Unipolar Signal Modification as a Guide for Lesion Creation during Radiofrequency Application in the Left Atrium: A Prospective Study in Humans in the Setting of Paroxysmal Atrial Fibrillation Catheter Ablation

Running title: Bortone et al.; Unipolar Signal and AF Ablation

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Abstract:

**Background** - In patients treated for paroxysmal atrial fibrillation (AF), the pulmonary vein (PV) reconnection rate is substantial and may be related to the lack of transmurality achievement while performing PV isolation (PVI). It has been experimentally demonstrated that positive unipolar atrial electrogram completion, when applying radiofrequency (RF) energy, was associated with transmural lesions. In this regard, we seek to determine whether the unipolar signal modification may be an appropriate end-point for point-by-point RF application and find out if it could improve the paroxysmal AF ablation results in humans.

**Methods and Results** - Fifty consecutive patients (61±8 years-old, 41 men) suffering from paroxysmal AF underwent PVI using Carto™ and Lasso™. Each RF application lasted until development of a completely positive unipolar electrogram. Fifty patients (63±9 years-old, 40 men), who previously underwent PVI following the standard approach of our institution, corresponded to the control group. All PVs were isolated in all patients of both groups. However, the procedural and ablation times were significantly lower in the unipolar group compared with those of the control group while the PV reconnection rate, after 30 minutes of waiting time, was not significantly different. Overall, 21±4 months after one PVI session, the sinus rhythm (SR) maintenance rate without anti-arrhythmic drugs was significantly higher (p=0.027) in the unipolar group (88%) compared with that of the control group (70%).

**Conclusions** - Unipolar signal modification is a useful end-point for RF energy delivery in patients afflicted by paroxysmal AF who undergo PVI and leads to a substantial mid-term SR maintenance rate.

**Key words:** atrial fibrillation, unipolar signal, pulmonary vein isolation.
Introduction

Pulmonary vein isolation (PVI) is the cornerstone for catheter ablation procedures in patients afflicted by paroxysmal atrial fibrillation (AF). However, there is current concern about the durability of PVI since the PV reconnection rate has been recognized as substantial and clearly associated with the recurrence of paroxysmal AF episodes.

Pulmonary vein reconnection may be related to the inability to create transmural and irreversible lesions around PV ostia. In this regard, it has been demonstrated in a porcine model that complete elimination of the negative component of the unipolar atrial electrogram (EGM), while applying radiofrequency (RF) energy, was always associated with transmural lesions whereas the persistence of such a negative component was constantly observed in case of nontransmural lesions.

In clinical practice, unipolar signal modification could be a suitable electrophysiologic (EP) criterion that indicates when to halt each RF energy application while performing point-by-point PVI (because a possible transmural lesion has been created) and when to continue its application (because the lesion deployed is presumed as not transmural).

We, therefore, conducted a prospective study in order to determine whether the unipolar signal modification may be useful or not as an end-point for point-by-point RF application and find out if it could improve the clinical results of paroxysmal AF ablations in humans by allowing more durable PVI achievement. We compared the results of the present study with those of a historical group of patients afflicted by paroxysmal AF who have undergone PVI following the standard ablative approach of our institution.
Methods

Population

The study cohort (designated as the unipolar group) consisted of 50 consecutive patients referred to our institution, from January 2011 to March 2012, for drug resistant and symptomatic paroxysmal AF ablation.

The control group consisted of 50 patients afflicted by drug resistant and symptomatic paroxysmal AF having undergone standard PVI at our institution between January 2009 and December 2010.

All patients received information and gave their written consent to the study, which was approved by the institutional ethics committee.

