World Journal of Cardiology

Online Submissions: http://www.wjgnet.com/1949-8462office
wjc@wjgnet.com
doi:10.4330/wjc.v2.i8.215

World J Cardiol 2010 August 26; 2(8): 215-222
ISSN 1949-8462 (online)

EDITORIAL

Role of three-dimensional imaging integration in atrial fibrillation ablation

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Received: June 17, 2010 Revised: July 13, 2010
Accepted: July 20, 2010
Published online: August 26, 2010

Abstract

Atrial fibrillation is the most common arrhythmia and in symptomatic patients with a drug-refractory form, catheter ablation aimed at electrically disconnecting the pulmonary veins (PVs) has proved more effective than use of antiarrhythmic drugs in maintaining sinus rhythm during follow-up. On the other hand, this ablation procedure is complex, requires specific training and adequate clinical experience. A main challenge is represented by the need for accurate sequential positioning of the ablation catheter around each veno-atrial junction to deliver point-by-point radiofrequency energy applications in order to achieve complete and persistent electrical disconnection of the PVs. Imaging integration is a new technology that enables guidance during this procedure by showing a three-dimensional, pre-acquired computed tomography or magnetic resonance image and the relative real-time position of the ablation catheter on the screen of the electroanatomic system. Reports in the literature suggest that imaging integration provides accurate visual information with improvement in the procedure parameters and/or clinical outcomes of the procedure.

Key words: Catheter ablation; Atrial fibrillation; Electroanatomic mapping; Multislice computed tomography; Magnetic resonance imaging

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De Ponti R, Marazzi R, Lumia D, Picciolo G, Biddau R, Fugazzola C, Salerno-Uriarte JA. Role of three-dimensional imaging integration in atrial fibrillation ablation. *World J Cardiol* 2010; 2(8): 215-222 Available from: URL: http://www.wjgnet.com/1949-8462/full/v2/i8/215.htm DOI: http://dx.doi.org/10.4330/wjc.v2.i8.215

INTRODUCTION

Over the last decade, catheter ablation has been a treatment option increasingly offered to patients with symptomatic atrial fibrillation (AF) refractory to antiarrhythmic drug therapy. In the updated survey on catheter ablation for AF[1], an almost 2-fold increase in the number of patients treated between 2003 and 2006 was observed as compared with the number between 1995 and 2002. In this survey, this treatment option shows to be effective in roughly 80% of patients after 1.3 procedures per patient, on average, with about 70% of the patients not requiring further antiarrhythmic drugs during a 10 ± 8 mo follow-up. These data are corroborated by the results of several, recently published meta-analyses on the efficacy of catheter ablation and of antiarrhythmic drug therapy for the prevention of AF[2-5]. Particularly, the most updated

meta-analysis of randomized, controlled trials comparing antiarrhythmic drug therapy *vs* catheter ablation of AF[5] showed that catheter ablation with isolation of the pulmonary veins (PVs) was associated with markedly increased odds of maintaining sinus rhythm as compared to antiarrhythmic drug therapy (77% *vs* 29%) in a patient population with predominantly paroxysmal AF (70%), refractory to 2 antiarrhythmic drugs with a mean left atrial diameter of 42 ± 3 mm. Moreover, a study performed in the United States[6] using a simulation mode showed that catheter ablation of symptomatic, drug-refractory AF with or without continuation of antiarrhythmic drug therapy during follow up appeared reasonably cost-effective compared to antiarrhythmic drug therapy alone, based on improved quality of life and avoidance of future health care costs.

In the past, different techniques and tools for catheter ablation of the PVs in patients with AF have been proposed and used. More recently, the HRS/EHRA/ECAS expert consensus statement[7] underlined that ablation of PVs with demonstration of complete electrical isolation is the cornerstone for most AF ablation procedures. Furthermore, this document stated that careful identification of the PV ostia is mandatory to avoid ablation within the PVs, which carries a significant risk of PV stenosis, which is a severe complication. Therefore, it appears mandatory that the operator should use an appropriate technology to identify the PV ostia and, more importantly, the real-time relative position of the ablation catheter.

