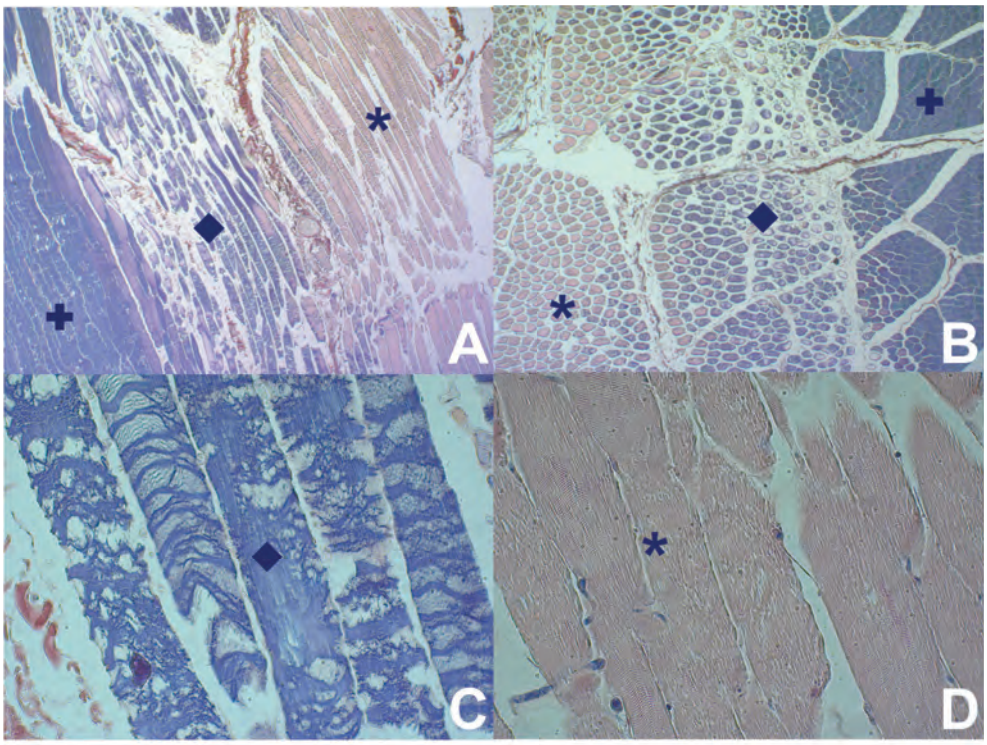

Figure 5: Histological illustrations of the lesions using phosphotungstic acid-hematoxylin (PTAH) staining. (*A*) Overview of the lesion border (magnification 4x, longitudinal section). (*B*) Overview of the lesion border (magnification 4x, cross-section). (*C*) Border zone of the lesion (magnification 40x). (*D*) Central coagulation necrosis (magnification 40x). * Central coagulation necrosis; ♦ Reactive zone with hypercontraction, interstitial edema and degenerative reaction of the muscle cells. + Intact muscle.

Lesion Dimensions, Temperatures, and Power Delivery

In Table II the lesion dimensions and recorded data during ablation are presented. Homogeneous lesions were less deep and had a smaller maximum lesion diameter as compared to inhomogeneous lesions (6.2 ± 1.5 vs 7.9 ± 1.4 mm, P = 0.003; 12.3 ± 1.8 vs 14.2 ± 2.1, P = 0.011, respectively). This resulted in significantly lower lesion volumes for homogeneous lesions (514.0 ± 198.8 vs 914.8 ± 399.1 mm^3, P = 0.003). The SGIT catheter is associated with larger lesion volumes as compared to the FGIT catheter (912.8 ± 438.6 vs 624.2 ± 234.7 mm^3, P = 0.025). In Figure 6 the mean lesion volumes for each number of observed bands is illustrated. No differences were observed for the mean and maximum electrode, interface, and tissue temperatures between the homogeneous and

inhomogeneous group (Table II). However, there is a trend that inhomogeneous lesions occur more frequently using the 30 W power setting than with the 50 W power output but this could not be demonstrated with statistical significance (77.1% vs 40.0%, P = 0.117).

Table 1
Distribution of ablation settings

Variable	Homogeneous Lesion	*N*	Inhomogeneous Lesion	*N*	Total	OR	95% CI	*P* value
Au † catheter	16.7%	4	83.3%	20	24	0.3	0.1 – 1.1	0.065
PtIr ‡ catheter	43.8%	7	56.2%	9	16	3.9	0.9 – 16.7	
Parallel orientation	31.6%	6	68.4%	13	19	1.5	0.4 – 6.0	0.422
Perpendicular orientation	23.8%	5	76.2%	16	21	0.8	0.2 – 3.4	
Power 30 W	22.9%	8	77.1%	27	35	0.2	0.0 – 1.4	0.117
Power 50 W	60.0%	3	40.0%	2	5	5.1	0.7 – 35.8	
Flow rate 8 mL/min	12.5%	2	87.5%	14	16	0.2	0.0 – 1.3	0.083
Flow rate 15 mL/min	36.4%	8	63.6%	14	22	2.9	0.6 – 13.0	0.151
Flow rate 30 mL/min	50.0%	1	50.0%	1	2	2.8	0.2 – 49.1	0.479

† Gold, ‡ Platinum-iridium
The data are presented as percentage, odds ratio (OR), 95% confidence interval (CI) and *P* value.

Table 2
Lesion dimensions and recorded data during ablation

Variable	Homogeneous Lesion	Inhomogeneous Lesion	*P* value
Lesion depth (mm)	6.2 ± 1.5	7.9 ± 1.4	0.003
Maximum lesion diameter (mm)	12.3 ± 1.8	14.2 ± 2.1	0.011
Lesion depth at maximum diameter (mm)	0.0 [0.0 – 0.0]	0.0 [0.0 – 3.3]	0.218
Lesion diameter at surface (mm)	11.6 ± 2.0	13.0 ± 2.5	0.116
Volume (mm^3)	514.0 ± 198.8	914.8 ± 399.1	0.003
Mean $T_{electrode}$ (°C)	39.8 ± 7.1	39.7 ± 6.2	0.988
Mean $T_{interface}$ (°C)	46.6 [39.1 – 61.8]	44.7 [38.9 – 57.9]	0.720
Mean $T_{3.5\ mm}$ (°C)	40.9 [36.7 – 44.4]	39.3 [38.0 – 45.6]	0.788
Mean $T_{7.0\ mm}$ (°C)	41.3 [36.7 – 42.3]	38.8 [36.2 – 42.0]	0.591
Maximum $T_{electrode}$ (°C)	41.7 [37.8 – 46.0]	38.6 [37.1 – 48.1]	0.570
Maximum $T_{interface}$ (°C)	61.0 ± 21.1	57.8 ± 17.9	0.638
Maximum $T_{3.5\ mm}$ (°C)	46.2 [37.8 – 49.9]	44.1 [39.1 – 52.9]	0.765
Maximum $T_{7.0\ mm}$ (°C)	49.0 ± 18.2	44.0 ± 7.3	0.216
Mean Power Delivery (W)	34.7 ± 8.9	30.1 ± 3.7	0.024
Mean Impedance (Ω)	84.6 ± 8.6	84.4 ± 6.3	0.922

The data are presented in mean ± standard deviation or median (interquartile range) and *P* value

Multiple Logistic Regression Model

Multiple logistic regression analysis was performed to determine independent predictors for inhomogeneous lesion formation. Catheter type, power setting, and 8 mL/min flow rate

setting were entered into the model since univariate analysis showed a P-value <0.150. The results indicate that the use of the SGIT catheter (OR 6.5, 95% CI 1.1–38.8; P = 0.040) is a statistically significant predictor for inhomogeneous lesion formation independent from power setting (OR 0.1, 95% CI 0.0–1.5; P = 0.107) and flow rate (OR 3.1, 95% CI 0.5–20.5; P = 0.235).

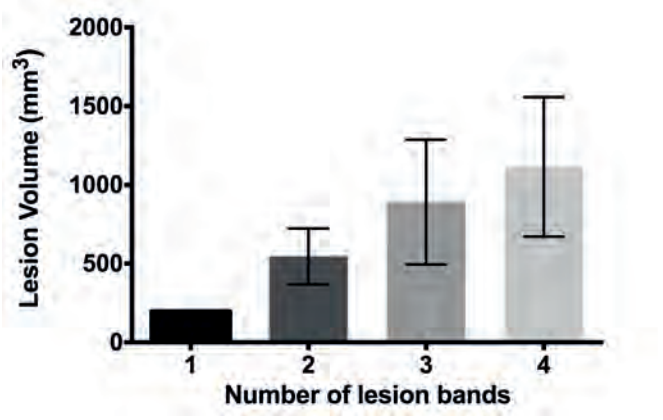

Figure 6: Lesion volumes presented for each number of observed bands. The mean values ± standard deviation of the lesion volumes are presented. Four categories of bands were observed: lesions with one band (n = 1), two bands (n = 10), three bands (n = 26), and four bands (n = 3).