Atrial Fibrillation Catheter Ablation

Unipolar Group

Prior to ablation, patients were put on efficient vitamin K antagonists (INR 2-3) for at least 2 consecutive months, with a shift, one week before the intervention, to low weight molecular heparin. All procedures were conducted under general anaesthesia without discontinuation of anti-arrhythmic drugs (AAD). Trans-esophageal echocardiography was performed for each patient within 24 hours before the procedure and permitted to exclude LA thrombi. Two long sheaths (Preface™, Biosense Webster, Diamond Bar, CA) were advanced into the LA after two trans-septal punctures under fluoroscopy guidance. Intravenous heparin was administered with a target activated clotting time of 350 to 400 seconds. Three catheters, inserted through the right femoral vein, were used for mapping and ablation: a 6F non deflectable hexapolar 2.5-2.5-2.5-2.5-247.5 mm interspacing electrodes catheter placed at the high right atrium (RA) or into the coronary sinus (CS) whenever possible (Curve: A-Josephson type, Biosense Webster), with its
proximal electrode placed at the level of the inferior vena cava (IVC), a 7F circular decapolar catheter (Lasso™) placed into the LA through one of the constantly perfused long sheaths and used to monitor PVI, and a 3.5 mm 7F externally irrigated-tip ablation catheter (Navistar™), placed within the LA through the second constantly irrigated long sheath. A LA anatomy shell was built by using a three-dimensional (3D) electro-anatomic navigation system (Carto™). This shell was merged with a 3D computed tomography scan acquired prior to the ablation procedure. Pulmonary veins were isolated two-by-two at their antral level by creating a continuous and wide circular lesion. The carina regions were not targeted unless PVs could not be isolated despite complete circular lesion creation around PVs ostia. Radiofrequency ablation settings used were: 30 W/48°C/17 cc per minute.

Every single RF application lasted until the unipolar atrial EGM, recorded by the ablation catheter, which always demonstrates positive-negative morphology before ablation, became complete positive signal. During each RF application, the modification of the unipolar atrial EGM was monitored in real-time with the Carto™ system at a sweep speed of 200mm/s (Figures 1 and 2, Videos 1 and 2). Reference annotation signal was recorded from the bipolar signal of either electrodes 1-2 or 3-4 of the non-deflectable 6F hexapolar catheter, depending on whether the latter was placed into the CS or at the high RA. Unipolar signal was recorded from the 3.5mm distal electrode of the ablation catheter and was filtered on the Carto™ system with a [0.5-120] Hz band-pass filter and displayed in the Carto™ annotation viewer. The indifferent electrode was used as the cathode and was located at the level of the IVC.

All procedures in this group were performed in SR since the analysis of the unipolar signal modification was not feasible during AF due to the instability and variability of the reference channel. For these reasons, patients presenting with AF at the beginning of the ablation
procedure (n=2) or who developed AF during the procedure (n=3), underwent current cardioversion.

Of importance, although the unipolar signal modification was used to monitor every spot-like RF application, PVI (entrance and exit blocks) remained the ultimate end-point of the ablation procedures in accordance with current guidelines.\(^1\) Thirty minutes after PVI, entrance and exit blocks were rechecked for each PV. In case of PV reconnection, supplemental RF applications were performed in order to re-isolate PVs.

The cavo-tricuspid isthmus was ablated only in case of documented common flutter; LA nests were not targeted for ablation and no LA linear lesions were deployed.

**Control Group:**
The standard ablation approach used for PVI in the control group differed from that of the unipolar group by three points. First, the catheter inserted into the CS was a 6F deflectable catheter (Xtrem\(^\text{TM}\), ELA Medical, Le-Plessis-Robinson, France). Second, every single RF application lasted 30 seconds and at the site allowing for PVI, the RF application lasted 90 seconds. Third, 7 PVI procedures in this group were carried out while in AF. Sinus rhythm was restored in these 7 patients by achieving PVI without the need for current cardioversion. All the remaining details were similar to those of the unipolar group ablation method.

**Post-ablation Management and Follow-up**
All patients were discharged home within 4 days (limits 2-4 days). Post-procedure, AAD (except amiodarone) and vitamin K antagonists were prescribed for 3 months and 6 months respectively. Subsequently, AAD were discontinued and the vitamin K antagonists were continued or not, depending on the CHA\(_2\)DS\(_2\)-VASc score (for the unipolar group) or the CHADS\(_2\) score (for the control group) of each patient.
Patients were monitored in the outpatient clinic at 1, 3, 6, 9 and 12 months post-ablation, and every 6 months thereafter. A 12-lead ECG and continuous 24-hour Holter monitoring were done routinely in all patients at each follow-up visit. Atrial tachycardia/AF recurrence was considered, any episode lasting > 30 s (either symptomatic or asymptomatic) subsequent to a 3-month blanking period, as per current guidelines.¹

Statistical Analysis

Descriptive variables are presented as means±SD (min-max) or percentages. The Student’s t-test through the Kolmogorov-Smirnov test was used for comparisons between the continuous data with normal distribution. The Mann-Whitney test was used for comparison of continuous data with non-normal distribution. The chi-square test with a Pearson or Fisher’s exact test was used for comparisons between the categorical data. A P value <0.05 was considered as statistically significant.

