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When local impedance meets contact force: preliminary experience from the CHARISMA registry

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47 Abstract

48 Purpose. Highly localized impedance (LI) measurements during atrial fibrillation (AF) ablation 49 have emerged as a viable real-time indicator of tissue characteristics and the consequent 50 durability of the lesions created. We investigated the impact of catheter-tissue contact force (CF) 51 on LI behavior during pulmonary vein isolation (PVI). 52 Methods: Forty-five consecutive patients of the CHARISMA registry undergoing *de novo* AF 53 radiofrequency (RF) catheter ablation with a novel open-irrigated-tip catheter endowed with CF and LI measurement capabilities (StablepointTM catheter, Boston Scientific) were included. 54 55 Results: A total of 2895 point-by-point RF applications were analyzed (RF delivery time 56 (DT)=8.7?4s, CF= $13\pm 8g$, LI drop= $23\pm 7\Omega$). All PVs were successfully isolated in an overall 57 procedure time of 118±34min (fluoroscopy time=13±8min). The magnitude of LI drop weakly 58 correlated with CF (r=0.13, 95% confidence interval (CI): 0.09 to 0.16, p<0.0001), whereas both 59 CF and LI drop inversely correlated with DT (r=-0.26, 95%CI: -0.29 to -0.22, p<0.0001 for CF; r=-0.36, 95%CI: -0.39 to -0.33, p<0.0001 for LI). For each 10 grams of CF, LI drop markedly 60 61 increased from $22.4\pm7\Omega$ to $24.0\pm8\Omega$ at 5 to 25g CF intervals (5-14 grams of CF vs 15-24 grams 62 of CF, p < 0.0001), whereas it showed smooth transition over 25g (24.8±7 Ω at \geq 25g CF intervals, 63 p=0.0606 vs 15-24 g of CF). No major complications occurred during the procedures or within 64 30 days.

65 Conclusions: CF significantly affects LI drop and probable consequent lesion formation during
66 RF PVI. The benefit of higher contact (>25g) between the catheter and the tissue appears to have
67 less impact on LI drop.

69 INTRODUCTION

70 Catheter ablation aimed at pulmonary vein (PV) isolation is the most effective treatment in 71 patients with atrial fibrillation (AF), and is now recommended as the first-line therapy (1, 2). 72 Despite acute safety and efficacy, a considerable number of recurrences are observed during 73 long-term follow-up, mainly as a result of PV reconnection (1-3). Several strategies have been 74 proposed in order to achieve durable, transmural lesions, thereby improving the efficiency of 75 catheter ablation (4). Highly localized impedance (LI) measurements during AF ablation have 76 emerged as a viable real-time indicator of tissue characteristics and the consequent durability of 77 the lesions created (5-7). A recently released catheter has combined CF detection with LI 78 assessment in a single catheter-tissue contact force (CF)-LI catheter (8). In swine and in vitro, 79 the addition of LI to CF has provided feedback on both electrical and mechanical loads and 80 allows the evaluation of tissue resistivity, and thus of the type of tissue with which the catheter is 81 in contact. It has also provided feedback on whether volumetric tissue heating is inadequate, 82 sufficient, or excessive. In addition, in a point-by-point workflow with consistent CF, the 83 visualization of LI significantly reduced RF time (8). We investigated the impact of CF on LI 84 behavior during PV isolation.

85 METHODS

86 Patient population and study design

CHARISMA was a prospective, multi-center cohort study designed to describe Italian clinical practice regarding the approach to ablation of various arrhythmias. The study complied with the Declaration of Helsinki, the locally appointed ethics committee approved the research protocol, and informed consent was obtained from all patients. From January 2021 to July 2021, 45 consecutive patients indicated for AF ablation who were undergoing their first high-resolution mapping and ablation procedure with a novel CF- and LI-featured catheter in 9 Italian centers
were included in our analysis. All patients were followed up at the same hospital, from the time
of first ablation to the last follow-up visit.

