

# Ablation of atrial fibrillation: does the addition of three-dimensional magnetic resonance imaging of the left atrium to electroanatomic mapping improve the clinical outcome?

## A randomized comparison of Carto-Merge vs. Carto-XP three-dimensional mapping ablation in patients with paroxysmal and persistent atrial fibrillation

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### Aims

To compare in a randomized and prospective fashion the outcome of atrial fibrillation (AF) ablation either after one procedure or after two procedures using the Carto-XP vs. the Carto-Merge mapping system in two different AF populations.

### Methods and results

Two hundred and ninety-nine patients with paroxysmal and persistent AF were enrolled in the study. One hundred and fifty patients with paroxysmal or persistent AF were randomly assigned to the Carto-Merge group and 149 patients to the Carto-XP group. The Carto-Merge patients underwent magnetic resonance imaging (MRI) of left atrium (LA) the day before the ablation. The ablation scheme included electrical disconnection of the pulmonary veins plus linear lesions. In the Carto-Merge patients, the three-dimensional MRI of the LA reconstruction merged with the electroanatomical map, and in the Carto-XP patients, the electroanatomical map guided the procedure. Considering the overall population with paroxysmal AF, 54% maintained sinus rhythm (SR), whereas in the persistent AF population, SR was present in 43% of the patients at the 12-month follow-up. In patients with paroxysmal AF, 52% in the Carto-XP group and 55% in the Carto-Merge group maintained SR without drugs. Procedure durations and exposure to X-ray in the Carto-XP group were  $94.6 \pm 17.5$  and  $40.4 \pm 13.5$  min, respectively. In the Carto-Merge group, duration and X-ray exposure were  $89 \pm 41.6$  and  $22.1 \pm 11.4$  min, respectively. Considering the patients with persistent AF at the 12-month follow-up, 44% in the Carto-XP group and 42% in the Carto-Merge group maintained SR without drugs. Procedure durations and X-ray exposure in the Carto-XP group were  $102.9 \pm 22.9$  and  $58 \pm 8.7$  min, respectively. In the Carto-Merge group, both duration and X-ray exposure were  $114.4 \pm 50.9$  and  $28.8 \pm 14.3$  min, respectively.

### Conclusion

Image integration using Carto-Merge in patients undergoing catheter ablation for paroxysmal and persistent AF does not significantly improve the clinical outcome, but shortens the X-ray exposure.

### Keywords

Atrial fibrillation • Ablation • Mapping systems

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## Introduction

The management of atrial fibrillation (AF) is still under debate. Radiofrequency (RF) catheter ablation as an AF treatment has significantly improved in recent years. Although different approaches have been proposed, currently, the principal ablation strategies include electrical disconnection of the pulmonary veins (PVs) with the addition of further linear lesions depending on the underlying substrate of AF.<sup>1–7</sup> Performing these procedures is technically challenging because the creation of lines of the conduction block in the three-dimensional (3D) geometry of the left atrium (LA) using fluoroscopy alone is difficult and time-consuming. This difficulty has encouraged the development of new non-fluoroscopic mapping techniques to increase the success rate and to reduce the side effects and the X-ray exposure. The latest technological developments allow merging of electroanatomic maps with magnetic resonance imaging (MRI)- or computed tomography (CT)-based 3D reconstruction.<sup>8–15</sup> However, until now, a clear demonstration of the advantages of performing AF ablation with the aid of these non-fluoroscopic systems has not been provided and the data available are conflicting. In a randomized study by Kistler *et al.*,<sup>10</sup> image integration used to guide catheter ablation for AF did not significantly improve the clinical outcome; on the other hand, Bertaglia *et al.*<sup>16</sup> reported the results from the Carto-Merge Italian Registry which showed that in patients with paroxysmal AF, circumferential PV isolation (PVI) guided by image integration significantly improved the outcome.

