

Safety and Feasibility of Contrast Injection During Pulmonary Vein Isolation with the nMARQ™ Multi-Electrode Catheter

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Abstract

Introduction: Pulmonary vein isolation (PVI) using the irrigated multi-electrode ablation system (nMARQ™) remains challenging in complex atrial anatomy cases and when CARTOMERGE™ technology is not available, due to absence of a leading guide-wire.

Objectives: Our objective was to assess feasibility and safety of PVI using nMARQ™ catheter with intra-procedural contrast injections through the deflectable sheath compared to nMARQ™ alone.

Methods: This is a prospective non-randomized observational study of 78 consecutive patients who underwent PVI only with nMARQ™. The first group (n=37, 64±10.5 years, 62% male, 13.5% persistent AF) underwent the procedure with the guidance of signal mapping, fluoroscopy, and electro-anatomical mapping (EAM) alone. Since 12/2013 an automatic closed-loop contrast media injector was added to improve catheter location (n=41, 62.5±11 years, 71% male, 34% persistent AF).

Results: Total procedure time was 78±19 and 85.5±18.5 minutes, and mean fluoroscopy time was 30±9 and 29.5±8.7 minutes for the first and second groups, respectively (NS); acute success rate was 97% and 97.5%, with a mean of 14.7±5 and 17.6±5.4 RF applications, respectively (p=0.02); and mean total burning time of 10.3±3.6 and 12±4 minutes, respectively (p=0.08). Mean contrast used was 60±18 mL versus 203±65 mL, with no effect on renal function or major complications. One year freedom from AF was 77% and 83%, respectively (p=0.5).

Conclusions: Addition of contrast injections to standard nMARQ™ procedure is feasible and safe. It has no benefit in routine use but further studies may confirm its potential added value to EAM in catheter localization by newly trained operators and in selective cases of large/common PV anatomy.

Introduction

The irrigated multi-electrode electro-anatomically guided nMARQ™ catheter (Biosense Webster Inc., Diamond Barr, CA, USA) for atrial fibrillation (AF) ablation was recently launched in the market.¹

The first generation nMARQ™ consists of an 8.4F decapolar irrigated-based catheter with an adjustable circular array 20–35 mm in diameter. The catheter can be recognized by the CARTO 3 system (Biosense Webster Inc., Diamond Bar, CA, USA), which allows 3D electro anatomical mapping (EAM) of the left atrium (LA) and pulmonary veins (PVs). The RF energy is delivered in either unipolar or bipolar mode, and atrial and pulmonary vein PV signals can be

recorded during ablation.

Yet, this catheter's relatively large diameter and lack of a leading guide wire (which is used in another circular ablation method)^{2,3} frequently causes technical difficulties and some uncertainty regarding the exact location of the catheter relative to the PV ostia, especially during the training of new operators and in cases of patients who have large PVs or common PVs, where the EAM does not provide adequate guidance and the impedances are not accurate in reflecting PV boundaries. Also in small and medium sized PVs, the large size of the nMARQ™ catheter prevents operators from mapping inside the PVs, and the addition of intra-cardiac echocardiography for antral localization increases the procedural costs. Cartomerge™ technology may assist in catheter localization, but this option is not available in every center and is of lesser accuracy for guiding nMARQ™ procedure.

In order to overcome this difficulty, we introduced a tool for pulmonary vein isolation (PVI) when using the nMARQ™ system: we connected the steerable long sheath to a closed-loop automatic injector contrast delivery system: ACIST CVi System (ACIST Medical Systems Inc., Eden Prairie, MN, USA). Selective intra-procedural contrast media injections in cases of large/common PVs helped us in localizing the catheter at the PV antrum (Figure 1).

Key Words:

Atrial Fibrillation, Catheter Ablation; Multi-Electrode Ablation Catheter, nMARQ, Contrast Injection. Agnisciet quamus, simus si

Disclosures:
None.