95 Ablation procedure

96 After completion of the baseline evaluation, patients underwent ablation in accordance with 97 standard clinical practice guidelines [1]. All procedures were performed under conscious 98 sedation or general anesthesia. Vitamin K antagonist treatment was not interrupted, while non-99 Vitamin K anticoagulants were skipped on the morning of the procedure. A decapolar catheter 100 (e.g. Dynamic XTTM, Boston Scientific, Marlborough, MA, USA) was used to cannulate the 101 coronary sinus. After single or double transseptal punctures under fluoroscopic guidance, 102 intravenous unfractionated heparin boluses were administered, in order to maintain an activated 103 clotting time of >300 seconds. Intracardiac echocardiography probe was not used in any procedure. The basket mapping catheter (OrionTM, Boston Scientific, Marlborough, MA, USA) 104 and the ablation catheter (StablepointTM catheter, Boston Scientific, Marlborough, MA, USA) 105 106 were then inserted. A standard, non-steerable sheath was used. The OrionTM catheter was used in combination with the RhythmiaTM HDx mapping system (RhythmiaTM, Boston Scientific, 107 108 Marlborough, MA, USA) to create a 3-dimensional electro-anatomical voltage and activation 109 map of the left atrium. Mapping and ablation were primarily carried out in sinus rhythm; in 110 patients in AF, electrical cardioversion was attempted in order to restore sinus rhythm, at the 111 beginning of the procedure and before re-mapping. Point-by-point RF delivery was performed in 112 such a way as to create contiguous ablation spots encircling the PVs. CF settings were at the 113 individual operator's discretion, within the range of 5 to 40 g. Ablation was guided by the 114 magnitude and time-course of impedance drop during RF delivery. RF applications were targeted

115 to a minimum LI drop of 15 Ω within 15 seconds and were stopped when a maximum cutoff LI 116 drop of $\geq 40 \Omega$ was observed. We aimed to reach an LI drop of 20–30 Ohms, on the basis of 117 previous experimental data (8). Radiofrequency energy was applied in the power controlled 118 mode (45–50 W) with a temperature limit of 43° C. The irrigation rate was 30 ml/min during 119 applications and 2 ml/min during mapping. A normal saline solution (NaCl 0.9%) was used. The 120 recommended maximum distance between adjacent ablation spots (center-to-center) was ≤ 6 mm. The ablation points were marked automatically with 6 mm diameter, numbered AutoTagsTM. The 121 122 starting impedance, initial CF, LI drop during RF, and average force applied were recorded. The 123 endpoint of ablation was PV isolation, as assessed on the basis of entry and exit block by means of the 64-pole OrionTM catheter placed sequentially in each of the PVs. In the absence of first-124 125 pass PV isolation (i.e. no isolation upon completion of the encirclement of ipsilateral veins), PV 126 isolation was accomplished by means of additional RF applications at the investigator's

127 discretion.

128 Local impedance

129 A 3-electrode method with separate circuits for field creation and measurement was used to 130 measure LI. As previously described, non-stimulatory alternating current was delivered between 131 the tip electrode and the proximal ring; voltage was passively measured between the tip electrode 132 and the distal ring (9). As the catheter used does not have mini-electrodes, the resulting voltage 133 was measured from the catheter tip. Impedance was calculated by dividing the voltage by the 134 stimulatory current. To measure the baseline reference impedance of the blood pool, once the 135 reference map had been completed, the ablation catheter was positioned in the blood pool for 10 136 s and the value was calculated when no EGM recordings from the ablation catheter were present. 137 Baseline tissue impedance and impedance drop for each ablation lesion were measured. To

analyze the impedance information, the isolation line around each pair of PVs was divided into
seven distinct sections (Figure 1A) in accordance with the literature (10). Videos of the ablation
procedures were exported from the mapping system, to display the procedure in real time. RF

141 current applications were then retrospectively analyzed.

