Remote Magnetic Navigation with Irrigated Tip Catheter for Ablation of Paroxysmal Atrial Fibrillation

Running title: Miyazaki et al.; Conventional versus MNS ablation for AF

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Abstract:

**Background** - Remote magnetic navigation system (MNS) has been used with a non-irrigated magnetic catheter for atrial fibrillation (AF) ablation. To evaluate the feasibility and efficiency of the newly available irrigated-tip magnetic catheter for index isolation of pulmonary veins (PVI) in patients with paroxysmal AF (PAF).

**Methods and Results** - Between January 2008 and June 2009, 30 consecutive patients with drug-resistant PAF underwent circular mapping catheter guided PVI using MNS(MNS-group). The outcomes were compared retrospectively with that of conventional hand-controlled ablation technique during the same period in 44 consecutive patients(manual-group). All 4 PVs were successfully isolated in both groups except in 4 patients in the MNS-group. RF and procedure duration were higher in the MNS-group than manual-group (60 ± 27 vs 43 ± 16 min, p=0.0019, and 246 ± 50 vs 153 ± 51 min, p<0.0001). In the patients who underwent only PVI, total fluoroscopic time was also longer in the MNS-group than manual-group (58 ± 24 vs 40 ± 14 min, p=0.0002). At 12-month follow-up after a single procedure, 69.0% of patients in MNS-group and 61.8% of patients in manual-group were free of atrial tachyarrhythmia without antiarrhythmic drug. There was no significant difference in the atrial tachyarrhythmia-free survival between the 2 groups(p=0.961). Cardiac tamponade occurred in 1 patient in the manual-group.

**Conclusions** - In patients with PAF, MNS guided PVI with newly available irrigated-tip magnetic catheter backed up with manual ablation whenever required, is feasible. However it requires longer ablation, fluoroscopy and procedural times than the conventional approach in the early experience-stage.

**Key words:** atrium, catheter ablation, fibrillation, remote magnetic navigation, irrigated tip catheter
Introduction

Over the last decade, radiofrequency (RF) catheter ablation of atrial fibrillation (AF) has become an important therapy with good procedural success rates.[1,2] Remote magnetic navigation systems (MNS) [3-8] have been recently introduced into clinical practice, which allows the use of a soft-tip ablation catheter that can be guided to and positioned at the desired site by directional magnetic fields. On the other hand, MNS is available and has been used with a non-irrigated magnetic tip catheter for RF ablation. Furthermore, previous report [8] showed that MNS with non-irrigated 4-mm magnetic catheter could not achieve pulmonary vein isolation (PVI) in most of the cases and charring of the catheter tip was frequently observed during the procedure.

The purpose of the present study is to investigate whether AF ablation using newly available irrigated tip catheter and MNS is feasible and effective in patients with paroxysmal AF (PAF) when compared with widely established manually steerable catheter approach.

Methods

Between January 2008 and June 2009, among 50 patients who underwent AF ablation using MNS and a new irrigated tip magnetic catheter at our center, 30 consecutive
patients fulfilling the inclusion criteria mentioned below were enrolled in this study (MNS group): Electrical PVI for drug-resistant PAF as an index procedure without inducibility testing.

Over the defined time period, 139 patients underwent catheter ablation for paroxysmal AF as an index procedure. Among them, the procedural and clinical outcomes in the MNS group were compared with those of the conventional hand-controlled catheter ablation in all consecutive patients who underwent PVI (manual group, n=44). The patients who received hand-controlled catheter ablation therapy as a part of simultaneously running other investigational protocols using novel tools (n=68) and those who received hand-controlled catheter ablation therapy with inducibility testing (n=27) were not included in this study.

AF was defined as paroxysmal when AF terminated spontaneously and lasted less than 7 days according to the HRS/EHRA/ECAS 2007 Consensus Statement on Catheter and Surgical Ablation of AF.[2] All patients gave written informed consent prior to the procedure.

Electrophysiological study

All anti-arrhythmic medications, with the exception of amiodarone, were discontinued
at least for five half-lives prior to the ablation. All patients were anti-coagulated with warfarin for at least 1 month before the procedure (target INR 2–3) and therapeutic anti-coagulation was maintained with intravenous or low molecular weight heparin following warfarin discontinuation starting 3 days prior to the intervention.