DISCUSSION

The main findings of this study are (1) that inhomogeneous lesions are frequent entities that occur often with RF catheter ablation, (2) the occurrence of inhomogeneous lesions is associated with higher lesion volumes and is not related to tissue temperature, and (3) the use of the second-generation irrigated Au-tip catheter is an independent predictor for inhomogeneous lesion development.

Inhomogeneous Lesions

Lesion structures with a visible multiband pattern, which indicated an inhomogeneous lesion structure, are more prone to occur with the SGIT catheter. Using multiple logistic regression

we demonstrated that the use of this new catheter, independent from power output and irrigation flow rate, is associated with a higher incidence of inhomogeneous lesion development. An important question arises: what are the possible underlying mechanisms of these findings, since multiple factors are important determinants for lesion formation and could contribute to these results? Contact force of the catheter with the tissue, irrigation, power output, and catheter design (including irrigation design and metal type) are important factors that influence lesion development.[11] Weiss and colleagues[15] demonstrated that irrigation has important effects on lesion formation. The use of irrigation allows operators to safely prolong ablation time and increase power output to create higher lesion volumes.[12] Another factor that influences lesion formation is the type of metal from the catheter tip. Lewalter and colleagues[14] compared Au and PtIr nonirrigated-tip catheters and found that the Au-tip electrode is associated with deeper lesions, which is in line with our findings. The increased lesion volumes using Au-tip electrode are thought to be related to the superior thermal conductive properties of the metal as compared to PtIr. The thermoconductivity of Au is four times better than of the PtIr alloy. This allows improved and more efficient energy delivery to the tissue and therefore larger lesions.[4]

However, the manifestation of inhomogeneous lesions could not be attributed to one aspect alone. A theory in which multiple determinants of lesion formation are involved could provide an answer about the existence of homogeneous and inhomogeneous lesion structures. The SGIT catheter, with its novel irrigation design, allows for better cooling of the surrounding tissue and therefore less temperature increase.[12] The additional proximal irrigation holes of the SGIT catheter may lead to more homogeneous tissue cooling over a larger area in a parallel orientation specifically. However, with perpendicular catheter orientation, the proximal holes of the SGIT catheter reduce saline flow out of the distal holes and consequently tissue cooling can be reduced as compared to FGIT. Furthermore, the amount of saline irrigation determines the amount of cooling at the tissue surface. Nakagawa et al.[12] described competing effects of heating from the underlying tissue with the cooling from the saline irrigation. This eventually leads to lesion development several millimeters below the surface instead of the thin layer of myocardium surrounding the catheter. The differences in irrigation efficacy between the two catheter types could lead to lesion formation at different depths in the tissue. This “indirect” heating and the differences

in “direct” heating at the muscle surface due to the novel catheter design could lead an inhomogeneous lesion structure as has been described in this study. When these factors of the SGIT catheter are combined (improved irrigation and superior thermoconductivity), it will lead eventually to higher lesion volumes that are created under lower temperature conditions. This could possibly explain our observations of lesion structures with a multiband pattern indicating different histological characteristics.

This hypothesis on the development of inhomogeneous lesions is also supported by our findings on the mean delivered power. As our results demonstrate, the total delivered power to the tissue is significantly lower for inhomogeneous lesions as compared to homogeneous lesions, although the volume of the inhomogeneous lesions is significantly higher. As a result, a lower total amount of energy is delivered into the tissue and therefore it may create less necrotic tissue and more inhomogeneous lesions.

Clinical Implications

Previous in vitro studies on new developed ablation catheters focused on lesion volumes as a definition of catheter efficacy, which was the basis of the comparison with other catheters. In other studies, where the most ideal ablation setting was investigated for clinical practice, the focus was on lesion dimensions. It seems that previous research on the basis of catheter ablation defined lesion dimensions as the primary endpoint rather than lesion quality. Certainly, lesion volumes are very important for everyday practice, in particularly for linear ablation. However, the structure of the lesion could provide information about lesion quality in the long term.

Badger and colleagues[16] studied the correlation between the amount of atrial scar and the success of initial and repeat atrial fibrillation ablation procedures. Their results demonstrate a discrepancy between the acute ablation endpoint of PVI and the amount of complete circumferential scarring after 3 months (6.9% of patients). Their conclusion is that it is a difficult task to achieve long-lasting PVI, even with acute successful isolation. Furthermore, they demonstrated that differences in lesion morphology (scar patterns) could be observed during follow-up using delayed-enhancement magnetic resonance imaging.[17] The underlying mechanism of this acute and long-term difference could be determined by lesion quality and

consistency. As our results demonstrate, there is a possibility of two types of acute lesion development with either a homogeneous or inhomogeneous structure. Our results demonstrate that SGIT catheters are associated with both larger and more inhomogeneous lesions. FGIT catheters provide more homogeneous and smaller lesions. Inhomogeneous lesions are related to significantly lower delivered power and we observed a tendency that it occurs more often using 30 W power output. This difference in lesion structure after acute RF ablation could have important impact on the quality and development of chronic lesions and can theoretically be responsible for the differences between acute and chronic ablation success rates. The data of Badger and colleagues[17] provide indirect proof that RF lesion structures change over time and eventually result in a final scar. Our paper provides direct proof that there are differences in the histological composition of RF lesions. However, at this moment it remains unknown which combination will result in better chronic lesions. Therefore, based on our results, further evaluation is needed using a chronic model to clarify the effect of inhomogeneous lesion development.

Limitations

Based on the results of this study, some parameters showed a trend to be related to inhomogeneous lesion development, although statistical difference was not significant. An example is the distribution of homogeneous and inhomogeneous lesions for the SGIT catheter using univariate analysis. This might be related to the power of this study. Probably, statistical analysis would reach significant difference if more lesions would be included in this study. Besides, a proportion of the lesions was excluded from analysis due to the occurrence of steam pops. The unequal distribution of steam pops between the FGIT and SGIT group could interfere with the comparison of lesion volume. Due to the nature of this study, which first was a safety evaluation of the novel SGIT catheter, no sample size calculation was performed for this study. However, multivariate logistic regression analysis was performed to deal with this issue.

Based on the results it can be concluded that the SGIT catheter is a significant predictor for inhomogeneous lesion formation. However, it remains unknown whether this was caused by the new irrigation design or the metal from the catheter. At the time of this study this could not be investigated due to unavailability of certain catheters. Therefore, further evaluation

of a 12-hole irrigation PtIr- and a six-hole Au-tip catheter is needed to really clarify the underlying element, which causes inhomogeneous lesions. Furthermore, because we found these surprising results regarding lesion structure, only two catheter types were compared in this study. It would be beneficial to compare multiple catheter types in order to better understand the underlying mechanisms of inhomogeneous lesion development. Besides, one contact force level was used during this study. Although this is a clinically relevant value, it would be interesting to evaluate the impact of different contact force values on lesion structure and quality.

In our study a canine thigh muscle preparation has been used to perform RF lesions. One of the advantages of this model is the flat surface of the muscle tissue. This allowed us to accurately determine lesion dimensions and continuously record tissue temperatures at different depths. However, in the trabeculated and beating endocardium, lesion formation might not be equal compared to our experiments. To really elucidate the clinical effects of different ablation catheters on lesion homogeneity these experiments should be conducted in a beating heart model as well. Furthermore, we evaluated morphological differences of lesions after RF catheter ablation. In order to increase the predictive clinical value, functional evaluation of the lesions would be valuable, as been performed by Datino et al. regarding the use of adenosine to evaluate pulmonary vein dormant conduction in an experimental setup.[18]

CONCLUSION

Inhomogeneous lesion developments are frequent manifestations after acute RF catheter ablation. The occurrence of inhomogeneous lesions is associated with higher lesion volumes. Furthermore, the use of an SGIT Au-tip catheter is an independent predictor for inhomogeneous lesion formation. Further studies using a chronic model are needed to evaluate the development of different lesion structures in the long term.

