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Robotic magnetic navigation-guided catheter ablation establishes highly effective pulmonary vein isolation in patients with paroxysmal atrial fibrillation when compared to conventional ablation techniques

Anna M. E. Noten MD[1] | Alexander Romanov MD, PhD[2] | Koen De Schouwer MD, PhD[3] | Vladimir Beloborodov MD[2] | Rohit Bhagwandien MD, PhD[1] | Mark G. Hoogendijk MD, PhD[1] | Igor Mikheenko MD[2] | Sip Wijchers MD[1] | Sing-Chien Yap MD, PhD[1] | Bruno Schwagten MD, PhD[3] | Tamas Szili-Torok MD, PhD[1]

[1]Department of Cardiology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

[2]E. Meshalkin National Medical Research Center of the Ministry of Health of the Russian Federation, Novosibirsk, Russia

[3]Department of Cardiology, Ziekenhuis Netwerk Antwerpen, Antwerp, Belgium

Correspondence
Anna M. E. Noten, MD, Department of Clinical Electrophysiology, Thoraxcenter, Erasmus MC, Postbus 2040, 3000 CA Rotterdam, The Netherlands.
Email: a.noten@erasmusmc.nl

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Abstract

Introduction: Pulmonary vein isolation (PVI) is a pivotal part of ablative therapy for atrial fibrillation (AF). Currently, there are multiple techniques available to realize PVI, including: manual-guided cryoballoon (MAN-CB), manual-guided radiofrequency (MAN-RF), and robotic magnetic navigation-guided radiofrequency ablation (RMN-RF). There is a lack of large prospective trials comparing contemporary RMN-RF with the more conventional ablation techniques. This study prospectively compared three catheter ablation techniques as treatment of paroxysmal AF.

Methods: This multicenter, prospective study included patients with paroxysmal AF who underwent their first ablation procedure. Procedural parameters (including procedural efficiency), complication rates, and freedom of AF during 12-month follow-up, were compared between three study groups which were defined by the utilized ablation technique.

Results: A total of 221 patients were included in this study. Total procedure time was significantly shorter in MAN-CB (78 ± 21 min) compared to MAN-RF (115 ± 41 min; $p < .001$) and compared to RMN-RF (129 ± 32 min; $p < .001$), whereas it was comparable between the two radiofrequency (RF) groups ($p = .062$). A 3% complication rate was observed, which was comparable between all groups. At 12-month follow-up, AF recurrence was observed in 40 patients (19%) and was significantly lower in the robotic group (MAN-CB 19 [24%], MAN-RF 16 [23%],

Abbreviations: AAD, antiarrhythmic drugs; AF, atrial fibrillation; CA, catheter ablation; FPI, first-pass isolation; LA, left atrium; OSAS, obstructive sleep apnea syndrome; PV, pulmonary vein; PVI, pulmonary vein isolation; RF, radiofrequency; RMN, robotic magnetic navigation; TOE, transesophageal echocardiography; TSP, transseptal puncture; TU, touch-up; WACA, wide area circumferential ablation.

RMN-RF 5 [8%] AF recurrences, $p = .045$) (multivariate hazard ratio of RMN-RF on AF recurrence 0.32, 95% confidence interval: 0.12–0.87, $p = .026$).

Conclusion: RMN-guided PVI results in high freedom of AF in patients with paroxysmal AF, when compared to cryoablation and manual RF ablation. Cryoablation remains the most time-efficient ablation technique, whereas RMN nowadays has comparable efficiency with manual RF ablation.

KEYWORDS

atrial fibrillation, cryoablation, pulmonary vein isolation, radiofrequency ablation, remote magnetic navigation, robotic magnetic navigation

1 | INTRODUCTION

Atrial fibrillation (AF) is the most prevalent sustained cardiac arrhythmia worldwide, with a growing incidence.[1–3] It has a progressive disease course, characterized by worsening atrial structural remodeling and aggravating atrial cardiomyopathy during the evolution from a paroxysmal to a more persistent state.[4,5]

Early rhythm control strategies, such as catheter ablation (CA), offer an opportunity to halt the progressive pathoanatomical alterations associated with AF.[6] In symptomatic AF patients, CA is thus considered a first-choice treatment. Besides, it is an important treatment option once treatment with antiarrhythmic drugs (AADs) has failed.[1] The essential part of any AF ablative therapy is the electrical isolation of the pulmonary veins (PVs),[7] which can be achieved by various ablation techniques. These include manual point-by-point radiofrequency (RF) ablation and manual ablation using single-shot devices such as the cryoballoon (CB).[1,8,9] Long-term success and adverse events rates were similar between these two techniques, whereas the CB had a slightly shorter procedure time, though higher fluoroscopy exposure when compared to manual point-by-point RF ablation.[8,9]

Robotic (or remote) magnetic navigation (RMN)-guided ablation is considered an alternative RF CA strategy. In RMN, the movement of the ablation catheter is robotically and remotely directed by the magnetic force created by two external permanent magnets alongside the patient.[10] Various studies reported on the benefits of RMN due to the precision of catheter movement, its stability, and its catheter's flexible tip, enhancing both lesion formation[11] and procedural safety.[12–14] Moreover, the procedural efficiency of RMN-guided AF ablation increased significantly during the last years.[15]

Because of the expanding AF pandemic, ablative technologies are warranted that are both highly efficient and efficacious. There is a lack of large prospective trials comparing contemporary, further developed RMN with the other available CA techniques in the treatment of paroxysmal AF. Therefore, we aimed to systematically evaluate and compare long-term efficacy and procedural parameters between the available CA techniques.