142 *Contact force*

143 The ablation catheter used in the current study has the ability to measure both real-time LI

144 calculated from a local electric field generated at the tip of the catheter, and CF. The force

145 applied to the tip electrodes transferred to inductive sensors via a spring. The signal change

146 measured by the inductive sensors is then converted to a 3-dimensional force vector by means of

147 known spring dynamics. The target CF was 5-40 g, at the operator's discretion. We collected the

148 following data on each first-pass ablation point: power, minimum CF, maximum CF, mean CF,

149 duration of application, baseline LI and LI drop. In addition, the CF range during the applications

150 was calculated by subtracting the minimum CF from the maximum CF of the ablation point. All

151 numbered AutoTagTM points were exported from the system for off-line analysis. An example of

152 visualization of CF values and the DirectSenseTM tool on the RhythmiaTM mapping system

153 during ablation is depicted in figure 1B, C.

154 Follow-up

155 Complications were reported on the case report form and collected during follow-up. After

ablation, anticoagulation and antiarrhythmic drugs therapy were continued. At 3 months,

157 anticoagulation was continued according to the stroke risk, whereas antiarrhythmic drugs were

- 158 continued at the discretion of the treating physician. Clinical evaluation and ECG were
- 159 performed at 1, 3, 6, and 12 months. Holter ECG was performed at 3, 6 and 12 months post-

ablation or in the case of symptoms. For the purpose of this study, data were collected during the
index procedure and during an ambulatory visit 30 days after the procedure.

162 Statistical analysis

163 Descriptive statistics are reported as means±SD for normally distributed continuous variables, or

164 medians with 25th to 75th percentiles in the case of skewed distribution. Normality of

- 165 distribution was tested by means of the non-parametric Kolmogorov–Smirnov test. Differences
- 166 between mean data were compared by means of a t-test for Gaussian variables, and the F-test

167 was used to check the hypothesis of equality of variance. The Mann-Whitney non-parametric test

- 168 was used to compare non-Gaussian variables. Differences in proportions were compared by
- 169 applying χ^2 analysis or Fisher's exact test, as appropriate. Linear regression analysis was
- 170 performed to determine relationships between LI drop, CF and RF delivery time (DT). A *p* value
- 171 <0.05 was considered significant for all tests. All statistical analyses were performed with

172 STATISTICA software, version 7.1 (StatSoft, Inc., Tulsa, OK).

173 **RESULTS**

174 Study population and procedural parameters

175 The demographic and procedural data of the 45 consecutive *de novo* PV isolation patients are

- 176 reported in Table 1. Almost two-thirds of the patients suffered from paroxysmal AF (n=26, 58%)
- 177 whereas 19 (42%) had a history of persistent AF. The mean procedure duration and fluoroscopy
- times were 107.4±39 min and 11.1±8 min, respectively. A total of 3196 RF applications were
- delivered, with a mean number of 64±31 ablation spots during a mean RF delivery time of 8.7±4
- 180 sec, without any steam popping.
- 181 Local tissue impedance values

- 182 High-quality data were available on 2895 (91%) RF applications performed around PVs. The
- 183 baseline LI was $157.9\pm17\Omega$ prior to ablation and $136.9\pm14\Omega$ after ablation (p<0.0001, absolute
- 184 LI drop of 23.0 \pm 7 Ω) with an LI drop rate of 3.5 \pm 2 Ω /s. The mean blood-pool impedance was
- 185 152.7 \pm 10 Ω (p<0.0001 vs baseline LI). The magnitude of the impedance drop was predicted by
- 186 the baseline LI (correlation coefficient r=0.61, 95% confidence interval (CI): 0.59–0.63,
- 187 p<0.0001). Regarding AF type, no difference in baseline LI was found ($158\pm17\Omega$ for paroxysmal
- 188 AF vs $157.9\pm17\Omega$ $157.7\pm17\Omega$ for persistent AF, p=0.3878), whereas LI drops were larger in
- paroxysmal AF cases (23.3 \pm 7 Ω) than in persistent AF cases (22.7 \pm 7 Ω , *p*=0.0097). On
- 190 considering the underlying rhythm, no differences were found in terms of either baseline LI or LI
- 191 drop (baseline LI: $157.2\pm17\Omega$ for sinus rhythm vs $158.4\pm17\Omega$ for AF, *p*=0.0518; LI drop:
- 192 22.8 \pm 7 Ω for sinus rhythm vs 22.9 \pm 7 Ω for AF, *p*=0.8606).