The aim of this study was to assess in a large AF population the efficacy of ablation in terms of success rate, reduction of complications, procedural time, and X-ray exposure, using 3D electroanatomic reconstruction with the aid of only the Carto-XP vs. the 3D electroanatomic reconstruction integrated with MRI of the LA (Carto-Merge).

## Methods

### Study population

From September 2006 to September 2007, 299 consecutive patients who had RF catheter ablation for symptomatic, paroxysmal, or persistent AF, defined according to the AHA guidelines,<sup>17</sup> refractory to at least two anti-arrhythmic drugs (AADs) were enrolled in the study: 150 patients underwent RF ablation using the Carto-Merge and 149 patients using only 3D electroanatomic reconstruction with Carto-XP. The randomization process was built as follows: for any patient, a random number *X* was extracted from a uniform distribution. If *X* was lower than 0.5, the patient was assigned to the Carto-Merge group and otherwise to the Carto-XP group. Then, we compared the percentage of paroxysmal AF among the two groups with a proportional test. If the *P*-value was <0.1, we repeated the randomization. Finally, the patients were scheduled to be treated twice per day, one with Carto-Merge and one with Carto-XP.

The inclusion criteria were: patients aged <80 years with persistent or paroxysmal AF refractory to AADs such as flecainide, propafenone, or amiodarone. In particular, regarding the Carto-XP population, 49 out of 94 patients with paroxysmal AF and, in the case of persistent AF, 36 patients were on amiodarone before the procedure. On the other hand, as far as Carto-Merge population is concerned, 35 out of 93 patients with paroxysmal AF while 30 out of 57 patients with

persistent AF tried amiodarone before the procedure. The exclusion criteria were: previous AF ablation procedures either transcatheter or surgical, valvular heart disease, hypertrophic cardiomyopathy, clinical hyperthyroidism, reduced life expectancy as a result of severe illnesses, and patient unwilling to undergo a strict follow-up. To reduce the X-ray exposure, only MRI of the LA was utilized. All the patients underwent ablation according to the '7' scheme, which implies the electrical isolation of the PVs and the linear lesions at the roof of the LA and at the left isthmus. In addition, all the patients underwent right isthmus ablation. The primary endpoint was to assess the maintenance of sinus rhythm (SR) in the absence of AADs in two different groups of AF, paroxysmal and persistent after one procedure and after two procedures with the aid of the Carto-XP in one group of patients and the aid of the Carto-Merge in the other one. The secondary endpoints were the maintenance of SR with the addition of the AADs, the comparison of the fluoroscopy time, the procedural time, and the incidence of complications between the Carto-XP and the Carto-Merge populations.

### Magnetic resonance imaging

The Carto-Merge group patients underwent gadolinium-enhanced MRI of both the LA and the PVs. Studies were performed on a 1.5 Tesla MRI system (Magnetom Avanto®, Siemens, Erlangen, Germany) in the post-absorptive state the day before the RF ablation. Angio-RM was obtained with a 3D fast-field Spoiled Gradient Echo imaging sequence. Slices with a thickness of 1.4 mm were acquired. The acquisition was performed after the injection of gadobutrol (Gadovist®, Shering S.P.A., Berlin, Germany). A revelation system using the Care-bolus® (CARE = combined applications to reduce exposure) was used as a technique to synchronize the acquisition of the image at the exact time when the bolus passed the LA. The acquired images were then transferred to the PACS (Picture Archiving and Communications System) where, using an elaboration software (Volume Viewer Plus AWW Suite 5.5.3f®, GE Medical Systems, Milwaukee, WI, USA), they were reviewed by two radiologists.

### Integration of the magnetic resonance imaging image into the electroanatomic mapping system

The image obtained using MRI was imported into the electroanatomic mapping (EAM) system using custom-designed software (Carto-Merge, Biosense Webster, Inc., Diamond Bar, CA, USA).

Segmentation of the cardiac image in order to separate the LA and PVs from the surrounding cardiac structures using proprietary software tools on the EAM system was performed. The LA and PVs were then exported into the real-time mapping system for registration. The electroanatomic map of the LA was created. Points were sampled from the PVs, posterior wall, septum, roof, and inferior wall.

