

nMARQ™ ablation



UNIVERSITÀ DEGLI STUDI DI TORINO

This is the accepted version of the following article:
J Cardiovasc Electrophysiol. 2014 Jul 28. doi: 10.1111/jce.12500.
[Epub ahead of print]

which has been published in final form at:
<http://onlinelibrary.wiley.com/doi/10.1111/jce.12500/abstract>

Pulmonary vein isolation with a new multipolar irrigated radiofrequency ablation catheter (nMARQ™): feasibility, acute and short term efficacy, safety and impact on post-ablation silent cerebral ischemia

Short title: PVI with nMARQ™

Marco Scaglione MD^a, Domenico Caponi MD^a, Matteo Anselmino MD PhD^b, Francesca Di Clemente MD^a, Alessandro Blandino MD^b, Federico Ferraris MD^b, Paolo Di Donna MD^a, Elisa Ebrille MD^a, Franck Halimi MD^c, Jean Francois Leclercq MD^c, Costanza Iunco MD^d, Carloeugenio Vaudagna MD^d, Federico Cesarani MD^d, Fiorenzo Gaita MD^b.

^a Cardiology Division, Cardinal Guglielmo Massaia Hospital, Asti, Italy; ^b Division of Cardiology, Department of Medical Sciences, University of Turin, Italy; ^c Department of Rythmology, CMC Parly II Le Chesnay, Le Chesnay, France; ^d Division of Radiology, Cardinal Massaia Hospital, Asti, Italy

Conflict of Interest Disclosures: none

Funding Sources: none

Corresponding author:

Marco Scaglione, MD

Cardiology Division, Cardinal Guglielmo Massaia Hospital, Asti, Italy

Corso Dante 202, 14100 Asti, Italy

Phone: + 39 0141 487121

Fax: + 39 0141 487134

E-mail: marco.scaglione@tin.it

Abstract

Background: Simultaneous multipolar ablation catheters have been proposed to simplify pulmonary vein isolation (PVI) in paroxysmal atrial fibrillation (AF). Recently a new multipolar irrigated radiofrequency (RF) ablation catheter (nMARQ™, Biosense Webster Inc, Diamond Bar, California) combining both three-dimensional electroanatomic mapping and multipolar open-irrigated ablation capability has been developed. Aim of our study was to assess feasibility, acute and short term success and safety of PVI by the use of this new technology with particular regard to the incidence of post-ablation silent cerebral ischemia (SCI).

Methods and Results: Twenty-five patients (76% males; age 57 ± 13 years) with paroxysmal AF underwent PVI using the nMARQ™ catheter. PVI, confirmed by Lasso catheter mapping, was achieved in 100 out of 102 pulmonary veins (98%) identified and final PVI was obtained in 24 out of 25 (96%) patients. The overall concordance between Lasso and nMARQ™ signals in demonstrating PVI was 78%. No major procedural complications, occurred and no patient suffered SCI, on the basis of cerebral magnetic resonance imaging (MRI) performed before and after the procedure. Following a six-month follow-up 17/25 (68%) patients remained free from AF without antiarrhythmic drugs.

Conclusions: In our preliminary experience, PVI with nMARQ™ catheter appears to be feasible and safe, without incidence of SCI. Long term clinical efficacy has to be evaluated in further studies.

Key-words: pulmonary vein isolation; atrial fibrillation; ablation; silent cerebral ischemia; asymptomatic cerebral embolism; nMARQ™; signals

Introduction

Pulmonary vein isolation (PVI) is a well-established treatment for symptomatic paroxysmal atrial fibrillation (AF) and can be considered as a first-line therapy in patients with structurally normal heart.¹ However, the generally used “point by point” ablation technique to isolate pulmonary veins (PVs) is still time consuming and requires experienced operators to perform and create reliable contiguous transmural lesions. In order to overcome these limitations, a simultaneous multipolar nonirrigated radiofrequency (RF) ablation catheter has been introduced in clinical practice.² Unfortunately the use of this catheter has been correlated with a high incidence of silent cerebral ischemia (SCI).^{3,4} Recently a new catheter (nMARQ™ Circular, Biosense Webster Inc, Diamond Bar, California) combining both 3D electroanatomic mapping (EAM) and multipolar RF ablation capability through open-irrigation design has recently been developed. Preliminary reports on PVI with nMARQ™ showed a good acute success but still with a high incidence of complications such as SCI and atrio-esophageal fistulas.^{5,6,7} Moreover, most of these preliminary studies did not provide confirmation of PVI with the standard circular multipolar mapping method and did not strictly apply the methodology proposed at the present time to reduce the incidence of SCI using the RF multielectrode ablation catheter.⁸

The present study aimed to assess, in patients with paroxysmal AF undergoing PVI with the use of this new catheter, the followings: 1) feasibility; 2) acute success validated with the Lasso catheter (BiosenseWebster, Diamond Bar, USA); 3) safety with particular interest on the incidence of periprocedural SCI by performing cerebral diffusion-weighted magnetic resonance imaging (DW-MRI) before and after the procedure; 4) short term follow-up (6 months).

