JAFIB
Original Research
Journal of Atrial Fibrillation
www. jafib.com

Robotic Navigation Shows Superior Improvement in Efficiency for Atrial Fibrillation Ablation

Anna M.E. Noten[1], Zsuzsanna Kis[1], Ferdi Akca[1], Rohit Bhagwandien[1], Sip Wijchers [1], Sing-Chien Yap[1], Tamas Szili-Torok[1]

[1] *Department of Cardiology, Erasmus MC, University Medical Center, Rotterdam, the Netherlands.*

Abstract

Background: Because of the expanding atrial fibrillation (AF) burden, AF catheter ablation (CA) techniques have to become more efficient. Efficient AF CA procedures are characterized by successful pulmonary vein isolation (PVI) within reasonable procedure time. Currently there are many PVI techniques available and all show substantial improvements over time. However, the magnitude of improvement in procedural efficiency has not yet been compared between different techniques. The aim of this study was to compare efficiency improvement between manually (MAN) guided, cryoballoon (CB) and remote magnetic navigation (RMN) guided PVI.

Methods: A total of 221 patients were included in this retrospective study. Procedural parameters of 115 patients treated with first-generation PVI techniques (MAN-1, CB-1, RMN-1) performed in 2010, were compared to 106 patients who were treated with the latest, second generation techniques (MAN-2, CB-2, RMN-2). Efficiency was characterized by the following parameters: total ablation time, total procedure time, first pass isolation (FPI) (i.e. successful isolation after the first pulmonary vein (PV) encirclement) and touch-up rates.

Results: Every technique showed significant improvement of procedure times from the first to the second generation (P<0.001). In-between second generation techniques, the procedure times were comparable. The greatest magnitude of procedure time improvement was observed within the RMN groups (Δ-180min), which was significantly greater compared to CB (Δ-48 min, P<0.001) and MAN (Δ-98min, P=0.011) groups. The highest FPI rates were observed in RMN-2 (78% and 74%; left and right PVs respectively), which was significantly higher compared to other techniques (MAN-2: 24% and 24%; CB-2: 50% and 48%; P<0.001).

Conclusions: The highest magnitude of efficiency improvement was detected in RMN guided PVI.

Introduction

The atrial fibrillation (AF) prevalence is rapidly increasing[1]. Already 33.5 million patients were diagnosed with AF worldwide in 2013[1]. The AF pandemic constitutes a significant public health problem, as well as it has a substantial financial impact on healthcare. Catheter ablation (CA) has become a first-choice treatment for patients with drug refractory AF[2-4]. Electrical isolation of the pulmonary veins (PVs) is the cornerstone of AF ablation[5,6]. CA procedures have to become more efficient in order to be available for a larger share of the AF population. Efficient AF CA procedures are characterized by successful pulmonary vein isolation (PVI) within reasonable ablation and procedure time. Many PVI techniques are currently available and all experienced substantial improvements over time.

Initially, PVI was performed manually by series of point-by-point radiofrequency (RF) lesions encircling the PVs, which had the inevitable risk of gaps persisting within the ablation lines[4,7]. The efficacy of manual (MAN) guided RF ablation improved significantly with the advent of contact force (CF) sensing catheters, resulting in less recurrence of arrhythmia and significantly shorter ablation times[8]. Besides, single-shot techniques emerged, of which the cryoballoon (CB) is nowadays most frequently used. The CB had the advantage of combining facile positioning and ablation, while decreasing procedure time[4,9,10]. Its disadvantage was the poor adaptation to anatomical variations of PVs[4,11]. The second generation CB exhibited higher freedom of AF within shorter isolation, fluoroscopy and procedure times when compared to its precursor[12]. Subsequently, remote magnetic navigation (RMN) guided ablation was introduced as an alternative RF CA strategy. In RMN, two magnetic platforms are utilized to remotely guide the movement of the ablation catheter by magnetic fields[13,14]. Various publications reported on the benefits of RMN due to precision of catheter movement, its soft tip and its stability, causing superior lesion formation[15] and improved procedural safety[16,17]. However, the disadvantages of RMN guided RF ablation were the prolonged ablation and procedure times and increased operator learning curve[18,19].

Although all techniques underwent progressive improvements resulting in simpler workflow, better efficiency and outcome, there still continues to be an ongoing discussion on which ablation technique

Key Words

Robotic Navigation Guided Ablation, Radiofrequency Ablation, Cryoballoon Ablation, Pulmonary Vein Isolation, Remote Magnetic Navigation Guided Ablation, Atrial Fibrillation

Corresponding Author
Tamas Szili-Torok,
Thoraxcenter, Department of Clinical Electrophysiology, Erasmus MC, Postbus 2040, 3000 CA, Rotterdam, The Netherlands

is preferable. Multiple studies have been published comparing procedural outcome between two ablation techniques[18-23]. However, there is no clear study available that investigates the potential of efficiency improvement of certain techniques. The aim of this study was to compare the advancements of procedural efficiency over time of three different ablation techniques (MAN guided RF, CB and Robotic navigation (RMN) guided RF), to distinguish which technique has highest potential for further efficiency improvement in the future.

Methods

Study design

This study is a retrospective, single-center study, investigating PVI procedures performed with CB, manual guided RF and RMN guided RF. We analyzed and compared procedural efficiency parameters between two generations of each of these three techniques. Procedural efficiency was defined by the following endpoints: total procedure time, total ablation time, first pass isolation rates and touch up rates. Additionally, we analyzed AF recurrence (documented on ECG) and redo procedure rates at 12-months post-procedure, with use of a 3-month blanking period[3].

Study population and data collection

All patients who underwent the first PVI for AF, utilizing the latest available techniques for MAN guided RF, CB or RMN guided RF ablation between September 2016 - July 2017, were selected for analysis (second generation procedures, defined as MAN-2, CB-2 and RMN-2 groups). From January 2010, age and sex-matched controls were selected consecutively for each of the three treatment techniques (first generation procedures, defined as MAN-1, CB-1 and RMN-1 groups). All patients were eligible for AF ablation based on the respective ACC/AHA/ESC Guideline valid at the date of procedure[2,24-26]. Patients with anatomical variants of PVs were valid for inclusion. Patients with intra-cardiac thrombus were contra-indicated for a CA procedure. Patients aged ≤18 years and redo PVI procedures were excluded from study participation. Baseline demographic and clinical characteristics were collected using the electronic health records (Elpado version 2.56.0). Procedural data was derived both from the electronical medical files, as well as from the electronical procedural log files recorded with the EP-workmate™ (St. Jude Medical Inc., St. Paul, MN, USA), the Ensite™ NavX™ (St. Jude Medical Inc., St. Paul, MN, USA), the CryoConsole® (Medtronic, Minneapolis, MN, USA) and the the Odyssey™ Cinema (Stereotaxis Inc., St. Louis MO, USA) systems. Data collection for this study from our registry was approved by the institutional review committee and was carried out in accordance with the ethical principles for medical research involving human subjects founded by Helsinki's declaration. All patients provided informed consent prior the ablation procedure.