2 | METHODS

2.1 | Design

This study is a prospective, multicenter study investigating paroxysmal AF ablative therapies. Three study groups were defined by the CA technique used: Manual-guided cryoballoon ablation (MAN-CB), manual point-by-point radiofrequency ablation (MAN-RF), and RMN-guided RF ablation (RMN-RF). The primary endpoint was the freedom of AF recurrence during 12 months of follow-up (FU). We also analyzed the following secondary endpoints: procedural efficiency (characterized by total procedure time, the duration of various successive procedure steps, and application duration), fluoroscopy exposure, acute success (including first-pass isolation [FPI], touch-up [TU] rates and successful PVI at the end of the procedure) and complication rates. The study protocol conforms to the ethical guidelines of the Declaration of Helsinki and was registered at ClinicalTrials.gov (NCT03695484).

2.2 | Study population

This prospective, multicenter study consecutively included patients ≥18 years of age, with documented paroxysmal AF who received their first AF ablation procedure between October 2018 and June 2021. Patients were not eligible for inclusion when they had any of the following criteria: persistent AF, any previous AF ablation procedure, other ablations performed in addition to PVI during the index procedure (e.g., additional ablation lines), active endocarditis or systemic infection, pregnancy, or absence of signed informed consent. All patients were eligible for CA according to the current guidelines.[1,16] All patients provided their signed informed consent before the ablation procedure.

2.3 | Data collection

Baseline demographic and clinical data were collected from the institutional electronic patient dossiers. Procedural data was

collected during the procedure using worksheets and/or the electronic patient dossier. Complications and FU data were also collected in the same manner. All de-identified data were collected in the online database (OpenClinica).

2.4 | Study sites

This study was initiated by the Society of Cardiac Robotic Navigation (SCRN), an independent platform for users of robotic technology in cardiology. RMN operating electrophysiologists were invited by the SCRN to participate in this study. Centers were only able to participate when they performed all three CA techniques for paroxysmal AF at their center. Investigators had to meet volume criteria to be able to participate (i.e., at least 50 patients treated in each of the past 2 years for any given technology). Eventually, three centers participated in this study. These included: the Erasmus Medical Center, Ziekenhuis Netwerk Antwerpen, and the E. Meshalkin National Medical Research Center of the Ministry of Health of the Russian Federation (Meshalkin National Medical Research Center).

2.5 | Procedural protocol

PV anatomy was evaluated in all patients preoperatively with a CT scan. Patients with a left common ostium, anatomical variants, and/or a PV size >24 mm were scheduled for PVI with RF (either MAN or RMN guided) as standard of care. All patients awaiting their AF ablation were distributed from the waiting list based on availability to the RMN-equipped or the conventional electrophysiology (EP) laboratory. Presence of intracardiac thrombus was evaluated preprocedurally by transesophageal echocardiography (TOE).

Procedures were performed with local anesthesia, conscious sedation, or general anesthesia up to the operator's preference. A groin puncture was performed to obtain femoral vein access. Subsequently transseptal puncture (TSP) was performed, using an EP Swartz SL1 sheath (Abbott) and a BRK (St. Jude Medical Inc.) or NRG transseptal needle (Baylis Medical). Guidance of TSP with fluoroscopy only, TOE, or intracardiac echocardiography was used up to operators' preferences. Unfractionated heparin was administrated with target-activated clotting time >300 to 350 s.

In MAN-CB, a quadripolar catheter was placed in the right ventricular during ablation of left-sided PVs or right subclavian vein for phrenic nerve pacing while ablating the right-sided PVs. Via single transseptal access, the CB was advanced into the left atrium (LA), and the individual PVs were treated subsequently. Indication of good occlusion was a grade 4 occlusion (i.e., no contrast leakage). The standard duration of cryotherapy was 180 s, which was prolonged up to the operator's preference when the time to isolation was >60 s or the temperature drop was suboptimal. Successful isolation of PVs was checked in all patients at the end of the procedure and if not, additional applications were made. Patients in the CB group were treated with the second- or fourth-generation Arctic Front Advance CB (Medtronic).

Regarding MAN-RF and RMN-RF groups, following TSP, passive recrossing of the intra-atrial septum was performed using the Agilis 8.5Fr NTX medium curl sheath (Abbott) and a flexible wire, to obtain double transseptal LA access. A 20-electrode lasso mapping catheter (Biosense Webster Inc.) and the ablation catheter were advanced into the LA subsequently. RF procedures were performed using either the EnSite NavX (St. Jude Medical Inc.) or the CARTO 3D (Biosense Webster) mapping systems. Fast anatomical mapping of the LA was performed with a multielectrode Lasso catheter to map the body of the LA (using a low resolution of around 10.0–13.0). More detailed mapping of the PV ostia and LAA was performed using the ablation catheter (higher resolutions around 15.0–18.0). Subsequently, wide area circumferential ablation (WACA) of the left-sided and right-sided PVs was performed. In MAN-RF this was done by point-by-point RF applications. In RMN-RF this was done by either point-by-point ablation or continuous dragging of the ablation catheter while ablating, up to the operator's preference. In all the MAN-RF patients contact force sensing catheters were used, including: the TactiCath contact force sensing catheters (St. Jude Medical) or the Thermocool Smarttouch catheters (Biosense Webster). RMN-RF procedures were performed using the Niobe ES Magnetic Navigation System (Stereotaxis), with the use of the NaviStar ThermoCool RMT catheter (Biosense Webster). MAN-RF ablation settings were: anterior wall 35 W, posterior wall 30 W, temperature limit 43°C, flow 17 mL/min, in Carto procedures an ablation index of 500 (400 for posterior wall), in EnSite procedures a Lesion Index of 5.0 (posterior wall 4.0) and contact force >10 <40 g.[17] RMN-RF ablation settings were: anterior wall 50 W, posterior wall 45 W, temperature limit 43°C, flow 17 mL/min, with guidance of the E-Contact Module and Ablation History features.[18]

All patients were observed at the cardiac unit after the procedure, with hemodynamic and respiratory monitoring and continuous electrocardiogram (ECG) recordings. The presence of pericardial effusion was checked in all patients postoperatively with transthoracic echography as the standard of care.