The registration of the MRI image was then performed: a single endocardial site defined as 'landmark point' was sampled from the posterior aspect of the left superior PV. The estimated corresponding location of this endocardial point was marked on the imported 3D MRI LA surface reconstruction, thus creating a 'landmark pair'. At this point, the Carto-XP system superimposed the 3D MRI LA surface reconstruction onto the real-time LA electroanatomic map by two algorithms: visual alignment and surface registration. If necessary, the points were deleted and additional landmark and surface registration points were taken to obtain an overall accuracy of <3 mm. The total duration time required to obtain an electroanatomic reconstruction of the LA and to register the MRI image was calculated as the EAM time.

## Electrophysiological study and radiofrequency catheter ablation

After written informed consent was obtained, patients underwent the electrophysiological (EP) study. Before the EP study, a transoesophageal echocardiography was performed in all the patients to rule out the presence of atrial thrombi. Patients had been on warfarin for at least 1 month before the procedure. Warfarin was discontinued 3 days before admission and low-molecular-weight heparin was administered instead. An oral bolus of barium was given before the EP study in order to visualize the oesophagus. An octapolar electrode catheter was positioned in the coronary sinus (CS) for pacing and recording. The LA was accessed by transseptal puncture or through a patent foramen ovale, when present. In the case of a lack of a patent foramen ovale, a guidewire was introduced into the LA by a transseptal puncture using an 8 F long sheath (Daig, St Jude or Preface, Cordis-Webster). The sheath was perfused during the procedure with heparinized NaCl 0.9% at 120 mL/h. A multipolar catheter (Orbiter, Bard or Lasso, Biosense Webster) was inserted through the long sheath to map the PV ostia in both the ablation procedures. All the procedures were performed using a 3.5 mm irrigated-tip ablation catheter (Navistar, Biosense Webster) advanced into the LA through the same hole whenever possible, otherwise a second transseptal puncture was performed. The venous sheath was moved to the right atrium and continuously perfused with heparinized 5% dextrose–water solution, or heparinized 0.9% NaCl. Intravenous heparin was given bolus to maintain an activated clotting time at least 200 s throughout the procedure. Deep sedation was achieved by means of intravenous phentanyl, midazolam, and propofol.

In the Carto-XP patients, PV angiography was performed at the beginning of the procedure and at the end of the procedure, whereas in the Carto-Merge patients, it was performed only at the end of the procedure. A 3D reconstruction of the LA and PV ostia, using an EAM system (Carto, Biosense Webster) was performed in all the patients and PV electrical activity was assessed using a decapolar ring catheter (Orbiter PV Bard and Lasso, Biosense Webster). The aim of the ablation was to obtain a complete electrical isolation plus the creation of linear lesions interconnecting the upper PV ostia (roof line) and the left inferior PV, down to the mitral annulus according to the procedure already described<sup>4</sup> (Figure 1).

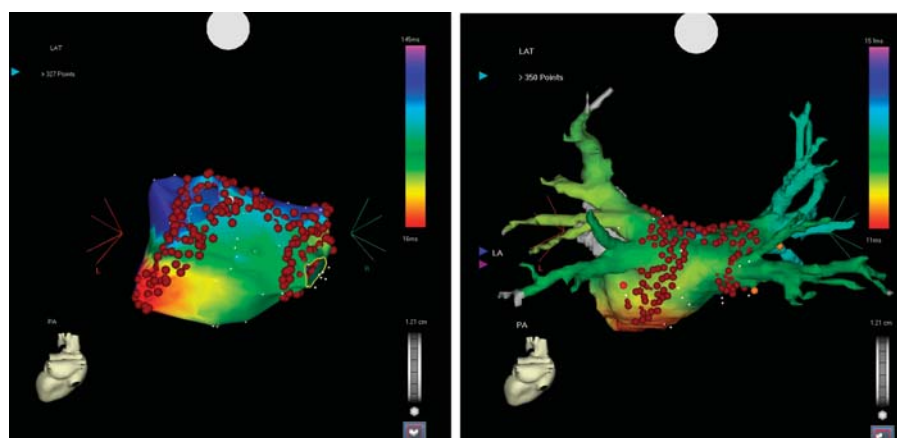
Radiofrequency was applied using an open irrigated-tip catheter (Navistar Thermocool, Biosense Webster) with a power output of up to 30 W, close to the PV ostia and up to 45 W while creating the roof line and the left mitral isthmus line, using an irrigation rate of 20–30 mL/min (0.9% saline infused with the Cool Flow Pump, Biosense Webster) in order to maintain a tip temperature of  $<45^{\circ}$ .