In this review, the rationale, methods, and results of using electroanatomic mapping with imaging integration to orient catheter ablation of AF aimed at electrical disconnection of the PVs will be described in detail.

RATIONAL FOR USING ELECTROANATOMIC MAPPING WITH IMAGING INTEGRATION

Initially, to visualize the PVs during the AF ablation procedure, two methods have been reported: PV angiography and intracardiac echography. When these methods are used, different techniques and tools can be utilized to improve the quality of visualization of PV anatomy during the AF ablation procedure[7]. However, these techniques provide two-dimensional images, sometimes with suboptimal resolution and, in the case of intracardiac echography, it requires extra costs, dedicated access and personnel. Moreover, the PVs anatomy in terms of number and morphology of oses, branching and supernumerary PVs is very individual, as already reported[8-11]. This anatomic variability may influence both success and safety of the procedure, if the PV os/antrum is not adequately visualized during the procedure. In fact, if the presence of supernumerary veins is not recognized and their os not treated, the success rate can be suboptimal[7,12]. On the other hand, the ablation performed inside the PV due to mislocalization of the true ostium may affect both the complication rate, since the risk of PV stenosis may increase significantly, and the success rate, since proximal PV foci can be left untreated.

Table 1 Anatomic variants of the pulmonary veins in 147 consecutive patients with atrial fibrillation undergoing a 64-slice computed tomography scan the day before the ablation procedure

Anatomy	*n* (%)
Four distinct PV oses	81 (55)
Common os	66 (45)
Left PVs	55
Right PVs	7
Left and right PVs	1
Inferior PVs	3
Adjunctive PVs	21 (14)
Right	16
Left	2[1]
Roof	4

[1]1 patient showed an adjunctive pulmonary vein both right and left. PV: Pulmonary vein.

Based on these considerations and the experience accumulated in several centers over recent years, the best way to visualize the individual variants of PVs is three-dimensional imaging, which can be obtained before the procedure, by computed tomography (CT) scanning or magnetic resonance imaging (MRI), or during the procedure, by three-dimensional rotational angiography[13]. The latter technology provides on-line intraprocedure angiographic data of the left atrium (LA) and PVs but, so far, its availability is limited. Therefore, the most frequently used technique is CT or MRI scan of the LA and PVs, which is acquired off-line, usually the day before the procedure. MRI avoids radiation exposure, but it might be tolerated less well, especially by claustrophobic patients, and the three-dimensional rendering might be operator-dependent. On the other hand, CT obviously implies radiation exposure, which depends on the method used for imaging acquisition.

Our personal experience in 147 consecutive patients with AF undergoing a 64-slice CT scan for imaging of the LA and the PVs the day before the ablation procedure shows high individual variability, including rare forms of anatomic variants (Table 1). As shown, the most expected anatomy with four separated PV oses is observed in only 55% of the patients and in 14% of cases adjunctive PVs are present, with an os close to the right or left PVs, but independently draining or, more peculiarly, located in the medial roof of the LA. The finding of a common trunk is by far more frequently observed in the left PVs. Interestingly, the already described[14-17] presence of a common os of the left and right inferior PVs, although rare (2%), significantly distorts the LA anatomy (Figure 1). In this patient population, the radiation exposure was very much dependent on the acquisition technique. In fact, the radiation