Methods

Study Population and Protocol

Twenty-five consecutive patients with drug-refractory paroxysmal AF undergoing PVI were prospectively enrolled. Exclusion criteria were: age <20 and >80 years, severe valvular heart disease, acute coronary syndrome in the last 3 months, previous AF catheter ablation, previous pacemaker or implantable cardioverter-defibrillator implant, any contraindication to cerebral MRI. All patients gave written informed consent before enrollment.

On admission all patients underwent a thorough cardiac assessment including transesophageal echocardiogram. All the patients underwent cerebral MRI 24 hours before and 24 hours after the ablation. The antithrombotic therapy was discontinued 5 days before admission and replaced by low molecular weight heparin (LMWH) dosed according to the body weight (1 mg/kg BD), until 12 hours before the procedure.

Cerebral MRI Imaging

Cerebral MRI was performed, using a 1.5 T scanner (1.5 Tesla Magnetom Avanto, Siemens, Erlangen, Germany). The detailed cerebral MRI imaging protocol has been previously reported⁹. Briefly, the imaging protocol included a sagittal T1-weighted spin echo sequence; an axial fluid-attenuated inversion recovery (FLAIR) sequence; a diffusion-weighted (DW) sequence. In the postablation MRI, acute embolic lesion was defined as a new focal hyperintense area detected by the FLAIR sequence, corresponding to a restricted diffusion signal in the DW sequence and confirmed by the apparent diffusion coefficient mapping to rule out a shine through artifact. The size and the location of the focal lesions were analyzed. Two blinded certified radiologists independently analyzed all MRI images. Interobserver variability for the MRI assessment was tested with the McNemar test and was not statistically significant.

Ablation Procedure: General Protocol

A contrast-enhanced cardiac MRI of the left atrium (LA) was performed 24 hours before the AF ablation. Deep sedation was achieved by means of intravenous fentanyl, midazolam and propofol.

Through femoral vein access, a decapolar electrode catheter was inserted into the coronary sinus. The LA was accessed by a single transseptal puncture using an 8.5 F long sheath continuously perfused with heparinized solution. Intravenous unfractionated heparin (100 IU/kg) was administered as follows: a third of the dose after femoral access and two-thirds of dose immediately after the transseptal puncture. The activated clotting time (ACT) was determined every 30 min and additional boluses were administered aiming to maintain ACT >320 seconds throughout the procedure. Catheters were introduced in the LA through the long sheath that was systematically withdrawn back to the right atrium after the positioning of the catheters in the LA. As far as concerning the acute efficacy, we decided to validate the supposed PVI obtained with the nMARQ™ catheter by using a multipolar catheter (Lasso, BiosenseWebster, Diamond Bar, USA) to map all the PVs at the baseline and after the PVI. At the beginning of the procedure, using the CARTO 3 system (Biosense Webster, Diamond Bar, USA), a fast electroanatomic map was created by nMARQ™ and subsequently merged with the 3D MRI shell. Ablation endpoint was the PVI, defined by a complete elimination or dissociation of PV potentials. The nMARQ™ was positioned at the ostium of each PV guided by 3D LA reconstruction. In order to avoid the phrenic palsy, before delivering RF at the right-sided veins ostium, pacing at high output (10 mA) was performed from each nMARQ™ electrodes to exclude the phrenic nerve capture. In case of diaphragm capture, the local site was first tagged and the corresponding electrodes were switched off during the RF delivery. At the end of PVI, validated according to nMARQ™

signals, Lasso catheter was re-advanced into the LA in order to confirm the effective PVI. If this target was not achieved, the nMARQ™ catheter was re-advanced at the PVs ostia to deliver further RF pulses aiming PVI. If PVI was not confirmed by Lasso mapping after this second round of multiple multielectrodes RF delivery by the nMARQ™, a 3.5-mm tip open irrigated catheter (SmarthTouch Thermocool, Biosense Webster Inc, Diamond Bar, California) was inserted through the same transseptal hole and used to complete the PVI. At the end of the procedure, after ruling out any pericardial effusion by echocardiogram, heparin infusion was started and titrated to maintain an activated partial thromboplastin time value of 60–80 seconds. The patient was discharged home bridging warfarin and LMWH (1 mg/kg BD until INR was \geq 2) the day after.