2.6 | Definitions

Total procedure time was defined as the time from the first puncture until the removal of sheaths. TSP time was defined as the time from the first groin puncture until double transseptal LA access was achieved. The mapping time was described as the time from the first mapping point taken until the completion of the map, whereas ablation duration was defined as the time from the first RF application until the last RF application. Regarding RF ablation, FPI was regarded when completion of the WACA-line resulted in successful PV isolation. If this first encirclement of PVs did not result in the isolation of the PV, additional applications were regarded as TU. In cryoablation, FPI was regarded when the first fully completed application resulted in successful PVI. Additional applications were regarded as TU. Acute procedure success was regarded when there was complete electrical isolation of the PVs at the end of the

procedure, to be demonstrated by either: an entry block or exit block of paced or spontaneous beats or exit block of PV ectopy.

2.7 | Follow-up

Following the index procedure, patients were regularly checked at the outpatient clinic. Standard follow-up visits were: 3, 6, and 12 months after the procedure. Symptoms, AAD treatment, vitals, and ECG recordings were evaluated during all FU visits. Seven-day Holter monitoring was conducted at every 12-month FU visit as standard of care. Following the ablation procedure, patients underwent a 90-day blanking period where arrhythmias were allowed to resolve. During this period, complications were accumulated but no other outcome measurements were done. Freedom of AF was regarded when no recurrent AF was documented by either 12-lead ECG, Holter rhythm observation, and/or implanted cardiac devices (reveal, pacemaker, or implantable cardioverter defibrillator) during FU.

2.8 | Statistical analysis

Normality was assessed by distribution on the normality plots and the Kolmogorov–Smirnov test. Mean and standard deviation were calculated for normally distributed continuous variables. Median and interquartile range (IQR) were computed for continuous variables with non-normal distribution. Continuous variables were compared between the three groups with the one-way analysis of variance (ANOVA), or the Kruskal–Wallis test in case of non-normal distribution. When a significant main effect was observed using the one-way ANOVA, the differences in-between the groups were evaluated using Tukey's post hoc honest significant difference test. Descriptive statistics for categorical data were expressed in absolute numbers and percentages and compared with the χ^2 test, or when appropriate the Fisher's exact test. Univariable and multivariable Cox proportional hazards models were used to examine the relationship between the treatment group and long-term outcomes, adjusting for potential confounders. Subsequently, when a clear benefit of one technique over others was observed, a multivariate model using a propensity score was designed. The propensity score was calculated using a logistic regression model including multiple co-variates as well as the ablation technique (RMN-RF vs. non-RMN-RF groups). Subsequently, propensity score adjustment was performed including ablation technique and propensity score in the Cox regression models. A two-sided p value of <.05 was considered significant. The data was analyzed using SPSS 26.0 (SPSS Inc.).

3 | RESULTS

In total, 211 patients were included in this study. Eighty patients were treated with MAN-CB, whereas 71 were treated with MAN-RF and 60 with RMN-RF, respectively (Figure 1). There were no crossovers between ablation techniques.

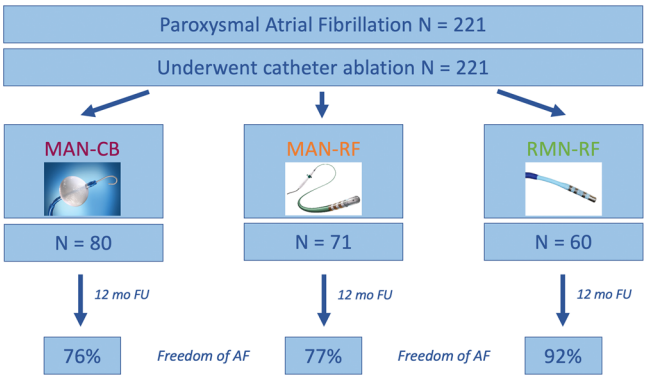

FIGURE 1 This prospective multicenter study investigated ablative therapy techniques as a treatment of paroxysmal atrial fibrillation (AF). This figure presents a schematical overview of the study population and distribution among the treatment groups. After 12 months of follow-up, there was an 81% freedom of AF in general, which was significantly higher in patients treated with robotic magnetic navigation-guided radiofrequency (RMN-RF). FU, follow-up; MAN-CB, manual-guided cryoballoon; MAN-RF, manual-guided radiofrequency.

3.1 | Baseline demographic and clinical data

Baseline demographic and clinical data of patients are presented in Table 1. The mean age of patients was 60 ± 10 years and there was a male predominance (39% female). Patients were diagnosed with AF for a median duration of 29 (IQR: 10–67) months. The majority of patients had a history of hypertension (53%). Nine percent had known coronary artery disease. Most of the patients had a normal or only mildly reduced left ventricular ejection fraction (LVEF) (99% had an LVEF ≥ 45%). The mean LA volume was 66 ± 19 mL. Various AADs were used by patients (see Table 1), whereas 45% did not receive daily treatment with AAD. Baseline characteristics were comparable between groups, with the exception of a history of congestive heart failure, which was more frequently present in the RMN-RF group (0% vs. 3% vs. 27%, $p < .001$, for MAN-CB, MAN-RF, and RMN-RF, respectively).