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CHAPTER 17

Summary and Future Perspectives

Since the beginning of invasive electrophysiology it developed very fast during the last decades.[1, 2] Arrhythmia mechanisms are better understood, new ablation techniques are invented, advanced mapping systems are developed, and better catheters are introduced. All these developments are based on at least one of the following fundamental principles: to improve safety, efficacy, efficiency and reproducibility of ablation procedures. In this thesis new developments in the field of invasive electrophysiology are studied and discussed. The aim of this work is to find strategies to optimize safety and efficacy of catheter ablation procedures. The most important developments that are studied in this thesis are the magnetic navigation system, the use of contact force sensing catheters and the introduction of new gold-tip ablation catheters.

PART I – ROBOTICS

In Part I of this thesis we discussed the use of the first available magnetic navigation system (MNS). The MNS is an advanced system using magnetic fields to manipulate the ablation catheter within the heart.[3, 4] Two external magnets are located on either side of the patient and generate a magnetic field strength of 0.08 or 0.1 T within the patient. The position of these magnets can be altered leading to different magnetic vectors. As the ablation catheter is very floppy and incorporates small magnets at the distal tip, it will align according to the magnetic vector. Therefore, by changing the magnetic vectors the ablation catheter can be maneuvered without any limitations. Since this system has enhanced maneuverability with an atraumatic catheter it is thought to provide benefits regarding safety and efficacy of ablation procedures compared to conventional ablation catheters.

In **Chapter 1** we studied the use of the MNS in a large cohort of patient including different arrhythmias arising from all four heart chambers. We were the first group to study the efficacy and safety of ablation using MNS and manual ablations in a large cohort. Overall, we observed that the MNS was associated with less major complications compared to conventional strategies. As we know from previous studies, catheter manipulation and ablation is accompanied by the risk of pericardial effusion and tamponade.[5, 6] In our series of patients no pericardial effusion or tamponade was observed in the MNS group, whereas for manual ablation this was the most occurring major complication. The design of the MNS could be held responsible for the significant reduction of complications. These findings were also confirmed by studies from other international research groups.[7-12] Furthermore, we

observed that the MNS is associated with less procedural fluoroscopy use. Due to the atraumatic catheter tip, continuous fluoroscopy to determine the position of the catheter is redundant and catheter manipulation can be performed using three-dimensional anatomical maps. Concerning acute procedural success, MNS was overall equally effective compared to manual ablation. For ventricular tachycardia (VT) ablation a higher acute success rate was observed using MNS. However, in further chapters we evaluated this more thorough.

In **Chapter 2** we studied the outcomes of MNS procedures for repeat catheter ablation for atrial fibrillation (AF), supraventricular tachycardia (SVT) and VT procedures. We compared the MNS with manual ablation and analyzed the procedures considering the technique that has been used during the initial procedure. Independent of the initial ablation technique, our findings suggest that MNS does not increase acute success rates for repeat catheter ablation. For repeat SVT and AF ablation MNS prolonged procedure times with an average of 30 and 60 minutes, respectively. However, when acute success was achieved the effect sustained over time, which was reflected by the 15% lower overall recurrence rate for MNS procedures. Therefore, it may be considered as an alternative technique for repeat catheter ablation although it has the potential to prolong procedure times.

In **Chapter 3** an overview of the literature is provided for the MNS in the treatment of atrial fibrillation. International surveys showed that the risk of cardiac tamponade is 1 – 1.5 % using manual catheter manipulation, even in experienced centers.[6, 13, 14] The MNS demonstrated to offer benefits regarding procedural safety and catheter-induced perforation. Early reports on the MNS in AF using non-irrigated ablation catheters describe char formation at the catheter tip after LA ablation.[9, 15] After the introduction of the first- and subsequently the second-generation irrigated MNS catheters the problem was solved and no tip charring and related embolic events occurred.[16] After evaluating the available literature, no major complications were reported which were directly related to the MNS. Concerning procedural efficacy, success rates for pulmonary vein isolation using MNS are comparable with conventional techniques, although it is related to longer procedure times. Lüthje et al. found that procedures lasted 35-60 minutes longer using the MNS, without a clear learning curve for procedure duration.[17] This could be explained by the separate actions of changing the magnetic vector, the movements of the two external magnets and

subsequently the catheter movement. This increases navigation time and thus procedure and ablation duration.

In **Chapter 4** we studied the ablation of longstanding persistent atrial fibrillation (LSP-AF). For paroxysmal atrial fibrillation electrical pulmonary veins isolation (PVI) is an accepted and often successful treatment.[18-20] However, the efficacy of PVI for LSP-AF is poor with single procedure drug-free success around 20%.[21, 22] Additional creation of ablation lines proved to increase procedural success rates.[23, 24] Other techniques, such as atrial defragmentation, has been proposed to increase the success rate of LSP-AF ablation as well.[25, 26] During this procedure electrogram-based ablation is performed targeting specific areas in the atrial substrate, showing complex fractionated atrial electrograms. In this chapter we studied the use of complete defragmentation using MNS in addition to conventional PVI and linear ablation. The major finding was that defragmentation for the ablation of LSP-AF after PVI and linear ablation is associated with a higher number of minor complications and more time-consuming procedures. After 12 months of follow-up no differences in freedom of AF were observed. Therefore, our data suggest that complete defragmentation therapy for LSP-AF compromises procedural efficiency without improving long-term efficacy.

Chapter 5 describes a new ablation strategy for the treatment of slow-fast atrioventricular nodal reentrant tachycardia (AVNRT). Conventional techniques require the insertion of several diagnostic catheters into the heart.[27] In this chapter we describe that a single-catheter approach using the MNS is a feasible technique with shorter procedures and less radiation exposure for both patient and physician as compared to conventional techniques. The high maneuverable ablation catheter allows accuracy up to 1 mm or 1 degree. As long as the magnetic field is applied, the catheter will remain at the desired location, irrespective of deep breaths or during accelerated junctional rhythm. This characteristic of the MNS is particularly important if mapping and ablation needs to be performed in small regions such as the triangle of Koch and in direct proximity of the compact AV node and His bundle. Because of these advantages permanent heart block could be avoided in all patients. Additionally, different locations could be stored in the MNS workstation and exact re-navigation was accomplished by reapplying these vectors.[28] This feature of the MNS allowed making the diagnosis of AVNRT quickly and with the use of a single catheter. The overall procedure time was reduced by 52% to an average of 83 minutes

in comparison to previous reported results and with 29% to conventional RF in this study.[29] Catheter stability, enhanced navigation capabilities and tagging of the His on fluoroscopy all contributed to the safety and efficacy of this procedure.

From the literature, and supported by our own data, ablation of AVNRT is a highly successful therapy.[30-32] However, some patients have documentation of SVT suggestive of AVNRT but fail to demonstrate the induction of AVNRT during the electrophysiology study. Empiric slow pathway ablation (ESPA) as a plausible option in these patients, even in the absence of proven AVNRT, can be considered.[33] The practice of ESPA is common (± 5–10% of SVT cases), but very few studies have reported on the efficacy of ESPA.[34] In **Chapter 6** we report that ESPA is effective in eliminating SVT recurrence in patients with documented tachycardia which is noninducible at the time of the procedure. We demonstrated that the pre-procedure ECG documentation of SVT, in particular short RP tachycardia, has a powerful role in predicting long-term clinical success of ESPA.

In this thesis the use of MNS for ablation of VT has been discussed. In **Chapter 7** we present a systematic review of the literature for MNS guided VT ablation. The available data indicate that MNS is used to achieve successful outcomes in various patient populations and VT subtypes with low complication rates. Patients with structurally normal hearts have the best outcomes in comparison to ischemic or non-ischemic cardiomyopathy patients. However, due to the very limited amount of published data, more knowledge on MNS guided VT ablation was required. In **Chapter 8** we presented the first large-scale study on MNS VT ablation involving statistically equivalent groups and including both idiopathic and scar-related VTs. The major finding of this study is that MNS was found to have a higher rate of acute success for catheter ablation of idiopathic VT, while for patients with scar-related VT the success rate was equal as conventional ablation. Furthermore, this advantage remained apparent during the follow-up, as fewer recurrences occurred in the MNS group compared to the MAN group.