nMARQ™ catheter and RF delivery details

The nMARQ™ system combines the 3D magnetic navigation system and multielectrode open-irrigated ablation technology. The main elements are: the nMARQ™ circular ablation catheter, the nMARQ™ Multichannel generator and a dedicated software interface of Carto3® system. The circular catheter has three magnetic sensors placed on the loop to allow the visualization on Carto3® system and consists of a 7.6 F shaft catheter, which has an 8.4F circular loop at the distal part of the shaft with centered helical design and variable diameter (20-35 mm). Ten irrigated ring electrodes (10 irrigation holes, 3mm length, 4mm inter-electrode spacing) are contained on the loop of the catheter that is internally designed to assure the same irrigation flow per each electrode. An irrigation pump (Cool Flow®, Biosense Webster Inc, Diamond Bar, California) is used to control the heparinized saline irrigation (4mL/min during mapping, 60mL/min during ablation). A thermocouple is welded to each electrode on the outer edge of the loop. The circular catheter is connected to the nMARQ™ Multichannel generator that has 10 channels, one for

each electrode. Each channel acts independently and one does not interact with the other in order to avoid any energy transferring. The generator may operate in unipolar or bipolar mode and continuously monitors impedance, temperature at each electrode and power delivered by each electrode/pair. The modality of the ablation is temperature control mode. During ablation, the generator controls the temperature of each electrode involved and reduces the power if the target temperature exceeded. In our study, after catheter placement at the desired location, RF energy was delivered only in unipolar mode, simultaneously from 1 up to 10 electrodes at the sites presenting PV potentials. The maximum duration of each multielectrodes application session was 40 sec. The target temperature was set to 45°C. The power delivered was set to 20W, decreased to 18W in the posterior wall in order to reduce the risk of esophageal injury, and increased up to 25W in the left lateral ridge and in the reconnection sites. In case of suspicion of electrodes overlapping due to a small catheter loop seen on fluoroscopy or 3D catheter visualization of the CARTO3 system and the presence of artifacts on endocardial signals, RF energy was delivered only through one of them, in order to avoid any energy cross-talk that may favor over-heating and thrombus formation^{10,11}.

Summary of specific techniques aiming to reduce the incidence of periprocedural complication with the use of nMARQ™

Previous experiences with the use of PVAC (pulmonary vein ablation catheter-PVAC, Ablation Frontiers, Inc., Carlsbad, CA, USA)^{8,10,11} and with the use of nMARQ™^{5,7} showed that specific procedural settings correlated with the incidence of embolic complications. Based on these considerations the following work-flow aiming to reduce periprocedural complications was instituted:

1. the procedures were performed on intravenous unfractionated heparin (UFH) to keep ACT >320 seconds, monitored every 30 min. UFH (100 UI/Kg) was administered as follows: 1/3 after the femoral access and the remaining 2/3 immediately after the transseptal puncture.
2. Catheters introduction and withdrawal were performed always aspirating from the sheath during their manipulation.
3. Transseptal sheath was continuously perfused with heparinized solution and it was systematically withdrawn back to the right atrium after LA catheters positioning.
4. RF energy was delivered only in unipolar mode.
5. In case of distal and proximal nMARQ™ electrodes overlapping, RF energy was delivered only through one of them, in order to avoid any energy cross-talk that may favor over-heating and thrombus formation^{10,11}.
6. The maximum duration of each multielectrode application session was set to no more than 40 sec.
7. The target temperature was set to 45°C.
8. The power delivered was set to 20W and decreased to 18W in the posterior wall in order to reduce the risk of esophageal injury,
9. The electrodes showing the absence of heating over 36°C or reaching less than 10 Watt were turned off.
10. Pacing at high output (10 mA) was performed from each nMARQ™ electrodes at the right-sided veins ostium, before RF delivery, in order to avoid the phrenic nerve palsy. Therefore the electrodes showing diaphragm capture, were switched off during RF delivery.

