Role of catheter location on local impedance measurements and clinical outcome with the new direct sense technology in cardiac ablation procedures

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Abstract

Background: A novel catheter technology (direct sense, DS) enables periprocedural local impedance (LI) measurement for estimation of tissue contact during radiofrequency ablation (RFA) for real-time assessment of lesion generation. This measure reflects specific local myocardial conduction properties in contrast to the established global impedance (GI) using a neutral body electrode. Our study aimed to assess representative LI values for the cardiac chambers, to evaluate LI drop in response to RF delivery and to compare those values to established GI measures in patients undergoing RFA procedures.

Methods and Results: Seventy-three patients undergoing RFA with the DS technology were included. Within the cardiac chambers, baseline LI was significantly different, with the highest values in the left atrium (LA 107.5 ± 14.3 Ω; RV 104.6 ± 12.9 Ω; LV 100.7 ± 11.7 Ω, and RA 100.5 ± 13.4 Ω). Baseline LI was positively correlated to the corresponding LI drop during RF delivery (R² = 0.26, p = 0.01) representing a promising surrogate of lesion generation. The observed mean LI drop (15.6 ± 9.5 Ω) was threefold higher as GI drop (4.9 ± 7.4 Ω), p < 0.01. We evaluated the clinical outcome in a subgroup of patients undergoing DS-guided pulmonary vein isolation, which was comparable regarding arrhythmia recurrence to a conventional ablation cohort (57 % vs 50 %, p = 0.2).

Conclusion: We provide detailed information on LI measures in electrophysiological procedures with significant differences within the cardiac chambers highlighting that RFA-related LI drop can serve as a promising surrogate for real-time assessment of lesion generation. Guiding the electrophysiologist in RFA procedures, this additional information promises to improve safety profile and success rates in the interventional treatment of arrhythmias.

1. Introduction

With expanding indications and increasing safety profile, catheter ablation has established the cornerstone therapy for cardiac arrhythmias [1]. In many invasive electrophysiological interventions there is an established clear procedural endpoint for successful treatment of the clinical arrhythmia, which is directly correlated to long-term outcome (e.g. bidirectional cavo-tricuspid isthmus block in typical atrial flutter (AFlut) or ablation of the slow pathway in AV-nodal reentry tachycardia (AVNRT)). In contrast, the procedural endpoints in atrial fibrillation (AF) and ventricular tachycardia (VT) ablation are not always directly related to the long-term freedom from the arrhythmia (e.g. acute isolation of atrio-pulmonary vein conduction in the treatment of AF). Especially in the field of interventional therapy of AF and ventricular arrhythmias, the role of catheter location on local impedance measurements and clinical outcome with the direct sense technology remains to be elucidated.

Abbreviations: AF, Atrial fibrillation; AFlut, Atrial flutter; AT, Atrial tachycardia; AVNRT, AV nodal reentry tachycardia; CF, Contact force; DS, Direct sense; ECG, Electrocardiogram; FAT, Focal atrial tachycardia; FU, Follow Up; GI, Global generator impedance; LA, Left atrium; LI, Local impedance; LV, Left ventricle; LVEF, Left ventricular ejection fraction; PVC, Premature ventricular complex; PVI, Pulmonary vein isolation; RA, Right atrium; RFA, Radiofrequency application; RFC, Radiofrequency current; RV, Right ventricle; SD, Standard Deviation; VT, Ventricular tachycardia.

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arrhythmias, the long-term clinical outcome might be limited by the difficulty in achieving durable and transmural ablation lesions which seems to be one important variable to improve clinical outcome with respect to arrhythmia recurrence after ablation. A poor or suboptimal catheter tip-to-tissue contact during radiofrequency application (RFA) is believed to reduce clinical efficacy by creating non-transmural lesions.