Improvements in surgical techniques for young patients with congenital heart disease (CHD) resulted in significant life prolongation. As these patients reach adulthood, they become high susceptible to late complications associated with the reparative surgery, such as cardiac arrhythmias.[35, 36] These might originate from either the myocardial substrate owing to the abnormal physiology or the presence of surgical scars. Catheter ablation is increasingly recognized as curative treatment for these, often complex, arrhythmias.[37]

Because the anatomy of the heart is different from the normal cardiac anatomy, it can be difficult to localize and reach the origin of the tachycardia. In **Chapter 9** we studied the use of MNS for catheter ablation of arrhythmias in CHD patients. Conventional catheters are often limited by the pre-defined curve of the catheter.[38] Our study showed that with the MNS a retrograde approach is very well possible and baffle punctures could be avoided during the procedure. It demonstrated to be safe without the occurrence of major complications. Our data reflect the advantages of the MNS for catheter ablation in complex anatomy without compromising outcome data. It is a feasible method to treat arrhythmias in CHD patients with high success rates that sustains well on the long term.

Correct diagnosis of the arrhythmia in CHD patients can be a major challenge for the electrophysiologist.[39] The surgical scars and the progression of the underlying disease can hinder the diagnosis for atrial tachycardias (ATs).[40-42] In structural normal hearts a distinction could be made between focal ATs and macro-reentrant ATs based on the total atrial activation time (TAAT) and the cycle length (CL) of the arrhythmia.[43, 44] Each of these arrhythmias has a different ablation strategy. The rate between these two values (TAAT/CL) is an important predictor to determine the etiology. According to the literature, a TAAT/CL ratio below 40% strongly suggests a focal activation pattern, a ratio above 40% a macroreentrant tachycardia.[43] However, since the diseased myocardium in CHD patients can influence conduction speed, the predictive value of the TAAT/CL ratio could be questioned. In **Chapter 10** our data demonstrate that 66.7% of the CHD patients with focal AT would be misdiagnosed based on this value. We found that the feasibility of these diagnostic parameters is related to the mean bipolar signal amplitude (BiSA) values. To allow correct differentiation between focal and macroreentrant AT in CHD patients, a mean BiSA of at least 0.90 mV is required. In case of low mean BiSA values, further diagnostic tests are needed to determine the correct mechanism of the AT. Therefore, our study demonstrates that mean BiSA values should be integrated into the diagnostics to establish correct diagnoses and improve procedural outcome.

PART II – CONTACT FORCE SENSING

In Part II of this thesis the use of contact force sensing catheters is studied. The success of catheter ablation procedures depends on accurate substrate localization, followed by optimal delivery of energy provided by good tissue contact.[45] It remains clear that the

patient's safety has the highest priority during catheter ablation. However, there is always a risk of cardiac perforation leading to hemodynamical instability.[46] One of the major determinants for cardiac perforation is the force of the catheter with the myocardium.[47] Previously the amount of pressure was only based on tactile feedback of the operator, and surrogate parameters such as movement of the catheter tip on fluoroscopy, ST elevation in the unipolar electrogram and impedance monitoring.[48, 49] However it seemed that these parameters were a poor predictor for the actual contact force. Previous studies showed that, even with experienced operators, often dangerous forces are applied during catheter manipulation based on tactile feedback.[46] Recently a new catheter was introduced that could measure the contact force directly at the catheter tip.[50] In **Chapter 11** we compared procedural safety between this contact force (CF) catheter, the MNS system and conventional techniques. Furthermore, we found that major complications occurred in 2.8% of the procedures with a cardiac perforation rate of 0.9%. We observed that CF catheters could reduce the risk of cardiac perforation compared to conventional ablation catheters, particularly in patients with AF. Our data demonstrate that using CF catheters procedural complications could be avoided leading to complication rates equal to MNS procedures.

CF guided procedures do not only have possible benefits regarding safety, but it plays a major role in procedural efficacy. It is known that CF is an important determinant of lesion formation to create effective lesions and reduce arrhythmia recurrence.[51-53] In this thesis we studied the role of CF sensing catheter for VT ablation. In **Chapter 12** we describe the initial experience of CF guided ablation during epicardial VT ablation. Radiofrequency (RF) catheter ablation in the epicardial space is substantially different from endocardial ablation. First of all, there is the absence of circulating blood in the epicardium and therefore lack of convective cooling during ablation; the catheter orientation is usually different, and the varying presence of epicardial adipose tissue interferes with lesion formation.[52] These factors all have significant influence on RF lesion formation and should be taken into account during epicardial VT ablation. We present two cases of epicardial ablation in patients with ARVC where CF catheters were used during mapping and ablation. Technical challenges, such as calibration of the CF catheter, were described in this chapter.

Endocardial VT ablation using CF catheters is presented in **Chapter 13**. We compared manual ablation, magnetic ablation and CF guided VT ablation. In our study CF ablation did not improve safety or efficacy of VT ablation. However, we recognize that there is

insufficient knowledge on the use of CF in VT ablation, for which we encourage more research.

PART III – LESION FORMATION

The introduction of the irrigated-tip RF catheter was a great improvement for invasive electrophysiology and increased success rates for many arrhythmias compared to nonirrigated-tip catheters.[54-57] Several types of catheters are currently available, mostly using a platinum-iridium (PtIr)- or gold (Au)-tip electrode with six irrigation holes. The irrigated Au-tip electrode allows for improved energy delivery at lower catheter-tip temperatures compared to irrigated PtIr-tip catheters.[58] However, a lot of saline infusion is often used during ablation, which could limit lesion size and sometimes even fluid overload in patients with impaired ventricular function. In **Chapter 14** we assessed the safety and efficacy of a novel 12-hole Au open-irrigation catheter for RF ablation at low irrigation flow rates compared to a conventional catheter (six-hole PtIr) at standard irrigation flow rates. Our data demonstrate that the Au electrode with 12 irrigation holes is safe for RF ablation at low irrigation flow rates. During ablation no coagulum was observed on the tissue interface after any of the RF application. Furthermore, during low flow settings the Au electrode with 12 irrigation holes creates larger lesions with lower electrode temperatures than the PtIr electrode. However, despite these promising results further clinical investigation is needed to reveal the true value of this new 12-hole Au irrigated-tip catheter in everyday practice.

Energy delivery of the ablation catheter is dependent on multiple factors such as contact force, irrigation flow rate, power output, ablation time, ablated tissue characteristics, catheter tip orientation, and the type of metal from which the catheter tip is manufactured.[45] These individual factors influence the efficacy of energy delivery to the tissue and therefore contribute to lesion formation and lesion quality. However, in clinical studies there is often a discrepancy between acute and chronic success rates.[59] Obviously, patients can develop a new arrhythmogenic substrate that leads to recurrent arrhythmias, but an inappropriate development of a chronic ablation lesion is also a possibility that explains this discrepancy. In **Chapter 15** we histologically compared two types of catheters to understand the different manifestations of lesion structures and to investigate major determinants for lesion formation. Histologically the ablation lesion has distinctive zones, including a part of central coagulum necrosis and a reactive zone with interstitial edema.

However, the structure of the lesion is not consistent for all ablation lesions and we found that inhomogeneous lesions are frequent entities that occur often with RF catheter ablation. We observed that the occurrence of inhomogeneous lesions is associated with higher lesion volumes and is not related to tissue temperature. Furthermore, the use of an Au-tip catheter with 12 irrigation holes is an independent predictor for inhomogeneous lesion development. At this moment it remains unknown which lesion will result in better chronic lesions and what the ideal settings are to improve chronic procedural success. However, the answer on the difference between acute and chronic success may be in the histological differences of the lesions. Therefore, this approach for lesion assessment should be used for further studies rather than just comparing lesion volume. Hopefully, future studies will present us the optimal ablation settings to improve procedural outcome.

FUTURE PERSPECTIVES

In this thesis new developments in the field of invasive electrophysiology are discussed to optimize safety and efficacy of catheter ablation procedures. Electrophysiology is a highly developing field and lot of issues still need to be improved or even discovered. As this thesis demonstrated, robotic catheter ablation has important benefits regarding safety and efficacy of procedures. However important issues still needs to be addressed. It is important to realize that robotics in catheter ablation would make sense only if they will address the most important challenges in clinical cardiac electrophysiology. These challenges include inefficient workflow, enormous interoperator differences, serious safety issues and suboptimal efficacy. In the future robotic technology will further develop leading to a more efficient and fully remote workflow. Secondly, we realize that contact force sensing catheters will be increasingly used during ablation procedures. A lot of research is currently ongoing to understand the value of contact force feedback during procedures and its effect on safety and efficacy of the ablations. Currently, the ideal amount of contact force for each region of the heart is unknown. This will certainly follow in the near future. Hopefully, the progresses with CF sensing catheters will eventually lead to the introduction of CF sensing MNS catheters. This would combine two very important techniques and will absolutely lead to better and safer ablation procedures. The increasing awareness of lesion formation using CF catheters will be combined with progressive knowledge on lesion formation, especially on the histological level. Future research should not only focus on lesion dimensions, but should

evaluate the structure of the lesion and its effect on chronic lesion formation. We believe that this could significantly improve chronic success rates. Furthermore, we hope that we will achieve a gaining understanding of the etiology of complex arrhythmias and strategies to perform ablation at sites that are inaccessible with current techniques (e.g. sites close to the coronary arteries).