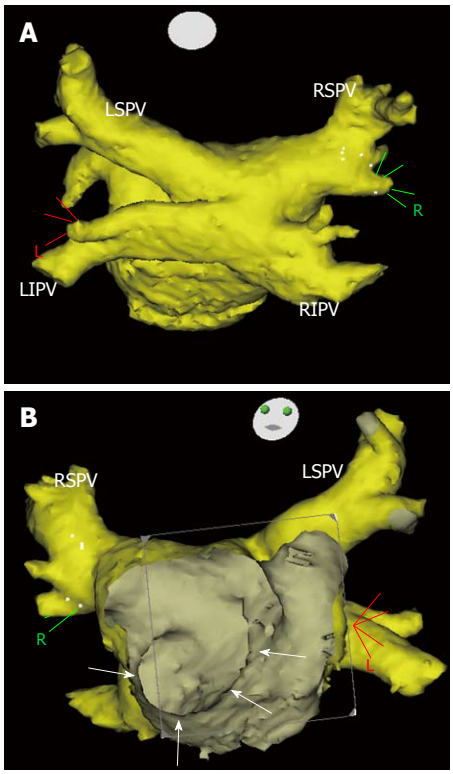

Figure 1 Three dimensional computed tomography image of a peculiar anatomic variant of the pulmonary veins in a patient with atrial fibrillation and no structural heart disease. A: The postero-anterior view of the left atrium and pulmonary veins; B: The endocardial aspect of the pulmonary vein oses after removal of the anterior wall of the left atrium. The common os of the left and right inferior pulmonary veins is evident both on the epicardial and endocardial (arrows) aspects. The oses of the right and left superior pulmonary veins are adjacent and more anterior, to the common os. LIPV: Left inferior pulmonary vein; LSPV: Left superior pulmonary vein; RIPV: Right inferior pulmonary vein; RSPV: Right superior pulmonary vein.

exposure was 7.6-fold higher in the first 30 patients, in whom the CT scan was performed in ECG-gated mode, as compared to the following patients, scanned in a non ECG-gated mode [23 ± 8 mSv (range 9.7-44 mSv) *vs* 3 ± 1 mSv (range 0.9-5.7 mSv), respectively, $P < 0.0001$].

The high resolution anatomical information provided by three-dimensional preprocedure imaging can be useful to the operator before the procedure. However, the best use of this imaging is obtained when, during the procedure, they are imported and integrated in the electroanatomic mapping, so that on the system screen the icon of the ablation catheter is visualized in real-time, with due accuracy, on the high resolution image of the PV os/antrum. In this way, it is possible to both accurately establish were the ablation lesion is performed and to manipulate the ablation catheter around the PV os with minimal or no use of fluoroscopy.

METHODS FOR ACCURATE IMAGING INTEGRATION OF THE LA AND PVS

For the purpose of better understanding the integration process, it can be subdivided in four different steps. First, the CT or MRI pre-acquired data set is imported in the electroanatomic system and it is "segmented" using dedicated software, so that the three-dimensional rendering of the LA and PVs is extracted. This image can be evaluated both from the epicardial and endocardial aspect, as shown in Figure 1. Second, at the beginning of the procedure, after transseptal catheterization has been accomplished, the LA is electroanatomically reconstructed by acquiring a variable number of points in this heart chamber. The third step is represented by the "registration" phase. One or more pairs of landmarks, each one positioned on the electroanatomic map and on the assumed corresponding site of the CT/MRI surface, are identified. Usually, sites easy to identify are used for this purpose (e.g. left atrial roof and os of the PVs). Then using the "landmark registration" and the "surface registration" options, each landmark on the two surfaces is superimposed and the two surfaces are superimposed as well, in such a way that the best match between the two images is obtained. In the fourth and last step, the accuracy of the superimposition of the two surfaces is checked. If imaging integration was performed accurately, the icon of the mapping/ablation catheter, visualized in real-time on the screen of the electroanatomic system, can be navigated in the high resolution anatomy image provided by the CT/MRI with optimal accuracy of localization.

As reported in Table 2, several published studies have mainly focused on the methods to integrate the CT or MRI images of the LA/PVs into an electroanatomic system and to evaluate the accuracy of this process. Overall, these studies have included more than 500 patients with a variable proportion of patients with paroxysmal AF, ranging from 31% to 83%. The CartoMerge technology and 64-slice CT have been used in the vast majority of the studies as an electroanatomic system and preprocedure three-dimensional imaging modality, respectively. Intracardiac echocardiography has been also sparingly used. In almost all cases, using the electroanatomic system, the LA and the oses of the PVs have been reconstructed as a single chamber and the number of acquired sites to reconstruct these anatomical structures varied in different studies, from 224 ± 59 to 24 ± 7 sites. Generally, all the studies reported that the integration process was successful in the majority of patients, so that the mapping/ablation catheter could be reliably navigated in the imported three-dimensional rendering of CT or MRI. The accuracy of the integration process has been evaluated by the distance between an electroanatomic point and the correspondent point on the CT/MRI, which is automatically given by the system. This value represents the average error, being the distance between the site where the catheter is shown to be on the CT/MRI image and the site where it actually is. In these reports, this value varied from 2.9 ± 0.7 mm to 1.4 ± 0.3 mm, on average, which confirms an accurate and clinically useful integration process since the catheter tip is 3.5 mm in length and every distance below