Therefore, established as well as novel approaches are warranted to monitor acute lesion creation aiming for durable ablation lesions with a high safety profile. The measurement of local impedance (LI) at the catheter tip and the corresponding drop during energy delivery are a highly innovative approach holding promise to improve safety profile with respect to prevention of overheating (coming along with steam pop and increased perforation risk) and clinical outcome by real-time assessment of lesion creation. [3-5] As previous data suggests that near-field impedance measurement is depending on additional co-variables (electrical tissue properties, pre-ablated tissue, intracardiac location) [6-7] it appears crucial to assess the impact of different cardiac locations on LI properties to provide reference values for optimized lesion creation. Prior work [8] showed a difference in impedance measures between the left atrium (LA) and the pulmonary veins (PVs), but did also find lower impedances in the LA and PVs in patients undergoing repeat catheter ablation. Therefore, being able to provide valid reference values for the 4 cardiac chambers this technology holds promise to be able to differentiate between healthy and scarred/diseased myocardium as well as to differentiate between pre-ablated and ablation-naïve myocardium.

2. Objectives

The aim of the present analysis was to determine the range of LI values in the four cardiac chambers in order to provide LI reference values and relate them to established generator impedance (GI) values. Further, we sought to assess the role of LI drop in response to RF delivery to compare those values to the established GI drop measures. Last, we sought to evaluate the outcome with respect to arrhythmia recurrence rates in a selected subgroup of patients undergoing pulmonary vein isolation (PVI) using the new direct sense (DS) technology.

3. Methods

3.1. Study design and patient characteristics

This single-center cohort study was conducted at the University Hospital Essen, Germany, in accordance with the Declaration of Helsinki and its amendments and was approved by the institutional review board of the University of Essen (number 19-8714-BO). Written informed consent was obtained from all study participants. Ablation procedures were performed with the DS catheter systems for different ablation procedures including typical and atypical AFLut, AF, focal atrial tachycardia (FAT), AVNRT, ventricular tachycardia (VT) and premature ventricular complexes (PVCs). Therefore, seventy-three consecutive patients undergoing interventional catheter ablation with the DS system were included in the current study. Baseline patient characteristics and outcome data were extracted from the patients’ medical records and a self-designed encrypted database.

3.2. Work flow of the procedure

Ablation was performed under conscious sedation with midazolam and remifentanil intravenously. Depending on the procedure performed, cardiac access was obtained by three venous sheaths (in case of left ventricular procedures via one additional 9 French sheath in the left common femoral artery). After placing a coronary sinus catheter (Inquiry™, St. Jude Medical, St. Paul, MN, USA) the ablation catheter (IntellaNav MiFi™ OI) was advanced in the intended cardiac chamber (right atrium (RA), right ventricle (RV), left atrium (LA), and left ventricle (LV)). In case of LA procedures, access was obtained via a transseptal puncture with a steerable sheath (Agilis™ Steerable Intro- ducer, St. Jude Medical, St. Paul, MN, USA) with advancing the ablation catheter passively through the transseptal orifice into the LA.

3.3. The DS system

Main element of the DS system is an open-irrigated single-tip mapping and ablating catheter as previously described. [7] Fig. 1A depicts the LI generation by the ablation catheter with the impedance information embedded in the 3D electroanatomical map. In brief, the catheter has 3 incorporated mini electrodes, enabling high-density local field signal detection, each with 2 mm distance to the tip of the catheter and a diameter of 0.8 mm. A local potential field is generated by non-stimulatory alternating current (5.0 μA at 14.5 kHz) between the tip electrode and the proximal ring. Within the 3 miniature electrodes and the distal ring, undulations of the electric field (expressed in voltage) by adjacent cardiac structures can be detected (Fig. 1B and C). By dividing voltage measurements through the stimulatory current the LI values are obtained. [7] The LI system is incorporated in a 3-dimensional navigation system for catheter and anatomy visualization (Rhythmia™, Boston Scientific, Marlborough, MA, USA).

3.4. Impedance measurements during the procedure

Local impedance embedded in the 3D system as well as GI (provided and shown on the RF generator (Stockert GmbH, Freiburg, Germany)) were obtained in real-time and were accessible to the treating electrophysiologist throughout the whole procedure. Global and LI values were recorded simultaneously during the ablation procedure and documented in a pre-defined spreadsheet. Only RF deliveries > 10 s were assessed for the present study. Initially, blood pool impedance representing the non-tissue impedance was assessed in the intended cardiac chamber, placing the ablation catheter in the cavity without contact to the myocardial wall. Missing wall contact was confirmed visually by use of the 3D-map, fluoroscopy and intracardiac electrograms. For every RF application, initial baseline GI and LI were documented, proximity to the myocardial wall was confirmed visually by the 3D system, tactile feedback or by fluoroscopy, if required. Radiofrequency deliveries were performed until the endpoint of the ablation was achieved. At the end of each RF application GI and LI were documented in order to assess the impedance drop as a change (∆) of LI as well as ∆GI compared to baseline values. An empiric baseline LI > 100 Ohm was aimed for before RF delivery to establish sufficient wall contact with the catheter [8] with aiming for a minimum impedance drop of > 10–15 Ohm. For consistency reasons enabling later comparison of the individual applications a strict point-by-point ablation was performed without dragging with a maximum duration of 60 s per RF delivery.