Transesophageal echocardiography was performed within 48 h prior to the procedure to exclude left atrial thrombus. Warfarin was resumed on the day of the procedure and effective anti-coagulation maintained with heparin until the INR was greater than 2.0.

Surface electrocardiogram and bipolar endocardial electrograms (filtered from 30 to 500 Hz) were continuously monitored and stored on a computer-based digital amplifier/recorder system (LabSystem Pro, Bard EP, Lowell, MA).

Electrophysiological studies were performed in the fasting state using mild sedation. The following catheters were introduced via the right femoral vein: (i) a deflectable quadripolar catheter (5-mm interelectrode spacing, Xtrem, ELA Medical, France) positioned within the CS with the distal electrode positioned at 4-5 o’clock along the mitral annulus in the 30° left anterior oblique radiographic projection; (ii) a 10 pole, fixed-diameter (20mm) circumferential mapping catheter to guide PVI (Lasso; Biosense-Webster, Diamond Bar, CA), introduced with the aid of a long sheath (Preface multipurpose, Biosense-Webster or SLO, St. Jude, MN, USA) and continuously
perfused with heparinized saline; (iii) a 3.5-mm tip externally irrigated magnetic tip catheter (Thermocool RMT, Biosense Webster, Diamond Bar, CA, USA) with the aid of 2nd long sheath in the MNS group or a 3.5-mm externally irrigated tip ablation catheter (Thermocool, Biosense-Webster, Diamond Bar, CA, USA) in the manual group.

A single trans-septal puncture was performed in the anteroposterior radiographic position under pressure monitoring. Left atrial access was confirmed by an appropriate atrial pressure waveform and contrast injection. The circumferential mapping catheter was introduced into the left atrium (LA) via the trans-septal sheath and the sheath was withdrawn into the right atrium to facilitate the passage of the ablation catheter to the LA through the same but dilated puncture site. Following the trans-septal puncture, a bolus of 50 IU/kg of heparin was administered and repeated only if the procedure lasted beyond 4 hours.

Catheter ablation

PVI was performed as widely in the antrum as possible with the endpoint of abolition or dissociation of activities in all the PVs and PV ostia during the sinus rhythm. PV potential and far-field potential were distinguished with pacing technique from the LA,
LA appendage or CS using the ablation or the quadripolar catheter.[9,10] Cavotricuspid isthmus (CTI) ablation was added, when CTI-dependent flutter was documented on 12 lead ECG before or during the procedure, with the endpoint of bidirectional conduction block. In the MNS group, manual versus robotic ablation for CTI was left to the operator’s choice. PVI of all the veins was confirmed at the end of the procedure.

RF ablation was performed in the power-control mode with target tissue temperature of not more than 45°C. Power of 25-35W was used with manual titration of the saline perfusate from 10 to 60 mL/min to achieve the desired power. The power was limited to 30W in the LA and 35W on the CTI. Three-dimensional electroanatomical mapping system was not used in the manual group. The Cathpax radioprotection cabin (Lemer Pax, Carquefou, France)[11] was used to protect the operator from radiation during all the procedures in both the groups.

MNS-group

The remote magnetic navigation system consists of 2 weak permanent magnets that generate a uniform magnetic field (0.08 T) and that are computer controlled and located on either side of the patient’s body. The MNS consists of 2 components: the Niobe Stereotaxis magnetic navigation system (Niobe, Stereotaxis Inc., St. Louis, MO, USA)
and an electroanatomical mapping system (CARTO RMT, Biosense-Webster Inc., Diamond Bar, CA, USA). The CARTO-RMT system sends catheter tip location and orientation data to the Stereotaxis system. It also sends target locations, points, and anatomical geometrical information from the reconstructed map to the MNS. The real-time catheter location is displayed on the X-ray images, enabling continuous real-time monitoring of the catheter tip position. Remote catheter advancement and retraction from the control room are performed using a catheter advancing system (Cardiodrive, Stereotaxis Inc., St. Louis, MO, USA) positioned anteriorly on the thigh. Even fluoroscopy can be undertaken remotely from the control room. The catheter contains 3 magnets within the distal tip segment and an irrigation channel. It aligns with the field produced by the external magnets, allowing effective tip orientation.