3.2 | Procedural efficiency

Procedural efficiency parameters are presented in Table 2. Procedures were performed under general anesthesia in 44% of patients, and this was significantly more frequently used in patients treated with RF techniques (19% vs. 63% vs. 56%, $p < .001$, for MAN-CB, MAN-RF, and RMN-RF, respectively). The mean procedure time was 105 ± 38 min (see Figure 2). The procedure time was significantly shorter in MAN-CB compared to MAN-RF (78 ± 21 vs. 115 ± 41 min, $p < .001$) and MAN-CB compared to RMN-RF (78 ± 21 vs. 129 ± 32 min, $p < .001$), whereas it was comparable between the two RF techniques ($p = .062$) (see Table 2). This was mainly due to the employed mapping time in both RF groups (23 ± 12 and 27 ± 13 min, for MAN-RF and RMN-RF, respectively; compared to a CB setup time of 7 ± 6 min in MAN-CB) and an increased ablation duration in both

TABLE 1 Baseline demographic and clinical data.

	MAN-CB, *N* = 80	MAN-RF, *N* = 71	RMN-RF, *N* = 60	Total, *N* = 211	*p* Value
Age (years)	60 ± 12	58 ± 9	61 ± 8	60 ± 10	.36
Female	27 (34%)	32 (45%)	23 (39%)	82 (39%)	.36
BMI (kg/m^2)	28 ± 4	28 ± 4	28 ± 4	28 ± 4	.93
Diabetes mellitus	6 (8%)	4 (6%)	10 (17%)	20 (10%)	.07
Hypertension	33 (41%)	38 (53%)	40 (67%)	111 (53%)	.01
Dyslipidemia	15 (19%)	7 (10%)	8 (13%)	30 (14%)	.29
OSAS	2 (3%)	2 (3%)	1 (2%)	5 (2%)	.91
Stroke	3 (4%)	5 (7%)	3 (5%)	11 (5%)	.66
Prior PCI	8 (10%)	1 (1%)	7 (12%)	16 (8%)	.05
Prior CABG	1 (1%)	1 (1%)	1 (2%)	3 (1%)	.98
Congestive heart failure	0 (0%)	2 (3%)	16 (27%)	18 (9%)	<.001
Valvular heart disease	4 (5%)	2 (3%)	2 (3%)	8 (4%)	.76
CHADS2-VASC2 = 0	22 (28%)	15 (21%)	10 (17%)	47 (22%)	.30
CHADS2-VASC2 = 1	19 (24%)	14 (20%)	6 (10%)	39 (19%)	.11
CHADS2-VASC2 = 2	21 (26%)	26 (37%)	21 (35%)	68 (32%)	.34
CHADS2-VASC2 ≥ 3	18 (23%)	16 (23%)	23 (38%)	57 (27%)	.07
AF duration (months)	32 (9–82)	26 (10–48)	27 (14–64)	29 (10–67)	.59
Other arrhythmias					
Atrial flutter	8 (10%)	14 (20%)	11 (18%)	33 (16%)	.21
AV(N)RT	4 (5%)	1 (1%)	0 (0%)	5 (2%)	.13
VT	1 (1%)	0 (0%)	0 (0%)	1 (1%)	.44
Prior non-AF ablation					
CTI	0 (0%)	4 (6%)	3 (5%)	7 (3%)	.11
AV(N)RT	2 (3%)	0 (0%)	0 (0%)	2 (1%)	.19
VT	1 (1%)	0 (0%)	0 (0%)	1 (1%)	.44
DOAC	76 (95%)	65 (92%)	54 (90%)	195 (92%)	.51
Coumadine	4 (5%)	6 (9%)	6 (10%)	16 (8%)	.51
Class 1a AAD	5 (6%)	2 (3%)	3 (5%)	10 (5%)	.61
Class 1c AAD	22 (28%)	20 (28%)	11 (18%)	53 (25%)	.36
Betablockers	28 (35%)	27 (38%)	18 (30%)	73 (35%)	.63
Sotalol	21 (26%)	21 (30%)	20 (33%)	62 (29%)	.66
Amiodarone	5 (6%)	9 (13%)	6 (10%)	20 (10%)	.40
Verapamil	8 (10%)	6 (9%)	4 (7%)	18 (9%)	.78
No AAD	38 (48%)	35 (49%)	22 (37%)	95 (45%)	.30
LVEF (%)	61 ± 6	59 ± 5	59 ± 8	59 ± 6.3	.55
LVEF ≥ 45%	80 (100%)	71 (100%)	59 (98%)	210 (99%)	.28
LVEF < 45%	0 (0%)	0 (0%)	1 (2%)	1 (1%)	.28
LA volume (mL)	67 ± 19	62 ± 18	71 ± 21	65.6 ± 18.9	.49

Abbreviations: AAD, antiarrhythmic drugs; AF, atrial fibrillation; AV(N)RT, atrioventricular (nodal) reentrant tachycardia; BMI, body mass index; CABG, coronary artery bypass grafting; CTI, cavotricuspid isthmus; DOAC, direct-acting oral anticoagulant; LA, left atrium; LVEF, left ventricular ejection fraction; MAN-CB, manual-guided cryoballoon; MAN-RF, manual-guided radiofrequency; OSAS, obstructive sleep apnea syndrome; PCI, percutaneous coronary intervention; RMN-RF, robotic magnetic navigation-guided radiofrequency; VT, ventricular tachycardia.

TABLE 2 Procedural parameters.