Table 2 Overview of the studies designed to evaluate the methods and accuracy of imaging integration of the left atrium/pulmonary veins in an electroanatomic mapping system during the atrial fibrillation ablation procedure

Author	No. of pts	Percentage of pts with parox. AF	System	3D-imaging (No. of pts)	ICE	Type of EA reconstruction: single/multi chamber	No. of EA points	Distance between EA and CT/MRI points (mm)		
								Mean	Maximum	Minimum
Tops *et al*[18]	16	31	CartoMerge	64-slice CT	N	Single	224 ± 59	2.1 ± 0.2	2.8 ± 1.8	1.7 ± 1.2
Dong *et al*[19]	16	62	CartoMerge	MRI (8)/ 64-slice CT (8)	N	Single	24 ± 7	2.1 ± 0.5	2.7 ± 1.8	0.9 ± 0.8
Kistler *et al*[20]	30	40	CartoMerge	8-slice CT	N	Single	39 ± 8	2.3 ± 0.4	9.3 ± 2.4	0 ± 0
Martinek *et al*[21]	40	65	CartoMerge	16-slice CT	N	Single	63 ± 14	1.6 ± 1.2	N/A	N/A
Heist *et al*[22]	61	57	CartoMerge	MRI (50)/ 64-slice CT (11)	N	Multi (LA + Ao)	LA (49 ± 25) Ao (148 ± 41)	1.9 ± 0.6	4.3 ± 3.4	1.2 ± 1.0
Fahmy *et al*[23]	124	55	CartoMerge	64-slice CT	N	N/A	59 ± 22	2.2 ± 1.7	N/A	N/A
Daccarett *et al*[24]	18	58	CartoMerge	64-slice CT	Y	Single	41 ± 8	5-10[1]	N/A	N/A
Bertaglia *et al*[25]	40	55	CartoMerge	MRI	N	Single	37 ± 10	1.3 ± 1.0	N/A	N/A
Richmond *et al*[26]	23	61	NAVx Fusion	8-slice CT	N	Single	N/A	3.2 ± 0.9	6.1 ± 1.0	2.9 ± 0.7
Brooks *et al*[27]	55	53	NAVx Fusion	64-slice CT	N	Single	N/A	2.6 ± 2.2	6.6 ± 2.8	1.9 ± 0.4
Rossillo *et al*[28]	40	45	CartoMerge	Multislice CT	Y	Single	47 ± 9	1.4 ± 0.3	N/A	N/A
Nölker *et al*[29]	38	50	CartoMerge	Rotational angiography	N	Single	104 ± 59	2.2 ± 0.4	N/A	N/A
Ejima *et al*[30]	24	83	CartoMerge	64-slice CT	N	Single	88 ± 34	1.7 ± 0.5	6.1 ± 2.7	0.04 ± 0.03

[1]Distance between an electroanatomic (EA) point and the same point localized by ICE. 3D: Three dimensional; AF: Atrial fibrillation; Ao: Aorta; CT: Computed tomography; ICE: Intra-cardiac echocardiography; LA: Left atrium; MRI: Magnetic resonance imaging; N: No; Y: Yes; N/A: Not available; Parox.: Paroxysmal; pts: Patients.