Switching over to the manual navigation was allowed for device failure, malfunction, patient anatomy or medical necessity at the discretion of the investigator. The procedure duration was defined as the time from the start of the first venous puncture until just before the sheath withdrawal at the end of the procedure. RF duration was defined as the cumulative length of all RF applications necessary to achieve the endpoint. There was no difference in terms of ablation strategy and ablation condition between both the study groups.
Follow-up

Patients were routinely hospitalized for 2 days post-procedure and again for 1 day at 1, 3, 6, and 12 months for clinical interview and ambulatory monitoring in addition to the routine follow-up by the referring cardiologist which included Holter monitoring in the event of symptoms. Blanking period of 3 month was applied. Antiarrhythmic medication was stopped following the index procedure or after 3 months in case of early recurrence of atrial arrhythmia. Warfarin anti-coagulation was continued for at least 3 months. Success was defined as the absence of all documented arrhythmia or symptoms suggestive of an arrhythmia recurrence off drugs.

Statistical analysis

Continuous variables are reported as mean± standard deviation or median and interquartile range (IQR; 25th and 75th percentiles) depending on the normality of distribution. Comparison between the two groups was performed with the Student’s t-test or the Wilcoxon Rank-Sum test (nonnormally distributed data). Categorical variables are reported as number and percentage and were compared using the Fisher’s exact test. Cumulative event rates were calculated according to the Kaplan–Meier
method, and any differences in the arrhythmia-free survival were evaluated using the log-rank test. All tests were two-tailed and statistical significance was established at $P < 0.05$.

**Results**

**Study Patient**

There was no significant difference in patient characteristics between the two groups (Table 1).

**PVI**

In the MNS group, 114/120 (95%) veins could be isolated with MNS only. In the manual group, all veins were successfully isolated. Totally, 6 veins amongst 4 patients in the MNS group required the conventional catheter approach to ablate ostial PV potentials (2 patients - right inferior PV, 1 patient - right PVs, and 1 patient - left PVs). RF duration for PVI was higher in the MNS group than the manual group (60 ± 27 vs 43 ± 16 min, $p=0.0019$). The procedural duration from first femoral puncture to the end of PVI was also higher in the MNS group than the manual group (246 ± 50 vs 153 ± 51 min, $p<0.0001$). In the patients who underwent only PVI, the total fluoroscopic time
was also longer in the MNS group than the manual group (58 ± 24 vs 40 ± 14 min, p=0.0002).

CTI Ablation

CTI ablation was added in 6 (20.0 %) and 15 (34.1 %) patients in the MNS and manual groups, respectively (p=0.187). In the MNS group, CTI ablation was started with MNS system in all the patients and it was completed in 3 (50%) patients with RF time of 14 ± 11 min. In rest of the 3 patients, CTI line was created by switching over to the conventional ablation in 1 (16%) patient and it could not be created in 2 patients (33%). In the manual group, CTI line was completed in 14 (93%) patients with RF time of 11 ± 8 min and was not completed in 1 (7%) patient.

Total Fluoroscopy, Procedural and RF Times

Total fluoroscopy (63 ± 18 vs 45 ± 16 min, p=0.0002), procedural (263 ± 72 vs 165 ± 52 min, p<0.0001) and RF times (67 ± 33 vs 47 ± 17 min, p=0.0016) were significantly longer in the MNS group than the manual group.

Clinical Outcome
Follow-up period was 14 ± 5 months in the MNS group and 15 ± 5 months in the manual group. At 12-month follow-up after single procedure, 69.0 % of patients in the MNS group and 61.8 % of patients in the manual group were free of atrial tachyarrhythmia without antiarrhythmic drug. There was no significant difference in terms of atrial tachyarrhythmia-free survival between the 2 groups (Figure 1, log-rank test p=0.961). In total 11 (14%) patients including 4 (13%) patients in MNS group and 7 (16%) patients in manual group (p=0.498), underwent second procedure 12.3 ± 2.5 months and 12.7 ± 5.2 months after the index procedure (p=0.874), respectively. Electrical PV-reconduction was observed in at least 1 vein in all patients except 1 patient in the MNS group. The average number of re-connected PV was 1.5 (IQR, 0.25 to 3.5) and 2.0 (IQR, 1.0 to 3.0) in MNS and manual groups, respectively. There was no significant difference between the 2 groups in terms of PV reconnection (p=0.777).