Follow up

Follow-up visits were scheduled at 3 and 6 months with physical examination, ECG, and 24-hour Holter monitoring. All the patients were encouraged to document any symptoms suggestive for AF/atrial tachycardia recurrence by a 12-lead ECG. After the ablation procedure, oral anticoagulant therapy (OAT) was maintained for at least 3 months. Thereafter, clinical decision about OAT interruption/continuation was made according to CHA₂DS₂-VASc score. The antiarrhythmic drugs (AADs) were continued for 12 weeks after the procedure, and then stopped if no recurrences occurred.

Statistical Analysis

Categorical variables are reported as count and percentages, while continuous variables as mean and standard deviations (SD). Comparison was tested in cross tabulations tables by means of the Pearson Chi-Square or Fisher's Exact Test and by one-way ANOVA respectively for categorical and continuous variables. A two sided p-value <0.05 was considered statistically significant. All analyses were performed with SPSS 17.0 (SPSS Inc, Chicago, IL, USA).

Results

Out of 25 patients with paroxysmal AF enrolled, 19 (76%) were male with a mean age of 57±13 years. Three (12%) patients showed ischemic heart disease while systemic hypertension was present in 13 (52%). The mean LA antero-posterior diameter was 44±8 mm while the mean left ventricular ejection fraction (LVEF) was 61±6%. A patent foramen ovale was found in 2 patients (8%). CHA₂DS₂-VASc score was 0 in 7 (28%), 1 in 9 (36%), ≥ 2 in 9 (36%) patients. The

neurological examination performed before ablation was normal in all the patients. Details about clinical characteristics are summarized in table 1.

Feasibility and procedural details

The ablation procedure was feasible in all the patients (Fig.1). The nMARQ™ catheter was easily manoeuvred without requiring the use of a steerable sheath in all the patients.

Procedural details, including fluoroscopic and procedural times at different ablation steps, are summarized in table 2 while table 3 shows, for each vein, overall RF time, mean power and mean number of active electrodes. Nineteen out of 25 enrolled patients showed 4 PVs, 2 a left common trunk, and 4 patients had a right middle PV. In these latter patients, the anatomical encircling around the right superior and/or inferior PVs allowed to electrically isolate the right middle PV using the nMARQ™ only (Fig.2). Overall, the mean RF time was 14.95 min while the mean power was 18.07 W and the mean number of activated electrodes was 6.62 for each vein. No significant difference among veins in term of procedural parameters considered was observed except for a longer RF time needed to achieve PVI in left superior PV (LSPV) and right superior PV (RSPV) when compared to left inferior PV (LIPV) ($p=0.019$) and right inferior PV (RIPV) ($p=0.011$), respectively.

Acute success

After a first round of several multielectrodes RF deliveries with the nMARQ™ at each PV ostia obtaining the supposed PVI, Lasso catheter mapping confirmed the PVI in 80 (78%) out of 102 PVs. In the remaining 22 (22%), Lasso mapping still demonstrated venoatrial connection and further nMARQ™ RF applications were required at the LSPV in 5, LIPV in 4, RIPV in 6, and RSPV in 7 patients to obtain PVI).

At the end of the ablation procedure, PVI obtained with the use of the nMARQ™ only and confirmed with the Lasso mapping, was achieved in 100 out of 102 (98%) identified and targeted PVs and in 24 out of 25 (96%) treated patients. In the remaining patient, despite two rounds of multielectrodes RF delivery attempts with nMARQ™ catheter, a residual conduction gap still remained in the area of the ridge between LSPV and left atrial appendage (LAA). PVI was safely and effectively achieved using a 3.5-mm tip open-irrigated catheter. Moreover, in the same patient, phrenic nerve capture was observed in a quite large area around the anterior and inferior aspect of RSPV ostium and antrum (Fig. 3). PVI of this RSPV was obtained with an anatomy-tailored point-by-point ablation strategy using the 3.5-mm tip open-irrigated catheter.

Safety outcome

Out of 25 procedures performed no major complications were observed. Post-procedural cerebral DW-MRI did not show any new SCI in all the patients. Only 3 groin hematomas occurred.

Six-months follow up

All patients completed the six-month follow up. No late adverse events (including cerebral thromboembolic events) were reported. Out of 25 patients 17 (68%) were in sinus rhythm and free from symptomatic or documented asymptomatic atrial arrhythmias, without AADs. Of the remaining 8 patients, 3 had documented AF episodes, 2 had symptomatic episodes without ECG/ECG Holter documentation and 3 had atypical atrial flutter.