193 Correlation between local impedance and key procedural parameters

- 194 The mean RF delivery time was 8.7 ± 4 s and the mean CF was 13.0 ± 8 g. On assessing the various
- 195 key ablation parameters, the magnitude of LI drop proved to be weakly correlated with CF
- 196 (r=0.13, 95%CI: 0.09 to 0.16, p<0.0001) whereas both CF and LI drop inversely correlated with
- 197 DT (*r*=-0.26, 95%CI: -0.29 to -0.22, p<0.0001 for CF; *r*=-0.36, 95%CI: -0.39 to -0.33, p<0.0001
- 198 for LI). Figure 2 (A to C) shows the resulting mean DT stratified by CF values and LI drop
- 199 values. For each 10 grams of CF, LI drops markedly increased from $22.4\pm7\Omega$ to $24.0\pm8\Omega$ at 5 to
- 200 25g CF intervals (5-14 grams of CF vs 15-24 grams of CF, p < 0.0001), whereas it showed a
- smooth transition above 25g (24.8 \pm 7 Ω at \geq 25g CF intervals, p=0.0606 vs 15-24 g of CF)
- 202 (Supplementary figure 1). There was a correlation between shorter DT and larger drop in LI:
- 203 27.2 $\pm 8\Omega$ at 0-5 seconds of DT interval vs 22.8 $\pm 7\Omega$ at 6-10 seconds of DT interval vs 19.7 $\pm 6\Omega$ at

>10 seconds of DT interval (all comparisons p<0.0001). Details of the relationships among the three parameters are reported in figure 3.

206 Characterization of pulmonary vein location sites

207 Of the 2895 RF applications, 1544 (53.3%) were sited on the RPVs and 1351 (46.7%) on the

208 LPVs. Baseline impedance was homogenous across the various location sites $(158.5\pm17\Omega \text{ at})$

209 LPVs vs $157.4\pm17\Omega$ at RPVs, p=0.0822; $157.2\pm17\Omega$ at anterior sites vs $159.4\pm18\Omega$ at posterior

sites, p=0.0643; and 159.4 \pm 17 Ω at inferior sites vs 157.5 \pm 15 Ω at superior sites, p=0.1028). LI

drop was higher at anterior sites ($23.4\pm7\Omega$ vs $22.8\pm8\Omega$ at posterior sites, p=0.029) and at inferior

sites $(23.5\pm7\Omega \text{ vs } 22.5\pm7\Omega \text{ at superior sites}, p=0.0447)$, whereas it was similar between RPVs

and LPVs (22.8 \pm 7 Ω in RPV pairs vs 23.2 \pm 7 Ω at LPVs, p=0.0565) (Figure 4A, 4B). RF delivery

time was longer at superior sites (8.9±4 sec vs 8.4±4 sec at inferior sites, p=0.0437) and in RPV

215 pairs (8.8±4 sec vs 8.6±4 sec in LPV pairs, p=0.0334), whereas no differences were found

between posterior and anterior sites (8.6±4 sec at posterior sites vs 8.7±4 sec at anterior sites,

217 p=0.7824) (Figure 4C). CF values were higher in LPV pairs (13.5±8 g vs 12.5±7 g in RPV pairs,

p=0.0025), whereas no differences were found between superior and inferior sites (13.2±8 g vs

219 12.6±8 g, p=0.2358) or between posterior and anterior sites (12.7±7 g vs 13.2±8 g, p=0.5062)

220 (Figure 4D). Details of the distribution of RF applications, CF values, LI drops and RF delivery

times, according to location sites, are reported in Figure 5 and Supplementary Table 1. Details of

baseline and ablated tissue impedance values are reported in Supplementary Figure 2 and

223 Supplementary Table 1.

224 First pass isolation and acute outcome

225 No steam pops or major complications, including atrio-esophageal fistula or tamponade, were

reported during or after the procedures. In our series a total 169 PVs (94%) were isolated at first