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Nederlandse Samenvatting en Discussie

Sinds het begin van invasieve electrofysiologie hebben er in korte tijd veel grote veranderingen plaatsgevonden.[1,2] Mechanismen van ritmestoornissen worden momenteel beter begrepen, nieuwe ablatietechnieken zijn ontdekt en betere catheters zijn geïntroduceerd. Al deze ontwikkelingen zijn gefundeerd op ten minste één van de volgende basisprincipes: het verbeteren van veiligheid, effectiviteit, efficiëntie en reproduceerbaarheid van ablatieprocedures. In dit proefschrift staan nieuwe ontwikkelingen op het gebied van invasieve electrofysiologie beschreven. Het doel van dit werk is strategieën te vinden die de veiligheid en effectiviteit van catheterablatie procedures verbeteren. De belangrijkste ontwikkelingen die in dit proefschrift worden besproken zijn het magneetnavigatie systeem, het gebruik van *contact force* registrerende catheters en de introductie van een nieuwe ablatiecatheter met een gouden electrode.

DEEL I – ROBOTS

In Deel I van dit proefschrift wordt het magneetnavigatie systeem (MNS) besproken die als eerste beschikbaar was voor het gebruik bij ablatieprocedures. Het MNS is een zeer geavanceerd systeem dat gebruik maakt van magnetische velden om de ablatiecatheter te manipuleren in het hart.[3,4] Aan weerszijden van de patiënt bevinden zich twee externe magneten, die een magnetisch veld in de patiënt genereren met een sterkte van 0.08 of 0.1 Tesla. De positie van deze magneten kan door de operateur veranderd worden en geeft de mogelijkheid verschillende magnetische vectoren te creëren. Gezien het feit dat de ablatiecatheter gemaakt is van een zeer flexibel materiaal met kleine magneten aan het uiteinde, zal deze zich parallel aan de magnetische vector oriënteren. Door het veranderen van de magnetische vectoren kan de ablatiecatheter zonder restricties worden gemanoeuvreerd. Aangezien dit systeem een betere manipulatie van de catheter mogelijk maakt – met deze atraumatische catheter – was de hypothese dat het MNS voordelen kon bieden met betrekking tot de veiligheid en effectiviteit van ablatieprocedures in vergelijking tot conventionele ablatiecatheters.

In **Hoofdstuk 1** hebben we het gebruik van het MNS onderzocht bij een grote patiëntenpopulatie met verschillende ritmestoornissen uit alle hartkamers. Wij waren de eerste groep die de effectiviteit en veiligheid van het MNS en manuele ablaties onderzochten bij een grote groep patiënten. Wij observeerden dat het MNS geassocieerd was met minder majeure complicaties in vergelijking tot conventionele ablatiestrategieën.

Eerdere onderzoeken hebben aangetoond dat bij manipulatie van catheters in het hart en bij het verrichten van ablaties, er een risico bestaat op pericardeffusie en harttamponade.[5,6] In onze patiëntengroep hebben we geen pericardeffusie of harttamponade geobserveerd voor de MNS groep, terwijl voor manuele ablaties dit de meest voorkomende complicaties waren. Het ontwerp van het MNS zou een verklaring kunnen geven voor de significante reductie van complicaties. Deze bevindingen werden ook bevestigd door studies van andere internationale onderzoeksgroepen.[7-12] Verder zagen we dat het gebruik van het MNS leidt tot een verminderd gebruik van röntgenstraling. Vanwege de atraumatische catheterpunt is continue controle van de ablatiecatheter middels röntgenstraling overbodig en kan manipulatie van de catheter plaatsvinden met behulp van driedimensionale anatomische reconstructies van het hart. Wat betreft het acuut procedurele succes was het MNS even effectief in vergelijking tot manuele ablatie. Voor ablatie van ventriculaire tachycardieën (VT's) werd wel een hoger acuut succes percentage geobserveerd met het MNS. In verdere hoofdstukken hebben we dit verder onderzocht.

In **Hoofdstuk 2** hebben we de uitkomsten van MNS procedures onderzocht na een tweede catheterablatie (*redo*) voor atriumfibrillatie (AF), supraventriculaire tachycardie (SVT) en VT procedures. We hebben het MNS vergeleken met manuele procedures en hebben de uitkomsten geanalyseerd, rekening houdend met de techniek die tijdens de eerste procedure is gebruikt. Voor een redo SVT en AF ablatie middels magneetnavigatie duurden de ablatieprocedures respectievelijk 30 en 60 minuten langer. Onze bevindingen suggereren dat het MNS niet het succes van een redo-procedure vergroot, onafhankelijk van de techniek die is gebruikt tijdens de eerste ablatieprocedure. Echter, indien er een succesvolle procedure werd verricht middels MNS was het aantal recidieven 15% lager vergeleken met manuele procedures. Hierom zou het gebruik van het MNS overwogen kunnen worden als alternatieve techniek voor redo catheterablaties; wel in overweging nemend dat proceduretijden kunnen toenemen.

In **Hoofdstuk 3** wordt een overzicht gegeven van de beschikbare literatuur voor de behandeling van atriumfibrillatie middels het MNS. Internationale studies hebben aangetoond dat het risico op een harttamponade 1 – 1.5% is bij manuele cathetermanipulatie, zelfs in ervaren centra.[6,13,14] Het MNS biedt voordelen met betrekking tot procedureveiligheid en catheter-geïnduceerde perforaties. Vroege rapporten over het MNS voor de behandeling van AF middels niet-geïrrigeerde ablatiecatheters beschrijven

thrombusvorming op de catheterpunt na ablatie in het linker atrium.[9,15] Echter, na de introductie van de eerste- en daarna tweede generatie irrigatie MNS catheters was dit probleem verholpen en traden geen thrombusvorming of gerelateerde embolische events op.[16] Na het analyseren van de beschikbare literatuur konden wij concluderen dat er geen majeure complicaties zijn gerapporteerd die direct gerelateerd zijn aan het gebruik van het MNS. Met betrekking tot procedurele effectiviteit waren de succespercentages voor pulmonaalvenenisolatie middels MNS vergelijkbaar met conventionele technieken, alhoewel dit gerelateerd was aan langere proceduretijden. Lüthje en collegae beschreven dat MNS procedures gemiddeld 35-60 minuten langer duurden, zonder een duidelijke leercurve voor proceduretijd.[17] Dit kan worden verklaard door de separate handelingen die de operateur moet uitvoeren bij het veranderen van de magnetische vector, de daaropvolgende bewegingen van de twee externe magneten en tenslotte het bewegen van de catheter. Hierdoor neemt de tijd voor cathetermanipulatie toe, resulterend in een langere procedure- en ablatieduur.

In **Hoofdstuk 4** hebben we het onderzoek beschreven naar ablatie van "*longstanding"* persisterend atriumfibrilleren (LSP-AF). Voor paroxysmaal atriumfibrilleren is electrische pulmonaalvenenisolatie (PVI) een geaccepteerde en vaak succesvolle behandeling.[18-20] De effectiviteit van PVI voor LSP-AF is echter zeer matig, en slechts 20% van de patiënten is niet meer medicatiebehoeftig na één procedure.[21,22] Het aanbrengen van additionele ablatielijnen heeft een bewezen toegevoegde waarde voor de succeskans.[23,24] Andere technieken, zoals atriale defragmentatie, zijn ook voorgesteld als mogelijke technieken die de succespercentages van LSP-AF ablatie kunnen vergroten.[25,26] Tijdens deze procedure wordt een ablatie verricht op plekken in het atriale substraat, met specifieke electrogrammen die complex gefractioneerde signalen laten zien. In het betreffende hoofdstuk hebben we het effect van complete defragmentatie met behulp van het MNS als toevoeging aan de conventionele PVI en lineaire ablatie beschreven. De belangrijkste bevinding van het onderzoek was dat defragmentatie als toevoeging aan PVI en lineaire ablatie voor de behandeling van LSP-AF geassocieerd was met een hoger aantal mineure complicaties en meer tijdrovende procedures. Gedurende 12 maanden follow up waren er geen verschillen in aantal recidieven AF geobserveerd met of zonder defragmentatie. Onze gegevens suggereren dat complete defragmentatie voor de behandeling van LSP-AF een

negatief effect heeft op de procedurele efficiëntie, zonder verbetering van de lange termijn uitkomsten.