Discussion

The major findings of the present study are the followings:

- PVI with the nMARQ™ catheter seems feasible with procedural and fluoroscopy times similar or even inferior to those reported with other existing ablation systems.

- The acute success of the procedure is high since PVI confirmed by Lasso mapping has been achieved in 100 out of 102 (98%) targeted PVs while in the remaining two veins further conventional RF delivery through a standard open-irrigated ablation catheter was necessary. However, the nMARQ™ catheter was able to predict PVI only in 78% of PVs. This finding may influence the outcome of the procedure if performed without the Lasso catheter validation.
- Our preliminary data showed that nMARQ™ catheter appears to be safe with no major procedural complications. In particular, applying a specific procedural work-flow, no new SCI were detected by post-ablation brain MRI.

“Point-by-point” ablation for PVI using conventional irrigated catheters is now widely used.¹²

However, the procedure still requires experienced operators to create reliable contiguous transmural lesions and, according to these limitations, PVI results are not completely reproducible and vary among different centres. In order to overcome all these limitations, simultaneous multipolar ablation catheters have been introduced in clinical practice. The last of these catheters is the nMARQ™, a new multipolar mapping and ablation catheter using an open-irrigated RF ablation technology and integration into the CARTO3 system. Previous studies reported that AF ablation by the use of nMARQ™ is feasible and represents a reliable alternative for PVI with a high acute success rate.^{5,6}

Our experience showed similar results in terms of procedural times and acute success rate.

Comparing the procedural time between the “point by point” ablation technique and the nMARQ™ ablation in our experience, no reduction was seen. It can be explained by our study protocol that imply extra procedural time due to the use of Lasso catheter mapping to validate the supposed PVI by the nMARQ™. Thus, considering the learning curve and the avoidance of the

use of the Lasso catheter mapping in standard procedures, a further reduction of the procedural time may be expected. In addition, the manoeuvrability of the catheter was satisfactory since PVI was obtained in all the cases without the use of steerable sheath in contrast to other experiences^{5,6,13}. It is well known that PVs anatomy variability is remarkable¹⁴ and, because of that, the use of circular multipolar ablation catheter may present some limitations. Nevertheless, in our study, the nMARQ™ catheter allowed us to achieve PVI in all the patients but 1 (96%). In this patient, LSPV was not isolated due to the impossibility to achieve a transmural lesion at the ridge between the left PVs and the LAA with the nMARQ™ and additional “point-by-point” ablation was required. Furthermore, phrenic nerve capture was also demonstrated in a quite large area around the RSPV antrum, so that, despite several attempts, a safe and complete PVI with the nMARQ™ catheter was not achieved and conventional ablation was needed to tailor the lesion line according to this specific anatomy.

An important limit of the nMARQ™ catheter pointed out by our results is that it was able to predict PVI only in 78% of PVs according to the Lasso catheter mapping. The evidence of a discordance between nMARQ™ and Lasso recording has been reported also by Rosso et al¹³. Possible explanations may be the difference in inter-electrode spacing, the electrodes size and more proximal position in the PVs ostia of the nMARQ™ that may influence the endocardial electrograms characteristics. Further studies are necessary to evaluate the long term outcome of PVI obtained by the use of the nMARQ™ only in order to assess the impact of confirmation of PVI with Lasso mapping on the procedural outcome.

Regarding the X-ray exposure it should be considered that the nMARQ™ technology, combining ablation capability with the 3D navigation, allows to visualize the catheter and consequently to maneuver it without the need of fluoroscopy. In our series the mean total X-ray time was

1.8'±2", similar to that previously published¹⁵ with conventional "point-by-point" RF ablation. Fluoroscopy was used almost only for the transseptal puncture and the initial positioning of the catheters, while the combination with the CARTO 3 system allowed to perform mapping and RF delivery fluorlessly. This result has an important clinical implication for the reduction of fluoroscopy exposure for the patient and medical staff.