227 pass ablation, resulting in 40 (89%) patients who had a first pass isolation, whereas 11 residual 228 gaps in 5 (11%) patients were observed after initial encirclement and required additional RF 229 applications. LI drop values were larger and CF values were higher where first pass isolation was 230 achieved (LI drop: 23.1 \pm 7 Ω at successful sites vs 16.8 \pm 3 Ω at unsuccessful sites, p<0.0001; CF: 231 13±8g at successful sites vs 10.2±6g at unsuccessful sites, p=0.0207, respectively). At the end of 232 the procedures, all PVs had been successfully isolated in all study patients. Minor complications 233 were reported in 3 patients (6.6%) after the procedure: one pericarditis with mild pericardial 234 effusion, and groin hematomas in 2 patients. Conservative treatment and medical therapy were 235 effective in all cases, without prolongation of hospital stay.

236 **DISCUSSION**

237 Main findings

238 In this single-arm prospective study, we performed AF catheter ablation by means of a novel 239 ablation catheter with integrated CF- and LI-sensing capabilities. The ablation strategy, which 240 was guided by LI information, had a 100% acute procedural effectiveness rate, without causing 241 any steam pops or major complications. CF significantly impacted on effective lesion formation 242 during RF PV isolation. The use of higher than 25g contact between the catheter and the tissue 243 proved to have less impact on LI drop. The inverse correlation of both CF and LI drop with RF 244 DT indicates that a significant reduction in RF time can be achieved at 45-50 W power in a 245 point-by-point workflow when LI guidance is combined with CF. These points reflect the value 246 of LI plus CF in discerning both mechanical contact and electrical coupling, thereby enabling 247 safe and effective lesions to be created.

248 Ablation guided by local impedance and contact force

249	The use of highly localized impedance measurements to provide insight into tissue
250	characteristics and their real-time evaluation seems to be helpful in order to precisely assess the
251	electrical contact of the catheter and tip stability and to serve as a viable real-time indicator of
252	tissue characteristics and durability of the lesions created (5-7; 11). Two commercially available
253	catheters capable of recording LI are currently available. The IntellaNav MiFi OI catheter
254	(Boston Scientific) generates LI measurements through mini-electrodes on the tip of the ablation
255	catheter, the maximum value being reported within a three-dimensional mapping environment
256	(Rhythmia; Boston Scientific). A recently released StablePoint catheter (Boston Scientific)
257	incorporates CF-sensing capability in addition to LI (8). The ablation strategy for PV isolation
258	guided by LI technology has proved safe and effective, resulting in a very low rate of AF
259	recurrence over 1-year follow-up (7). However, as the dedicated ablation catheter (IntellaNAV
260	Mifi OI, Boston Scientific) used in these studies was not able to collect data on CF sensing, it
261	was not possible to compare CF and impedance measurements.
262	It is well recognized that, when RF energy is applied, CF is one of the variables, in addition to
263	catheter stability, power output, temperature, and duration of RF output, that impact on lesion
264	size and transmurality (4). CF-guided RF catheter ablation has been associated with a
265	significantly greater AF/atrial tachycardia-free survival benefit than non-CF-guided ablation in
266	patients with paroxysmal AF rather than persistent AF. In addition, the CF-guided ablation
267	strategy also reduced procedure time, fluoroscopy time and RF time, though it had no distinct
268	effect on the alleviation of procedure-related complications (12). Adding CF sensing to the LI-
269	sensing technology has the potential to further increase the efficiency of LI-guided catheter
270	ablation. Indeed, we found that CF significantly impacted on effective lesion formation during
271	RF PV isolation. However, the benefit of higher than 25g contact between the catheter and the