3.5. Mapping and ablation protocol

The preferred ablation strategy depended on the target-arrhythmia. Briefly, in case of RA arrhythmias the ablation catheter was used to generate a 3D electroanatomic map of the RA with energy deliveries at the identified target until the endpoint of the respective ablation procedure had been achieved. In case of paroxysmal or persistent AF, sole PVI or re-isolation in the case of re-do procedures was performed. If a patient was referred for VT ablation, substrate modification was performed after detailed high-density mapping of the LV with a dedicated mapping catheter (Intellamap Orion™, Boston Scientific, Marlborough, MA, USA) followed by RF deliveries targeting fractionated and late potentials. In case of arrhythmias accessible to activation mapping (typical/atypical AFLut, FAT, VT), a 3D electroanatomical local activation map was performed guiding the ablation procedure. Each RFA was applied for a maximum of 60 s with a minimum target drop of > 10–15
Ohm, in a temperature-controlled mode with an irrigation rate of 17–30 mL/min. The only deviation from the maximum duration of 60 s per RFA was performed when the energy delivery had to be stopped prematurely due to a excessive local impedance drop (>30–35 Ohm) for safety concerns. A maximum of 30 W (W) for atrial and 50 W for ventricular ablations with a temperature limit of 45 °C was applied to the tissue.

3.6. Study endpoints and clinical follow-up in the PVI subgroup

Patients undergoing LI-guided first-do PVIs with the DS catheter system for AF treatment were followed in our outpatient clinic. A historic cohort which had undergone PVI (first-do procedure) with an open-irrigated 3.5 mm single tip catheter (SurroundFlow™, Biosense Webster, Inc., Baldwin Park, CA, USA) or Therapy Cool Flex™ (St. Jude Medical, St. Paul, MN, USA) between 05/2009–03/2014 served as control group, these procedures were guided by the CARTO-3 (Biosense Webster, Inc., Baldwin Park, CA, USA) or the Ensite NavX (St. Jude Medical, Inc., St. Paul, MN) electro-anatomical navigation system. These patients had been matched for age, sex and type of AF in order to adjust for these three main characteristics. The procedural endpoint in the DS as well as in the control group was complete electrical isolation of all PVs with entrance- and exit block, which was confirmed by the use of the diagnostic mapping catheter (DS group: IntellamapOrion™, Boston Scientific, Marlborough, MA, USA; control group: cicular mapping catheter). In the control group, RFA was performed for a maximum duration of 60 s aiming for a significant decrease of the local signal whereas ablation in the DS group was LI-guided, again for a max. duration of 60 s with a target LI drop of >10–15 Ohm.

3.7. Statistical analysis

Data are presented as mean ± standard deviation unless otherwise indicated. Binary-coded and categorical data were described as counts and relative frequencies for group comparisons and analysis of the different anatomical locations. The non-parametric Kruskall-Wallis test (one-way ANOVA) ranking the scores for the whole sample and then the mean rank for each group was performed. Dunn’s post hoc pairwise tests were carried out for the different pairs of groups and adjusted using the
Bonferroni correction. Linear regression analysis was calculated to determine the relationship between LI and GI as well as Δ LI and Δ GI. A statistical significance was defined as a p-value < 0.05, with a 95% confidence interval. Survival curves censored to 365 days were plotted using the Kaplan-Meier estimation, with differences evaluated by log-rank testing. Statistics were calculated using SPSS Statistics (Version 26.0; SPSS Institute, Chicago, IL, USA).