Hoofdstuk 5 beschrijft een nieuwe ablatiestrategie voor de behandeling van een slow-fast atrioventriculaire nodale re-entry tachycardie (AVNRT). Conventionele technieken vereisen het gebruik van meerdere diagnostische catheters in het hart.[27] In dit hoofdstuk beschrijven we een benadering middels het MNS waarbij één catheter wordt gebruikt. We hebben aangetoond dat deze techniek mogelijk is en resulteert in kortere proceduretijden en minder röntgenexpositie voor zowel de patiënt als de operateur in vergelijking tot conventionele technieken. De zeer manoeuvreerbare ablatiecatheter geeft de mogelijkheid om de catheter met een accuraatheid van 1 mm te manipuleren. Zolang het magnetische veld effectief is, zal de catheter in de gewenste positie blijven, onafhankelijk van diepe ademteugen of bij een snel junctioneel hartritme. Deze eigenschappen van het MNS zijn met name belangrijk voor mapping en ablatie in kleine regio's, zoals de driehoek van Koch en in de directe nabijheid van de compacte AV knoop en de His bundel. Door deze voordelen kon een permanent hartblok als complicatie van de procedure worden vermeden bij alle patiënten. Verder kunnen met het MNS verschillende locaties worden opgeslagen in het werkstation en kan de catheter exact worden teruggeleid naar een specifieke locatie door de opgeslagen vectoren toe te passen.[28] Deze functie maakte het mogelijk de diagnose AVNRT snel vast te stellen en met behulp van één catheter. De totale proceduretijd was met 52% gereduceerd in vergelijking tot eerder gepubliceerde resultaten, en met 29% vergeleken met conventionele radiofrequente ablatie in onze studie.[29] Catheter stabiliteit, verbeterde catheter manipulatie en het vastleggen van de His locatie op de röntgen hebben bijgedragen aan de veiligheid en effectiviteit van deze procedure.

Uit de beschikbare literatuur, en ondersteund door onze eigen data, is bekend dat ablatie van AVNRT een zeer succesvolle therapie is.[30-32] Bij sommige patiënten met documentatie van een supraventriculaire tachycardie (SVT) die suggestief is voor AVNRT is de hartritmestoornis echter niet te induceren tijdens een electrofysiologisch onderzoek. Empirische ablatie van een *slow pathway* (ESPA) is een mogelijke overweging, zelfs wanneer het AVNRT niet definitief bevestigd kan worden.[33] ESPA wordt geregeld toegepast (± 5–10% van de SVT patiënten), maar de effectiviteit hiervan is slechts door een klein aantal studies onderzocht.[34] In **Hoofdstuk 6** beschrijven we dat ESPA een effectieve therapie is voor de eliminatie van SVT bij patiënten waarbij de ritmestoornis niet induceerbaar is ten tijde van

de procedure. We hebben aangetoond dat de documentatie van SVT vóór de procedure, in het bijzonder een tachycardie met een kort RP-interval, een sterke voorspeller is voor het lange-termijn succes van ESPA.

In dit proefschrift is het gebruik van het MNS voor de ablatie van VT onderzocht. In **Hoofdstuk 7** presenteren we een systematic review van de beschikbare literatuur over VT ablatie middels MNS. De beschikbare data laten zien dat het MNS wordt toegepast voor verschillende patiëntenpopulaties en voor meerdere VT subtypes met goede uitkomsten en een laag complicatierisico. Patiënten met een structureel normaal hart hebben de beste uitkomsten in vergelijking tot patiënten die lijden aan een ischemische of niet-ischemische cardiomyopathie. Echter, gezien de zeer beperkte hoeveelheid gepubliceerde data is meer kennis over MNS-gestuurde VT ablatie noodzakelijk. In **Hoofdstuk 8** presenteren we de eerste grootschalige studie over VT ablatie middels MNS waarbij zowel idiopathische als litteken-gerelateerde VT's zijn opgenomen. De belangrijkste bevinding van dit onderzoek is dat MNS een hoger acuut succespercentage heeft dan conventionele therapie voor ablatie van idiopathische VT, en een vergelijkbaar succespercentage voor patiënten met litteken-gerelateerde VT. Dit verschil persisteerde tijdens follow up, aangezien er minder recidieven optraden in de MNS groep dan in de manuele ablatiegroep.

Verbeteringen in chirurgische technieken bij jonge patiënten met een congenitale hartziekte (CHD) hebben geresulteerd in een significante verlenging van de levensverwachting. Echter, met het ouder worden van deze patiënten, hebben ze een hoge kans op het ontwikkelen van late complicaties die gerelateerd zijn aan de chirurgische correctie, waaronder hartritmestoornissen.[35,36] Deze kunnen ontstaan door zowel een abnormale fysiologie van het myocardiale substraat als de aanwezigheid van chirurgische littekens. Catheterablatie wordt steeds meer toegepast als een curatieve therapie om deze – vaak complexe – ritmestoornissen te behandelen.[37] Aangezien de cardiale anatomie bij deze patiënten vaak verschillend is van de normale situatie, kan het moeilijk zijn de oorsprong van de tachycardie te bepalen en vervolgens te bereiken. In **Hoofdstuk 9** hebben we het gebruik van het MNS beschreven voor de behandeling van ritmestoornissen bij patiënten met CHD. Conventionele catheters zijn vaak beperkt door de voorgefabriceerde kromming van de catheter.[38] Onze studie wijst uit dat met het MNS een retrograde benadering zeer goed mogelijk is en puncties tijdens de procedure door een *baffle* vermeden kunnen worden. Onze uitkomsten demonstreren dat het een veilige techniek is zonder het optreden van

majeure complicaties. Het betreffende hoofdstuk beschrijft de voordelen van het MNS voor catheterablatie bij een complexe anatomie zonder negatief effect op de uitkomsten. Het is een goed toepasbare techniek voor de behandeling van ritmestoornissen bij patiënten met CHD, met goede succespercentages die persisteren op lange termijn.

Een correcte diagnose van de ritmestoornissen bij patiënten met CHD kan een grote uitdaging zijn voor de electrofysioloog.[39] De chirurgische littekens en de progressie van de onderliggende ziekte kunnen de diagnose van een atriale tachycardie (AT) bemoeilijken.[40-42] In structureel normale harten kan er onderscheid gemaakt worden tussen focale AT's en macro-reëntry AT's gebaseerd op de totale atriale activatie tijd (TAAT) en de cycluslengte (CL) van de tachycardie.[43,44] Beide typen ritmestoornissen hebben een andere ablatiestrategie. De verhouding tussen deze twee waarden (TAAT/CL) is een belangrijke voorspeller om de etiologie te bepalen. Uit de literatuur is bekend dat een TAAT/CL ratio onder de 40% sterk suggestief is voor een focaal activatiepatroon, en een ratio boven de 40% voor een macro-reëntry tachycardie.[43] Echter, bij patiënten met CHD kan het beschadigde myocard de geleidingssnelheiden beïnvloeden en kan de voorspellende waarde van de TAAT/CL ratio worden betwijfeld. In **Hoofdstuk 10** laten wij zien dat 66.7% van de CHD patiënten met een focale AT verkeerd zou worden geclassificeerd gebaseerd op deze waarde. Onze data wijzen uit dat de toepasbaarheid van deze diagnostische parameters gerelateerd is aan de gemiddelde amplitude van de bipolaire signalen (BiSA). Voor een juiste differentiatie tussen een focale en macro-reëntry AT bij CHD patiënten is een gemiddelde BiSA waarde van tenminste 0.90 mV vereist. In geval van lagere gemiddelde BiSA waarden zijn verdere diagnostische onderzoeken nodig om de correcte etiologie van de AT vast te stellen. Ons onderzoek demonstreert daarom dat de gemiddelde BiSA waarde geïntegreerd moet worden in het diagnostische proces om een correcte diagnose mogelijk te maken en procedurele uitkomsten te verbeteren.