272 tissue had less impact on the increase in LI drop. Our findings may have relevant implications in 273 the clinical setting: 1) good catheter-tissue contact improves the drop in LI and shortens the time 274 needed to achieve it; 2) the lack of benefit of a CF value of above 25 g might avoid excessive 275 catheter pressure and potential complications. Similar data have already been reported with other 276 CF-sensing technologies (10, 13); 3) the CF value may help to differentiate the LI value of the 277 blood pool from that of diseased tissue. Indeed, both the blood pool and diseased tissue display 278 lower LI values than healthy tissue (5,14). Of note, the magnitude of the mean LI drop observed 279 in our study (23.0 \pm 7 Ω) was significantly higher than that reported with previous LI technology 280 (IntellaNAV Mifi OI, Boston Scientific) by other authors: Segreti et al. (5), $14\pm8\Omega$; Das et al. 281 (6), $19.8 \pm 11.1 \Omega$, and Solimene et al. (7), $13 \pm 8\Omega$. To date, only one pilot study, which used the 282 StablePointTM ablation catheter (15), showed that a local impedance drop > 21.8 Ohms on the 283 anterior wall and > 18.3 Ohms on the posterior wall significantly increased the probability of 284 creating a successful lesion. The CF-LI catheter does not have microelectrodes; instead, its distal 285 tip serves as the return pole of the LI circuit. The larger electrical field created gives rise to CF-286 LI values that are typically 40%–50% greater than those measured by the non-CF-LI catheter 287 (16). Further studies will therefore be required in order to determine the magnitude of LI drop 288 that predicts acute PV segment conduction block.

289 Right power, right duration

Winkle et al. first showed that AF ablations can be performed at 45–50 W for short durations with very low complication rates. High-power, short-duration ablations have the potential to shorten procedural and total RF times and to create more localized and durable lesions (17). In addition, high-power short-duration RF ablation has proved able to significantly shorten

294 procedure time, fluoroscopy time, left atrial dwell time, and RF ablation time in comparison with

295 a conventional approach, with no difference in safety outcomes between the two groups (18). 296 When high-power short-duration ablation is performed, several parameters can indicate that a 297 lesion has been formed and that no further ablation is needed, thereby avoiding ablation for 298 longer than needed to selectively destroy the target tissue. These parameters include: monitoring 299 the loss of pacing capture during RF delivery, observing a drop in impedance, and following 300 such metrics of lesion formation as the Lesion Size Index or the Ablation Index. (19-21). Our 301 findings showed an inverse correlation of both CF and LI drop with DT, together with a 302 significant reduction in RF time at 45-50 W power in a point-by-point workflow. This reflects 303 the value of LI plus CF in discerning both mechanical contact and electrical coupling, thereby 304 enabling safe and effective lesions to be created.

305 Limitations

306 This investigation focused on the effect of each single RF application, and no data on medium-307 and long-term clinical outcomes were available. Impedance drop was used to assess lesion 308 formation; however, it is only a surrogate and could be affected by several factors. The LI values 309 that we used were empirically chosen. However, they were based on our previous experience in 310 clinical practice, in which they had allowed us to achieve considerable clinical success. Further 311 studies are required to identify the best workflow and targeted parameters also for achieving 312 long-term success. The effect of using a steerable sheath during ablation may need further 313 investigation. Lastly, esophageal temperature monitoring was not performed. However, in our 314 preliminary experience, applying this procedural workflow, no steam pops or major 315 complications, including atrio-esophageal fistula or tamponade, occurred during or after the 316 procedures.

317 CONCLUSIONS

318	CF significantly impacts on effective lesion formation during RF PVI. The benefit of higher than
319	25g contact between the catheter and the tissue appears to have less impact on LI drop.
320	
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324	Scientific. The other authors have no conflicts of interest to declare that are relevant to the
325	content of this article.
326	Availability of data and material: The data underlying this article will be shared on reasonable
327	request to the corresponding author.
328	Code availability: Not applicable.
329	Ethics approval: This study was performed in line with the principles of the Declaration of
330	Helsinki. The locally appointed Ethics Committee approved the research protocol.
331	Consent to participate: Informed consent was obtained from all individual participants
332	included in the study.
333	Consent to publish: Patients signed informed consent regarding publishing their data.
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441 Table legends