Results

Population

A total of 50 consecutive patients were enrolled in the study and corresponded to the unipolar group. A historical group of 50 patients, who have undergone PVI following the standard ablative approach of our institution prior to the present study, corresponded to the control group. Clinical characteristics of the 2 groups of patients were similar and are shown in Table 1.

Index AF Ablation Procedure

The index AF ablation procedure of both groups of patients is presented in Table 2. All PVs were isolated with bidirectional block completion in all patients of each group. However, the mean ablation time, the mean procedural time and the X-ray exposure were significantly lower in the unipolar group compared to those of the control group while the PV reconnection rate, after
30 minutes of waiting time, tended to be lower in the unipolar group, although the difference did not reach statistical significance. Furthermore, only minor complications were reported for each group (i.e. hematomas of the groin).

**Unipolar Group:**

The mean RF application time to elimination of the negative component of the unipolar atrial EGM was 15±1 seconds.

Pulmonary veins were isolated in 35 patients without the need for RF application to the carina regions whereas, in 15 patients, PVs could be isolated only after RF application to the carina regions despite circular lesions creation around ipsilateral PVs exhibiting exclusive positive unipolar EGMs.

After 30 minutes of waiting time, 19 patients presented PV re-connection. Among these 19 patients, PVs were initially isolated in 12 patients without the need for RF energy application to the carina regions while in the remaining 7 patients, RF application to the carina regions was necessary to complete PVI.

*In 6 out of these 19 patients:* reversed unipolar atrial EGMs demonstrating positive-negative morphology were found along the circular lesion created around PV antra. Pulmonary veins were re-isolated in these 6 patients by targeting those reversed unipolar EGMs. It is interesting to note that in 2 of these 6 patients, the earliest PV potentials recorded by the Lasso™ catheter were next to the reversed unipolar EGMs whereas in 4 patients, the earliest PV potential recorded by the Lasso™ catheter were distant from reversed unipolar EGMs. Among these 6 patients, PVs were initially isolated in 5 patients without the need for RF application to the carina regions, while in the remaining patient; PVI could be achieved only after RF application to the carina regions.
In 13 out of these 19 patients: reversed unipolar EGMs could be found neither along the circular lesions nor along the carina regions. Among these 13 patients, initial PVI completion needed RF application to the carina regions in 6 patients, while, in 7 patients, PVI could be achieved without the need for RF application to the carina regions. In these 13 patients, PVs were re-isolated by targeting earliest PV potentials recorded by the Lasso™ catheter inside the circular lesions created.

Control Group:
Pulmonary veins were isolated in 34 patients without the need for RF application to the carina regions while in 16 patients, PV could be isolated only after RF application to the carina regions.

After 30 minutes of waiting time, 26 patients presented PV re-connection. In these 26 patients, PVs were re-isolated by targeting the earliest PV potentials recorded by the Lasso™ catheter.

Follow-up and Redo AF Ablation Procedures
Unipolar Group:
After a mean follow-up of 21±4 months (limits 14-28 months) following the first ablation procedure, 44 patients (88%) have not presented AF/AT recurrence without the use of AAD.

However, 6 patients (12%) have presented paroxysmal AF recurrence and, therefore, underwent a second PVI session. Among these 6 patients, AF recurrence took place in 3 of them approximately 3 months after the first AF ablation procedure while AF recurred in 2 patients 6 months after the first AF ablation procedure. Finally, in 1 patient, AF recurred 15 months after the first ablation procedure.