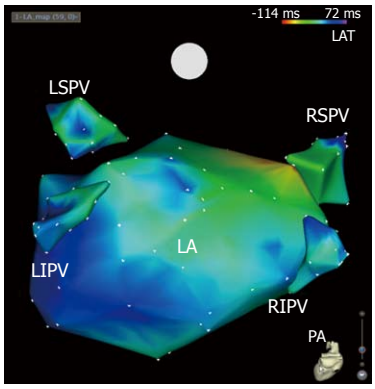

Figure 2 Postero-anterior view of the electroanatomic activation mapping of the left atrium and pulmonary veins. These have been reconstructed as five separate chambers using the Carto system and acquiring a few sites while the mapping catheter is manipulated in these anatomic structures. Colors indicate the activation sequence from the earliest in red (antero-medial part of the left atrium) to the latest in dark blue (postero-lateral part of the left atrium and distal part of the pulmonary veins). LA: Left atrium; LIPV: Left inferior pulmonary vein; LSPV: Left superior pulmonary vein; RIPV: Right inferior pulmonary vein; RSPV: Right superior pulmonary vein.

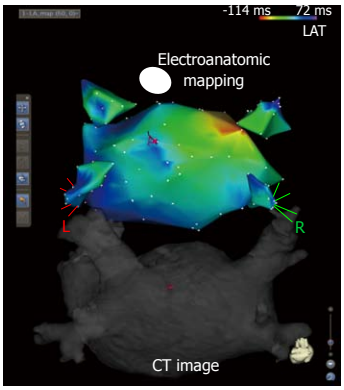

Figure 3 Postero-anterior view of the electroanatomic map shown in Figure 2 and of the three-dimensional rendering of the computed tomography scan, both in a postero-anterior view. A couple of points (small red flags on the electroanatomic mapping and computed tomography) have been identified on the left atrial roof. These two landmarks will be used to initially guide the superimposition of the two surfaces. CT: Computed tomography.

this value can be considered, with the due precautions, as acceptable.

In our experience, the method to integrate a 64-slice CT image (Aquilion 64, Toshiba Medical Systems, Tokyo, Japan) of the LA and PVs is slightly different from what has been reported in other studies. Briefly, after transseptal catheterization has been accomplished, the LA and the PVs are electroanatomically reconstructed by using the Carto 3 electroanatomic mapping system (Biosense-Webster, Diamond Bar, CA, USA) as five separate chambers, shown in Figure 2. On average, 40 sites in the body of the LA are acquired, while 20 sites and 15 sites in the proximal part of the superior and inferior PVs, respectively, are also acquired. Generally, the acquired sites are homogeneously distributed in the chamber and particular care is taken when points are acquired in the PVs, so that catheter manipulation does not distort the PV anatomy. Subsequently, as shown in Figure 3, a single site in the left atrial roof is identified, both on the CT image and the electroanatomic mapping to serve as the landmark for the first raw superimposition of the two surfaces. Afterwards, superimposition is improved by the "surface registration" option, which finds the best match between the electroanatomic maps and the CT images by rotating the two surfaces relatively. Then, an accuracy check is performed by evaluating the

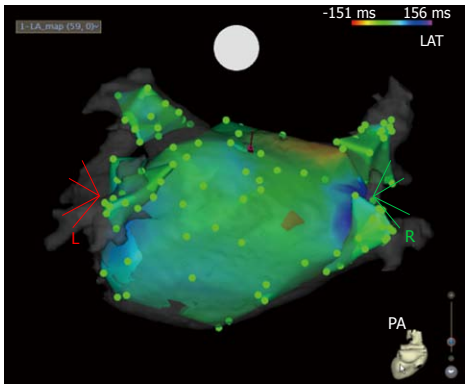

Figure 4 The two surfaces have been superimposed based on the guide provided by the two landmarks. The match of the two surfaces has been further improved with the so-called "surface registration" option, obtaining optimal integration. The accuracy of this process is then checked by verifying the distance between each electroanatomic point and the corresponding site on the computed tomography surface. In this case, all sites in the electroanatomic maps are marked by a green dot, which identifies the distance between the two surfaces as < 5 mm.

