## The impact of radiofrequency wide circumferential pulmonary vein isolation on left atrial geometry in patients with recurrent atrial fibrillation

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## Abstract

Introduction: We sought to investigate the net effect of wide area circumferential radiofrequency catheter ablation (WACA) on the atrial (LA) geometry. Methods and results: Seventy-one patients, who underwent a second PVI procedure, after index procedure of point-by-point WACA, for recurrent paroxysmal (n=31) or persistent (n=40) atrial fibrillation (AF) in our center were included. A three-dimension rotational angiography of the left atrium (3D-RA) under rapid ventricular pacing was performed immediately before ablation, at index and repeat ablation in all patients. LA geometry in terms of volume, sphericity and surface were assessed in all patients between first and second PVI. There was a statistical significant reduction of the LA volume ( $65,6 \pm 14 \text{ ml/m2}$  vs  $62,2 \pm 15 \text{ ml/m2}$ , p<0,001) and of the surface of the LA ( $74,4 \pm 11,2 \text{ vs } 70,4 \pm 11,2 \text{ cm2/m2}$ , p<0,001), whereas the sphericity of the LA increased significantly ( $82 \pm 2\%$  vs.  $83 \pm 2\%$ , p=0,004) in all 71 patients. Patients with paroxysmal AF showed significant decrease of the LA volume ( $121,8 \pm 25,7 \text{ vs } 116 \pm 32 \text{ ml}$ , p=0,008) and increase of the LA sphericity ( $82,3 \pm 2,1 \text{ vs } 83,1 \pm 2\%$ , p=0,009). Patients with persistent AF showed significant decrease of the LA volume ( $133,5 \pm 32 \text{ vs } 126 \pm 32 \text{ ml}$ , p=0,005), but only a trend towards increased sphericity ( $82,4 \pm 2,8 \text{ vs } 83 \pm 2,4\%$ , p=ms). Conlusions: WACA results into significant reduction of the LA volume, LA surface area and into significant increase of the LA sphericity in treated patients with recurrent AF.

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#### **Conflict of interest**

None.

#### Abstract:

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Methods and results: Seventy-one patients, who underwent a second PVI procedure, after index procedure of point-by-point WACA, for recurrent paroxysmal (n=31) or persistent (n=40) atrial fibrillation (AF) in our center were included. A three-dimension rotational angiography of the left atrium (3D-RA) under rapid ventricular pacing was performed immediately before ablation, at index and repeat ablation in all patients. LA geometry in terms of volume, sphericity and surface were assessed in all patients between first and second PVI.

There was a statistical significant reduction of the LA volume ( $65.6 \pm 14 \text{ ml/m}^2 \text{ vs } 62.2 \pm 15 \text{ ml/m}^2$ , p<0,001) and of the surface of the LA ( $74.4 \pm 11.2 \text{ vs } 70.4 \pm 11.2 \text{ cm}^2/\text{m}^2$ , p<0,001), whereas the sphericity of the LA increased significantly ( $82 \pm 2\%$  vs.  $83 \pm 2\%$ , p=0,004) in all 71 patients. Patients with paroxysmal AF showed significant decrease of the LA volume ( $121.8 \pm 25.7 \text{ vs } 116 \pm 32 \text{ ml}$ , p=0,008) and increase of the LA sphericity ( $82.3 \pm 2.1 \text{ vs } 83.1 \pm 2\%$ , p=0,009). Patients with persistent AF showed significant decrease of the LA volume ( $133.5 \pm 32 \text{ vs } 126 \pm 32 \text{ ml}$ , p=0,005), but only a trend towards increased sphericity ( $82.4 \pm 2.8 \text{ vs } 83 \pm 2.4\%$ , p=ns).

*Conlusions:* WACA results into significant reduction of the LA volume, LA surface area and into significant increase of the LA sphericity in treated patients with recurrent AF.