Procedural protocols

PV anatomy was evaluated in all patients pre-operatively with a CT-scan. Patients with a left common ostium and/or a PV size >28mm, were scheduled for PVI with RF (either MAN or RMN guided) as standard of care. All procedures were performed under local or general anesthesia. Presence of intra-cardiac thrombus was evaluated at the start of procedure by trans-esophageal echocardiography. All MAN procedures were performed using the EnSite NavX (St. Jude Medical Inc., St. Paul, MN, USA) mapping system. The following catheters were used in the MAN-1 group: the Celsius ThermoCool® 4mm catheter and the Navistar ThermoCool® catheters (Biosense Webster Inc., CA, USA). In the MAN-2 group, all procedures were performed using CF sensing catheters, i.e. the TactiCath™ contact force catheter (St. Jude Medical Inc., St. Paul, MN, USA). Patients in the CB groups were treated with first generation Artic Front® (CB-1 group) or second generation Arctic Front Advance® (CB-2 group) cryoballoon (Medtronic, Minneapolis, MN, USA). RMN procedures were performed using either the Niobe II (RMN-1 group) or the Niobe ES (RMN-2 group) Magnetic Navigation System (Stereotaxis, St Louis, MO, US), with use of the NaviStar RMT ThermoCool catheter (Biosense Webster Inc., CA, US) in both generations. During all PVI procedures, thirty minutes of waiting time were executed as standard of care to identify early PV reconnection. All patients were observed at the intensive care unit or cardiac care unit after the procedure, with continuous hemodynamic, respiratory and ECG recordings. Presence of pericardial effusion was checked in all patients with trans-thoracic echography (TTE) as standard of care.

Remote Magnetic Navigation

The Niobe RMN system (Stereotaxis, Inc., St Louis, MO, USA) is a medical platform designed for electrophysiology and interventional procedures. The RMN system utilizes two permanent magnets, one on each side of the patient, to remotely guide the movement of the distal tip of compatible ablation catheters via magnetic fields. This technique has been described and validated extensively elsewhere[13,14]. In RMN-2 ablation was performed with the following radiofrequency settings: power 45-50 W, temperature 43°C. In all RMN-2 procedures the latest RMN technologic advancements were implemented: the Ablation History feature and the e-Contact module. Ablation History provides a visual display of the history of the catheter's power output and duration of energy application at each location at the map during the ablation. The 'e-Contact module' provides contact feedback, by a visual indicator (starburst) when the catheter tip is in contact with the cardiac tissue.

Definitions

Procedural efficiency is characterized by successful PVI isolation within reasonable procedure and ablation time. Therefore, we analyzed the following procedural parameters: total application duration, total procedure time, PV encirclement times, first pass isolation rate (FPI) and touch-up (TU) rate. Total procedure time was defined as the time from start of the procedure (1st puncture) until the end of procedure (removal of catheters). The PV encirclement time was defined as the start of the first application for either the left or the right sided wide-area circumferential ablation (WACA), until the last application enclosing the vein. In case of CB ablation, encirclement time was calculated as the duration of the first adequate balloon application. First pass isolation (FPI) was regarded when the first PV encirclement or first adequate CB application, resulted in successful PV isolation. If the first encirclement did not result in isolation of the PVs, additional applications were regarded TU. For CB, the second and all additional applications were regarded TU. The PV encirclement time, number of touch ups (TU) and first pass

isolation (FPI) rates were evaluated in second generation procedures only, because of the use of different procedural protocols in the past. When additional ablations of non-PVI triggers were performed, the procedure times were adjusted accordingly, as well as the number of applications and total application duration. The single procedure AF recurrence rates were evaluated. When a redo procedure was performed during the 12 months of follow-up, it was regarded as AF recurrence.

Complications

Major complications were defined as per ISO 14155 definition, as events that led to death, or led to serious deterioration in the health of the subject (i.e. resulted in a life-threatening illness or injury, or a permanent impairment of a body structure or a body function, or in-patient or prolonged hospitalization, or medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function). Minor complications were defined as events that resulted in minimal transient impairment of a body function or damage to a body structure, or which did not require any intervention other than monitoring.

Statistical analysis

Continuous variables were checked for normal distribution with normality plots and the Shapiro-Wilk test. Normally distributed continuous variables were described with mean and standard deviation. Normal distributed continuous variables were analyzed using the 1-way ANOVA. A post-hoc Tukey's honestly significant difference test was performed to investigate significant differences in-between the 6 groups when a significant main effect was present. Continuous variables with a non-normal distribution were described by median and interquartile ranges (IQR). The Kruskal-Wallis test was used to examine continuous variables with a non-normal distribution. Descriptive statistics for categorical data were expressed in absolute numbers with percentages and analyzed using the Chi-square test, or, when appropriate, Fisher's exact test. A 2-sided P-value of <0.05 (2-tailed) was considered significant. Data were analyzed using SPSS 24.0 (SPSS Inc., Chicago, IL, USA).

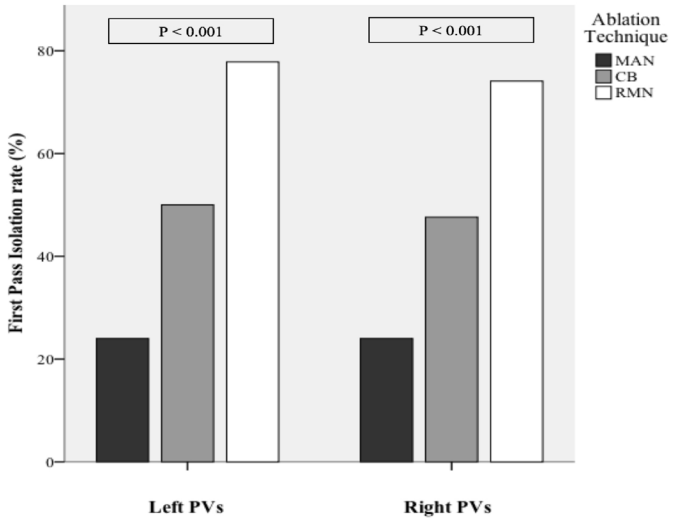

Figure 1: First pass isolation rates - 2nd generation groups only

The first pass isolation rates of the three second generation treatment techniques are displayed in figure 1. First pass isolation (FPI) was regarded when the first ablation encirclement of the PVs or the first CB application, resulted in successful PV isolation. Only second generation groups are displayed, as first pass isolation could only be calculated in these groups.
PVs = pulmonary veins.