	MAN-CB, *N* = 80	MAN-RF, *N* = 71	RMN-RF, *N* = 60	Total, *N* = 211	*p* Value
Local anesthesia only	61 (76%)	3 (4%)	3 (5%)	67 (32%)	<.001
General anesthesia	15 (19%)	43 (63%)	32 (56%)	90 (44%)	<.001
Conscious sedation	4 (5%)	25 (37%)	25 (44%)	54 (27%)	<.001
Total procedure time (min)	78 ± 21	115 ± 41	129 ± 32	103 ± 38	<.001[a]
TSP time (min)	13 ± 8	5 ± 6	8 ± 5	9 ± 8	<.001[a]
Mapping time (min)	N.A.	23 ± 12	27 ± 13	25 ± 12	.038
Cryoballoon setup time (min)	7 ± 6	N.A.	N.A.	N.A.	N.A.
Ablation duration (min)	35 ± 14	59 ± 26	63 ± 24	51 ± 25	<.001[a]
Left WACA time (min)	N.A.	26 ± 14	28 ± 13	27 ± 14	.49
Right WACA time (min)	N.A.	27 ± 13	27 ± 14	27 ± 13	.92
Waiting time (min)	6 ± 4	9 ± 9	9 ± 8	8 ± 7	.002[a]
Application number	6 ± 2	65 ± 29	50 ± 44	37 ± 37	<.001[b]
Application duration (min)	1099 ± 445	1911 ± 630	1581 ± 712	1527 ± 699	<.001[b]
Fluor time TSP (min)	3 ± 3	6 ± 3	6 ± 4	5 ± 3	<.001[a]
Fluor time ablation (min)	12 ± 6	9 ± 7	7 ± 9	10 ± 8	.001[a]
Total fluor time (min)	16 ± 6	15 ± 7	13 ± 10	15 ± 8	.15

Note: Analysis was performed using the one-way analysis of variance. When a significant main effect was present, the differences in between the groups were evaluated using Tukey's post hoc honest significant difference test. The following in-between group differences are annotated in the table.

Abbreviations: MAN-CB, manual-guided cryoballoon; MAN-RF, manual-guided radiofrequency; N.A., not applicable; RMN-RF, robotic magnetic navigation-guided radiofrequency; TSP, transseptal puncture; WACA, wide area circumferential ablation.

[a]Significant differences were observed in-between MAN-CB ⇔ MAN-RF and MAN-CB ⇔ RMN-RF.

[b]Significant relations were observed in-between all three groups.

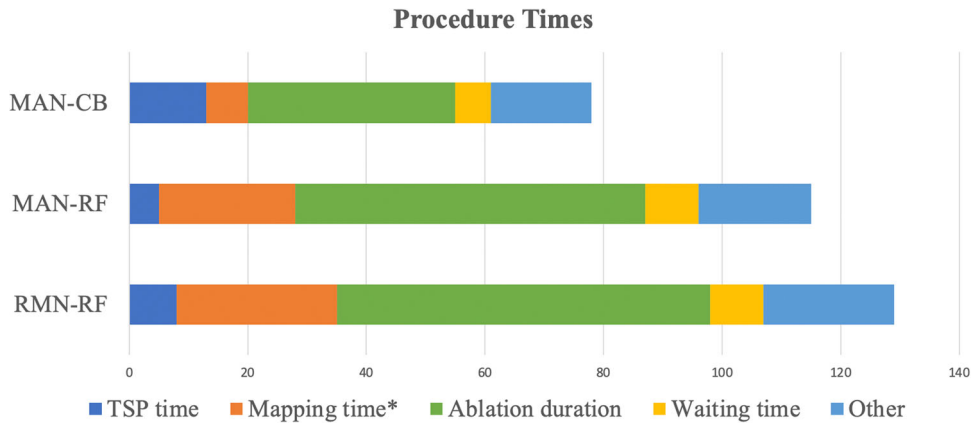

FIGURE 2 Procedural efficiency. The duration of various procedural steps, including the time of transseptal puncture (TSP), mapping time, ablation duration, and waiting time at the end of the procedure, is presented in this figure. The total procedure time was significantly different between MAN-CB and MAN-RF as well as between MAN-CB and RMN-RF, whereas it was comparable between the two RF techniques. *Of note: In MAN-CB, no mapping was performed, the time presented in orange represents cryoballoon setup time. Other included time of groin puncture and catheter manipulations in between the various procedural steps. MAN-CB, manual-guided cryoballoon; MAN-RF, manual-guided radiofrequency; RMN-RF, robotic magnetic navigation-guided radiofrequency.

RF groups (35 ± 14 vs. 59 ± 26 vs. 63 ± 24 min, for MAN-CB vs. MAN-RF vs. RMN-RF, respectively) (see Table 2).

The total fluoroscopy time was 15 ± 8 min and comparable between groups. When looking at the TSP and ablation parts of the procedure separately, we noticed that the fluoroscopy times to guide TSP were significantly shorter in MAN-CB compared to the RF techniques (3 ± 3 vs. 6 ± 3 vs. 6 ± 4 min, respectively, $p < .001$), whereas the fluor times during the ablation part of the procedure

were significantly longer in MAN-CB compared to the other two groups (12 ± 6 vs. 9 ± 7 vs. 7 ± 9 min, respectively, $p = .001$).

3.3 | Procedural efficacy

FPI/single-freeze isolation was significantly more often observed in MAN-RF and RMN-RF compared to MAN-CB for both the left-sided and the right-sided PVs (see Figure 3 and Table 3). Correspondingly, significantly more TUs/additional freeze cycles were applied in the MAN-CB group (Table 3). In MAN-RF and RMN-RF, a 100% acute success rate was observed for all PVs. In MAN-CB a significantly lower acute success rate was found at three PV sites (LSPV 94%, $p = .015$; LIPV 94%, $p = .015$; RIPV 93%, $p = .007$). The acute success of the RSPV with MAN-CB was comparable with the RF techniques (99%, $p = .435$).

3.4 | One-year follow-up outcomes

At 12 months of follow-up, we observed AF recurrence in 40 patients (19%). The recurrence of AF was significantly lower in the RMN-RF group (MAN-CB 19 [24%], MAN-RF 16 [23%], RMN-RF 5 [8%] AF recurrences, $p = .045$).