While performing the index procedures, all these 6 patients had PV reconnection after the 30-minute waiting time. In 2 patients, reversed unipolar EGMs exhibiting positive-negative
morphology were found along the circular lesions created (no RF application to the carina regions was performed) and were the target of supplemental RF energy applications whereas in the remaining 4 patients (to whom RF applications to the carina regions were performed) no reversed unipolar EGM was found and PVI was achieved by targeting the earliest PV potentials recorded by the Lasso™ catheter.

While performing redo procedures, 2 patients had the left PVs reconnected only while the remaining 4 had all PVs reconnected. Pacing (10 mA/2ms) 6 along the previous circular lesions created around ipsilateral PVs and at the carina regions (when appropriate) was performed. Sites exhibiting unipolar positive-negative morphology could be captured while at sites demonstrating positive-only unipolar morphology capture was not possible. Radiofrequency energy application to sites demonstrating unipolar positive-negative morphology (reversed unipolar EGMs) allowed successful PVI in all patients (Figures 3 and 4). It is worth-noting that the sites exhibiting reversed unipolar morphology during redo procedures did not match with those exhibiting reversed unipolar morphology during the index procedures nor were next to sites allowing PVI by targeting the earliest PV potentials recorded by the Lasso™ catheter.

There were no complications related to redo procedures and these six patients have been arrhythmia-free 6±3 months after their second PVI session without AAD.

Control Group:

After a follow-up period of 21±5 months (limits 14-27 months) (arbitrarily stopped in order to have a similar follow-up period with regard to the unipolar group), 35 patients (70%) remained arrhythmia-free without AAD use after a single PVI session. The remaining 15 patients underwent redo PVI procedures due to AF/AT recurrence.

Among these 15 patients, 7 had all PVs reconnected, 4 had 2 PVs reconnected and 4
patients had only one PV reconnected. Targeting the earliest PV potentials recorded by the Lasso™ catheter disconnected all reconnected PVs.

Discussion

Main Findings

The principal findings of the present study are the following: (1) unipolar signal modification is a useful end-point for RF energy delivery while performing PVI in the setting of paroxysmal AF ablation; (2) its utilization is associated with a drastic decrease of the total ablation time with regard to a conventional AF ablative approach; (3) its application leads to a substantial rate of mid-term SR maintenance after PVI.

Unipolar atrial EGM modification analysis as a guide for RF energy delivery in the PVI setting

Background:

In patients afflicted by paroxysmal AF episodes, PVI is the cornerstone for catheter ablation procedures. However; electric reconnection between PVs and the LA has been recognized as a frequent situation directly linked to paroxysmal AF episodes recurrence. There is, therefore, a great concern about the manner with which to render PVI more durable.

Pulmonary vein isolation is currently performed by means of a large circular lesion creation around PVs ostia. Such a circular lesion may be created by a one-fits-all device or following a point-by-point ablative method. In both cases, however, transmurality of the circular lesion created is not assessed and the energy application duration is somewhat empiric. Furthermore and of particular importance, transient PVI can be achieved without complete circular lesion creation both in terms of transmurality and contiguity likely related to edema formation and/or reversible cell injury. Similarly but at the opposite side of the spectrum, in
certain parts of the circular lesion created, energy application may have been excessively and unnecessarily long, thus, exposing patients to LA perforation or surrounding organs injury. Consequently and despite substantial progress in tissue lesion creation understanding, there is a current need for a reproducible and easy-to-implement EP criterion capable of predicting transmurality completion while delivering energy and, therefore, capable of indicating when to cease ablation or when to continue it. This criterion may theoretically enhance both, PVI results and safety.

In a recent and elegant fundamental study, Otomo et al \(^5\) demonstrated in a porcine model that elimination of the negative component of the unipolar atrial EGM, while delivering RF energy, was always associated with transmural lesions while the persistence of such a negative component translated the lack of transmurality regardless of the catheter’s tip orientation and atrial wave-front. This EP parameter was used in our study, after its integration into a commercially available navigation electro-anatomic system.