Results

Baseline demographic and clinical characteristics

A total of 221 patients were included in this study (MAN-1 n=39; CB-1 n=39; RMN-1 n=37; MAN-2 n=37; CB-2 n=43; RMN-2 n=27). Patient demographic and clinical data are summarized in [Table 1]. Age was significantly different between groups ([Table 1], P=0.009). Post-hoc analysis showed that the only significant difference was found between CB-1 group with a mean of 55.44 ± 9.18 years and MAN-2 group with a mean of 62.36 ± 8.36 years (P=0.022). In both CB groups, significantly more patients with paroxysmal AF were present, as compared to MAN and RMN groups ([Table 1], P<0.001). Treatment with amiodarone was less frequently used in CB and second-generation groups ([Table 1], P=0.002). Prevalence of ischemic heart disease was significantly different between groups as well, which however did not result in a difference in ejection fraction. All patients were treated with anti-coagulation. Vitamin K antagonists were often prescribed in the first generation groups, while direct-acting oral anticoagulants (DOAC) were more prevalent in the second generation groups ([Table 1], P<0.001).

Procedural characteristics

Procedural data is depicted in [Table 2] and 3. The mean procedure time significantly differed between the 6 groups ([Table 2], P<0.001). Additionally, significant differences were observed in the number of applications and application duration, with the lowest number of applications noted in the CB groups ([Table 2], P<0.001) and the shortest application durations noted in second generation procedures ([Table 2], P<0.001). The PV encirclement time, number of touch ups (TU) and first pass isolation (FPI) rates were evaluated in second generation procedures only. Encirclement times of left and right sided PVs were significantly different between the three second generation techniques ([Table 3], P<0.001). Interestingly, the first pass isolation rates of the left and right sided PVs differed considerably between the three second generation techniques. The highest FPI rates were observed in RMN-2: 78% for left PVs and 74% for right PVs, while in the MAN-2 group and CB-2 group significantly lower rates were found ([Table 3] and [Figure 1], P<0.001). The TU rates reflected the FPI rates and highlighted a significant difference as well ([Table 3], P<0.001).

Post-hoc analysis

Post-hoc analysis investigated the significant differences in-between groups identified by the one-way ANOVA tests. The mean PVI procedures times were comparable between the second generation groups ([Table 2] and supplemental files). The mean procedure time significantly improved within each treatment technique over time ([Table 2] and supplemental files). The greatest magnitude of improvement of procedure time was observed within the RMN groups (Δ -180min), which was significant higher when compared to CB (Δ -48 min, P<0.001) and MAN (Δ -98min, P=0.011) groups ([Figure 2] and supplemental files). Post-hoc analysis showed that the encirclement time for left PVs was the longest in MAN-2 group

(27 ± 13.76 min), intermediate in RMN-2 (13 ± 5.40 min), while the shortest time was observed in the CB-2 group (6 ± 1.83 min) (MAN-2 vs. CB-2, P<0.001; MAN-2 vs. RMN-2, P<0.001; CB-2 vs. RMN-2, P=0.003). The encirclement times for right PVs showed the same pattern ([Table 3] and supplemental files).

12 month outcomes

Documented AF recurrence rates and redo procedure rates were analyzed for patients with paroxysmal and persistent AF separately. The results are presented in [Table 4]. The overall recurrence rate in paroxysmal AF was 31%, whereas in persistent AF the recurrence rate was 42%. In both paroxysmal and persistent AF, recurrence rates were comparable between groups ([Table 4], P=0.708 and P=0.622, respectively). In patients with paroxysmal AF treated with first generation CB (CB-1), a high redo procedure rate was detected (42%), which was significantly higher compared to the

Table 1: Patient demographic and clinical data

	MAN-1 (n=39)	CB-1(n=39)	RMN-1 (n=37)	MAN-2 (n=36)	CB-2(n=43)	RMN-2 (n=27)	All patients (n=221)	P-value
Age (years)	59 ±11.2	55 ±9.2A	57 ±9.4	62 ±8.4B	61 ±9.0	62 ±8.9	59 ±9.6	0.009
Female	12 (31%)	10 (26%)	11 (30%)	9 (25%)	7 (16%)	8 (30%)	57 (26%)	0.691
BMI (kg/m2)	28 ±4	27 ±4.0	28 ±4.5	27 ±4.7	27 ±3.2	28 ±3.0	27 ±4.0	0.733
AF duration (years)	2 (1 - 6)	2 (1 - 3)	3 (1 - 7)	3 (2 - 6)	3 (1 - 6)	3 (1 - 6)	1 (2 - 6)	0.056
Paroxysmal AF	26 (67%)	36 (92%)	18 (49%)	28 (78%)	39 (91%)	14 (52%)	161 (73%)	<0.001
Previous EP procedure (No PVI)	7 (18%)	5 (13%)	3 (8%)	8 (22%)	6 (14%)	5 (19%)	34 (15%)	0.629
Hypertension	13 (33%)	14 (36%)	14 (38%)	17 (47%)	21 (49%)	7 (26%)	86 (39%)	0.367
Hyperlipidemia	9 (23%)	7 (18%)	4 (11%)	7 (19%)	13 (30%)	6 (22%)	46 (21%)	0.422
Diabetes Mellitus	5 (13%)	3 (8%)	5 (14%)	2 (6%)	2 (5%)	2 (7%)	19 (9%)	0.640
Ischemic HD	8 (21%)	0 (0%)	4 (11%)	1 (3%)	4 (9%)	5 (19%)	22 (10%)	0.019
Dilated CMP	2 (5%)	0 (0%)	2 (5%)	0 (0%)	0 (0%)	0 (0%)	4 (2%)	0.169
OSAS	0 (0%)	3 (8%)	3 (8%)	2 (6%)	4 (9%)	0 (0%)	12 (5%)	0.311
CVA / TIA / PE	7 (18%)	1 (3%)	3 (8%)	1 (3%)	3 (7%)	4 (15%)	19 (9%)	0.102
CHA2DS2-VASc 0	12 (31%)	19 (49%)	12 (32%)	11 (31%)	15 (35%)	8 (30%)	77 (35%)	0.507
CHA2DS2-VASc 1	9 (23%)	12 (31%)	16 (43%)	13 (36%)	13 (30%)	7 (26%)	70 (32%)	0.491
CHA2DS2-VASc ≥2	18 (46%)	8 (21%)	9 (24%)	12 (33%)	15 (35%)	12 (44%)	74 (34%)	0.315
Beta-blocker	14 (36%)	21 (55%)	21 (57%)	21 (58%)	16 (37%)	14 (52%)	107 (49%)	0.162
Amiodarone	13 (33%)	5 (13%)	17 (46%)	9 (25%)	7 (16%)	2 (7%)	53 (24%)	0.002
Flecainide	8 (21%)	7 (19%)	7 (19%)	13 (36%)	13 (30%)	7 (26%)	55 (25%)	0.411
Sotalol	9 (23%)	6 (14%)	5 (14%)	7 (19%)	12 (28%)	7 (26%)	46 (21%)	0.598
Calcium antagonist	2 (5%)	3 (8%)	4 (11%)	0 (0%)	4 (9%)	2 (7%)	15 (7%)	0.515
Anticoagulation								
None	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1.000
VitaminK antagonist	36 (92%)	39 (100%)	37 (100%)	15 (42%)	18 (42%)	11 (41%)	155 (71%)	<0.001
DOAC	3 (7%)	0 (0%)	1 (3%)	21 (58%)	25 (58%)	16 (59%)	65 (30%)	<0.001
EF (%)	45 ±15.7	62 ±10.8	57 ±12.8	60 ±14.9	58 ±8.6	55 ±11.4	57 ±13.0	0.056
EF ≥55%	27 (69%)	34 (87%)	23 (68%)	29 (81%)	39 (91%)	22 (82%)	174 (80%)	0.065
EF 45 - 54%	9 (23%)	3 (8%)	6 (18%)	5 (14%)	3 (7%)	2 (7%)	28 (13%)	0.196
EF 30 - 44%	2 (5%)	2 (5%)	3 (9%)	2 (6%)	1 (2%)	3 (11%)	13 (6%)	0.716
EF <30%	1 (3%)	0 (0%)	2 (6%)	0 (0%)	0 (0%)	0 (0%)	3 (1%)	0.185
LA volume (ml)	87(67-103)	78 (65-89)	88(55-110)	79 (64-98)	76 (63-97)	92(67-108)	83 (65-100)	0.686
LA size (mm)	45 ±6.6	42 ±5.4	43 ±6.5	43 ±8.1	42 ±5.5	42 ±5.1	43 ±6.3	0.289