CA procedures performed with RMN guidance were associated with improved AF-free survival during the 12 months of FU when compared to the other study groups (multivariate hazard ratio [HR] of RMN-RF on AF recurrence 0.32, 95% confidence interval [CI]: 0.12–0.87, $p = .026$; with MAN-CB + MAN-RF as the reference group) (Figure 4 and Table 4). Age, gender, LA volume, history of hypertension, obstructive sleep apnea syndrome (OSAS), and diabetes mellitus, were subsequently consecutively added to the univariate and multivariate models and did not have a significant association with the outcome. As a sensitivity analysis, the center of the procedure and the presence of high blood pressure preoperatively or during follow-up (i.e., systolic RR > 140 and/or diastolic RR > 90 mmHg), were also added to the models and did not show any significant associations with the primary outcome either (data not shown). Subsequently, multivariate analysis using a propensity score (including age, gender, diabetes mellitus, hypertension, OSAS, and center of procedure in the propensity score), showed a significant benefit of RMN-RF versus non-RMN-RF technique irrespective of the propensity score adjustment (HR: 0.38 [95% CI: 0.14–1.03] of RMN-RF vs. non-RMN-RF techniques, $p = .019$).

3.5 | Safety

Postprocedurally, seven complications (3%) were observed, and these were comparable between the groups. These consisted of five minor complications and two major complications. In MAN-CB were five complications observed (of which two were major), whereas there were 0 complications in the MAN-RF group and two minor complications in the RMN-RF group. One major complication was a cardiac tamponade due to LA wall perforation by the CB tip for which emergency pericardiocentesis and thoracic surgery were performed. The patient recovered completely. The other major complication was a patient who had permanent paralysis of the right hemidiaphragm caused by the CB application. The minor complications were all access site-related.

4 | DISCUSSION

This is one of the first studies systematically and prospectively comparing contemporary RMN-guided CA as a treatment of paroxysmal AF, with the conventional ablation techniques of manual cryoablation and manual point-by-point RF ablation. The main finding is that RMN-guided PVI results in improved freedom of AF after 12 months of follow-up.

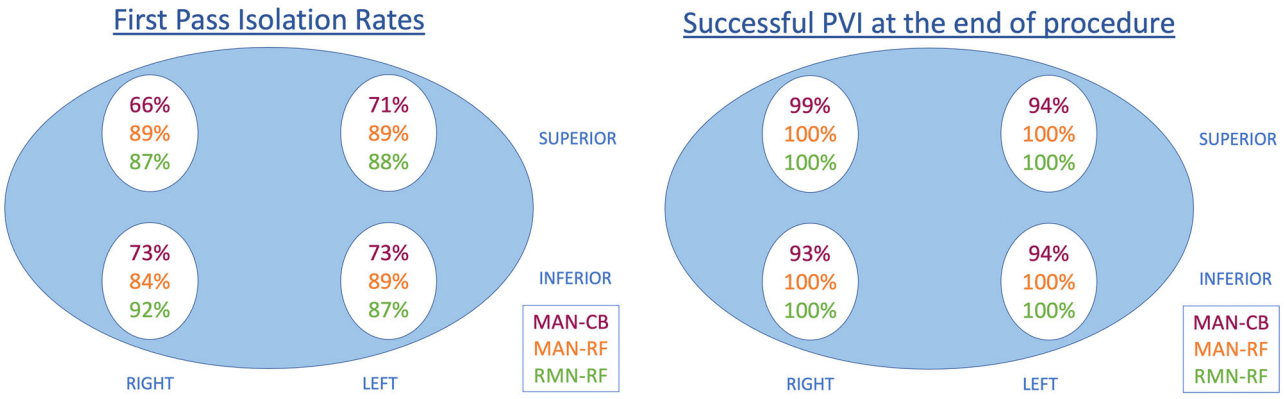

FIGURE 3 First-pass isolation/single-freeze isolation and acute success. This figure schematically shows the four pulmonary veins and the respective first-pass isolation/single-freeze isolation rates for each of the three ablation techniques, as well as the acute success rates (i.e., successful pulmonary vein isolation [PVI] at the end of the procedure). MAN-CB, manual-guided cryoballoon; MAN-RF, manual-guided radiofrequency; RMN-RF, robotic magnetic navigation-guided radiofrequency.

TABLE 3 Procedural efficacy.

	CB, *N* = 80	MAN-RF, *N* = 71	RMN-RF, *N* = 60	Total, *N* = 211	*p* Value
First-pass isolation or single-freeze isolation					
LSPV	55 (71%)	62 (89%)	53 (88%)	170 (82%)	.005
LIPV	57 (73%)	62 (89%)	52 (87%)	171 (82%)	.027
RSPV	53 (66%)	62 (89%)	52 (87%)	167 (80%)	.001
RIPV	58 (73%)	59 (84%)	55 (92%)	172 (82%)	.018
TU or additional freeze cycles					
LSPV	22 (28%)	8 (11%)	7 (12%)	37 (18%)	.010
TU count	1 (1–2)	2 (1–5)	3 (2–14)	2 (1–3)	.009
LIPV	20 (26%)	8 (11%)	8 (13%)	36 (17%)	.046
TU count	1 (1–2)	2 (1–4)	3 (2–5)	2 (1–2)	.005
RSPV	25 (31%)	8 (11%)	8 (13%)	41 (20%)	.003
TU count	1 (1–2)	5 (3–6)	2 (1–3)	1 (1–3)	.010
RIPV	21 (27%)	11 (16%)	5 (8%)	37 (18%)	.018
TU count	1 (1–3)	3 (1–8)	5 (2–7)	2 (1–4)	.119
Successful PVI (end of procedure)					
LSPV	75 (94%)	71 (100%)	60 (100%)	206 (98%)	.015
LIPV	75 (94%)	71 (100%)	60 (100%)	206 (98%)	.015
RSPV	78 (99%)	71 (100%)	60 (100%)	209 (99%)	.44
RIPV	74 (93%)	71 (100%)	60 (100%)	205 (100%)	.007

Abbreviations: CB, catheter ablation; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; MAN-RF, manual-guided radiofrequency; PVI, pulmonary vein isolation; RIPV, right inferior pulmonary vein; RMN-RF, robotic magnetic navigation-guided radiofrequency; RSPV right superior pulmonary vein; TU, touch-up.