At 1, 3, 6 and 12 months after the procedure, 56 (22 (73%) vs 34 (77%)), 53 (21 (70%) vs 32 (73%)), 49 (19 (63%) vs 30 (68%)) and 48 (19 (63%) vs 29 (66%)) patients were hospitalized and monitored at our center in the MNS and manual groups, respectively. There was no significant difference between the 2 groups. However, all patients who could not be hospitalized at our center were followed by the referring cardiologist and were subjected to Holter monitoring at each follow-up period.
Complications

Access site hematoma was observed in 2 patients in each of the two groups (6.7 % vs 4.6 %, p=0.692). Cardiac tamponade with audible pop requiring percutaneous drainage occurred in 1 patient (2.3 %) in the manual group.

Discussion

We report our initial experience with PVI using MNS and irrigated-tip magnetic ablation catheter. To our knowledge, these are the first published data evaluating feasibility and efficacy of ablation using a novel irrigated tip ablation catheter and MNS in PVI.

Potential Advantage of MNS

The magnetic catheter has a flexible shaft and limited maximal force exerted by the magnetic vector. Several advantages have been mentioned for the MNS compatible RMT catheter versus the conventional catheter during cardiac mapping. First, it is possible that less endocardial trauma (compared with manual mapping) would result from the MNS system. Therefore, the risk of procedure-related cardiac perforation is
low. Second, the “lighter” tissue-touch of remote magnetic mapping catheter is likely to cause less deformation of the cardiac chamber and thereby result into a more accurate mapping than the manual mapping. Third, this has the potential to reduce fluoroscopic exposure for both the patient and the operator, especially the latter.

Wood et al reported reduction in fluoroscopic time and radiofrequency lesion deliveries for the ablation of supraventricular arrhythmias with MNS when compared with manual catheter navigation, although there were no significant differences in procedural time and success rate.[5] Arya et al reported that CTI block was successfully completed in 24/25 (96%) patients using 8-mm tip magnetic catheter with high RF delivery settings (70°C with a maximum power of 70 W), however there is no data in comparison with manual ablation.[7] In patients with congenital heart disease and anatomical variants, MNS can be a useful tool for reaching the areas otherwise inaccessible with conventional catheters.[12.13]

**Potential Disadvantage**

On the other hand, MNS system has several potential disadvantages. It needs longer time to set up. The operator must commute frequently between the remote control room and operation room to change the circular mapping catheter position when it is unstable.
and the sheath position to facilitate accessing the target with the magnetic catheter.

These processes would lead to longer total procedural duration, but will be overcome by remote control of the new driving device. The limited contact force may also limit the lesion size, which might lead to more frequent PV reconnection after PVI. The necessity of a 2nd long sheath for the ablation catheter leads to a higher procedural cost.

Observation and evaluation of the patient’s state are relatively difficult because the operator stays in the remote room. During conventional ablation procedure, the operator can estimate the force of the tissue contact by the tactile feedback during catheter manipulation. In contrast, no tactile feedback of the catheter tip contacting the atrial wall can be perceived by the operator using MNS.

In comparison with other ablation procedures, AF ablation is much more complicated and needs many RF lesions to reach the end point. Actually, Biase et al reported lasso-guided AF ablation using MNS and non-irrigated tip 4-mm CARTO RMT catheter.[8] The report clarified that electrical PVI was not completed in most of the PVs and needed additional manual ablation even with high RF delivery settings (55°C with a maximum power of 50 W). Furthermore, the charring of the catheter tip was observed in 33% of the patients.[8]
**MNS with Irrigated Tip Catheter**