All continuous variables represent mean ± standard deviation and were analyzed with the one-way ANOVA. For variables with a significant ANOVA test, post-hoc analysis by Tukey's honestly significance difference test was performed. The significant relations found with the post-hoc analysis are marked by letter annotations. Labeled means in a row with a different letter annotation differ significantly. All categorical variables represent count (percentage) and were analyzed using the Chi-square test. When variables do not have a normal distribution, the median (IQR) is given and these were analyzed using the Kruskal-Wallis test. BMI = body mass index, AF = atrial fibrillation, EP = electrophysiology, PVI = pulmonary vein isolation, HD =heart disease, CMP = cardiomyopathy, OSAS = obstructive sleep apnea syndrome, CVA = cerebrovascular accident, TIA = transient ischemic attack, PE = pulmonary embolism, DOAC = direct acting oral anticoagulation, EF = ejection fraction, LA = left atrium.

Table 2: Procedural data

	MAN-1 (n=39)	CB-1 (n=39)	RMN-1 (n=37)	MAN-2 (n=36)	CB-2 (n=43)	RMN-2 (n=27)	All patients (n=221)	P-value
Procedure time (min) *	251 ±89.4 A	197 ±78.0 C	293 ±65.1 A	153 ±52.0 B	150 ±32.1 B	113 ±48.1 B	184 ±83.4	<0.001
Number of applications *	57 (41-77)	10 (8-13)	87 (56-122)	39 (27-53)	8 (6-11)	17 (15-25)	16 (9-48)	<0.001
Application duration (sec) *	1814 (1319-2284)	3253 (2667-4026)	2396 (1789-3135)	1522 (1244-2089)	1445 (1197-2012)	1568 (1211-1844)	1845 (1331-2681)	<0.001
Additional ablations (non-PVI triggers)	12 (31%)	7 (18%)	20 (54%)	16 (43%)	0 (0%)	15 (56%)	70 (32%)	<0.001

[Table 2] shows procedural data. When additional ablations (non-PVI triggers) were performed in addition to PVI, the presented procedure times, number of applications and application durations were corrected for this. All continuous variables represent mean ± standard deviation and were tested with the one-way ANOVA. For variables with a significant ANOVA test, post-hoc analysis by Tukey's honestly significance difference test was performed. The significant relations found with the post-hoc analysis are marked by letter annotations. Labeled means in a row with a different letter annotation differ significantly. Labeled means in a row with a common letter annotation are not significantly different. See the supplemental files for the detailed post-hoc analysis results. All categorical variables represent count (percentage) and were tested using the Chi-square test. When variables do not have normal distribution, the median (IQR) is given and these were analyzed using the Kruskal-Wallis test. * When additional ablations of non-PVI triggers were performed, the procedure times, number of applications and total application duration were corrected accordingly. PVI = pulmonary vein isolation.

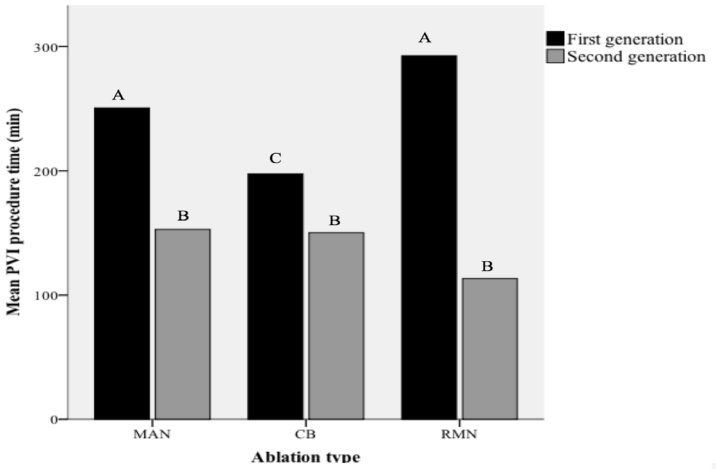

Figure 2: Mean procedure time

Figure 2 demonstrates the mean procedure time of the first and second generation treatment techniques. Mean procedure times were analyzed with the one-way ANOVA, which demonstrated a significantly different distribution in general (P<0.001). Results of the post-hoc analysis by Tukey's honestly significance difference test are marked by letter annotations. Labeled means with a different letter annotation differ significantly. Labeled means with a common letter annotation are not significantly different.
PVI = pulmonary vein isolation

Table 3: Procedural data of second generation procedures

	MAN-2 (n=36)	CB-2 (n=43)	RMN-2 (n=27)	All patients (n=221)	P-value
Left PVs encirclement time (min)	27 ±13.8 A	6 ±1.8 B	13 ±5.4 C	13 ±10.9	<0.001
Left PVs FPI rate	6 (24%)	21 (50%)	21 (78%)	50 (38%)	<0.001
Left PVs TU done	19 (76%)	21 (50%)	6 (22%)	83 (62%)	<0.001
Left PVs TU number	3 (0.5 - 7)	0.5 (0 - 2)	0 (0 - 0)	2 (0 - 4)	<0.001
Left PVs TU duration (sec)	64 ±66.4 A	229 ±322.3 B	37 ±78.4 A	413 ±558.7	0.002
Right PVs encirclement time (min)	28 ±15.3 A	5 ±2.0 B	13 ±7.3 C	13 ±12.0	<0.001
Right PVs FPI rate	6 (24%)	20 (47%)	20 (74%)	48 (36%)	<0.001
Right PVs TU done	19 (76%)	22 (52%)	7 (26%)	85 (64%)	<0.001
Right PVs TU number	2 (0.5 - 4.5)	1 (0 - 2)	0 (0 - 1)	2 (0 - 3)	<0.001
Right PVs TU duration (sec)	81 ±108.3	184 ±235.6	96 ±197.3	317 ±398.2	0.096