4.1 | AF recurrence

In general, CA results in an improved freedom of AF when compared to AAD.[1,19,20] Most studies investigating ablative therapy of paroxysmal AF report a freedom of arrhythmia around 80% during long-term follow-up.[8,21,22] Over time, recurrence rates have been remarkedly consistent and comparable between ablation techniques.[8,9,23] Proposed sources of arrhythmia recurrence are (early) PV reconnection, the presence of other non-PV AF triggers, and the formation of novel substrate by the initial ablation and/or the maturation of LA substrate.[16] For instance, the manifestation of atrial tachycardia following CA of AF is well recognized and thought to result from incomplete lesions or gaps in the ablation lines that become a substrate for a reentry circuit.[24] Multiple RF TUs or additional freeze cycles could theoretically provide a proarrhythmogenic substrate in the future, reducing the long-term freedom of arrhythmia.[25]

Previous studies evaluating RMN-guided AF ablation showed similar freedom of AF recurrence rates between manual and RMN-guided RF ablation.[26,27] A recent prospective study observed an inferior performance of RMN compared to manual RF ablation, but investigated a different population including >60% of patients with persistent AF.[28] The current study observed for the first time an improved efficacy of RMN in the treatment of paroxysmal AF. We postulate that multiple factors contributed to this result, including technological developments made to the RMN system, an improved RMN ablation strategy, and improved lesion formation and lesion-to-lesion continuity—among other things—caused by RMN's catheter stability in combination with the use of relatively higher power settings. In addition, the size of the WACA/freezed area could have influenced our outcomes, as a wide antral approach was shown to have higher freedom from total atrial tachyarrhythmia recurrence at long-term follow-up compared to ostial PVI.[29]

4.2 | RMN technological advances

RMN-guided CA has been used in the treatment of cardiac arrhythmias for almost 20 years.[10] The currently most frequently utilized system worldwide employs remote navigation of magnetically enabled catheters in the heart via magnetic fields.[10] Over time, various technological upgrades have been made to this system. For

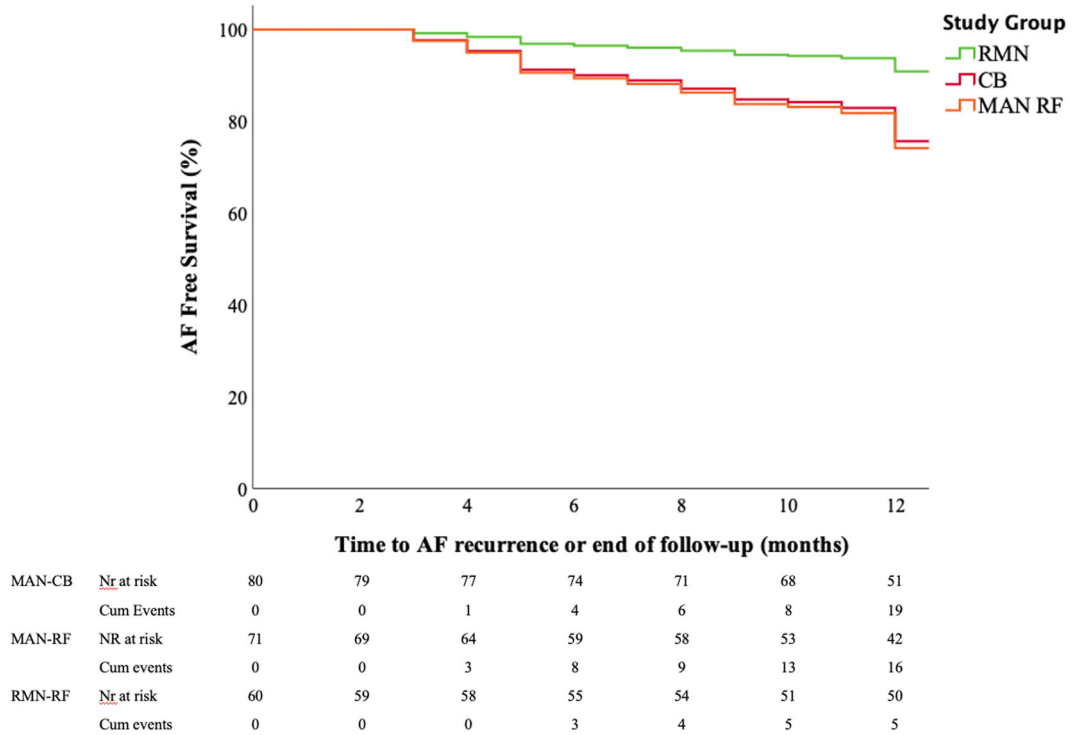

FIGURE 4 AF-free survival. This figure illustrates the AF-free survival for the three study groups. CA procedures performed with RMN guidance were associated with improved AF-free survival during the 12 months of follow-up when compared to the other study groups (multivariate HR of RMN-RF on AF recurrence 0.32, 95% CI: 0.12–0.87, $p = .026$; with MAN-CB + MAN-RF as the reference group). AF, atrial fibrillation; CA, catheter ablation; CI, confidence interval; HR, hazard ratio; MAN-CB, manual-guided cryoballoon; MAN-RF, manual-guided radiofrequency; RMN-RF, robotic magnetic navigation-guided radiofrequency.

TABLE 4 Cox proportional hazard models for AF recurrence.