Recently much attention has been raised regarding the occurrence of post-AF ablation SCI⁸. With the use of multipolar non irrigated RF ablation catheters, PVAC, post-ablation SCI were detected in 38.9% of the cases³. Similar incidence (33%) has been reported by Deneke et al⁵ using the nMARQ™. Several periprocedural variables may play a potential role¹⁶. Using a porcine ablation model, Haines et al¹⁰ found that microemboli and microbubbles formation with PVAC were more common in the following settings: (1) bipolar over unipolar RF delivery; (2) during catheter introduction and manipulation; (3) during energy delivery with the overlap of proximal and distal electrodes. The results of a recent trial⁸ demonstrated that, performing ablation with a careful attention to avoid the above mentioned procedural settings^{10,11,16}, the rate of SCI with PVAC decreased dramatically to 1.7%. Applying the same procedural precautions, as described in the methods sections, in our series no SCI were detected by post-ablation DW MR, in contrast with the results reported by Deneke et al.⁵ Possible explanations of this difference may be: 1) longer total RF time (19' vs 14.95'); 2) lower ACT level (334" vs 372"); 3) the use of the steerable sheath left in the LA during all the procedure and 4) possible simultaneous RF delivery when the proximal and distal electrodes overlapped⁶ (Deneke⁵ did not specify if the interaction between electrodes 1 and 10 was avoided).

Deneke⁷ also reported the occurrence of esophagopericardial fistula with a fatal outcome after an uneventful ablation of atrial fibrillation using the nMARQ™ catheter. Furthermore, the same

authors reported also 33% of esophageal lesions detected by endoscopy.⁵ This complication was attributed to the use of high RF power in the posterior wall. In our series we declined the use of esophageal temperature monitoring because of a possible causal connection between multielectrode ablation and esophageal lesion by passive heating of the temperature probe.¹⁷ However, for safety reason, we delivered a maximum of 18 watts RF energy in the posterior wall for no more than 40 seconds.

Finally, in our study, with the use of the nMARQ™ catheter a short-term success rate of 68% was achieved without AADs. However, our short-term follow up does not allow any firm conclusion and the outcome of the procedure needs to be assessed in further studies with longer-follow-up and with more accurate detection tools to exclude asymptomatic arrhythmias episodes.

Study limitations

This is a study with a limited sample size and a short follow up. Moreover, the follow-up was carried out only on a clinical basis, so that asymptomatic AF episodes may be missed.

Secondly, our acute and short term outcome cannot be attributed only to the use of the nMARQ™ technology because, in our study protocol, the Lasso catheter was used to confirm PVI. In addition, in one patient the use of the standard 3.5-mm tip open irrigated catheter was needed to complete PVI.

Another consideration regards the uncertainty of re Lasso recordings related to our study protocol since Lasso and nMARQ™ signals were not recorded simultaneously, but in temporal sequencing.

Moreover, another limitation is that the procedure was not performed with the widely used on-warfarin protocol, but with the bridge protocol between warfarin and LMWH with intra-procedural heparin infusion.

Finally, esophageal lesions were not assessed with endoscopy.

Conclusions

The limited size of our patient population does not allow any firm conclusion. However, our preliminary experience demonstrated the feasibility, the safety and the good acute procedural success of the PVI performed with the nMARQ™ catheter.

In addition an important result of our study is the complete absence of periprocedural SCI, in contrast with other experiences⁵ using the same ablation catheter. This finding underlies the importance of following a specific and careful procedural workflow.

Our preliminary results need to be confirmed with long-term studies.

Author contribution:

Marco Scaglione: concept/design, data analysis/interpretation, critical revision of article, approval of article

Domenico Caponi: data analysis/interpretation, draft article, approval of article

Matteo Anselmino: data analysis/interpretation, critical revision of article, approval of article

Francesca Di Clemente: data collection, clinical follow up, draft article, approval of article

Alessandro Blandino: data analysis/interpretation, statistics, draft article, approval of article

Federico Ferraris: data collection, clinical follow up, critical revision of article, approval of article

Paolo Di Donna: data analysis/interpretation, critical revision of article, approval of article

Elisa Ebrille: data analysis/interpretation, critical revision of article, approval of article

Franck Halimi: data collection, clinical follow up, critical revision of article, approval of article

Jean Francois Leclercq: data analysis/interpretation, critical revision of article, approval of article

Costanza Iunco: data collection, critical revision of article, approval of article

Carlo Eugenio Vaudagna: data collection, critical revision of article, approval of article

Federico Cesarani: data analysis/interpretation, critical revision of article, approval of article

Fiorenzo Gaita: data analysis/interpretation, critical revision of article, approval of article