[Table 3] depicts procedural data of second generation procedures. All continuous variables represent mean ± standard deviation and were tested with the one-way ANOVA. For variables with a significant ANOVA test, post-hoc analysis by Tukey's honestly significance difference test was performed. The significant relations found with the post-hoc analysis are marked by letter annotations. Labeled means in a row with a different letter annotation differ significantly. Labeled means in a row with a common letter annotation are not significantly different. See the supplemental files for the detailed post-hoc analysis results. All categorical variables represent count (percentage) and were tested using the Chi-square test. When variables do not have normal distribution, the median (IQR) is given and analyzed using the Kruskal-Wallis test. PVs = pulmonary veins, FPI = first pass isolation, TU = touch up.

other groups (P=0.004). Moreover, the CB redo procedure rate improved significantly from first to second generation (CB-1 42% vs. CB-2 21%, P=0.005). No significant improvements over time were observed in-between first and second generation MAN and RMN.

Complication rates

Complication rates are shown in [Table 5] Total complication rates were higher in first generation procedures as compared to second generation procedures: 21% vs. 9% (P=0.010). In-between the three second generation treatment techniques, no significant differences were found (P=0.784), as well as in-between the three first generation techniques (P=0.662). The minor complication rate exhibited the same configuration, with significant improvement over time from first generation (16%) to second generation procedures (5%) (P=0.008). The major complication rate was comparable between first and second generation procedures (5% vs. 4% respectively, P=0.606). The majority of minor complications were access site complications not requiring intervention (N=10; 5%) and minor pericardial effusion not requiring intervention, noted during routine post-operative evaluation with TTE (N=7; 3%).

Discussion

This is the first clear study to compare the improvement of efficiency of three recognized treatment modalities of CA for AF: MAN guided RF, CB and RMN guided RF ablation. In accordance with other studies, all ablation techniques exhibited significant improvement of efficiency over time. However, the major finding of this study is that the magnitude of procedure time improvement was most explicit in RMN guided RF CA procedures. The progress made

Table 4: 12-month outcomes

Paroxysmal AF	MAN-1 (n=26)	CB-1 (n=36)	RMN-1 (n=18)	MAN-2 (n=28)	CB-2 (n=39)	RMN-2 (n=14)	All patients (n=161)	P-value
AF recurrence	8 (31%)	14 (39%)	7 (39%)	6 (21%)	11 (28%)	4 (29%)	50 (31%)	0.708
Redo procedure	4 (15%)	15 (42%)	3 (17%)	1 (4%)	8 (21%)	1 (7%)	32 (20%)	0.004
Paroxysmal AF	**MAN-1 (n=26)**	**CB-1 (n=36)**	**RMN-1 (n=18)**	**MAN-2 (n=28)**	**CB-2 (n=39)**	**RMN-2 (n=14)**	**All patients (n=161)**	**P-value**
AF recurrence	6 (46%)	1 (33%)	9 (47%)	4 (50%)	1 (25%)	4 (31%)	25 (42%)	0.880
Redo procedure	1 (8%)	1 (33%)	2 (10%)	0 (0%)	1 (25%)	2 (15%)	6 (10%)	0.622

[The documented AF recurrence rates and redo procedure rates 12-months following the PVI procedure are presented in [Table 4]. Results were analyzed for patients with paroxysmal AF and patients with persistent AF separately. Analysis was performed using the Chi-square test. ECG = electrocardiogram

Table 5: Complication rates

1st generation procedures	MAN-1 (n=39)	CB-1 (n=39)	RMN-1 (n=37)	Total (n=115)	P-value
All complications	10 (26%)	7 (18%)	7 (19%)	24 (21%)	0.662
Major complications	2 (5%)	3 (8%)	1 (3%)	6 (5%)	0.620
Minor complications	8 (21%)	4 (10%)	6 (16%)	18 (16%)	0.457
2nd generation procedures	**MAN-2 (n=36)**	**CB-2 (n=43)**	**RMN-2 (n=27)**	**Total (n=106)**	**P-value**
All complications	4 (11%)	3 (7%)	2 (7%)	9 (9%)	0.784
Major complications	1 (3%)	2 (5%)	1 (4%)	4 (4%)	0.909
Minor complications	3 (8%)	1 (2%)	1 (4%)	5 (5%)	0.437
All procedures	**1st generation (n=115)**	**2nd generation (n=106)**	**Total (n=221)**	**P-value**	
All complications	24 (21%)	9 (9%)	33 (15%)	0.010	
Major complications	6 (5%)	4 (4%)	10 (5%)	0.606	
Minor complications	18 (16%)	5 (5%)	23 (10%)	0.008	

Major, minor and total complication rates are visualized in [Table 5]. Percentages represent occurrence within procedure type. Comparison within first generation procedure types and within second generation procedure types was performed, as well as comparison between all first generation and between all second generation procedures. Analysis was performed using the Chi-square test.

in robotic navigation guided CA has resulted that nowadays ablation and procedure times are comparable with CB and MAN guided CA. Furthermore, the RMN guided RF CA has the highest potential for future advance.

Procedure and ablation times

The study by Kataria et al evaluated long-term outcome data of 336 patients undergoing PVI with MAN and RMN guided RF[22]. The investigators observed a significantly higher mean procedure time in the RMN group, when compared to the MAN group. Also, a significant difference in mean ablation time was found in favor of the MAN group. Similar results of higher procedural time of RMN guided RF ablation, in comparison to MAN guided RF ablation, were also described by Miyazaki et al. and Arya et al. and found in two meta-analyses[18,19,27,28]. A mean CB procedure time of 124 ± 39 minutes was observed in the Fire and Ice trial [23], whereas the current study noted a higher mean CB procedure time. This could be attributed to the standard 30 minutes of waiting time which is performed in all procedures in our center as standard of care. Moreover, due to the retrospective nature of our study with consecutive enrollment, procedures were sometimes performed by less experienced electrophysiologists.