4. Results

4.1. Patient characteristics

In the overall cohort (n = 73 patients) the mean age was 62 ± 8 years, with 42/73 (58%) male patients. The baseline characteristics for the overall cohort and stratified for patients depending on the cardiac chamber where the ablation has been performed are provided in Table 1. With respect to differences between the different groups, we observed a significantly enlarged LA diameter in the LA ablation group (43.2 ± 25 vs 39.1 ± 24 mm in the overall cohort, p < 0.05). Regarding the sub-analysis for the PVI cohort, which has been compared to a historic control, the baseline characteristics of the two groups were comparable except for left ventricular ejection fraction (LVEF) which was slightly lower in the DS cohort (online supplement, table S1).

4.2. Procedural data

With respect to the ablation location, n = 39 ablations were performed in the LA, of those n = 34 for AF and n = 5 for atrial flutter, respectively. Right atrial procedures (n = 25) comprised interventions for AVNRT (n = 8), FAT (n = 3) and typical AF (n = 14). Left ventricular procedures comprised VT ablations only (n = 5), while all RV procedures (n = 4) were performed for treatment of PVCs originating in the RV outflow tract. In the LA, LV, RA and RV the mean number of RFA was 31 ± 18 (total n = 1353), 24 ± 13 (total n = 77), 17 ± 10 (total n = 390) and 11 ± 4 (total n = 44), respectively. Within a total of 1864 RF applications, we documented 1213/1864 (65.1%) RFA with a local baseline impedance before RF delivery of greater or equal 100 Ohm. In this subgroup of PVI first-do procedures (n = 32), all PVs (n = 128) could acutely be isolated (100% acute success rate, with a mean of 43 RFA per procedure).

4.3. Safety outcome

In total, four groin hematomas (n = 2 in PVI group and n = 2 in the VT ablation group) were observed, all without the need for surgical or interventional treatment. No hemodynamic relevant pericardial effusion/tamponade or cerebrovascular complications occurred in the evaluated procedures.

4.4. Specific impedance measurements

4.4.1. Blood pool

The mean local blood pool impedance value for the overall cohort was 97.1 Ω ± 13.8 Ω (LA 97.2 Ω ± 15.2 Ω; LV 94.3 Ω ± 6.2 Ω; RA 96.0 Ω ± 8.5 Ω and RV 109.7 Ω ± 10.0 Ω; p = 0.91 for intergroup comparison), with no significant difference of blood pool impedance between the four assessed chambers (Fig. 2).

Baseline tissue impedance values and subsequent impedance drop within the 4 cardiac chambers.

Chamber-specific comparison between LI and GI showed consistently higher values for GI when compared to the corresponding LI values in all chambers (overall GI 150.3 ± 19 Ω vs LI 105.6 ± 14 Ω; p < 0.01). The difference between baseline LI and GI ranged from 43.4 Ω to 63.4 Ω, with the largest difference obtained between LI and GI in the RV (Fig. 3A).

In a next step we specifically compared the LI values within the different chambers (Fig. 3B) finding that baseline chamber-specific LI values were significantly different (p < 0.01 for intergroup comparison). We observed differences in baseline LI values between the LA vs LV (107.5 Ω ± 14.3 Ω vs 100.7 Ω ± 11.7 Ω, p < 0.01), LA vs RA (107.5 Ω ± 14.3 Ω vs 100.5 Ω ± 13.4 Ω, p < 0.01) and RA vs RV (100.5 Ω ± 13.4 Ω vs 104.6 Ω ± 12.9 Ω, p = 0.04), respectively. The highest absolute LI baseline values were observed in the LA and RV.

4.5. Impedance drop

Analysis of the subsequent impedance drop in the overall cohort after RFA revealed that mean LI drop of 15.6 ± 9.5 Ω was threefold higher covering a wider range of impedance drop values as compared to overall mean GI drop of 4.9 Ω ± 7.4 Ω (p < 0.01). When stratifying the impedance drop for the four assessed chambers, the observed difference was consistent for all chambers (p < 0.01), with a range of 12.2–17.7 Ω and 3.5–6.6 Ω for LI and GI drop, respectively. The highest proportional difference between LI and GI drop was observed in the RV (see Fig. 3C).

4.6. Correlation of local and global impedance and impedance drop

Linear regression analysis revealed that baseline LI was positively correlated to the LI drop (R² = 0.26, p = 0.01) in the overall cohort, while baseline GI was not significantly associated to GI drop in the overall cohort. Fig. 4 depicts the correlation of LI and GI with the corresponding impedance drop. Looking at the correlation of baseline LI and the corresponding LI drop in the four chambers, we observed the best correlation within the RV, with a R² of 0.31 (p < 0.01).