442 **Table 1.** Baseline characteristics and procedural parameters

Parameter	n = 45			
Age, years	61.6±9			
Male Gender, n (%)	28 (62.2)			
Indication for ablation:				
• Paroxysmal AF, n (%)	• 26 (57.8)			
• Persistent AF, n (%)	• 19 (42.2)			
History of atrial flutter/atrial tachycardia, n (%)	6 (13.3)			
LVEF, %	55.1±8			
Cardiomyopathy, n (%)	15 (33.3)			
Hypertension, n (%)	26 (57.8)			
Coronary artery disease, n (%)	5 (11.1)			
History of heart failure, n (%)	3 (6.7)			
COPD, n (%)	2 (4.4)			
CKD, n (%)	1 (2.2)			
ACE-ARB, n (%)	14 (31.1)			
Beta-blockers, n (%)	28 (62.2)			
Statin, n (%)	7 (15.6)			
Diuretics, n (%)	5 (11.1)			
Antiarrhythmics, n (%)	33 (73.3)			
Procedure duration, min	107.4±39			
Fluoroscopy time, min	11.1±8			
RFC applications, n	64±31			
RFC duration time, sec	8.7±4			
Mean Power, W	47.2±3			
Complications during the procedure, n (%)	0 (0)			
Minor complications	3 (6.6)			
Mild pericardial effusion	• 1			
Groin hematomas	• 2			

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⁴⁴⁴ AF=atrial fibrillation; PVI=pulmonary vein isolation; LVEF=left ventricular ejection fraction; RFC=radiofrequency

⁴⁴⁵ catheter; COPD=chronic obstructive pulmonary disease; CKD=chronic kidney disease; ACE=angiotensin-

⁴⁴⁶ converting enzyme; ARB=angiotensin receptor blocker.

447 Figure legends

- 448 Figure 1. Panel A: Identification of 7 ablation sites around the right (RPV) and left (LPV) pairs of pulmonary veins.
- 449 Anterior superior: R1, L1; Anterior inferior: R2, L2; Inferior: R3, L3; Posterior inferior: R4, L4; Carina: R5, L5;
- 450 Posterior superior: R6, L6; Superior: R7, L7. LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary
- 451 vein; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein. *Panel B*: Example of
- 452 visualization of CF and DirectSenseTM tool on the RhythmiaTM mapping system during ablation. *Panel C:* Point-by-
- 453 point RF delivery created contiguous ablation spots encircling the PVs. The maximal inter-lesion distance between
- 454 two neighboring lesions was set ≤ 6 mm and was automatically measured through the AutotagTM software. CF
- 455 settings were at the individual operator's discretion, within the range of 5 to 40 g.



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459 Figure 2. Panel A: Multidimensional relationship between RF delivery time, CF values and LI drop values. Panel

460 **B:** Radar plot showing the relationship between RF delivery time and CF values according to different degrees of LI

461 drop. This Kiviat chart displays multivariate data (RF delivery time) with values represented on axes starting from

- 462 the same point. The apexes of the Kiviat charts represent different CF intervals (5-14g, 15-24g and \geq 25g) whereas
- 463 the lines represent different degrees of LI drop (blue line for $10-19\Omega$ LI drop values, orange line for $20-29\Omega$ LI drop
- 464 values and grey line for LI drop values $\geq 30\Omega$). RF delivery time is represented according to CF and LI drop
- 465 intervals.
- 466 *Panel C:* Radar plot showing the relationship between RF delivery time and LI drop values according to different
- 467 degrees of CF. This Kiviat chart displays multivariate data (RF delivery time) with values represented on axes
- 468 starting from the same point. The apexes of the Kiviat charts represent different LI drop intervals $(10-19\Omega, 20-29\Omega)$
- 469 and $\geq 30\Omega$), whereas the lines represent different degrees of CF (blue line for 5-14g CF values, orange line for 15-
- 470 24g CF values and grey line for CF values \geq 25g). RF delivery time is represented according to CF and LI drop
- 471 intervals.



- 473 Figure 3. Details of relationships among the three key parameters: RF delivery time and LI drop according to
- 474 different levels of CF (panel A); RF delivery time and CF according to different degrees of LI drop (panel B) and
- 475 CF and LI drop according to different values of RF delivery time *(panel C)*.