To the best of our knowledge, no clear studies comparing the advancements of efficiency of three CA modalities (MAN, CB and RMN) have been performed. We found a significant improvement of both procedure and ablation times within each treatment modality over time, highlighting the technological advances made in each of them. The higher procedural time in the RMN guided RF ablation found in previous studies, was attributed to the additional time required to set up the navigational system, positioning of the patient and time required for placing the circular mapping catheter into different veins. In the present study, a notable evolvement of RMN procedure times was observed, which now makes procedure times comparable with CB. These advancements could be attributed to the use of a dedicated EP lab for RMN procedures, where the EP staff has a broad experience using the RMN hard- and software, as well as in positioning of the patient. Second, RMN guided PVI was performed only by highly experienced electrophysiologists, whereas in CB procedures less experienced electrophysiologists were sometimes performing the procedures. Third, multiple improvements were implemented to the RMN Niobe ES system, which for instance significantly improved the response time (defined as time of vector movement by the operator, until movement of the magnetic field) [29]. Moreover, we introduced a new ablation strategy in the RMN-2 group, implementing the latest technological advancements made in RMN guided RF CA. With the use of the 'Ablation History feature' and contact feedback by the 'e-Contact module', a new ablation approach for RMN guided PVI was designed: the 'Continuous Dragging' technique. While ablating, the catheter is dragged around both ipsilateral PVs by wide area circumferential ablation (WACA) with help of the e-Contact and Ablation History feedback, using high power settings. It was attempted to interrupt ablation as least as possible. Only after completing the encirclement of either right or left sided PVs, electrical isolation was evaluated. If necessary, additional touch ups were performed to acquire PV isolation. This approach resulted in our opinion, in an efficient and safe RMN guided PVI procedure.

First pass isolation

First pass isolation (FPI) was defined as the first encirclement (WACA) resulting in successful PV isolation. FPI in CB was regarded when the first cryo-application resulted in successful PV isolation. Interestingly, a high rate of FPI was observed in the RMN-

2 groups, which in our belief, is an affirmation of our new RMN ablation strategy. In CB-2, the first adequate application did not often result in successful isolation. However, when first pass isolation in CB occurs, the procedure is much shorter than other techniques. In our opinion, this emphasizes the convenience of CB ablation, but also its susceptibility to anatomic variants of PVs. Where CB and manual ablation catheters are still confined to uni- or bidirectional movement using pull wires[30], magnetic navigation ensures enhanced maneuverability of the ablation catheter that makes reach of difficult anatomical structures possible[13,31]. Therefore, in our opinion RMN is the preferential technique for ablation of anatomical variants of PVs.

12-month outcomes

Whereas the highest efficiency improvement was detected in RMN, the highest efficacy improvement was observed in CB. Although the current study was designed to evaluate procedural efficiency, we also observed a significant improvement of the CB redo procedure rates over time, which correspond with literature[12]. The efficacy improvement was not detected to such extent in the other techniques. In our opinion, this is because first generation MAN and RMN techniques already had acceptable long-term outcomes.

Complication rates

Numerous studies reported on complication rates of CA ablation techniques for AF, but data comparing three techniques is limited. A large meta-analysis by Cardoso et al[32] evaluated complication rates between CB and MAN guided RF CA. CB ablation was associated with a lower incidence of pericardial effusions or tamponade, but with a higher rate of transient phrenic nerve palsies. The Fire and Ice trial found a comparable primary safety endpoint between CB and MAN guided RF (a composite of death, cerebrovascular events or serious treatment related adverse events)[20]. Shurrab et al observed a non-significant overall complication rate between MAN guided PVI and RMN guided PVI procedures[27]. However, the meta-analysis by Proietti et al investigating MAN and RMN guided PVI, revealed that major complications were rare, but significantly different between MAN 5% and RMN 2% groups (OR 0.41, 95% CI 0.19 - 0.88, P=0.02)[28]. Both studies observed a significantly lower rate of significant pericardial complication in RMN guided ablation[27,28]. Unfortunately, the literature does not yet report a comparison between the three treatment techniques performed here. The present study, observed no significant improvement of major complications over time. The number of patients in this study however, may not be powered to detect a difference in major adverse events. Nevertheless, minor complication rates improved significantly over time between first and second generation procedures, accentuating advances in technology and operator experience.

Limitations

The techniques presented in this study, seem to have different learning curves. In our believe, it takes more time to master RMN and MAN ablation techniques, whereas CB ablation technique is most easily adopted. The present study is a retrospective, single-center study investigating an average cohort of patients who underwent CA for AF. The study aimed to investigate as many patients possible per group, but still only an average of 37 patients per group was included. Unfortunately, FPI and TU rates and encirclement times could only be evaluated in second generation procedures. In first generation procedures, different ablation strategies were used as standard of care, which made the data incomparable (e.g. in CB-1 group a standard of two applications per PV were performed regardless of electrical isolation). Prospective studies comparing the efficiency and outcomes of the three treatment modalities, as well as the presented new ablation strategy for RMN guided PVI, are desired to clearly define the role of RMN in CA of AF.

Conclusions

The highest magnitude of procedural efficiency improvement, as defined by procedure times, ablation times and first-pass isolation rates, was detected in RMN guided PVI. Because of the technical advances made in the robotic navigation ablation technique, it has become as efficient as CB and MAN guided PVI. The efficiency evolution observed in RMN guided PVI, highlights that this technique has most potential for future advance.

References

1. Chugh SS, Havmoeller R, Narayanan K, Singh D, Rienstra M, Benjamin EJ, Gillum RF, Kim YH, McAnulty JH, Jr., Zheng ZJ, Forouzanfar MH, Naghavi M, Mensah GA, Ezzati M, Murray CJ. Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. Circulation. 2014; 129: 837-847.
2. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener HC, Heidbuchel H, Hendriks J, Hindricks G, Manolis AS, Oldgren J, Popescu BA, Schotten U, Van Putte B, Vardas P, Agewall S, Camm J, Baron Esquivias G, Budts W, Carerj S, Casselman F, Coca A, De Caterina R, Deftereos S, Dobrev D, Ferro JM, Filippatos G, Fitzsimons D, Gorenek B, Guenoun M, Hohnloser SH, Kolh P, Lip GY, Manolis A, McMurray J, Ponikowski P, Rosenhek R, Ruschitzka F, Savelieva I, Sharma S, Suwalski P, Tamargo JL, Taylor CJ, Van Gelder IC, Voors AA, Windecker S, Zamorano JL, Zeppenfeld K. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J. 2016; 37: 2893-2962.
3. Calkins H, Hindricks G, Cappato R, Kim YH, Saad EB, Aguinaga L, Akar JG, Badhwar V, Brugada J, Camm J, Chen PS, Chen SA, Chung MK, Cosedis Nielsen J, Curtis AB, Davies DW, Day JD, d'Avila A, Natasja de Groot NMS, Di Biase L, Duytschaever M, Edgerton JR, Ellenbogen KA, Ellinor PT, Ernst S, Fenelon G, Gerstenfeld EP, Haines DE, Haissaguerre M, Helm RH, Hylek E, Jackman WM, Jalife J, Kalman JM, Kautzner J, Kottkamp H, Kuck KH, Kumagai K, Lee R, Lewalter T, Lindsay BD, Macle L, Mansour M, Marchlinski FE, Michaud GF, Nakagawa H, Natale A, Nattel S, Okumura K, Packer D, Pokushalov E, Reynolds MR, Sanders P, Scanavacca M, Schilling R, Tondo C, Tsao HM, Verma A, Wilber DJ, Yamane T. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. Europace. 2017.
4. Haegeli LM, Calkins H. Catheter ablation of atrial fibrillation: an update. Eur Heart J. 2014; 35: 2454-2459.
5. Haissaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G, Garrigue S, Le Mouroux A, Le Metayer P, Clementy J. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med. 1998; 339: 659-666.
6. Arentz T, Haegeli L, Sanders P, Weber R, Neumann FJ, Kalusche D, Haissaguerre M. High-density mapping of spontaneous pulmonary vein activity initiating atrial fibrillation in humans. J Cardiovasc Electrophysiol. 2007; 18: 31-38.
7. Oral H, Knight BP, Tada H, Ozaydin M, Chugh A, Hassan S, Scharf C, Lai SW, Greenstein R, Pelosi F, Jr., Strickberger SA, Morady F. Pulmonary vein isolation for paroxysmal and persistent atrial fibrillation. Circulation. 2002; 105: 1077-1081.