4.7. Clinical outcome of LI-guided PVI in AF patients

Out of the 39 LA procedures, the outcome of 32 patients who had undergone a first PVI procedure for symptomatic AF treatment was compared to a matched historic PVI cohort (n = 32) as described above. With respect to freedom from arrhythmia recurrence no significant difference could be observed in the LI-guided PVI group when compared to the historic PVI control group. One-year recurrence rates were 43% in the DS and 50% in the control group, which is illustrated in the Kaplan-Meier analysis in Fig. 5.

5. Discussion

This study aimed to specifically determine clinical reference values for LI in cardiac ablation procedures for baseline impedance as well as...
for impedance drop in response to RF ablation, serving as a potential surrogate for lesion formation. We measured LI values using a novel nearfield impedance technique enabled by a novel ablation catheter for the four cardiac chambers and compared those parameters to established values of GI. We found that baseline measures for LI differed between the four chambers, with the highest baseline values in the LA. Further, we confirmed that LI values were significantly lower compared to GI, going along with significantly higher values for LI compared to GI drop during RF delivery. Last, baseline LI, not GI was significantly correlated to the corresponding impedance drop, suggesting LI being a more specific surrogate for catheter-tissue coupling and subsequent lesion generation in RF ablations.

5.1. Differences in baseline LI measurements

Local impedance values measured in the blood without contact to myocardial tissue were comparable between the four cardiac chambers and go along with reported values from literature. [9] In this study we provided baseline values for LI measurements before RF-energy delivery for all four cardiac chambers, showing that baseline LI values were significantly different within the four cardiac chambers prior RF ablation. One hypothesis was that the different size and/or structure of the assessed location led to the deviation of baseline LI within the four cardiac chambers as it is for example established for GI measures being higher in smaller cavities. This has already been shown for the coronary sinus, where the electrode-catheter interface is fully wrapped with tissue rather than blood. [10] As our study revealed highest baseline LI values in the LA and RV, one underlying reason could be the distinct wall contact in the four chambers immediately before RF delivery. We are not able to provide information on local wall contact during the LI measurements as the used catheter was not capable of simultaneous real-time CF assessment. Nevertheless, pre-clinical experimental data suggest that local CF and LI show a good correlation pointing at the impact of tissue contact on dynamic baseline LI. [11] Preclinical findings that tissue thickness is not correlated to baseline LI go along with our data of the highest LA values in the (thin) LA and RV outflow tract. [11] The differences in myocardial tissue in the four chambers play an important role in the varying LI values, especially the status of the myocardium (healthy myocardium with higher voltage values vs scarred myocardium) has been shown to be a significant indicator of baseline LI [9] which can be suggested to be due to the lower resistance of fibrotic tissue compared to healthy myocardium. [6].

This could potentially explain the low baseline LI values in the LV as the detailed analysis of LV ablation patients suggested extensive myocardial remodeling/scarring in these patients (online supplement, table S1).

Taking our results, we confirm differences between regional LI measures in the heart and report on different locations of the maximum LI values (LA, RV) when compared to available literature. [6] This underlines that the impact of clinical co-variates (tissue properties, intrinsic constitution, scar level, regional blood flow) on LI measures is still not finally elucidated. In this context the lack of available CF information seems to be relevant, since observed differences in local LI could also be due to varying contact in different locations. Therefore, the role of LI on tissue characterization will probably require additional CF measures to adjust for potential CF-dependent differences.