The PVI was carried out anatomically and confirmed electrophysiologically. The 3D reconstructed anatomy guided the encircling of the PVs, performed by ablating a wide area at 1–2 cm from their ostia with the aim of eliminating all the atrial potentials, or their abatement  $<0.05$  mV. If a complete PV electrical disconnection was not present after the anatomical encircling, a segmental ablation of the PV was carried out. Pulmonary vein isolation was defined by complete elimination, or dissociation, of PV potentials, determined by the circular mapping catheter, positioned at the PV ostia.

The lines were performed with an anatomical approach, using a CARTO map. This map allowed us to guide the catheter along the pre-determined lines on the LA roof and the left isthmus, making it also possible to return to the previously ablated points. Moreover, the CARTO map allowed for the identification of the disappearance of the atrial potentials, or their reduction  $<0.05$  mV. The creation of an effective mitral isthmus linear lesion was assessed by mapping the activation detour during pacing from both sides of the lesion and assessing the CARTO activation map post-ablation. If a complete block was not achieved, epicardial ablation within the CS was not considered because of the risk of complications, but adjacent lines were added to slow conduction to an interval of the local double potential  $>80$  ms. The conduction block along the roof was assessed demonstrating a corridor of double potentials along the entire length of the roof during pacing from the distal CS by point-by point mapping.

## Follow-up

During hospitalization, the electrocardiogram (ECG) was continuously monitored and standard heparin infusion maintained for 24 h after the procedure. Transthoracic echocardiography was performed immediately after ablation in all patients to assess the presence of pericardial effusion and the LA function. Patients were discharged the day after the procedure with warfarin and low-molecular-weight heparin which was stopped when the international normalized ratio was in



**Figure 1** (Left panel) Posteroanterior (PA) view of 3D EAM (Carto-XP); (right panel) PA view of 3D EAM merged with 3D MRI reconstruction of the LA. The red dots represent the points of ablation.

the therapeutic range between 2 and 3. The AAD was discontinued after 2 months. At 3, 6, and 12 months, patients were followed up with a clinical evaluation, a 12-lead ECG, and Holter monitoring. Any episode of AF, atrial flutter, or tachycardia of at least 30 s duration occurring after the blanking period was defined as a recurrence.<sup>18</sup>

## Statistical analysis

Data are given as mean  $\pm$  SD for continuous variables and as percentage values for a categorical variable. Normality was tested with Shapiro–Wilk procedures. All the population included in our analysis agrees with the hypothesis of normality or non-normality seems to be extremely moderate. A comparison of continuous variables between the two groups was made by the Welch *t*-test.<sup>19</sup> Percentages between the two groups were compared by the test of equal proportions. A significant difference was obtained if  $P \leq 0.05$ . The statistical package used was R 2.8.1.

## Results

The clinical characteristics of the patients and the procedural results are presented in *Tables 1* and *2*.

The mean surface registration error in the MRI group was  $1.88 \pm 1.6$  mm.

Complete PVI was acutely achieved in all patients. A complete mitral isthmus block was obtained in 33% of the cases; in the remaining patients, acute conduction slowing along the mitral isthmus during CS pacing was observed, with a mean atrial electrogram interval of  $120 \pm 18$  ms. A conduction block along the roof was achieved in 89% of the patients.