8. Reddy VY, Dukkipati SR, Neuzil P, Natale A, Albenque JP, Kautzner J, Shah D, Michaud G, Wharton M, Harari D, Mahapatra S, Lambert H, Mansour M. Randomized, Controlled Trial of the Safety and Effectiveness of a Contact Force-Sensing Irrigated Catheter for Ablation of Paroxysmal Atrial Fibrillation: Results of the TactiCath Contact Force Ablation Catheter Study for Atrial Fibrillation (TOCCASTAR) Study. Circulation. 2015; 132: 907-915.
9. Manolis AS. Ablation of atrial fibrillation: single-shot techniques poised to dominate rhythm control strategies/the future is hereJ Thorac Dis. China 2017: E313-e321.
10. Packer DL, Kowal RC, Wheelan KR, Irwin JM, Champagne J, Guerra PG, Dubuc M, Reddy V, Nelson L, Holcomb RG, Lehmann JW, Ruskin JN. Cryoballoon ablation of pulmonary veins for paroxysmal atrial fibrillation: first results of the North American Arctic Front (STOP AF) pivotal trial. J Am Coll Cardiol. 2013; 61: 1713-1723.
11. Nobre Menezes M, Cortez-Dias N, Carpinteiro L, de Sousa J. One-Shot Ablation For PV Isolation. J Atr Fibrillation. 2014; 7: 1111.
12. Di Giovanni G, Wauters K, Chierchia GB, Sieira J, Levinstein M, Conte G, de Asmundis C, Baltogiannis G, Saitoh Y, Ciconte G, Julia J, Mugnai G, Irfan G, Brugada P. One-year follow-up after single procedure Cryoballoon ablation: a comparison between the first and second generation balloon. J Cardiovasc Electrophysiol. 2014; 25: 834-839.
13. Faddis MN, Blume W, Finney J, Hall A, Rauch J, Sell J, Bae KT, Talcott M, Lindsay B. Novel, magnetically guided catheter for endocardial mapping and radiofrequency catheter ablation. Circulation. 2002; 106: 2980-2985.
14. Faddis MN, Chen J, Osborn J, Talcott M, Cain ME, Lindsay BD. Magnetic guidance system for cardiac electrophysiology: a prospective trial of safety and efficacy in humans. J Am Coll Cardiol. 2003; 42: 1952-1958.
15. Bhaskaran A, Barry MA, Al Raisi SI, Chik W, Nguyen DT, Pouliopoulos J, Nalliah C, Hendricks R, Thomas S, McEwan AL, Kovoor P, Thiagalingam A. Magnetic guidance versus manual control: comparison of radiofrequency lesion dimensions and evaluation of the effect of heart wall motion in a myocardial phantom. J Interv Card Electrophysiol. 2015; 44: 1-8.
16. Pappone C, Vicedomini G, Frigoli E, Giannelli L, Ciaccio C, Baldi M, Zuffada F, Saviano M, Pappone A, Crisa S, Petretta A, Santinelli V. Irrigated-tip magnetic catheter ablation of AF: a long-term prospective study in 130 patients. Heart Rhythm. 2011; 8: 8-15.
17. Jin QI, Pehrson S, Jacobsen PK, Chen XU. Efficacy and Safety of Atrial Fibrillation Ablation Using Remote Magnetic Navigation: Experience from 1,006 Procedures. J Cardiovasc Electrophysiol. 2016; 27 Suppl 1: S23-28.
18. Arya A, Zaker-Shahrak R, Sommer P, Bollmann A, Wetzel U, Gaspar T, Richter S, Husser D, Piorkowski C, Hindricks G. Catheter ablation of atrial fibrillation using remote magnetic catheter navigation: a case-control study. Europace. 2011; 13: 45-50.
19. Miyazaki S, Shah AJ, Xhaet O, Derval N, Matsuo S, Wright M, Nault I, Forclaz A, Jadidi AS, Knecht S, Rivard L, Liu X, Linton N, Sacher F, Hocini M, Jais P, Haissaguerre M. Remote magnetic navigation with irrigated tip catheter for ablation of paroxysmal atrial fibrillation. Circ Arrhythm Electrophysiol. 2010; 3: 585-589.
20. Kuck KH, Furnkranz A, Chun KR, Metzner A, Ouyang F, Schluter M, Elvan A, Lim HW, Kueffer FJ, Arentz T, Albenque JP, Tondo C, Kuhne M, Sticherling C, Brugada J. Cryoballoon or radiofrequency ablation for symptomatic paroxysmal atrial fibrillation: reintervention, rehospitalization, and quality-of-life outcomes in the FIRE AND ICE trial. Eur Heart J. 2016; 37: 2858-2865.
21. Luik A, Radzewitz A, Kieser M, Walter M, Bramlage P, Hormann P, Schmidt K, Horn N, Brinkmeier-Theofanopoulou M, Kunzmann K, Riexinger T, Schymik G, Merkel M, Schmitt C. Cryoballoon Versus Open Irrigated Radiofrequency Ablation in Patients With Paroxysmal Atrial Fibrillation: The Prospective, Randomized, Controlled, Noninferiority FreezeAF Study. Circulation. 2015; 132: 1311-1319.
22. Kataria V, Berte B, Vandekerckhove Y, Tavernier R, Duytschaever M. Remote Magnetic versus Manual Navigation for Radiofrequency Ablation of Paroxysmal Atrial Fibrillation: Long-Term, Controlled Data in a Large Cohort. Biomed Res Int. 2017; 2017: 6323729.
23. Kuck KH, Brugada J, Furnkranz A, Metzner A, Ouyang F, Chun KR, Elvan A, Arentz T, Bestehorn K, Pocock SJ, Albenque JP, Tondo C. Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation. N Engl J Med. 2016; 374: 2235-2245.
24. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC, Jr., Conti JB, Ellinor PT, Ezekowitz MD, Field ME, Murray KT, Sacco RL, Stevenson WG, Tchou PJ, Tracy CM, Yancy CW. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2014; 64: e1-76.
25. Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S, Van Gelder IC, Al-Attar N, Hindricks G, Prendergast B, Heidbuchel H, Alfieri O, Angelini A, Atar D, Colonna P, De Caterina R, De Sutter J, Goette A, Gorenek B, Heldal M, Hohloser SH, Kolh P, Le Heuzey JY, Ponikowski P, Rutten FH. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Eur Heart J. 2010; 31: 2369-2429.
26. Fuster V, Ryden LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, Halperin JL, Le Heuzey JY, Kay GN, Lowe JE, Olsson SB, Prystowsky EN, Tamargo JL, Wann S, Smith SC, Jr., Jacobs AK, Adams CD, Anderson JL, Antman EM, Hunt SA, Nishimura R, Ornato JP, Page RL, Riegel B, Priori SG, Blanc JJ, Budaj A, Camm AJ, Dean V, Deckers JW, Despres C, Dickstein K, Lekakis J, McGregor K, Metra M, Morais J, Osterspey A, Zamorano JL. ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. Circulation. 2006; 114: e257-354.
27. Shurrab M, Danon A, Lashevsky I, Kiss A, Newman D, Szili-Torok T, Crystal E. Robotically assisted ablation of atrial fibrillation: a systematic review and meta-analysis. Int J Cardiol. 2013; 169: 157-165.
28. Proietti R, Pecoraro V, Di Biase L, Natale A, Santangeli P, Viecca M, Sagone A, Galli A, Moja L, Tagliabue L. Remote magnetic with open-irrigated catheter vs. manual navigation for ablation of atrial fibrillation: a systematic review and meta-analysis. Europace. 2013; 15: 1241-1248.
29. Da Costa A, Guichard JB, Maillard N, Romeyer-Bouchard C, Gerbay A, Isaaz K. Substantial superiority of Niobe ES over Niobe II system in remote-controlled magnetic pulmonary vein isolation. Int J Cardiol. 2017; 230: 319-323.
30. Aagaard P, Natale A, Briceno D, Nakagawa H, Mohanty S, Gianni C, Burkhardt JD, L DIB. Remote Magnetic Navigation: A Focus on Catheter Ablation of Ventricular Arrhythmias. J Cardiovasc Electrophysiol. 2016; 27 Suppl 1: S38-44.
31. Parreira L, Cavaco D, Reis-Santos K, Carmo P, Cabrita D, Scanavacca M, Adragao P. Remote magnetic navigation for mapping and ablation of right and left ventricular outflow tract arrhythmias. Rev Port Cardiol. 2013; 32: 489-495.
32. Cardoso R, Mendirichaga R, Fernandes G, Healy C, Lambrakos LK, Viles-Gonzalez JF, Goldberger JJ, Mitrani RD. Cryoballoon versus Radiofrequency Catheter Ablation in Atrial Fibrillation: A Meta-Analysis. J Cardiovasc Electrophysiol. 2016; 27: 1151-1159.