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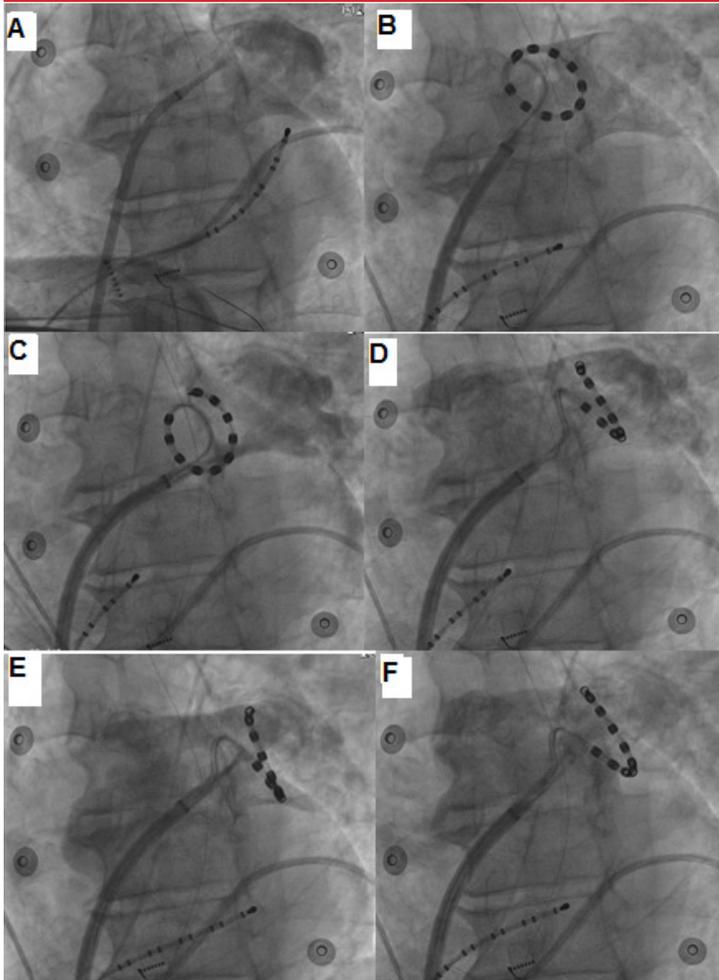


Figure:1

An example of a patient in group II with a large left common pulmonary vein. A. A selective angiogram through the deflectable sheath before introducing the nMARQ™ catheter. B-F. There was difficulty in isolating the vein, so injection through the ACIST CVI System was applied. Different positions of the catheter thought to be appropriate according to signal recordings and electro-anatomical mapping and impedances are demonstrated – but according to contrast injections by the ACIST CVI System – not in optimal areas of the vein. Finally an optimal target for ablation was found and the vein was eventually isolated.

The purpose of this study was to compare our preliminary experience of PVI using an nMARQ™ catheter with the aid of this closed-loop contrast injector versus nMARQ™ alone regarding feasibility, safety, as well as procedure and application times and one-year follow up, as reflected by our non-randomized single center registry. The study was not designed to prove superiority of the contrast injection method but to demonstrate its applicability in selective cases during training or complex PV anatomy.

Material and Methods

Patient Population

We studied all consecutive patients with symptomatic drug-refractory documented AF who underwent AF ablation using the irrigated multi-electrode circular ablation catheter in our center. Only paroxysmal and persistent AF patients who underwent PVI without additional lines of ablations were included in this study. They were included in a prospective non-randomized observational registry and were followed up in our institution.

Overall, out of 111 patients who underwent PVI with nMARQ™

Table 1:		Patient characteristics	
	Group I nMARQ™ (n=37)	Group II nMARQ™ with contrast (n=41)	p-value
Age (y)	64±10.5	62.5±11	0.5
Gender (%male)	23 (62%)	29 (71%)	0.4
CHA2DS2 VASC score	2.3±1.5	2.1±1.3	0.6
Anti-arrhythmic drugs AADs (mean N ± STD)	1.3±0.7	1.45±0.71	0.5
Left atrial size (AP, mm)	38.7±5.5	39.8±6.7	0.47
LV EF (%)			
Good/mild dysfunction	32 (86%)	37 (90%)	0.05
Moderate dysfunction	1 (3%)	4 (10%)	
Severe dysfunction	4 (11%)	0 (0%)	
H/O CVA/TIA	1 (3%)	1 (2.4%)	0.9
H/O CAD	7 (19%)	7 (17%)	0.8
cal GFR prior to procedure (ml/ min/1.73):			
>90	8 (22%)	11 (27%)	0.6
60-89	26 (70%)	25 (61%)	0.4
30-59	2 (5%)	5 (12%)	0.3
15-29	1 (3%)	0	0.3
<15	0	0	
>60	34 (92%)	36 (88%)	0.5
Persistent AF (%)	5 (13.5)	14 (34)	0.03