## Clinical outcome

### Paroxysmal atrial fibrillation

At the 12-month follow-up after the first procedure, 52% (49 out of 94) of the patients were in SR without AADs in the Carto-XP group, whereas in the Carto-Merge group, SR was present in 55% (51 out of 93) of the patients. If we consider the addition of AADs, the percentage of patients increased to 65% in the Carto-XP group (6 of 12 on amiodarone) and to 71% in the Carto-Merge group (4 of 15 on amiodarone). Recurrences were similar in the groups (*Figure 2*). A statistically significant difference was demonstrated between the groups considering the fluoroscopy

**Table 1** Patients characteristics

Clinical variable	Carto-XP (n = 149)	Carto-Merge (n = 150)	P-value
Age (years)	57.2 $\pm$ 10.1	59.5 $\pm$ 11.8	0.08
Males:females	111:38	127:23	0.04
Time since AF onset (years)	4.9 $\pm$ 3.8	4.5 $\pm$ 3.1	0.31
Paroxysmal AF/persistent (patients)	94/55	93/57	0.85
Structural heart disease (patients)	16	17	0.87
Ischaemic heart disease	12	11	
Hypertensive heart disease	4	3	
Dilated cardiomyopathy		2	
Valvular heart disease		1	

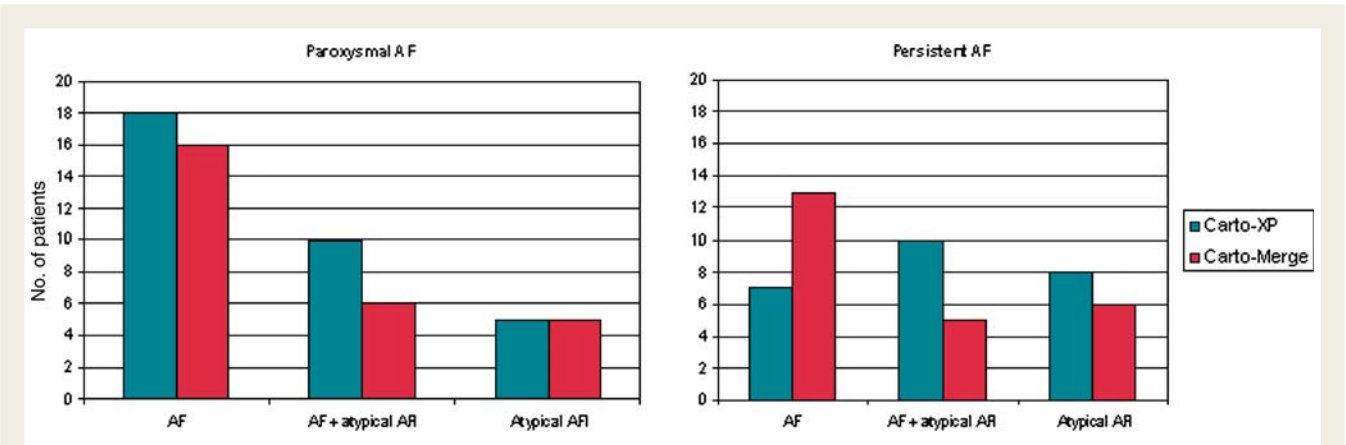
**Table 2** Acute procedural results

			Carto-XP	Carto-Merge	P-value
Skin to catheter positioning		Time	13'30'' ± 2'	14'30'' ± 1'30''	n.s.
		Fluoroscopy	2'40'' ± 35''	2'30'' ± 35''	n.s.
LA electroanatomic mapping		Time	26'30'' ± 3'	19' ± 7'	<0.01
		Fluoroscopy	11' ± 2'	2' ± 35''	<0.01
Ablation		Time	60' ± 16'	65' ± 29'	n.s.
		Fluoroscopy	28' ± 5'	15'30'' ± 10'	<0.01
Fluoroscopy time	Paroxysmal AF	CVT isthmus	6' ± 1'	6'20'' ± 30''	n.s.
		LA ablation	34' ± 40''	15'10'' ± 10''	<0.01
	Persistent AF	CVT isthmus	7'30'' ± 2'	7' ± 1'30''	n.s.
		LA ablation	50' ± 1'30''	21' ± 3'	<0.01
LA volume calculated with EAM (mL)			136 ± 25	128 ± 36	n.s.
# points to complete the EAM			129 ± 19	74 ± 10	<0.01
Mean fill threshold			25 ± 4	25 ± 3	n.s.
RF duration (min)			54 ± 15	50 ± 19	n.s.
Mean power (W)			31 ± 4	32 ± 3	n.s.

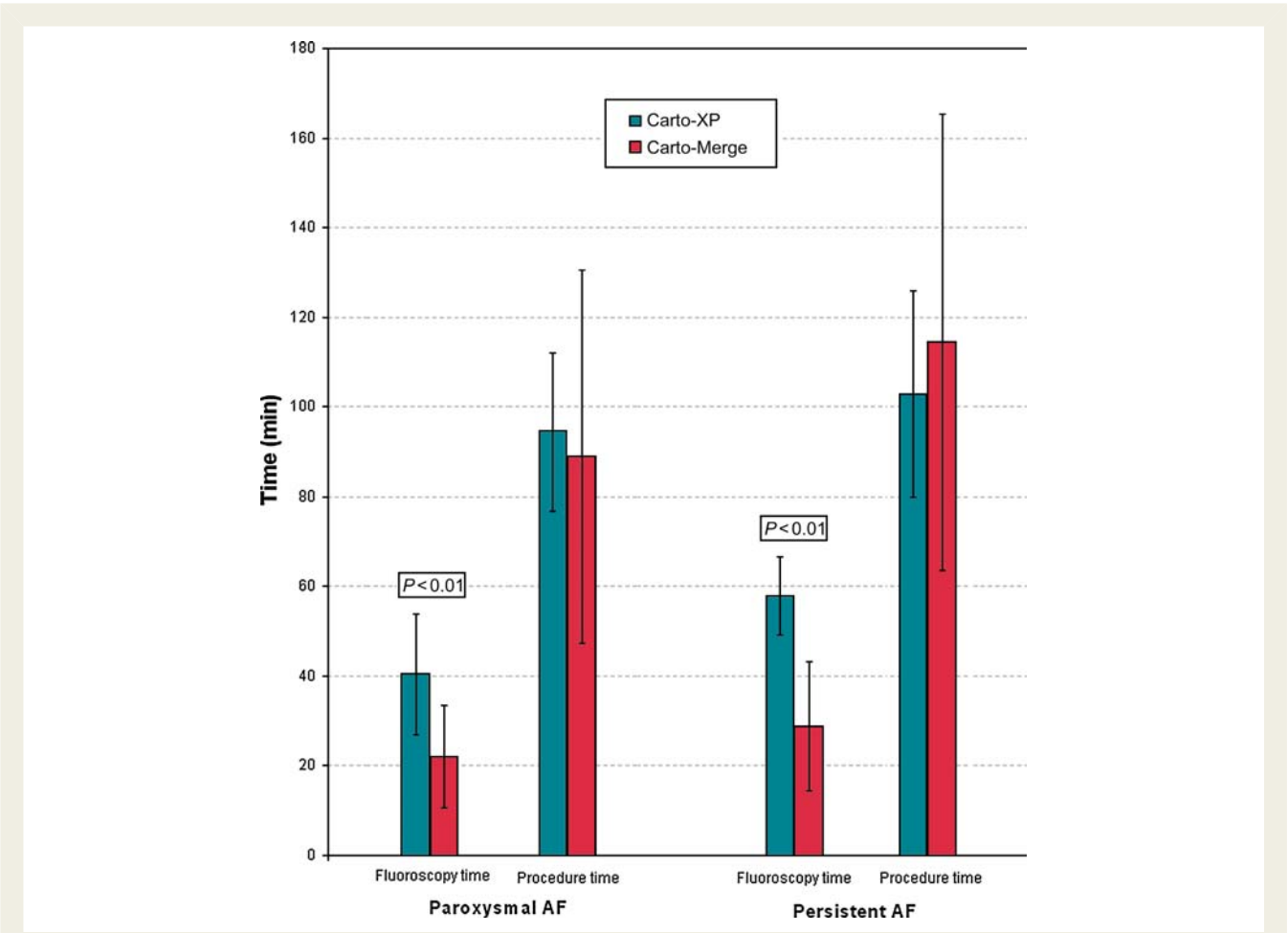
CVT, cavo-tricuspid isthmus; LA, left atrium; EAM, electroanatomic mapping.