## Keywords:

Left atrial geometry, radiofrequency ablation, three-dimension rotational angiography, atrial fibrillation

#### Introduction:

Atrial fibrillation (AF) is the most common supraventricular arrhythmia in adult patients leading to increased morbidity and mortality.<sup>1-2</sup> AF begets AF resulting in electrical, functional and structural alterations, summarized under the term remodeling of the left atrium (LA).<sup>3-4</sup> Pulmonary vein isolation (PVI) is currently the treatment of choice for the maintenance of sinus rhythm (SR) in patients suffering from paroxysmal and persistent AF.<sup>5-8</sup> Successful PVI leading to sustainable SR results into reduction of the LA volume and alteration of the LA geometry, a phenomenon known as LA remodeling.<sup>9-12</sup> However, there are limited data regarding the remodeling of the LA in patients with recurrent AF after PVI. The imaging modalities utilized currently for the assessment of LA remodeling are transthoracic echocardiography (TTE), cardiac computed tomography (cCT) and cardiac magnetic resonance tomography (CMR), which is considered the current gold standard for LA volume estimation, providing accurate endocardial border definition.<sup>13-15</sup>Alternatively, 3-dimensional rotational angiography (3D-RA) under rapid right ventricular pacing immediately before PVI, allows the 3-dimensional reconstruction of the LA geometry with high accuracy in real time, without dependency from the cardiac cycle. It has also the unique advantage of high-quality resolution by exhausting the elastic properties of the LA due to the direct and fast injection of radiopaque contrast within a short period of very low intracavitary pressures.<sup>16, 17</sup> Nevertheless, 3D-RA is an invasive procedure and can only be performed peri-interventionally during a scheduled PVI. In the current study we sought to analyse the impact of radiofrequency PVI on the LA geometry in patients, who underwent repeat PVI after documented AF recurrence.

## Methods:

From October 2014 to July 2018 a total of 1548 patients were referred in our center for first time and/or redo interventional treatment of medically refractory recurrent paroxysmal and persistent AF. Seventy-one of those patients (Age:  $61 \pm 12$  years, males: 47) developed recurrent AF after index RF-PVI and underwent a second procedure in our center. A 3D-RA was performed before index and redo procedure for the subset of patients in the presented analysis. This study was reviewed and approved by our institutional ethics committee and all patients granted their written consent to participate.

## Three-dimension-rotational angiography and image acquisition:

After positioning of the pigtail catheter in the LA, a short test injection with 10 cc of contrast was given to confirm that the tip of the pigtail catheter was both in the center of the LA and the center of the screen in posterior-anterior (PA) view. A second projection was acquired in the right lateral view (RAO:  $90^{\circ}$ , cranial:  $0^{\circ}$ ) to position the pigtail in the isocenter of the imaging system.

A test-rotation of the X-ray tube, covering from RAO  $102^{\circ}$  to LAO  $92^{\circ}$  angle was performed before image acquisition to ensure lack of collision. During apnea and fast ventricular pacing (220-250 ms), 100 cc of contrast was injected in the LA within four seconds and a fast rotation of the X-ray tube was performed to acquired and then processed to provide a CT-like dataset (*Fig.1*).

#### Analysis of left atrial geometry:

A 3D reconstruction of the LA was created from the obtained 3D-RA image. The final LA model was exported as a mesh for further analysis in a custom developed software

package to automatically calculate LA volume, surface and sphericity parameters (*Fig. 2*). The anteroposterior (AP) diameter was manually calculated from the obtained mesh by measuring the longest AP distance. All geometrical measurements, as well as the calculation of the LA sphericity and the LA center of mass were performed based on previously published literature.<sup>18</sup>

#### Radiofrequency ablation:

All index and redo PVI procedures were performed with the CARTO3 system (Johnson & Johnson, Biosense Webster). A 3.5 mm tip contact force sensing, open irrigated RF-catheter (Biosense Webster, Navistar STSF) was the ablation catheter used in all procedures. All patients underwent double transseptal puncture. An 8-Fr non-steerable long sheath was advanced in the left atrium and via the sheath a 6-Fr pigtail catheter was positioned in the center of the LA for the acquisition of the 3D-RA. A second transseptal puncture and an 8.5-Fr non-steerable sheath was advanced in the LA, housing the ablation catheter. The acquired image of the LA from the 3D-RA was integrated in the CARTO system and used, after correct alignment, as LA-model for PVI. For all index RF-PVI procedures a wide circumferential point-by-point ablation (WACA) was performed on the lateral and septal pulmonary veins. Isolation was confirmed using a 20-pole circular mapping catheter. Ablation was performed using a standardized workflow consisting of a pre-specified procedure sequence including 3D modeling, followed by radiofrequency encircling of the pulmonary veins (25 W posterior wall, 35 W anterior wall) with a THERMOCOOL SMARTTOUCH® Catheter guided by CARTO VISITAG Module (2.5 mm/5 s stability, 50% > 7 g) and ablation index (targets: 550 anterior wall, 400 posterior wall).<sup>19</sup>

#### Statistical analysis:

Quantitative variables are expressed as mean +- SD, whereas qualitative variables are expressed as number of cases and percentage. Student t-test and Mann-Whitney U for paired and unpaired data were used to compare quantitative variables between groups according to normality assumptions. All data were analyzed using the SPSS version 23.0 statistical package (SPSS Inc., Chicago, IL, USA).