distance of each electroanatomic point from the corresponding site on the CT image. As shown in Figure 4, this can be done simply by using the software option that identifies sites with a distance < 5 mm as green dots, sites with a distance between 5 mm and 10 mm as yellow dots and sites with a distance > 10 mm as red dots. Therefore, during this final phase, sites with a distance > 5 mm should be deleted, while the catheter, visualized in real-time as an icon on the system screen, is moved in the LA and especially around the PV os/antrum to check the concordance between the actual catheter position and its display on the CT image. During this phase, other sites can be acquired to improve the quality of the integration. After the integration process has been concluded, the electroanatomic maps of the LA and PVs become transparent and the operator can manipulate the catheter looking at the projection of the catheter icon on the epicardial and endocardial aspect of the CT image, with minimal or no use of fluoroscopy, to deploy sequential radiofrequency energy lesions around the PV oses (Figure 5). In our institution, the accuracy of this integration process has been carefully evaluated in 150 consecutive patients undergoing catheter ablation of AF with electrical disconnection of the PVs. For this purpose, the distance between the actual site of radiofrequency energy application, based on different parameters (electrical signal, PV angiography, value of impedance, and three-dimensional imaging) and the corresponding site at the PV os on the CT imaging was calculated. The accuracy of integration has been defined as optimal if this distance was < 2 mm, acceptable if between 2 and 5 mm and unacceptable if > 5 mm. In this patient series, the accuracy was evaluated along the perimeter of 532 junctions between the PV and LA; in 68 patients a common os was found. An optimal imaging integration was observed in 75% of the PV-LA junctions, while it was acceptable in 16% and unacceptable in only 9%. Thus, manipulation of the ablation catheter around

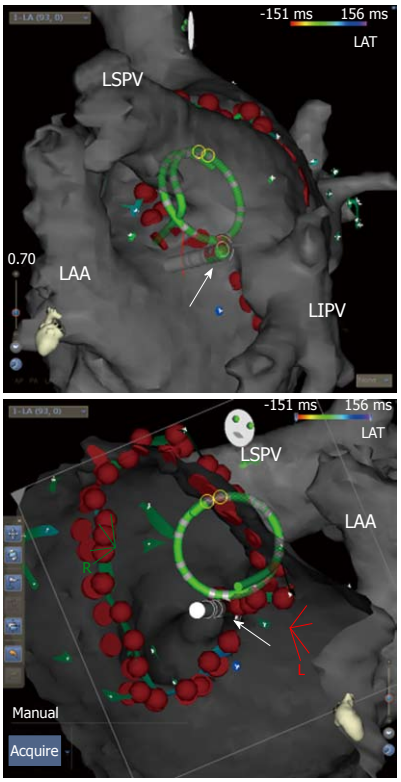

Figure 5 After completing the imaging integration process, pulmonary vein ablation is initiated. The screen of the electroanatomic system shows simultaneously the epicardial (upper) and endocardial (down) aspects of the high resolution computed tomography image of the common os of the left pulmonary veins present in this patient. The green circular icon identifies the multipolar circular mapping catheter, positioned inside the common os to verify its electrical disconnection. The icon of the ablation catheter (white arrows) is also visible, so that this catheter can be manipulated to navigate the three-dimensional computed tomography image with minimal or no use of fluoroscopy. Each red dot marks the site where radiofrequency energy has been applied along the veno-atrial junction of the left pulmonary veins to achieve their electrical disconnection. LIPV: Left inferior pulmonary vein; LSPV: Left superior pulmonary vein; LAA: Left atrial appendage.

the os of the PVs to place radiofrequency energy applications with no or minimal use of fluoroscopy was done in 91% of the cases. Both in our experience, as well as in other centers' experiences[20,21], the accuracy of integration was not affected by the difference of cardiac rhythm (sinus *vs* AF) during which the CT and the electroanatomic mapping were acquired. This is crucial, since the two images are acquired on two different days and it is likely that these patients exhibited different cardiac rhythms from 1 d to another. In fact, only 95/150 (63%) patients in our series were on the same cardiac rhythm (sinus rhythm or AF) during both (CT scan and electroanatomic mapping) imaging acquisition. In our experience, other factors that did not affect the accuracy of imaging integration were: mode of CT acquisition (ECG-gated *vs* non ECG-gated), left atrial volume, number of acquired sites in the LA and PVs and positioning of the multipolar circular mapping catheter to evaluate PV potentials during ablation. On the other hand, movements or respiratory artifacts during CT acquisition significantly altered the