times (Carto-XP:  $40.4 \pm 13.5$  vs.  $22.1 \pm 11.4$  min in the Carto-Merge patients,  $P < 0.01$ ). Instead, the procedural times did not show a statistically significant difference (Figure 3).

A second procedure was performed in 20 patients in the Carto-XP group and in 8 patients in the Carto-Merge group. With the addition of a second procedure, the clinical endpoint



**Figure 2** Arrhythmia recurrences in the follow-up. AF, atrial fibrillation. AFL, atrial flutter.



**Figure 3** Fluoroscopy times and procedural times in patients undergoing ablation for paroxysmal AF (on the left) and persistent AF (on the right).



was reached in 78.4% of patients in the Carto-XP group, whereas it increased to 72% in the Carto-Merge group.

### Persistent atrial fibrillation

At the 12-month follow-up after the first procedure, 44% (24 out of 55) of the patients were in SR without AADs in the Carto-XP group, whereas in the Carto-Merge group, SR was present in 42% (24 out of 57) of the patients. If we consider the addition of AADs, the percentage of patients increased to 55% in the Carto-XP group (four of six on amiodarone) and to 58% in the Carto-Merge group (three of nine on amiodarone). Recurrences were similar in the groups (Figure 2). A statistically significant difference was demonstrated between the groups considering the fluoroscopy times (Carto-XP  $58 \pm 8.7$  vs.  $28.8 \pm 14.3$  min in the Carto-Merge patients,  $P < 0.01$ ). Instead, the procedural times did not show a statistically significant difference (Figure 3).

A second procedure was performed in 14 patients in the Carto-XP group and in 11 patients in the Carto-Merge group. With the addition of the second procedure, the clinical endpoint was reached in 74.5% of the patients in the Carto-XP group while increased to 76.1% in the Carto-Merge group.

### Complications

In patients who had undergone AF ablation using the Carto-XP, one patient experienced cardiac tamponade requiring pericardiocentesis, and in two patients, pericardial effusion occurred. One patient had an inguinal haematoma, a transient ischaemic attack (TIA) occurred in one patient, and a right inferior PV stenosis was documented in another patient.

On the other hand, considering the Carto-Merge group, cardiac tamponade occurred in one patient, two patients had pericardial effusion, and in one patient, a pericarditis was present. One patient experienced a TIA.

### Discussion

Three-dimensional EAM has been developed to effectively guide the AF ablation. However, few data exist regarding the outcome of the AF ablation performed using these systems.<sup>8–15</sup> Some of the results are conflicting: in fact, data from the Carto-Merge Italian Registry showed that in a population of 573 patients with paroxysmal AF which underwent circumferential PVI, the use of image integration significantly improved the clinical outcome. The Carto-Merge patients experienced arrhythmia recurrences in 22.6% of the case compared with 41.1% in the Carto group during the 1-year follow-up.<sup>16</sup> On the other hand, Kistler *et al.* reported the results of a randomized prospective study of 80 patients with paroxysmal and persistent AF undergoing LA ablation. One group (40 patients) underwent catheter ablation guided by EAM alone and the second group (40 patients) guided by EAM with CT scan image integration. In this study, the addition of image integration did not significantly improve the clinical outcome at a mean follow-up of  $59 \pm 12$  weeks.<sup>10</sup> In our study, considering the procedures performed utilizing either the Carto-XP or the Carto-Merge, the overall clinical success of the procedure was similar after one procedure and after a second procedure at the 1-year follow-up either in