**Unipolar Signal Analysis and its Impact on the SR Maintenance Rate:**

In the present study, unipolar signal modification was a very useful end-point for every single RF energy delivery while creating a point-by-point circular lesion around PV antra as it clearly indicated when to cease each RF energy application (elimination of the negative component of the unipolar atrial EGM) and when to prolong RF application and/or differently place the ablation catheter (persistent unipolar atrial positive-negative morphology-Figure 2). This was not the case in the control group, where each RF application lasted during an empiric 30-second period without any accurate feedback (i.e. impedance drop, temperature, bipolar signal abatement) regarding the efficacy of the spot lesion created. As a consequence, unipolar signal modification analysis rendered local RF applications more rationale and may be the reason why
the SR maintenance rate was significantly higher in the unipolar group compared to that of the control group. Indeed, by indicating when and where to prolong RF energy and/or place differently the ablation catheter, the unipolar ablation approach may have tended to decrease the PV reconnection occurrence and, therefore, diminish the AF recurrence rate.

Furthermore, unipolar signal modification analysis drastically shortened the RF application time while performing PVI. Indeed, the vast majority of RF applications in the unipolar group led to elimination of the negative component of the unipolar atrial EGM after 10-20 seconds only compared to the empiric 30 seconds of each RF application in the control group. This aspect of the unipolar ablation approach may have safety implications by limiting the amount of RF energy delivered and, therefore, the possibility of surroundings organs injury and LA perforation. However, this remains to be proven, as the complications of both groups were rare and limited to minor hematomas of the groin.

Finally, as described by Otomo et al, the unipolar signal modification could be analyzed whatever the orientation of the ablation catheter was with respect to the LA wall, which permitted conventional ablation catheter manipulation without the need for any learning curve or particular maneuver.

**Perspectives:**

The present manuscript shows that elimination of the negative component of the unipolar atrial EGM can be a reversible phenomenon, likely reflecting transmural injury related to edema and/or reversible cell damage. Indeed, in 6 patients of the unipolar group presenting with acute PV reconnection and in the 6 patients of the same group having undergone redo AF ablation, unipolar atrial EGMs exhibiting a negative component were found while searching for gaps along the lesions created (Figure 4). It is worth-noting that pacing at sites exhibiting those
reversed unipolar atrial EGMs allowed capture (in the 6 patients undergoing redo PVI), which supports the viability of the atrial tissue. Furthermore, targeting such reversed unipolar signals allowed PVI achievement thus, demonstrating their implication within the PV reconnection.

Elimination of the negative component of the unipolar atrial EGM also appeared in our study as a possible irreversible phenomenon related to transmural necrosis. Accordingly, in the 6 patients of the unipolar group having undergone redo PVI, the LA sites exhibiting unipolar EGMs with exclusive positive morphology could not be captured by pacing (Figure 3), which, strongly suggests the absence at those sites of atrial viability.

Further studies are, however, required for defining the nature and the behaviour of lesions leading to elimination of the negative component of the unipolar atrial EGM in humans.

**Limitations**

The limitations of the present study are the following. First, this is a single-center and non-randomized study with a limited number of patients. Second, no challenge with adenosine administration for PV-LA dormant conduction unmasking was performed. Third, no pacing along the lesions created was carried out during the index PVI procedures. Finally, the explanation about the acute PV reconnection observed in 7 patients without any unipolar positive-negative morphology evidenced along the circular lesions deployed in which PVI was initially achieved without the need for RF application to the carina regions is lacking. One may hypothesize, however, that epicardial connections between PVs and the LA existed or that the absence of a dedicated unipolar catheter may have obscured the interpretation of certain unipolar signals and led to inaccurate conclusions in some cases.

**Conclusion**

Unipolar atrial EGM modification analysis is a useful end-point for RF energy delivery in
patients suffering from paroxysmal AF who undergo PVI. Furthermore, this easy-to-implement EP parameter is associated with a substantial mid-term SR maintenance rate and with a drastic decrease of the total ablation time compared to that of a conventional ablative approach without compromising the safety of patients.

Further studies are, however, required for defining the nature and the behaviour of lesions leading to elimination of the negative component of the unipolar atrial EGM in humans and improve PVI durability.

Conflict of Interest Disclosures: A. Bortone is a consultant for Biosense-Webster, Inc. A. Appetiti is an employee of Biosense-Webster, Inc. The other authors report no conflict.