References

1. Camm AJ, Lip GY, De Caterina R, Savelieva I, Atar D, Hohnloser SH, Hindricks G, Kirchhof P: 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. An update of the 2010 ESC Guidelines for the management of atrial fibrillation developed with the special contribution of the European Heart Rhythm Association. *Eur Heart J* 2012; 31:2719-2747.
2. Boersma LV, Wijffels MC, Oral H, Wever EF, Morady F: Pulmonary vein isolation by duty-cycled bipolar and unipolar radiofrequency energy with a multielectrode ablation catheter. *Heart Rhythm* 2008; 5:1635–1642.
3. Gaita F, Leclercq JF, Schumacher B, Scaglione M, Toso E, Halimi F, Schade A, Froehner S, Ziegler V, Sergi D, Cesarani F, Blandino A: Incidence of Silent Cerebral Thromboembolic Lesions After Atrial Fibrillation Ablation May Change According To Technology Used: Comparison of Irrigated Radiofrequency, Multipolar Nonirrigated Catheter and Cryoballoon. *J Cardiovasc Electrophysiol* 2011; 22:961-968.
4. Herrera Siklody C, Deneke T, Hocini M, Lehrmann H, Shin DI, Miyazaki S, Henschke S, Fluegel P, Schiebeling-Romer J, Bansmann PM, Bourdias T, Dousset V, Haissaguerre M, Arentz T: Incidence of asymptomatic intracranial embolic events after pulmonary vein isolation: comparison of different atrial fibrillation ablation technologies in a multicenter study. *J Am Coll Cardiol* 2011; 58:681-688.
5. Deneke T, Schade A, Müller P, Schmitt P, Christopoulos G, Krug J, Szöllösi G, Mügge A, Kerber S, Nentwich K: Acute safety and efficacy of a novel multipolar irrigated radiofrequency ablation catheter for pulmonary vein isolation. *J Cardiovasc Electrophysiol* 2013 Nov 14 [Epub ahead of print].

6. Shin DI, Kirmanoglou K, Eickholt C, Schmidt J, Clasen L, Butzbach B, Rassaf T, Merx M, Kelm M, Meyer C: Initial results of using a novel irrigated multielectrode mapping and ablation catheter for pulmonary vein isolation. *Heart Rhythm* 2013 Dec 6 [Epub ahead of print].
7. Deneke T, Schade A, Diegeler A, Nentwich K: Esophago-pericardial fistula complicating atrial fibrillation ablation using a Novel-Irrigated Radiofrequency Multipolar Ablation Catheter. *J Cardiovasc Electrophysiol* Oct 2013 [Epub ahead of print].
8. Verma A, Debruyne P, Nardi S, Deneke T, DeGreef Y, Spitzer S, Balzer JO, Boersma L; ERACE Investigators: Evaluation and reduction of asymptomatic cerebral embolism in ablation of atrial fibrillation, but high prevalence of chronic silent infarction: results of the Evaluation of Reduction of Asymptomatic Cerebral Embolism trial. *Circ Arrhythm Electrophysiol* 2013; 6:835–842.
9. Gaita F, Caponi D, Pianelli D, Scaglione M, Toso E, Cesarani F, Boffano C, Gandini G, Valentini MC, De Ponti R, Salimi F, Leclercq JF: Radiofrequency catheter ablation: A cause of silent thromboembolism? Magnetic resonance imaging assessment of cerebral thromboembolism in patients undergoing ablation of atrial fibrillation. *Circulation* 2010; 122:1667-1673.
10. Haines DE, Stewart MT, Ahlberg S, Barka ND, Condie C, Fiedler GR, Kirchhof NA, Halimi F, Deneke T: Microembolism and catheter ablation I. A comparison of irrigated radiofrequency and multielectrode-phased radiofrequency catheter ablation of pulmonary vein ostia. *Circ Arrhythm Electrophysiol* 2013; 6:16-22.
11. Wiczorek M, Lukat M, Hoeltgen R, Condie C, Hilje T, Missler U, Hirsch J, Scharf C: Investigation into causes of abnormal cerebral MRI findings following PVAC duty-cycled, phased RF ablation of atrial fibrillation. *J Cardiovasc Electrophysiol* 2013; 24:121-128.