AAD = anti arrhythmic drugs; AF = atrial fibrillation; CAD = coronary artery disease; cal GFR = calculated GFR according to the equation: $GFR (mL/min/1.73 m^2) = 175 \times (Scr)^{-1.154} \times (Age)^{-0.203} \times (0.742 \text{ if female})$; CVA = cerebrovascular event; EF = ejection fraction; H/O = history of; LA = left atrium; LV=left ventricle; STD = standard deviation; TIA = transient ischemic attack

ablation system in our center, 78 were included in this study. The others were excluded due to the addition of ablation lines beyond PVI. Cartomerge™ technology was unavailable. All patients provided an informed consent prior to the procedure; the study protocol was approved by our institution review board and was not influenced by Biosense Webster Company.

Group I (n = 37) underwent the procedure using nMARQ™ ablation system. Group II (n = 41) underwent AF ablation using the nMARQ™ ablation system with the aid of contrast injections through the deflectable sheath while the catheter was inside the LA to help localize the catheter in large/common PV ostia. This tool was introduced in December 2013.

Mapping and Ablation Procedure

The nMARQ™ ablation system was previously described.^{1,4-6} All patients underwent trans-esophageal echo (TEE) up to 48 hours prior to the procedure. An interrupted anti-coagulation approach was used. All patients underwent the ablation under conscious sedation with midazolam, propofol, and pethidine hydrochloride, without the presence of an anesthesiologist. We introduced a naso-gastric tube for marking the proximity of the esophagus to the ablation sites. Vascular access was obtained through a femoral vein with continuous hemodynamic monitoring through the radial or femoral artery. A decapolar catheter was positioned in the coronary sinus. Trans-septal puncture was performed using a long sheath (SL0, SJM, Minnetonka, MN, USA), a SafeSept™ J-shaped guide wire, and a Brockenbrough needle (BRK, SJM, Minnetonka, MN, USA) under fluoroscopic and contrast guidance. After accessing the left atrium LA, heparin was given intravenously with a target active clotting time (ACT) of 300–350 seconds. By placing a wire in the left superior PV (LSPV), the fixed sheath was exchanged for a steerable guided sheath (Channel 9.5F, Bard, Lowell, MA, USA; or FlexCath, 10F or 12F, Medtronic

Cryo Cath LP, Canada; or Oscor 10F, Oscor® Inc., FL, USA). Selective angiograms of all PVs were then performed through the deflectable sheath and before introducing the nMARQ™ catheter in all patients in order to demonstrate LA anatomy and PV size. The ablation catheter was then introduced into the deflectable sheath under continuous flushing of the deflectable catheter with heparinized saline and under continuous flushing of the nMARQ™ catheter by the Cool Flow Pump at 60 mL/min and at 4 mL/min inside the LA.

For both groups we started mapping and ablating at the right inferior pulmonary vein (RIPV), which was the last vein to be demonstrated by the selective angiogram. We used the selective pre-catheter-insertion angiograms, fluoroscopy, EAM, impedances, and intracardiac signals from the nMARQ™ catheter for targeting the ablation zone in all patients.

In Group II patients we connected a contrast delivery system to the deflectable sheath: ACIST CVi System. We used it for short injections of contrast media (8 mL each) through the deflectable sheath whenever there was a doubt regarding catheter localization in relation to PV orifice (Figure 1). Those patients were treated with intravenous saline (1000 mL/24h) during the procedure or until the day after, and routine renal function tests were taken the day post-procedure.

Before ablating the right superior PV (RSPV), a high energy pacing (10 mV/2 ms at CL 500 ms) was performed from each electrode of the circular catheter to rule out phrenic nerve stimulation, in which case this electrode was shut down.

We applied unipolar RF energy with power settings of 20 Watts for the non-posterior zones and 15 Watts for the posterior areas. Each application lasted until the PV signals disappeared, between 15–60 seconds each. In case of lack of atrial signals on some of the multi-electrodes, those displaying no signal were shut off during subsequent energy delivery.