Supplemental Material

Table 1: Post-hoc analysis of procedure time (min)

Procedure	Number	Mean	SD	Compared to procedure type	P-value
MAN-1	39	251	89.41	CB-1	0.018
				RMN-1	0.256
				MAN-2	<0.001
				CB-2	<0.001
				RMN-2	<0.001
CB-1	39	198	77.96	MAN-1	0.018
				RMN-1	<0.001
				MAN-2	0.046
				CB-2	0.033
				RMN-2	<0.001
RMN-1	37	293	65.14	MAN-1	0.256
				CB-1	<0.001
				MAN-2	<0.001
				CB-2	<0.001
				RMN-2	<0.001
MAN-2	36	153	52.09	MAN-1	<0.001
				CB-1	0.046
				RMN-1	<0.001
				CB-2	1.000
				RMN-2	0.141
CB-2	43	150	32.13	MAN-1	<0.001
				CB-1	0.033
				RMN-1	<0.001
				MAN-2	1.000
				RMN-2	0.212
RMN-2	27	113	48.10	MAN-1	<0.001
				CB-1	<0.001
				RMN-1	<0.001
				CB-2	0.212
				MAN-2	0.141

Table 1 presents results of the post-hoc analysis of procedure time. Post-hoc analysis was performed by the Tukey's honestly significance difference test as part of the one-way ANOVA to investigate the in-between relationships between the 6 ablation techniques.

Table 2a: Post-hoc analysis of encirclement time of left PVs

Procedure type	Number	Mean (min)	SD	Compared to procedure type	P-value
MAN-2	36	28	13.76	CB-2	<0.001
				RMN-2	<0.001
CB-2	43	5	1.83	MAN-2	<0.001
				RMN-2	0.004
RMN-2	27	13	5.40	MAN-2	<0.001
				CB-2	0.004

Table 2a presents results of the post-hoc analysis of the mean encirclement time of left PVs. Post-hoc analysis was performed by the Tukey's honestly significance difference test as part of the one-way ANOVA to investigate the in-between relationships between the 3 second generation ablation techniques. PVs = pulmonary veins

Table 2b: Post-hoc analysis of encirclement time of right PVs

Procedure type	Number	Mean (min)	SD	Compared to procedure type	P-value
MAN-2	36	28	15.27	CB-2	<0.001
				RMN-2	<0.001
CB-2	43	6	1.83	MAN-2	<0.001
				RMN-2	0.003
RMN-2	27	13	5.40	MAN-2	<0.001
				CB-2	0.004

Table 2b presents results of the post-hoc analysis of the mean encirclement time of right PVs. Post-hoc analysis was performed by the Tukey's honestly significance difference test as part of the one-way ANOVA to investigate the in-between relationships between the 3 second generation ablation techniques. PVs = pulmonary veins.

Table 3: Post-hoc analysis of TU application duration of left PVs

Procedure type	Number	Mean (min)	SD	Compared to procedure type	P-value
MAN-2	36	65	66.37	CB-2	0.026
				RMN-2	0.911
CB-2	43	229	322.28	MAN-2	0.026
				RMN-2	0.003
RMN-2	27	37	78.40	MAN-2	0.911
				CB-2	0.003

Table 3a presents results of the post-hoc analysis of the touch up application duration of left PVs. Post-hoc analysis was performed by the Tukey's honestly significance difference test as part of the one-way ANOVA to investigate the in-between relationships between the 3 second generation ablation techniques. TU = touch up. PVs = pulmonary veins.