5.2. Impedance drop and the potential benefit of LI over GI drop

Detailed assessment of the impedance data demonstrates that absolute LI drop was about 50 % higher compared to the GI drop, with the largest LI difference in the LV (17.7 ± 7.6 Ω) followed by the LA with 16.5 ± 9.3 Ω. Recently published data suggest that the LI drop measured with the DS catheter was about twice as high as the GI drop. [6] In animal studies the magnitude of impedance drop after RFA showed a strong correlation with lesion depth, diameter and volume. [12] Based on our data confirming literature [6–7] it could be hypothesized that LI measurement translates into a better graduation of variation in tissue-catheter coupling before and during RF delivery. [13] This is especially of importance as the delta of LI has been previously shown to be a better predictor of lesion creation than GI. [7] Further, calculation models using LI drop are able to markedly better predict lesion size than models incorporating CF parameters. [7] With respect to the distinct locations within the heart (Fig. 3C) we were able to show that LI drop in the LA was high (16.5 ± 9.3 Ω) according to the highest baseline value of 107.5 ± 14.3 Ω, a finding which goes along with reported literature. [6] Interestingly, we observed the highest LI drop in the LV where baseline LI has been within the two lowest measures (LV and RA). This finding might point at the important issue that not only baseline LI, but also other covariates might influence the magnitude of LI drop. Potential variables are catheter stability during RF application or myocardial blood flow. [4] Baseline GI could not be correlated to the GI drop which

![Fig. 2. Blood pool values for local impedance in the four cardiac chambers, suggesting no significant difference in the intergroup comparison (p = 0.91). LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.](image-url)
is in line with available literature and highlights the potential additive value of LI measurement during RF ablation procedures beyond the established GI assessment. [9].

5.3. Clinical outcome of PVI procedures performed with the DS system

Looking at the acute ablation result within the PVI cohort we were able to isolate all PVs using the DS catheter. Comparing our midterm outcome in the DS cohort to a historic PVI group treated with a conventional single tip catheter, we found comparable results with respect to the primary endpoint “freedom from any arrhythmia recurrence” after 1 year. It is too early to draw the conclusion that the use of DS systems does not translate into better clinical outcome as our studied cohort was small and a learning curve has to be taken into account. This is especially relevant as recently the LOCALIZE trial has demonstrated that LI drop during PVI was able to predict conduction block which is suggested to be relevant for optimizing outcome after PVI. [13] There are several considerations that have to be kept in mind. First, we aimed for a baseline impedance of 100 Ω and for a minimum LI drop of 10 to 15 Ω before stopping the RF delivery. [8] Further controlled studies based on larger clinical data have to show if there is a potential benefit of this novel system with respect to recurrence rates in AF ablations as well as in other ablation procedures. Since the technique of high-power short-duration procedures is emerging in AF treatment, the real-time assessment of lesion formation appears beneficial to monitor efficacy in lesion generation. The technique might increase the safety profile of RF ablations by preventing overheating and consecutive steam pop generation by implementing an upper LI drop limit while RF delivery.

Fig. 3. A. Comparison of baseline local and global baseline impedance, demonstrating significant difference in all four cardiac chambers. B. Local impedance (LI) measures after established tissue contact before RF delivery within the four cardiac chambers with pairwise comparison, with the lowest LI values in the LV and RA. C. Comparison of the local and global impedance drop, suggesting a significant difference in the four assessed chambers, with the highest proportional difference in the RV. Abbreviations as in Fig. 2.
6. Limitations

We describe a small cohort undergoing catheter ablation for heterogeneous cardiac arrhythmias. As we report on impedance values in the four cardiac chambers no other objective measures were assessed to be set in context, like simultaneously acquired CF parameters. Further, electrical properties of the myocardium in the assessed chambers were not assessed, i.e. no correlation of impedance values and voltage measures differentiating between healthy and remodeled myocardium could be performed. Especially the number of patients in the RV and LV group was small, nevertheless this patient group represents a heterogeneous real-life cohort in this pilot study which should serve as basis for conducting future studies on this novel ablation catheter technology.

7. Conclusion

This study assessed chamber-specific impedance properties with respect to the novel DS system measuring LI properties at the catheter tip. Local impedance is distinct from GI measurement with significant differences between the LI and GI values in the four chambers of the heart providing further information regarding chamber-specific impedance properties. Furthermore, LI kinetics seem to reflect a broader spectrum of the ablation-dependent impedance changes. Thereby, a cut-off value limiting the max. LI to 30–35 Ohm appears to increase safety with respect to local thermal damage. This indicates that the LI drop enables a more precise graduation of the effect of RF delivery on the tissue, a feature which has to be evaluated in larger studies, especially with respect to clinical outcome (effectiveness). The outcome analysis of the small PVI cohort guided by the new DS technology showed comparable results with respect to arrhythmia freedom in the context of previous outcome data.

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CRediT authorship contribution statement

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2022.101109.

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