PV isolation was proved by entrance and exit block technique for very large PVs, in which the whole catheter could enter. In smaller veins, RF delivery was continued until no PV signals were observed at the antrum (along the inner aspect of the circumferential ablation line) and atrial loss of capture could be proven (the pace-and-ablate technique)⁷ or dissociated PV activity could be shown.

Our approach for patients with persistent AF was as follows: in patients who entered the procedure in AF rhythm, ablation of right PVs was performed, then DC cardioversion and completing PVI in sinus rhythm was applied – for better signal recording and proving isolation.

Table 2:	Procedural data (mean±SD)		
	Group I nMARQ™ (n=37)	Group II nMARQ™ with contrast (n=41)	p-value
Procedure time - overall (min)	78±19	85.5±18.5	0.1
Fluoroscopy time - overall (min)	30±9	29.5±8.7	0.8
Applications (mean ± STD)	14.7±5	17.6±5.4	0.02
Total burning time (min)	10.3±3.6	12±4	0.08
Overall amount of contrast media used during the procedure (cc)	60±18	203±65	<0.0001
Charring of catheter	0	0	

Min= minutes

Post-Ablation

All patients were monitored overnight and underwent echocardiography the day post-procedure to rule out pericardial effusion. Oral anticoagulation was continued for three months for all patients and for lifetime for those with CHA2DS2-VASC score above 1. Antiarrhythmic drugs were continued for two to three months post-procedure and all patients were treated with proton pump inhibitors for one month post-procedure.

Statistics

Patient characteristics for comparing the two groups were described by percentage and mean±SD. Continuous variables were compared using independent Student t-test; categorical variables were compared using chi-square test or Fisher's exact test. A p-value < .05 was considered statistically significant. Analyses were carried out using SPSS version 21.0 statistical package (SPSS IBM Inc.).

Results

Patient Characteristics

We studied prospectively 37 consecutive patients in our center who underwent AF ablation using nMARQ™ ablation with contrast injection for demonstrating selective PV angiography through the deflectable sheath while the nMARQ™ catheter was not yet applied to LA (64±10.5 years; 62% male; 13.5% persistent AF) – group I. We compared them to 41 consecutive patients who underwent AF ablation using nMARQ™ ablation with contrast injection as in group I but with additional contrast injections through a closed loop automatic injector connected to the deflectable sheath while the nMARQ™ catheter was introduced in PV ostia (62.5±11 years; 71% male; 34% persistent AF) – group II.

There was no statistical difference between the groups regarding baseline characteristics, except for the ratio of patients with persistent AF and baseline ejection fraction (EF) (Table 1). All patients had symptomatic documented AF that was refractory to at least one antiarrhythmic drug AAD. There was no significant difference between the two groups regarding percentage of patients with good left ventricular function, left atrial LA size, history of stroke, history of coronary artery disease, CHA2DVASC2 score, number of anti-arrhythmic drugs AADs used, and baseline kidney function (Table 1).

Procedural Data

Table 2 shows intra-procedural data for both groups.

Overall mean procedure times (from cleaning the groin to pulling back all catheters) were 78±19 minutes for group I and 85.5±18.5 minutes for group II (p = 0.1). Overall mean fluoroscopy times were 30±9 minutes for group I and 29.5±8.7 minutes for group II (p = 0.8).

The number of applications was 14.7±5 for group I and 17.6±5.4 for group II (p = 0.02); the total burning times were 10.3±3.6 and 12±4 minutes, respectively (p = 0.08).

During the procedure overall 60±18 mL of contrast media were injected intravenously in group I patients (selective angiograms before introducing the catheter) versus 203±65 mL in group II (both selective angiograms and injection through the ACIST CVi System while catheter in LA) (p < .0001).

No charring of the catheter was noted in both groups.