12. Cappato R, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J, Kim YH, Klein G, Natale A, Packer D, Skanes A, Ambrogi F, Biganzoli E: Updated worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circ Arrhythm Electrophysiol* 2010; 3:32-38.
13. Rosso R, Halkim A, Michowitz Y, Belhassen B, Glick A, Viskin S: Radiofrequency ablation of paroxysmal atrial fibrillation with the new irrigated multipolar nMARQ ablation catheter. Verification of intracardiac signals with a second circular mapping catheter. *Heart Rhythm* Dec 2013. [Epub ahead of print]
14. Anselmino M, Blandino A, Beninati S, Rovera C, Boffano C, Belletti M, Caponi D, Scaglione M, Cesarani F, Gaita F: Morphologic Analysis of Left Atrial Anatomy by Magnetic Resonance Angiography in Patients With Atrial Fibrillation. A Large Single Center Experience. *J Cardiovasc Electrophysiol* 2011; 22:1-7.
15. Scaglione M, Biasco L, Caponi D, Anselmino M, Negro A, Di Donna P, Corleto A, Montefusco A, Gaita F: Visualization of multiple catheters with electroanatomical mapping reduces X-ray exposure during atrial fibrillation ablation. *Europace* 2011; 13:955-962.
16. Anselmino M, Gaita F: Unresolved issues in transcatheter atrial fibrillation ablation: silent cerebrovascular ischemia. *J Cardiovasc Electrophysiol* 2013; 24:129-131.
17. Deneke T, Bunz K, Bastian A, Päsler M, Anders H, Lehmann R, Meuser W, de Groot JR, Horlitz M, Haberkorn R, Mügge A, Shin DI: Utility of esophageal temperature monitoring during pulmonary vein isolation for atrial fibrillation using duty-cycled phased radiofrequency ablation. *J Cardiovasc Electrophysiol* 2011; 22(3):255-61.

Table 1. Baseline characteristics of enrolled patients.

Variables	
Number of patients	25
Gender (male)	19 (76%)
Age (years)	57±13
BMI (Kg/m ²)	26±3
Ischemic heart disease	3 (12%)
Hypertension	13 (52%)
Diabetes	1 (4%)
Dyslipidemia	10 (40%)
Dysthyroidism	6 (24%)
First AF (months)	44±46
Number of failed AADs	2 (1-5)
CHA ₂ DS ₂ -VASc score	
0	7 (28%)
1	9 (36%)
≥2	9 (36%)
Anticoagulation:	
<i>Oral anticoagulant therapy</i>	15 (60%)
<i>Aspirin</i>	8 (32%)
<i>None</i>	2 (8%)
LVEF (%)	61±6
LA APd (mm)	44±8
Patent Foramen Ovale	2 (8%)
PVs anatomy:	
<i>Left common trunk</i>	2 (8%)
<i>Right middle PV</i>	4 (16%)
<i>4 PVs</i>	19 (76%)

AADs, antiarrhythmic drugs; AF, atrial fibrillation; APd, antero-posterior diameter; BMI, Body Mass Index; LA, left atrium; LVEF, left ventricular ejection fraction; PV, Pulmonary vein

Table 2. Procedural variables.

Variables	
Total procedural time (min)	131±49
Total fluoro time (min)	1.8±2
Catheter placement time (min)	29±16
Fluoro time during catheter placement (min)	1.5±1.8
Time of LA mapping (min)	11±5
Fluoro time during LA mapping (min)	0.2±0.3
Mean RF time (min)	14.9±3.7
Fluoro time during RF (sec)	2±9
Mean ACT (sec)	372±40
Irrigation volume (ml)	1603±433

ACT, activated clotting time; LA, left atrium; RF, radiofrequency;

Table 3. Radiofrequency delivery details using nMARQ™ catheter

<i>Pulmonary Vein</i>	<i>n</i>	<i>Parameters</i>	<i>Mean</i>
LSPV	23	Radiofrequency time (min)	4.03
		Mean Power (W)	17.56
		Mean n°of active electrodes	6.94
LIPV	23	Radiofrequency time (min)	2.84
		Mean Power (W)	18.34
		Mean n°of active electrodes	6.15
LCT	2	Radiofrequency time (min)	5.07
		Mean Power (W)	16.79
		Mean n°of active electrodes	8.55
RSPV +RMPV	25	Radiofrequency time (min)	4.79
	3	Mean Power (W)	17.93
		Mean n°of active electrodes	6.33
RIPV +RMPV	25	Radiofrequency time (min)	3.26
	1	Mean Power (W)	18.29
		Mean n°of active electrodes	7.13
Total	102	Radiofrequency time (min)	14.95
		Mean Power (W)	18.07
		Mean n°of active electrodes	6.62

LCT, left common trunk; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; RIPV: right inferior pulmonary vein; RMPV, right middle pulmonary vein; RSPV, right superior pulmonary vein.