#### **Results:**

Patient population:

The mean age of the study population (n=71) was 62 +- 12 years old. Thirty-four patients (47,9%) had hypertension and 5 (7%) were diabetic. The mean ejection fraction (EF) was 58 +- 8%. There was no baseline difference in population demographics between patients with paroxysmal (n=31) and persistent (n=40) AF (age: 60 +- 12 vs. 62 +- 12 years old, p=ns, hypertension: 11/31 vs. 23/40, p=0,08, diabetes: 2/31 vs. 3/40, p=0,9, EF: 59 +- 6% vs. 57 +- 9, p=0,48) (*Table 1*).Comparing the LA parameters between patients with paroxysmal and persistent AF before index procedure, there were no differences noted on the LA volume (121,8 +- 25,8 ml vs. 133,5 +- 32 ml, p=0,1). The indexed LA volume for body surface showed a tendency for a significantly increased LA volume index (62 +- 11,5 ml/m<sup>2</sup> vs. 68,4 +- 16,4 ml/m<sup>2</sup>, p=0,06) in patients with persistent AF. Furthermore, no statistical significant differences were noted regarding the LA surface (140,6 +- 20,7 cm<sup>2</sup> vs. 148,8 +- 23 cm<sup>2</sup>, p=0,12), LA surface index (71,8 +- 9 cm<sup>2</sup>/m<sup>2</sup> vs. 76,3 +- 12,3 cm<sup>2</sup>/m<sup>2</sup> p=0,078), LA antero-posterior diameter (41,2 +- 5 mm vs. 42,1 +- 5,8 mm, p=0,5) and LA sphericity (82,3 +- 2,2% vs. 82,4 +- 2,8, p=0,9) in both group of patients (*Table 2*).

#### Follow-up:

Regular follow up visits including clinical evaluation, ECG as well as 24-hour-holter ECG and transthoracic echocardiography were scheduled for all 71 patients. Patient follow up was regularly scheduled at 3 months post ablation, and then at 6 months intervals. Intermediate follow up visits were scheduled in patients who developed recurrent AF episodes after initially successful PVI.

In all 71 patients recurrent onset of AF was documented after a mean 316 + 258 days. The mean time to AF recurrence was 305 + 238 days in patients with paroxysmal AF (n=31) and 325 + 276 days in patients with persistent AF (n=40), p = ns.

During follow up visits, additive medication such as ACE-inhibitors, or aldosterone receptor blockers with reverse remodeling potential for the LA was registered.<sup>20, 21</sup> Only three patients during follow up were prescribed one of the previously mentioned drugs after index PVI.

## Effect of catheter ablation on left atrial geometry

The mean absolute LA volume in all 71 patients was 128,4 + 30 ml before and 121,8 + 30 ml after PVI, p < 0,001 and  $65,6 + 14 \text{ ml/m}^2$  vs  $62,2 + 15 \text{ ml/m}^2$ , p<0,001 after correction for body surface area. The LA sphericity was calculated 82 + 2% before and 83 + 2% after index PVI, p=0,004. Furthermore, the calculated surface/BSA and antero-posterior diameter of LA before and after PVI was 74,4 + 11,2 vs 70,4 + 11,2 cm<sup>2</sup>/m<sup>2</sup>, p<0,001 and 41,7 + 5 vs 41,5 + 5 mm, p=ns respectively (*Table 1*).

We performed a subgroup analysis for patients with paroxysmal and persistent AF. The group of patients with paroxysmal AF (n=31) had a statistical significant difference in their LA volume (121,8 +- 25,7 vs 116 +- 32 ml, p=0,008), LA sphericity (82,3 +- 2,1 vs 83,1 +- 2%, p=0,009) and LA surface area (71,8 +- 9 vs 68,5 +- 9,5 cm<sup>2</sup>/m<sup>2</sup>, p=0,001), whereas the antero-posterior diameter remained unchanged (41,2 +- 5 vs 41,2 +- 6 mm, p=ns).