In this study we evaluated the feasibility and efficacy of lasso-guided electrical PVI using MNS and newly available irrigated tip ablation catheter and drew in a comparison with manual ablation with the same RF delivery settings. Our study establishes several points. First, circular mapping catheter guided PVI with MNS is difficult in some patients, especially for the antrum of RIPV even after using irrigated tip catheter and various manipulation techniques. It seems to be due to the anatomy (structural complexity, relationship between the transseptal hole and the PV ostium) and the weaker contact force when compared with the manual navigation. Deflectable long sheath seems to be one of the solutions for improving the manipulation. Second, PVI using MNS needed longer RF, procedural and fluoroscopic duration than manual ablation for the patients with PAF. Because the endpoint was defined as electrical PVI of all the PVs, all the durations were significantly prolonged due to the difficulty in achieving the endpoint. The difficulty in reaching some points and soft tissue contact of magnetic catheter may be some of the crucial factors that explain the significant difference in RF duration. Third, no charring of the catheter tip was observed during AF ablation using MNS and irrigated tip catheter, which stands as a substantial improvement in the previous non-irrigated magnetic tip catheter. Fourth, AF ablation
using MNS and irrigated tip catheter with back up manual ablation whenever required was as effective as the conventional ablation for index procedure with PVI as the primary endpoint.

_Limitations_

First, the study was not designed in a prospective randomized fashion, which implies the design’s inherent limitations. Nevertheless, the key data in the patients distributed between the two groups were similar, which allowed direct comparison between these 2 different systems. Furthermore, we compared the results obtained using the same ablation strategy and in the similar energy delivery conditions (power, temperature setting, etc). Second, the present experience is limited to a relatively small number of patients. Therefore, we can’t comment on the safety aspect of this system, although no complications were noted. Our data should be confirmed in a larger randomized trial. Third, we do not have the separate data of fluoroscopic time for PVI. However, the result did not get altered even after eliminating the patients who underwent CTI ablation. Fourth, the AF-recurrence rate might have been underestimated because asymptomatic AF episodes would remain undetected with interval monitoring post-ablation. Finally, outcome, procedure data may be institution specific and may be related to lack of
extensive experience with MNS. The use of pre-procedural anatomic imaging with CT
or MR with merging of the imaging with the electroanatomic mapping system may
result in shorter procedure times and less fluoroscopy exposure with MNS.

Conclusions

The efficacy of MNS with a novel irrigated tip catheter with back up of manual
ablation wherever required for patients with PAF undergoing index PVI is comparable
to the conventional technique in our early experience. The radiofrequency, fluoroscopy
and procedural times are significantly higher with MNS system than the conventional
approach. Technical modifications in the system including the contact force and wider
clinical experience may help to improve these outcomes.

Conflict of Interest Disclosures: Matthew Wright acknowledges financial support
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Hospital NHS Foundation Trust
References:


navigation in adults with complex congenital heart disease and in small children.


Table 1. Patient Clinical Characteristics

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<th>MNS-group</th>
<th>manual-group</th>
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<tr>
<td>N</td>
<td>30</td>
<td>44</td>
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<tr>
<td>Age (years)</td>
<td>60.2 ± 9.4</td>
<td>57.6 ± 11.3</td>
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<td>Sex (M/F)</td>
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<tr>
<td>Structural heart disease</td>
<td>3 (10%)</td>
<td>5 (11%)</td>
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<td>Ischemic heart disease</td>
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<td>3</td>
<td></td>
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<tr>
<td>Valvular heart disease</td>
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<tr>
<td>Cardiomyopathy</td>
<td>0</td>
<td>1</td>
<td></td>
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<td>Duration of AF (months)</td>
<td>60 (IQR, 40 to 96)</td>
<td>48 (IQR, 29 to 84)</td>
<td>0.670</td>
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<td>Ineffective AADs (n)</td>
<td>2 (IQR, 2 to 3)</td>
<td>2 (IQR, 1 to 3)</td>
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<td>Amiodarone (n)</td>
<td>10 (33%)</td>
<td>14 (32%)</td>
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<td>LAD (mm)</td>
<td>42.0 ± 6.3</td>
<td>40.7 ± 6.0</td>
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<td>LVEF (%)</td>
<td>65.4 ± 9.0</td>
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AADs=antiarrhythmic drugs; LAD=left atrial diameter; LVEF=left ventricular ejection fraction.

Figure Legend:

Figure 1. Kaplan-Meier curves of the maintenance of sinus rhythm in the follow-up after the initial procedure. There was no significant difference between MNS group (green line) and manual group (red line).
Freedom from AF recurrence

Months after the initial procedure

Number of patients at risk

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