Safety Issues

Table 3 describes the complications during the procedures in the two groups. There was one tamponade that occurred in group II during manipulation of the catheter from the left PVs to the

Table 3: Safety and follow-up

	Group I nMARQ™ (n=37)	Group II nMARQ™ with contrast (n=41)	p-value
Acute complications (N)			
Pericardial tamponade	0	1	0.3
TIA/CVA	0	0	
Clinical PV stenosis	0	0	
A-E fistula	0	0	
Phrenic nerve palsy	0	0	
Access site	4 (10.8%)	0	0.03
Transient STE (inferior leads)	3 (8%)	0	0.06
Acute success (%)	36 (97%)	40 (97.5%)	0.9
Worsening of renal function tests (%)	1 (2.7%)	0	0.3
1year freedom from AF (available f/u) after one PVI	27/35 (77%)	20/24 (83%)	0.56
with AAD	6/27 (22%)	10/20 (50%)	0.13
1year freedom from AF (available f/u) after two PVIs	29/35 (83%)	22/24 (92%)	0.3
with AAD	6/29 (21%)	10/22 (45%)	0.06

A-E fistula = atrio-esophageal fistula; AF = atrial fibrillation; CVA = cerebrovascular event; PV = pulmonary vein; PVI = pulmonary vein isolation; STE = ST segment elevation in electrocardiogram; TIA = transient ischemic attack

right PVs. No overt neurological sequel or symptomatic pulmonary stenosis or atrio-esophageal fistula was observed.

Four vascular access site complications (pseudoaneurysm without the need for a vascular surgery) and three transient ST elevations in inferior leads occurred in group I after injecting dye through the Brockenbrough needle.

Since these cases we have changed our protocol regarding two issues:

1) we infuse protamine-sulfate post-procedure before removing the sheaths from the groin and prescribe new oral anti-coagulants (NOACs) post-procedure in order to avoid bridging for warfarin with low-molecular weight heparin (LMWH);

2) we no longer inject contrast through the Brockenbrough needle after trans-septal puncture. Since the application of these changes in daily practice, no such complication has been seen (group II) (Table 3).

Despite a difference in the amount of contrast medium injected in the two groups we observed no worsening in renal function tests in both groups, except for one patient in group I in whom calculated GFR worsened from normal to mild renal dysfunction the day post-procedure ($p = 0.3$).

We observed no acute complication related to the injection of contrast media in group II. The contrast was injected and was irrigated prior to the application of RF ablation.

Acute Success

For one patient in group I and one in group II, PV isolation could not be proven for all PVs, either due to anatomy of very small PVs and instability of the catheter at PV ostium (group I) or due to phrenic nerve stimulation in the RSPV that prevented us from isolating this vein (group II). Thus the acute success rate was 97% for nMARQ™ (group I) and 97.5% for nMARQ™ with contrast (group II) (Table 3).

One-Year Follow Up

One-year follow up was available for 35 patients in group I and 24 patients in group II. One year freedom from AF in those patients was 77% in group I and 83% in group II ($p = 0.56$) (Table 3). Twenty-two percent of those free of AF in group I were treated with anti-arrhythmic drugs AADs, versus 50% in group II ($p = 0.13$).

One-year freedom from AF after two PVI procedures was 83% in

group I and 92% in group II ($p = 0.3$) (Table 3). Twenty-one percent of those free of AF in group I were treated with AAD, versus 45% in group II ($p = 0.06$).

Discussion

The irrigated multi-electrode electro-anatomically guided nMARQ™ catheter was recently launched in the market for AF ablation.¹ Despite its advantages (EAM-based, TissueConnect™ feature), the first generation nMARQ™ system consists of an 8.4F catheter with an adjustable circular array of 20–35 mm diameter and no guiding wire.

The learning curve of this technology might be long for new operators since the localization of the catheter in PV ostium is difficult without a guiding wire. In addition, for some PV anatomies, the relatively large diameter of the nMARQ™ catheter and the lack of a guiding wire frequently causes technical difficulties and some uncertainty regarding the exact location of the catheter relative to the PV ostia, despite EAM usage. PVI guided by EAM integrated with magnetic resonance/computed tomographic images of the left atrium LA (Cartomerge™ technology) may serve as a solution to these cases,^{8,9} but their availability might be sub-optimal in some centers.

In order to overcome this difficulty, we connected the steerable long sheath to a closed-loop automatic injector contrast delivery system. This helped us in localizing the catheter at the PV orifice by using short injections of contrast media through the deflectable sheath while the catheter was in the PV antrum before RF ablation of the vein (Figure 1). This study investigated the applicability of this option in selective cases.

Procedural Differences

Mean procedure time and fluoroscopy time were comparable for both groups. However, the number of applications was larger when we used the injector and the total burning time tended to be longer.