The group of patients with persistent AF (n=40) showed a statistical significant difference in their LA volume (133,5 +- 32 vs 126 +- 32 ml, p=0,005) and LA surface area (76,3 +- 12,3 vs 71,8 +- 12,4 cm<sup>2</sup>/m<sup>2</sup>, p=0,005), whereas the change of their LA sphericity (82,4 +- 2,8 vs 83 +- 2,4%, p=ns) and antero-posterior diameter (41,1 +- 5 vs 41,7 +- 6 mm, p=ns) did not reach statistical significance (*Table 3*).

#### Discussion:

Transthoracic echocardiography has the inherent advantage of being a fast bed-side tool, providing fast information about the cardiac chamber anatomy and function. Nevertheless, the quality of the acquired images may be severely compromised from the patient habitus and present significant inter-observer variability. In addition, it typically provides a 2D measure of a structure that it is not a perfect sphere, thereby potentially introducing significant error even in good quality images. On the other hand, CMR and cCT provide threedimensional (3D) datasets of the LA.<sup>14</sup> The acquisition of the LA geometry with all of the above-mentioned imaging modalities can vary due to the intravascular fluid state of the patient and timing of heart cycle. The current study is unique in its design for the examination of LA geometry by utilizing a near-real time invasive imaging method. 3D-RA has the inherit advantage of high-quality image acquisition of the LA, eliminating the impact of cardiac cycle and fluid status of the patient on the LA geometry. The direct and fast injection of radiopaque contrast under rapid ventricular pacing at the time point of short-term intracavitary pressure reduction allows the left atrial chamber to acquire its most spherical shape by exhausting at the same time its elastic properties, thus leading to exactly similar baseline hemodynamic conditions for each of the acquired images and allowing a more accurate and reproducible examination of geometrical parameters.<sup>22</sup> The scope of the current study was to evaluate the alteration of the LA geometrical parameters after WACA RF-PVI in patients with recurrent AF, in a hemodynamic model that eliminates the impact of cardiac cycle and volume status of the patient.

Our entire population (n=71) showed a decrease of LA volume/LA volume-index and surface and an increase of its LA sphericity after index RF-PVI procedure. A subgroup analysis between patients with paroxysmal and persistent AF was performed and we recorded no statistical difference at baseline values of LA sphericity and volume index between patients with paroxysmal and persistent AF. After RF-PVI however, patients with paroxysmal AF showed a significant increase of their initial LA sphericity. On the other hand, patients with persistent AF also showed a tendency towards increasing of their LA sphericity, without reaching statistical significance. In accordance with previous studies we report an increase of the LA sphericity in patients with recurrent AF after initially successful RF-PVI. <sup>12</sup>, <sup>18</sup>

Regarding the effect of RF-PVI on LA volume and surface, there was a significant reduction of parameters after index procedure in the entire population, as well as in each series of patients with paroxysmal and persistent AF separately. There are conflicting results regarding the net effect after WACA RF-PVI on the LA volume in patients with AF recurrence. A study by Tops et al. implementing transthoracic echocardiography as imaging modality reported a reduction of the LA volume from baseline only in patients without recurrent AF after PVI.<sup>23</sup> On the contrary, Hanazawa et al., report a significant decrease of the minimal and maximal LA volumes using 320-row cardiac MCT after RF-PVI, regardless of AF recurrences.<sup>24</sup> Similar findings are reported by Hof et al., when he assessed the LA volume with cardiac MRI after WACA PVI.<sup>25</sup> Our findings are in accordance with the two previously mentioned studies, confirming a significant reduction of the LA volume and surface in a series of patients failing to preserve SR after initially successful PVI. This can be explained from the net effect of WACA RF-PVI to the left atrium. The RF-lesions from the wide circumferential LA antrum isolation leads probably to shrinkage of the LA cavity.

## Conclusions:

Wide circumferential radiofrequency point-by-point PVI results into significant reduction of the LA volume, significant reduction of the LA surface area and into significant increase of the LA sphericity in treated patients with recurrent AF.

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#### **Figures legends:**

Figure 1: Performance of the three-dimensional rotational angiography (3D-RA) of the left atrium (panel A), three-dimensional reconstruction of the left atrium from the obtained 3D-RA image (panel B).

**Figure 2:** Processed three-dimensional (3D) reconstruction of the left atrium (panel A) and left atrial mesh from the obtained 3D-rotational angiography image (panel B) for calculation of the left atrial volume, surface, antero-posterior diameter and sphericity.

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