DEEL II – CONTACT FORCE

In Deel II van dit proefschrift is het gebruik van een "*contact force*" catheter beschreven die de hoeveelheid kracht tussen de catheter en de hartspier kan registeren en hiermee een maat is voor wandcontact. Het succes van catheterablatie procedures is afhankelijk van meerdere factoren waaronder localisatie van het juiste substraat, optimale afgifte van energie en adequaat contact met het weefsel.[45] Het moge duidelijk zijn dat de veiligheid van

de patiënt de hoogste prioriteit heeft tijdens een catheterablatie procedure. Er is echter altijd een risico op cardiale perforatie leidend tot een hemodynamisch instabiele toestand.[46] Eén van de belangrijkste determinanten voor een perforatie is de hoeveelheid kracht tussen de catheter en de hartspier.[47] Voorheen was de hoeveelheid *contact force* gebaseerd op het manuele gevoel van de operateur en andere surrogaat parameters zoals de beweging van de catheterpunt op de röntgenopname, ST elevatie in het unipolaire electrogram en monitoring van de impedantie.[48,49] Het bleek echter dat deze parameters een slechte voorspeller waren voor de daadwerkelijke *contact force*. Eerdere studies hebben aangetoond dat vaak gevaarlijk hoge krachten worden uitgeoefend op het hart tijdens manuele cathetermanipulatie, zelfs in handen van ervaren operateurs.[46] Recent is echter een nieuwe catheter geïntroduceerd die direct de hoeveelheid *contact force* aan de catheterpunt kan registeren.[50] In **Hoofdstuk 11** hebben we de procedurele veiligheid vergeleken van de contact force (CF) catheter, het magneetnavigatie systeem en conventionele ablatietechnieken. Onze studie liet zien dat majeure complicaties optraden in 2.8% van alle procedures met een risico op een cardiale perforatie van 0.9%. Het gebruik van de CF catheter kon echter het risico op een perforatie reduceren, met name bij patiënten met AF. Onze data tonen aan dat het gebruik van de CF catheter complicaties kan vermijden en de risico's vergelijkbaar zijn aan het MNS systeem.

Het gebruik van CF catheters heeft niet alleen mogelijke voordelen voor de veiligheid, maar speelt ook een grote rol voor de procedurele effectiviteit. Het is bekend dat CF een belangrijke determinant is voor de formatie van effectieve laesies.[51-53] In dit proefschrift hebben we het gebruik van CF catheters voor VT ablatie beschreven. In **Hoofdstuk 12** beschrijven we de initiële ervaringen van ablatie middels CF catheters voor epicardiale VT ablatie. Radiofrequente (RF) catheterablatie in de epicardiale ruimte verschilt substantieel van endocardiale ablatie. Ten eerste, de afwezigheid van circulerend bloed in het epicard leidt tot verminderde convectieve koeling tijdens ablatie; de catheteroriëntatie is vaak anders, en de aanwezigheid van epicardiaal vetweefsel interfereert met de laesieformatie.[52] Al deze factoren hebben een aanzienlijk effect op de RF laesieformatie en moeten in overweging worden genomen tijdens epicardiale ablatie. In het betreffende hoofdstuk presenteren wij twee casussen waarbij een epicardiale ablatie met CF catheters is uitgevoerd. Technische overwegingen, zoals calibratie van de CF catheter, zijn beschreven in dit hoofdstuk.

Het gebruik van CF catheters voor endocardiale VT ablatie staat beschreven in **Hoofdstuk 13**. In deze studie zijn manuele ablatie, magneet-gestuurde ablatie en CF ablatie vergeleken voor de behandeling van VT. In onze studie leidde het gebruik van CF catheters niet tot een verbetering van de veiligheid en effectiviteit tijdens VT ablaties. Wij realiseren echter dat er momenteel onvoldoende kennis is over het gebruik van CF catheters voor VT ablaties en aanvullende studies gestimuleerd moeten worden.

DEEL III – LAESIEFORMATIE

De introductie van geïrrigeerde RF catheters was een enorme verbetering en leidde tot verbeterde succespercentages voor veel soorten ritmestoornissen in vergelijking tot niet-geïrrigeerde catheters.[54-57] Momenteel zijn er verschillende typen catheters beschikbaar die meestal gebruik maken van een platinum-iridium (PtIr) of gouden (Au) electrode met zes irrigatiegaten. De geïrrigeerde Au electrode heeft een betere energieafgifte bij lagere electrodetemperaturen in vergelijking tot de geïrrigeerde PtIr electrode.[58] Echter, tijdens ablatie wordt er vaak veel irrigatievloeistof gebruikt waardoor de laesiegrootte beperkt wordt en zelfs volumeoverbelasting kan plaatsvinden bij patiënten met een slechte hartkamerfunctie. In **Hoofdstuk 14** hebben we de veiligheid en effectiviteit van een nieuwe geïrrigeerde Au catheter met 12 irrigatiegaten beschreven in vergelijking tot een conventionele ablatiecatheter (PtIr). Onze resultaten wijzen uit dat de Au electrode met 12 irrigatiegaten een veilige techniek is voor RF ablatie bij lage irrigatiesnelheden. Tijdens alle RF applicaties zijn er geen stolsels ontstaan op het weefsel. Verder resulteerden deze applicaties in een groter laesieoppervlak bij lagere electrodetemperaturen dan bij de PtIr electrode. Ondanks deze veelbelovende resultaten is verder klinisch onderzoek van belang om de waarde van deze nieuwe catheter voor dagelijks gebruik te evalueren.

De energieafgifte van de ablatiecatheter is afhankelijk van meerdere factoren zoals *contact force*, irrigatiesnelheid, wattage, ablatietijd, weefseleigenschappen, electrode positie, en het materiaal waarvan de electrode gemaakt is.[45] Deze individuele factoren hebben een invloed op de effectiviteit van energieafgifte aan het weefsel en dragen daarom bij aan de laesieformatie en –kwaliteit. Echter, in klinische studies is er vaak een discrepantie tussen acute en chronische succespercentages.[59] Patiënten kunnen mogelijk een nieuw aritmogeen substraat ontwikkelen dat leidt tot een recidief van ritmestoornissen, maar een inadequate ontwikkeling van een chronische ablatielaesie behoort ook tot de mogelijkheden

voor deze discrepantie. In **Hoofdstuk 15** hebben we op een histologisch niveau twee typen catheters vergeleken om de verschillende manifestaties van laesiestructuren te bekijken en te onderzoeken wat belangrijke determinanten zijn voor laesieformatie. Histologisch gezien heeft de ablatielaesie verschillende distinctieve zones, met een deel van centrale necrose en een reactieve zone met interstitieel oedeem. De structuur van de laesies is echter niet consistent bij alle ablatielaesies en onze resultaten tonen aan dat een inhomogene opbouw frequent voorkomt tijdens RF ablatie. We observeerden dat dit geassocieerd was aan grotere laesievolumes en er geen relatie bestond met weefseltemperatuur. Verder is het gebruik van de Au electrode met 12 irrigatiegaten een onafhankelijke voorspeller voor inhomogene laesies. Op dit moment is het echter onbegrepen welke laesies zullen resulteren in een betere chronische laesie en wat de ideale instellingen zijn om lange termijn succes te verhogen. De verklaring voor het verschil tussen acuut en chronisch succes kan zeer goed te vinden zijn in de histologische verschillen tussen de laesies. Hierom roepen wij op om een dergelijke histologische benadering meer toe te passen bij toekomstig onderzoek, in plaats van slechts laesievolume te vergelijken. Wij hopen dat toekomstig onderzoek ons de optimale ablatie-instellingen kan onthullen voor betere procedurele uitkomsten.

TOEKOMSTPERSPECTIEF

In dit proefschrift zijn nieuwe ontwikkelingen binnen de invasieve electrofysiologie besproken om de veiligheid en effectiviteit van catheterablatie procedures te verbeteren. Electrofysiologie is een snel ontwikkelend terrein met veel facetten die nog kunnen verbeteren of nog moeten worden ontdekt. Zoals is aangetoond in dit proefschrift, heeft robotische catheterablatie belangrijke voordelen met betrekking tot de veiligheid en effectiviteit van procedures. Echter, belangrijke zaken dienen nog te worden verbeterd. Het is van belang te realiseren dat robotica in catheterablatie alleen zinvol is als het de meest belangrijke uitdagingen weet te adresseren. Deze uitdagingen zijn onder andere een inefficiënt werkveld, grote verschillen tussen operateurs, veiligheidsaspecten en een suboptimale effectiviteit. Ten tweede, realiseren wij dat *contact force* registrerende catheters in toenemend aantal gebruikt zullen worden tijdens ablatieprocedures. Momenteel is er veel onderzoek gaande om de exacte waarde van deze catheter en de effecten op de veiligheid en effectiviteit van procedures te onderzoeken. Momenteel is de ideale hoeveelheid *contact force* voor elke regio in het hart nog onbekend. Dit zal zeker

duidelijk worden in de nabije toekomst. Hopelijk zullen de progressies met de *contact force* catheter uiteindelijk leiden tot de introductie van een *contact force* registerende MNS catheter. Dit zal twee zeer belangrijke technieken combineren en zal absoluut resulteren in betere en veiligere ablatieprocedures. De toenemende bewustwording van laesieformatie met het gebruik van *contact force* catheters zal gevolgd worden door een toenemende kennis over laesieformatie, met name op histologisch niveau. Toekomstig onderzoek dient zich niet slechts te richten op laesiedimensies, maar de structuur van de laesies en de effecten op de lange termijn dienen eveneens onderzocht te worden. Wij geloven dat dit het lange termijn succes van de ingrepen significant kan verbeteren. Verder hopen wij dat er een toenemende kennis vergaard zal worden over de etiologie van complexe ritmestoornissen en dat er strategieën bedacht zullen worden om ablaties uit te voeren op plekken die momenteel nog ontoereikbaar zijn met de huidige technieken.