We suspect that this stems from those situations where we think that the catheter is in the right place, but then, when we inject contrast media, we find that the catheter is not in an optimal location, despite satisfactory EAM, and that we need to ablate more (Figure 1). This is true especially for very large PVs and common PVs.

Acute End-Point and Success Rate

The acute success rate (isolation of all PVs) was high and similar for the two groups with or without contrast injection (Table 3). One case of anatomic difficulties in group I and another case of phrenic nerve stimulation all over PV ostium in group II resulted in acute success rates of 97% and 97.5%, respectively ($p = 0.9$). The contrast system could not help in this regard.

One-year follow up was similar for both groups after either one PVI or two, but with a trend of using more AAD during this period of time in group II ($p = 0.06$).

Safety

The overall complication rates were similar versus point-by-point ablation techniques, with one tamponade out of the whole study population (1.3%).¹⁰ This tamponade was not related to injection of contrast media. There was a high rate of vascular access site complications and transient ST elevation in inferior leads in group I. Changes in procedure protocol were described above and resulted in no such complications in group II patients that followed group I in time.

No patient showed symptoms related to cerebral thromboembolism.

Although there was an absence of clinically noticeable cerebral thromboembolic injuries, we cannot exclude or quantify possible asymptomatic cerebral events, which have been described with all available ablation techniques used for PVI,^{11,12} because no cerebral MRI scan was performed.

No symptomatic pulmonary stenosis was observed. However, the development of PV stenosis might occur after a delay of several months or weeks, which cannot be excluded by our present set of data.

In order to avoid esophageal damage with nMARQ™,⁴ our practice was to set the power during ablation along the posterior wall with a maximum energy level of 15 Watts (Unipolar only) and maximum impulse duration of 40 seconds. A nasal-gastric tube marked the esophagus location. Since no clinical signs for esophageal damage appeared, no endoscopy was performed. Thus, no data can be given for possible thermal esophageal lesions by ablation.

Despite a difference in amount of contrast injection in the two groups we observed no worsening in creatinine level and eGFR in Group II versus group I (Table 3). We believe that our common practice to treat group II patients preventively with intravenous saline (1000 mL/24h) during the procedure or until the day after has a role in those calming results.

We observed no acute complication related to the injection of contrast media in group II. The contrast media was injected and was irrigated prior to the application of RF ablation. The fact that this system is irrigation-based prevents the contrast media from sticking to the catheter. We observed no char on the catheter in all cases.

Target Population

Although the purpose of the study was to evaluate mainly feasibility and safety of the nMARQ™ catheter with contrast injection, our study showed no benefit in using this method routinely in every patient. On the other hand, we believe that this method should be taken into consideration in selective clinical scenarios:

In group II patients – in most PVs with “normal” anatomy, the selective angiograms done before introducing the catheter, the PV potentials, the fluoroscopy, the impedances, and the EAM guidance have provided sufficient information to assure us regarding proper catheter location.

However, in cases of large PVs and common PVs, the newly described introduction of a contrast delivery system, the ACIST CVI System, surely helped us localize the catheter at the PV orifice and avoid ablation inside the PVs (Figure 1). Further validation of this technique is needed.

In addition, we realized that another advantage of the contrast injections during catheter manipulation is its role in training new operators with the multi-electrode ablation system: especially when there is no “anchoring wire” and the learning curve to recognize the signals of the multi-electrode catheter takes time. Knowing the exact catheter location gives the operators online feedback.

Limitations

We could not rule out that the tendency for longer ablation time and larger number of applications in group II were related to the contrast media covering the electrodes, but we saw no change in temperature, power, and impedances of the electrodes before and after injecting the dye; thus we believe it is mostly the result of a better catheter-PV contact after more attempts of manipulations of the catheter.

Another limitation of the study is the sequential nature of the two

groups. The fact that increasing experience level could have influenced outcome cannot be ruled out.

Conclusion

Addition of contrast injections to standard nMARQ™ procedure is feasible and safe. Although it does not prolong the procedure significantly, it involves more applications. It does not have a benefit for a routine use in every patient, but this tool may have an added value to EAM in catheter localization by newly trained operators and in selective cases of large/common PV anatomy. Future studies are needed to prove its advantage in selective cases.

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