patients with paroxysmal or persistent AF. It seems that the aid of the LA MRI did not add advantages in terms of procedural success and long-term efficacy. This can be explained by the fact that the 'endpoint' of the procedure does not change in the two populations: the complete isolation of the PVs and the creation of linear lesions in the LA remained. This endpoint can be reached in different ways: with fluoroscopy alone or with the aid of EAM using either the Carto-XP or the Carto-Merge that allows the integration of LA anatomy and EAM. However, it must be mentioned that the amount of X-ray exposure was significantly reduced in the Carto-Merge group ( $22.1 \pm 11.4$  min in the Carto-Merge vs.  $40.4 \pm 13.5$  min in the Carto-XP in the paroxysmal AF group and  $28.8 \pm 14.3$  min in the Carto-Merge vs.  $58 \pm 8.7$  min in the Carto-XP in patients with persistent AF). The same trend of reduction in the X-ray exposure was reported by Kistler *et al.*<sup>10</sup> In contrast, Bertaglia *et al.* reported that the fluoroscopy time had not significantly decreased in patients with AF undergoing PVI using the Carto-Merge; however, in the paper by Bertaglia *et al.*,<sup>16</sup> it was stated that in most of the centres participating in the study, the operators were using this technique for the first time. The advantage of reducing X-ray exposure is important since X-ray exposure has been associated with an increased risk of cancer both in patients and medical personnel.<sup>20–21</sup> Besides, in most cases, the patient candidates for AF ablation must undergo more than one procedure so that the amount of X-ray exposure with its associated risks may double. On the basis of these considerations, a strict decision was made to choose the LA MRI instead of a CT scan. Our study confirmed that a high-quality image integration can be obtained by using MRI, thus avoiding significant exposure to ionic radiation when using CT scans.

Another interesting point is that with the MRI pre-procedure, the ostia of PVs can be identified providing detailed information on the number, location, and branching pattern of all PVs. This information is important since in a substantial number of cases, anomalies in the PVs distribution have been reported.<sup>22–23</sup> Therefore, the use of the Carto-Merge may allow us to deliver the ablation line just around the ostia of the PVs, increasing the efficiency of the PVI and tailoring the procedure to the individual anatomy. Besides, the addition of the 3D vision of the LA and the PV number and pre-ablation location may explain the reduction in the X-ray exposure because the 3D vision helps an experienced operator to feel confident in moving the catheter in the absence of fluoroscopy. In such a way, the precise positioning of the catheter in addition to the physical perception in manipulating the catheters combined to the EP data such as impedance and potential amplitudes may make the procedure easier. Furthermore, the detailed anatomic information provided by radiological image integration may assist lower case volume centres in decreasing the learning curve time.

In our series of cases, complications were not serious and were similar in the two groups of patients. In the Carto-XP group, a patient experienced PV stenosis, whereas no stenosis was reported in the Carto-Merge group. Significant PV stenosis generally occurs in 2–5% of patients in AF ablation.<sup>1,24–25</sup> The appreciation of the anatomy of the PVs and the knowledge of the PV numbers may increase the safety of the procedure.

## Limitations

An important limitation of the present study is the fact that the follow-up has been performed according to the actual clinical practice so that extended ECG monitoring was not used. It is conceivable therefore that asymptomatic episodes of AF occurring outside the monitoring periods were missed. As a consequence, asymptomatic episodes may have been overlooked.

## Conclusions

Image integration used to guide catheter ablation for patients with paroxysmal and persistent AF did not significantly improve the clinical outcome but image integration reduces the X-ray exposure in catheter ablation for AF.

**Conflict of interest:** none declared.

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