Dankwoord

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PhD Portfolio

Name PhD student:	Ferdi Akca
Department:	Electrophysiology / Cardiology
Research school:	Cardiovascular Research School Erasmus University Rotterdam
Title thesis:	Optimizing safety and efficacy of catheter ablation procedures
Promotor:	Prof.dr. F. Zijlstra
Date of thesis defence:	16 September 2015

	Year	Workload (ECTS)
ACADEMIC EDUCATION		
- Bachelor of Medicine, Erasmus Medical Center, Rotterdam, The Netherlands	2009 – 2012	
- Honours Class, Erasmus Medical Center, Rotterdam, The Netherlands	2010 – 2011	
- Medical Doctor, Erasmus Medical Center, Rotterdam, The Netherlands	2012 – 2015	
EXTRA-CURRICULAR ACTIVITIES		
- Student/nursing assistant Department of Cardiology, Erasmus Medical Center, Rotterdam, The Netherlands	2006 – 2014	
IN-DEPTH COURSES		
Erasmus Summer Programme (NIHES)		
- Principles of Research in Medicine and Epidemiology	2011	0.7
- Clinical Decision Analysis	2011	0.7
- Methods of Public Health Research	2011	0.7
- Social Epidemiology	2011	0.7
- Markers and Prognostic Research	2011	0.7
- The Practice of Epidemiologic Analysis	2011	0.7
Core courses (NIHES)		
- Study Design	2011	4.3
- Biostatistical Methods I: Basic Principles	2011	5.7
Advanced courses (NIHES)		
- Ever Thought of Doing Research	2012	2.8
- Clinical Trials	2012	0.7
- Health Economics	2012	0.7
- Case-control Studies	2012	0.7
- Principles of Genetic Epidemiology	2012	0.7
- History of Epidemiologic Ideas	2012	0.7
Cardiovascular Research School (COEUR)		
- Arrhythmia Research Methodology	2012	1.5
University of Cambridge – Institute of Public Health		
- Chronic Disease / Cardiovascular Disease Epidemiology	2015	1.1

PRESENTATIONS

Oral presentations

- Hearth Rhythm Society Congress (Boston, USA)	2012	0.6
- Cardiostim World Congress (Nice, France)	2012	0.6
- Netherlands Heart Rhythm Association (Ermelo, The Netherlands)	2012	0.6
- American Heart Association Congress (Los Angeles, USA)	2012	0.6
- International Symposium on Progress in Clinical Pacing (Rome, Italy) (3x)	2012	1.8
- European Cardiac Arrhythmia Society Congress (Paris, France)	2013	0.6
- European Society of Cardiology Congress (Barcelona, Spain)	2014	0.6
- Annual Spring Meeting of the Dutch Cardiology Society (Papendal, The Netherlands)	2014	0.6
- International Symposium on Progress in Clinical Pacing (Rome, Italy) (2x)	2014	1.2

Poster presentations

- Hearth Rhythm Society Congress (San Francisco, USA)	2011	0.6
- European Heart Rhythm Association Congress (Madrid, Spain) (4x)	2011	2.4
- European Society of Cardiology Congress (Paris, France) (2x)	2011	1.2
- Hearth Rhythm Society Congress (Boston, USA)	2012	0.6
- Cardiostim World Congress (Nice, France)	2012	0.6
- American Heart Association Congress (Los Angeles, USA)	2012	0.6
- European Cardiac Arrhythmia Society Congress (Paris, France)	2013	0.6
- European Society of Cardiology Congress (Amsterdam, The Netherlands)	2013	0.6
- Hearth Rhythm Society Congress (San Francisco, USA) (2x)	2014	1.2
- Cardiostim World Congress (Nice, France) (3x)	2014	1.8
- European Society of Cardiology Congress (Barcelona, Spain)	2014	0.6

INTERNATIONAL CONFERENCES

- European Society of Cardiology Symposium (Rotterdam, The Netherlands)	2010	1.5
- 5th International Symposium on Advances in Arrhythmias (Rotterdam, The Netherlands)	2011	1.5
- Hearth Rhythm Society Congress (San Francisco, USA)	2011	2.0
- European Heart Rhythm Association Congress (Madrid, Spain)	2011	2.0

- European Society of Cardiology Congress (Paris, France)	2011	2.5
- Hearth Rhythm Society Congress (Boston, USA)	2012	2.0
- Cardiostim World Congress (Nice, France)	2012	2.0
- European Society of Cardiology Congress (München, Germany)	2012	2.0
- Netherlands Heart Rhythm Association (Ermelo, The Netherlands)	2012	1.0
- American Heart Association Congress (Los Angeles, USA)	2012	2.5
- International Symposium on Progress in Clinical Pacing (Rome, Italy)	2012	2.0
- European Cardiac Arrhythmia Society Congress (Paris, France)	2013	1.5
- European Society of Cardiology Congress (Amsterdam, The Netherlands)	2013	2.5
- Hearth Rhythm Society Congress (San Francisco, USA)	2014	2.0
- Cardiostim World Congress (Nice, France)	2014	2.0
- European Society of Cardiology Congress (Barcelona, Spain)	2014	2.0
- Annual Spring Meeting of the Dutch Cardiology Society	2014	0.5
- International Symposium on Progress in Clinical Pacing	2014	2.0

GRANTS / PRIZES

- Award Best Moderated Poster – European Society of Cardiology Congress (Barcelona, Spain)	2014
- Acadamy Van Walree Travel Grant – The Academy Medical Sciences Fund	2014

PEER REVIEWING

- EP Europace	2012 – 2014	0.5

TEACHING

- Supervising 2nd year medical students in writing a systematic review, Erasmus MC, Rotterdam, The Netherlands	2013	0.6

TOTAL WORKLOAD (ECTS) **75.7**

Curriculum Vitae

CURRICULUM VITAE

Ferdi Akca was born in Rotterdam, The Netherlands on April 12th, 1991. After graduating "cum laude" from secondary school (Gymnasium, Nature & Health and Nature & Science, Wartburg College, Rotterdam, The Netherlands), he started Medical school in 2009 at the Erasmus University Rotterdam. Since he belonged to the top 5% of his class he was invited to participate at the Erasmus MC Honours Class. During the same time he worked as a department assistant at the cardiology department of the Erasmus Medical Center. Fascinated by cardiovascular diseases and cardiac arrhythmias he started doing research under guidance of dr. T. Szili-Torok. During this research period he attended a cardiovascular research seminar at the University of Cambridge (United Kingdom). In April 2015 he obtained his medical degree at the Erasmus University, Rotterdam. In September 2015, he completed his PhD thesis under supervision of Prof. Dr. F. Zijlstra and Dr. T. Szili-Torok entitled '*Optimizing safety and efficacy of catheter ablation procedures'*. Recently, Ferdi got married to his wife Carola.

List of Publications

1. T Bauernfeind, **F Akca**, B Schwagten, NMS De Groot, Y van Belle, S Valk, B Ujvari, L Jordaens, T Szili-Torok. The magnetic navigation system allows safety and high efficacy for ablation of arrhythmias. Europace 2011;13(7):1015-21.

2. T Szili-Torok, **F Akca**. Remote magnetic navigation in atrial fibrillation. Expert Rev Med Devices 2012;9(3):249-55.

3. **F Akca**, I Önsesveren, L Jordaens, T Szili-Torok. Safety and efficacy of the remote magnetic navigation for ablation of ventricular tachycardias – a systematic review. J Interv Card Electrophysiol 2012;34(1):65-71.

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BOOK CHAPTER

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