References:


7. Ranjan R, Kholmovski EG, Blauer J, Vijayakumar S, Volland NA, Salama ME, Parker DL, MacLeod R, Marrouche NF. Identification and acute targeting of gaps in atrial ablation lesion sets using a real-time magnetic resonance imaging system. Circ Arrhythm Electrophysiol. 2012;5:1130-1135.

### Table 1. Baseline characteristics of the study subjects.

<table>
<thead>
<tr>
<th>Patients characteristics</th>
<th>Unipolar group (50 pts)</th>
<th>Control group (50 pts)</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>61±8</td>
<td>63±9</td>
<td>0.24</td>
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<td>Gender (F/M)</td>
<td>9/41</td>
<td>10/40</td>
<td>0.79</td>
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<tr>
<td>LVEF (%)</td>
<td>58±9</td>
<td>56±12</td>
<td>0.31</td>
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<tr>
<td>Left atrial volume (ml)</td>
<td>135±28</td>
<td>131±46</td>
<td>0.13</td>
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<tr>
<td>Hypertension, n (%)</td>
<td>10 (20)</td>
<td>13 (26)</td>
<td>0.47</td>
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<tr>
<td>Diabetes Mellitus, n (%)</td>
<td>4 (8)</td>
<td>6 (12)</td>
<td>0.74</td>
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<tr>
<td>Previous TIA/Stroke, n (%)</td>
<td>1 (2)</td>
<td>0</td>
<td>1</td>
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<tr>
<td>Vascular disease, n (%)</td>
<td>4 (8)</td>
<td>3 (6)</td>
<td>1</td>
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<tr>
<td>Obesity, n (%)</td>
<td>4 (8)</td>
<td>2 (4)</td>
<td>0.68</td>
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<tr>
<td>Sleep Apnea, n (%)</td>
<td>2 (4)</td>
<td>4 (8)</td>
<td>0.68</td>
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<tr>
<td>History of AF episodes (years)</td>
<td>5±3</td>
<td>4±2</td>
<td>0.16</td>
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<tr>
<td>Duration of AF episodes (hours)</td>
<td>22±28</td>
<td>21±22</td>
<td>0.91</td>
</tr>
<tr>
<td>AAD failed, n</td>
<td>2.8±0.7</td>
<td>2.9±1</td>
<td>0.69</td>
</tr>
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<td>Patients on amiodarone at the moment of the index procedure, n (%)</td>
<td>10 (20)</td>
<td>14 (28)</td>
<td>0.47</td>
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Table 2. Index AF ablation procedures

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<th>Unipolar group (50 pts)</th>
<th>Control group (50 pts)</th>
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<tr>
<td>Procedural duration (minutes)</td>
<td>106±28</td>
<td>131±30</td>
<td>&lt;0.0001</td>
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<td>X-ray exposure (minutes)</td>
<td>14±4</td>
<td>20±7</td>
<td>&lt;0.0001</td>
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<td>Ablation time (minutes)</td>
<td>26±8</td>
<td>63±27</td>
<td>&lt;0.0001</td>
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<tr>
<td>Energy delivered per PVI procedure (kJ)</td>
<td>47±15</td>
<td>113±48</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Impedance decrease (Ω) during local RF applications</td>
<td>13±1</td>
<td>12±1</td>
<td>0.14</td>
</tr>
<tr>
<td>PVI (%)</td>
<td>100</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td>Patients with PV reconnection after 30 min of waiting time</td>
<td>19 (38%)</td>
<td>26 (52%)</td>
<td>0.16</td>
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<tr>
<td>Patients in whom RF applications at the carina regions were necessary for PVI completion</td>
<td>15 (30%)</td>
<td>16 (32%)</td>
<td>0.83</td>
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<tr>
<td>Cavo-tricuspid isthmus ablation (patients)</td>
<td>9</td>
<td>7</td>
<td>0.58</td>
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<tr>
<td>Complications</td>
<td>3 hematomas of the groin</td>
<td>2 hematomas of the groin</td>
<td>1</td>
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<tr>
<td>SR maintenance rate 21±4 months after the index PVI session (%)</td>
<td>88</td>
<td>70</td>
<td>0.027</td>
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</table>
Figure Legends:

Figure 1. Unipolar atrial EGM recorded before and after ablation. Panel A: Left atrium 3D computed tomography. Modified left lateral view. A Lasso™ catheter (in blue) is visualized inside a common left pulmonary vein trunk. The tip of the ablation catheter (in green) is visualized at the most inferior aspect of the common left pulmonary trunk. The hexapolar catheter placed inside the CS is shown in orange. A RF application already performed appears as a red dot at the posterior wall of the LA. Are shown the II surface ECG lead demonstrating sinus rhythm (in white), the unipolar (MAP 1 in blue) and bipolar (MAP 1-2 in yellow) EGMs recorded by the end-tip of the ablation catheter of a non-ablated LA tissue, and the proximal CS signal recorded by the hexapolar catheter (CS UNI 3-4 in pink). The atrial unipolar EGM (MAP 1) shows a positive-negative morphology. Panel B: The atrial unipolar EGM became exclusive positive morphology 12 seconds after the RF application.

Figure 2. Same patient as in figure 1. Unipolar atrial EGM before and after RF delivery. Panel A: The tip of the ablation catheter is located at the junction between the left superior PV and the LA appendage. The unipolar atrial EGM demonstrates positive-negative pattern. Panel B: After several attempts for catheter stabilization and prolonged RF application (50 seconds), the unipolar atrial EGM demonstrates somewhat incomplete positive morphology with a little persistent negative component. In this case, a supplemental more internal RF application was delivered in order to consolidate the circular lesion.

Figure 3. Persistent positive unipolar atrial morphology in a patient undergoing redo AF ablation.
procedure. Posterior LA view. In this example, while searching for gaps at the previous circular line created around the left PVs, the ablation catheter recorded positive unipolar atrial EGM (Map 1 in blue). Please note that the bipolar channel shows a very low voltage EGM (Map 1-2 in yellow). This point was tagged as ablated since there was no need to perform supplemental RF application. It is important to note that pacing at this site demonstrated no LA capture.

Figure 4. Reversed unipolar atrial EGM in a patient undergoing a second PVI session. Please note that the unipolar channel (Map 1 in red) demonstrates positive-negative morphology while the bipolar channel (Map 1-2 in bleu) shows a low amplitude signal. The right PVs were connected in this patient and could be disconnected by targeting such a unipolar atrial reversed signal. Of interest, pacing at that site captured the LA before ablation.
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SUPPLEMENTAL MATERIAL

**Video 1.** Radiofrequency Application in a Patient of the Unipolar Group - Left Atrial Posterior View.

The circular decapolar catheter (Lasso™) in yellow is located inside the right superior pulmonary vein. The hexapolar catheter in green is located at the high RA. The ablation catheter is located at the infero-posterior aspect of the right inferior PV. Please note that before the RF application, the unipolar atrial EGM (MAP-1 in yellow) exhibited a positive-negative pattern. Fourteen seconds after the onset of the RF application, the negative component of the unipolar atrial EGM has disappeared.

Once the RF application halted, the ablation catheter is moved around the RF application site. It can be easily appreciated that “outside” the ablation spot, the unipolar atrial EGM constantly exhibits a negative component while at the ablation spot such a negative component is absent. It is important to underline that, although some noise is present, the RF application and its impact on the unipolar atrial EGM can be accurately monitored in real-time.

In this video are also shown II and V1 surface ECG leads (in white and blue respectively) demonstrating sinus rhythm, the bipolar (MAP 1-2 in yellow) EGM recorded by the end-tip of the ablation catheter and the proximal and distal high RA signals recorded by the hexapolar catheter (CS UNI 1-2 and 3-4 in green).

**Video 2.** Same patient as in Video 1.

The RF application takes place at the infero-posterior aspect of the left inferior PV. The unipolar channel (MAP 1 in yellow) demonstrates, before RF application, a positive-negative
morphology. Please note the rapid elimination of the negative component of the unipolar atrial EGM while delivering RF energy, which can be easily appreciated in real-time.

As in the previous example (Video 1), once the RF application ceases (14 seconds), the ablation catheter is moved around the RF ablation spot. Outside the RF application spot, the unipolar atrial EGM constantly shows positive-negative pattern while at the ablation spot, unipolar atrial EGM does not show any negative component.