	Univariate model			Multivariate model		
AF recurrence	Hazard ratio	95% CI	*p* Value	Hazard ratio	95% CI	*p* Value
MAN-CB	1.41[a]	0.75–2.63	.30	2.92[a]	1.08–7.86	.034
MAN-RF	1.52[b]	0.80–2.86	.21	3.13[b]	1.15–8.56	.026
RMN-RF	0.33[c]	0.13–0.85	.009	0.32[c]	0.12–0.87	.026
Age	1.02	0.98–1.05	.31	1.02	0.99–1.06	.22
Female	1.79	0.94–3.33	.08	1.85	0.98–3.45	.06
Hypertension	1.39	0.74–2.60	.31	1.21	0.64–2.30	.56
Diabetes	1.34	0.41–4.34	.61	1.01	0.31–3.33	.99
OSAS	1.05	0.14–7.63	.96	1.14	0.16–8.32	.90
LA volume	0.99	0.96–1.03	.63	1.00	0.96–1.03	.79

Note: Hazard ratios were calculated using the reference groups (given as footnotes a–c).

Abbreviations: AF, atrial fibrillation; CI, confidence interval; LA, left atrium; MAN-CB, manual-guided cryoballoon; MAN-RF, manual-guided radiofrequency; OSAS, obstructive sleep apnea syndrome; RMN-RF, robotic magnetic navigation-guided radiofrequency.

[a]Compared to MAN-RF and RMN-RF as the reference groups.

[b]Compared to MAN-CB and RMN-RF as the reference groups.

[c]Compared to MAN-CB and MAN-RF as the reference groups.

instance, the third-generation RMN system (Niobe ES) significantly reduced procedure times compared to its prior generations, provided by an improved response time of the system to changes in the magnetic vector.[30] The "e-Contact Module" was developed specifically for RMN, which provides real-time contact feedback to the operator[18] and was associated with improved ventricular tachycardia ablation outcomes.[31] The "Ablation History" feature provides a visual display of the applied therapy (based on the applied Watt × s per location) on the 3D map.[18] All patients in this study's RMN group were treated with the most up-to-date RMN technology.

In addition, our RMN PVI strategy improved over time.[32] Nowadays, the participating centers frequently perform RMN-guided PVI by drawing WACA lines with continuous dragging of the catheter while ablating, in combination with the use of relatively higher power settings (i.e., posterior wall 45 W, anterior wall 50 W).[32] The technological tools described above— providing contact feedback and a visual display of the applied therapy—in combination with the use of 3D mapping systems, make the operator more comfortable manipulating and moving the catheter around the PV ostia while ablating, additionally without the need for continuous fluoroscopy confirmation of the catheter's position. This is confirmed by the low fluoroscopy exposure during the ablation part of the procedure observed in this study.

4.3 | High power short duration

While conventional settings during RF ablation involve applying low power for long times, a new setting based on high power and short duration has recently been suggested as safer and more effective.[33–36] Overall, high-power short-duration lesions were significantly wider, and of slightly lower or similar depth compared to standard settings.[33] The increased lesion-to-lesion uniformity and linear continuity, given the larger lesion diameter, is most beneficial in establishing permanent PVI.[36] Otherwise, the slightly diminished lesion depth is of less concern while ablating the relatively thin-walled atria (compared to the ventricle).[33] Whether high power short duration lesions result in improved outcomes, is still a matter of ongoing debate. However hypothetically, the RF lesion characteristics we've learned from these studies could explain why the relatively higher power settings used in RMN in this study, resulted in improved PVI when compared to manual point-by-point RF ablation.

4.4 | Procedural efficiency

The procedural efficiency of RMN-guided AF ablation increased significantly during the last years.[15] In this study, we observed comparable procedure times between manual- and RMN-guided RF ablation, which is in our believe an affirmation of the technological advances made in RMN. Single-shot devices, such as the CB, result in very efficient procedures. In the literature, utilization of the CB significantly reduced procedure times when compared to manual RF ablation.[8,9,37] The current study also observed significantly lower procedure times in favor of the CB, which can be regarded as a benefit of this technology.

4.5 | Allocation

Patients who gave their consent to participate in the study were consecutively allocated to a treatment arm based on the availability of the RMN-equipped laboratory or the conventional laboratories at the participating centers. There was one selection criterium: patients with large PV ostia and/or common ostium were adjudicated to treatment with the RF techniques. Unfortunately, because of a larger availability of non-RMN-equipped laboratories, the group sizes differed.

4.6 | Limitations

The present study's lack of blinded adjudication might have introduced bias, although this was moderated by the use of objective measures and allocation to a treatment group based on the EP laboratory's availability. This manner of allocation caused a difference in group sizes, which is a limitation of the study. In addition, there was selection bias introduced by the allocation of patients with large PV ostia and/or common ostium to one of the RF groups. The present study included patients from multiple centers. This might have introduced inter-operator or intercenter variability. Nevertheless, we observed significantly better long-term outcomes in procedures performed with RMN in general. In addition, the center of inclusion was added as a potential confounder to the Cox proportional hazard models and did not show a significant relation with the primary outcome. Unfortunately, we were not able to retrospectively evaluate the WACA/freezed area size and relate this to the outcome due to the prospective nature and design of this study, but we believe this should be incorporated in future research on this topic.

5 | CONCLUSION

Contemporary RMN-guided RF ablation establishes the most effective long-term freedom of AF when compared to manual cryoablation or manual point-by-point RF ablation. Cryoablation remains the most efficient ablation technique resulting in the shortest procedure times, whereas nowadays RMN-guided ablation has a comparable time efficiency with manual RF ablation.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Anna M. E. Noten http://orcid.org/0000-0003-1582-5315
Sing-Chien Yap http://orcid.org/0000-0003-4520-2725

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