- 484 Figure 4. Details of the distribution of baseline LI (Panel A), ablated tissue impedance (Panel B), RF application
- 485 time (*Panel C*) and CF values (*Panel D*) according to location sites: anterior sites vs posterior sites, LPV sites vs





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Figure 5. Details of the distribution of RF applications, CF, ablated tissue impedance values and RF delivery times according to location sites. This Kiviat chart displays multivariate data with values represented on axes starting from the same point. Each apex of the Kiviat charts represents a location site according with seven distinct sections of right (R) and left (L) pairs of PVs (Anterior superior: R1, L1; Anterior inferior: R2, L2; Inferior: R3, L3; Posterior inferior: R4, L4; Carina: R5, L5; Posterior superior: R6, L6; Superior: R7, L7). Blue, orange and grey dots represent

493 the mean LI drop values, CF values and RF delivery time values according to location sites.





511 Supplementary material

- 512 Supplementary Table 1. Details of the distribution of RF applications, CF, baseline and ablated tissue impedance
- 513 values according to location sites

Location Site			n (%)	Baseline LI, Ω	LI drop, Ω	CF, g	RF application time, sec
	Anterior superior	R1	233 (8.0)	161.1±18	25.4±7	12.5±7	9.2±4
	Anterior inferior	R2	149 (5.1)	153.9±18	23.7±8	13.3±8	9.5±4
	Inferior	R3	186 (6.4)	159.0±21	23.0±7	13.7±9	9.1±4
RPV	Posterior inferior	R4	209 (7.2)	157.0±16	20.3±7	13.3±8	9.0±4
	Carina	R5	334 (11.5)	156.1±18	22.4±8	12.7±7	8.7±4
	Posterior superior	R6	154 (5.3)	155.3±13	19.3±6	13.9±10	9.2±4
	Superior	R7	238 (8.2)	159.0±16	22.8±7	13.0±7	9.0±4
	Anterior superior	L1	219 (7.6)	154.3±16	23.0±8	11.8±7	10.0±5
	Anterior inferior	L2	146 (5.0)	157.7±16	24.3±7	13.1±8	8.1±3
	Inferior	L3	158 (5.5)	157.9±15	24.5±8	13.6±10	7.3±4
LPV	Posterior inferior	L4	196 (6.8)	158.3±15	23.1±6	13.0±7	7.4±4
	Carina	L5	295 (10.2)	156.8±17	22.8±8	13.0±8	8.6±4
	Posterior superior	L6	160 (5.5)	158.7±16	21.8±7	14.1±8	8.6±4
	Superior	L7	218 (7.5)	164.9±18	25.4±7	12.0±6	8.1±4

515 CF=contact force; LI=local impedance; RF=radiofrequency; RPV=right pulmonary vein; LPV=left pulmonary vein.

- 522 Supplementary figure 1. Details of LI drop values according to different values of CF. Although there is a
- 523 significant difference dichotomizing CF values below and above 25 grams ($22.8\pm7\Omega$ at < 25g CF intervals vs
- $24.8\pm7\Omega$ at \geq 25g CF intervals, p<0.0001), LI drops markedly increased from 5 to 25g CF intervals, whereas it
- 525 showed a smooth transition above 25g. No differences were found comparing 20-24g CF interval to both 25-29g and
- \geq 25g CF intervals. Polynomial trendline is displayed in red.



LI drop according to different values of CF

- 536 Supplementary figure 2. Details of the distribution of baseline and ablated tissue impedance values according to
- 537 location sites with seven distinct sections of right (R) and left (L) pairs of PVs. Anterior superior: R1, L1; Anterior
- 538 inferior: R2, L2; Inferior: R3, L3; Posterior inferior: R4, L4; Carina: R5, L5; Posterior superior: R6, L6; Superior:
- 539 R7, L7. The mean baseline LI and ablated tissue impedance values at sites of left pair of PVs are reported in red
- 540 tones, at sites of right pair of PVs are reported in blue tones. In green tones are reported the mean values at all sites.
- 541 Dark color denotes baseline LI, light color denotes ablated tissue impedance.