Table 3 Overview of the studies designed to evaluate the impact of imaging integration for atrial fibrillation ablation on the procedure and clinical outcomes

Author	No. of pts	Type of study	Imaging	Type of evaluation	FU	Effect of imaging integration			
						Fluoroscopy time	Procedure duration	Complications	Clinical outcome
Kistler *et al*[31]	94	Non-randomized	CT	3D *vs* Merge	6 mo	↓	=	=	↑
Martinek *et al*[32]	100	Non-randomized	CT	XP *vs* Merge	6 mo	=	=	↓	↑
Kistler *et al*[33]	80	Randomized	CT	XP *vs* Merge	1 yr	=	=	=	=
Tang *et al*[34]	81	Randomized	CT	XP *vs* Merge	1 yr	↓	↓	=	=
Della Bella *et al*[35]	290	Randomized	CT	Conv *vs* Merge	> 1 yr	↑	↑	=	↑
Bertaglia *et al*[36]	573	Non-randomized	CT/MRI	Conv *vs* XP *vs* Merge	> 1 yr	=	↓	=	↑
Caponi *et al*[37]	299	Randomized	MRI	XP *vs* Merge	1 yr	↓	=	=	=

3D: Three-dimensional; Conv: Conventional; CT: Computed tomography; FU: Follow-up; Merge: CartoMerge; MRI: Magnetic resonance imaging; XP: Carto XP; ↑: Increased; ↓: Decreased; =: No difference; pts: Patients.

PV/left atrial geometry, therefore affecting the quality of imaging integration. In our experience, the quality of imaging integration was poor in a small percentage of cases (less than 10% of the PV oses), however, since quality greatly depends on respiratory or movement artifacts, great care should be taken during CT scan acquisition.

RESULTS OF IMAGING INTEGRATION IN TERM OF CLINICAL IMPACT

Using imaging integration to support AF ablation, the most important issue is whether this highly technological approach results in an improvement of the procedure parameters and the clinical outcome. Table 3 shows an overview of the results of the studies undertaken to assess the clinical usefulness of this technology[31-37]. As shown, there are three non-randomized and four randomized studies published to date. While in the early reports the number of patients included was around 100, the 2009 multicentre Italian registry[36] reported on more than 500 patients. In these studies, as well as in the studies aimed at assessing imaging integration accuracy, the most frequently used three-dimensional imaging modality was CT; the postablation follow-up was at least 1 year in most of the studies. In 5 of 7 studies[31-34,37], the impact of imaging integration was compared with the use of three-dimensional mapping without imaging integration, whereas in the two remaining studies[35,36], a comparison with the conventional technique (based only on fluoroscopy and the use of a circular mapping catheter) was made. It is evident that, apart from one study[33], all the others reported significant improvement of procedure parameters and/or clinical outcome. Specifically, the two studies[35,36] that compared imaging integration *vs* conventionally performed AF ablation reported improvement of clinical outcome with lower arrhythmia recurrences in the imaging integration group during follow-up. Among the other studies that compared an electroanatomic system with and without imaging integration, only two reported[31,32] improvement in clinical outcome. However, of the 3 remaining studies, 2 reported improvement of the procedure parameters with reduction of fluoroscopy[34,37] and procedural time[34].

Apart from the Italian registry[36], which was a non-randomized study, all the other data are from single experiences. Indeed, the best results in term of evaluation of the clinical impact of imaging integration should be obtained by multicentre randomized studies enrolling a large cohort of patients. However, such studies are difficult to design, are long-lasting and sensitive to multiple different variables in different centers and, therefore, they are at risk of being inconclusive. Data provided to date favor the use of imaging integration technology in a complex procedure, such as AF ablation, to improve the quality of patient care.

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