Clinical utility of local impedance monitoring during pulmonary vein isolation

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May 20, 2020

Abstract

Introduction: A novel ablation catheter that can measure local impedance (LI) was recently launched. We aimed to explore target LI measurements at each radiofrequency application (RFA) for creating sufficient ablation lesions during pulmonary vein (PV) isolation. Methods: This prospective study included 15 consecutive patients scheduled to undergo an initial ablation of paroxysmal atrial fibrillation (AF). Circumferential ablation around both ipsilateral PVs was performed using a 4-mm irrigated ablation catheter with an LI sensor. Point-by-point ablation was used with a 4-mm inter-ablation-point distance. Operators were blinded to LI measurements during the procedure. Creation of sufficient ablation lesions was assessed by the absence of a conduction gap. Results: After first-pass encircling PV antrum ablation, left atrium to PV conduction remained in 12 of 30 (40%) ipsilateral PVs. Mapping using the mini-basket catheter identified 48 ablation points through which the propagation wave entered the PV. At ablation points with a gap, the LI drop during RFA was half that at points without a gap (12 $\pm$ 7 vs. 23 $\pm$ 12 ohm, $p<0.001$). The GI drop did not differ between ablation points with and without a gap (12 $\pm$ 7 vs. 14 $\pm$ 10 ohm, $p=0.10$). An LI drop of 15 ohm predicted sufficient lesion formation without a gap with a sensitivity of 0.71, specificity of 0.81, and predictive accuracy of 0.75. Conclusion: A target LI drop of 15 ohm at each RFA with a 4-mm distance between adjacent ablation points may facilitate creation of sufficient ablation lesions during PV isolation

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Short title: Local impedance monitoring during PVI

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Total word count:

Financial support: None

Conflict of interest: None

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Structured abstract

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Methods: This prospective study included 15 consecutive patients scheduled to undergo an initial ablation of paroxysmal atrial fibrillation (AF). Circumferential ablation around both ipsilateral PVs was performed using a 4-mm irrigated ablation catheter with an LI sensor. Point-by-point ablation was used with a 4-mm inter-ablation-point distance. Operators were blinded to LI measurements during the procedure. Creation of sufficient ablation lesions was assessed by the absence of a conduction gap.

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Conclusion: A target LI drop of 15 ohm at each RFA with a 4-mm distance between adjacent ablation points may facilitate creation of sufficient ablation lesions during PV isolation.

Key words; Local impedance, Radiofrequency ablation; Atrial fibrillation

Introduction

Pulmonary vein (PV) isolation is an essential procedure in catheter ablation of atrial fibrillation (AF). However, reconnection of left atrium to PV conduction is not rare, and is one of the main causes of AF recurrence after PV isolation.[1] Poor durability of PV isolation arises from insufficient ablation lesions. Multiple factors such as catheter-tissue contact, radiofrequency power, application time, and tissue factors influence radiofrequency ablation lesion formation, making it difficult to estimate the radiofrequency ablation lesion size.

Tissue impedance has been experimentally shown to decrease in heated myocardium.[2] A drop in generator impedance (GI) between the catheter-tip and skin patch during radiofrequency application (RFA) is used as a rough indicator of lesion formation.[3-5] However, the clinical utility of GI is limited because it is a bulk impedance measurement that reflects the electrical properties of not only the near-field myocardium but also other thoracic structures such as skin, lungs, subcutaneous tissue, and musculature.[6]

A novel ablation catheter (IntellaNav MiFi OI^{TM}; Boston Scientific, Marlborough [Cambridge] MA, USA) that can measure local impedance (LI) was recently launched. LI measures near-field impedance, and may be a more specific representation of myocardial impedance. The relationship between LI measurements and ablation lesion formation were previously reported in an experimental model[6] and two clinical studies.[7,8]However, there is little data on the clinical utility of LI monitoring during PV isolation.

The purpose of this study was to explore the clinical utility of LI measurements for estimating ablation lesion formation during PV isolation, and to clarify the target LI measurements at each RFA.

Methods

Patients

This prospective study included 15 consecutive patients scheduled to undergo an initial ablation of paroxysmal AF at Kansai Rosai Hospital from October 2019 to March 2020. Exclusion criteria were age < 20 years and prior cardiac surgery.

This study complied with the Declaration of Helsinki. Written informed consent for the ablation and participation in the study was obtained from all patients, and the protocol was approved by our institutional review board.

Catheter settings and left atrial mapping

Electrophysiological studies and catheter ablation were performed under general anesthesia using intravenous propofol at 5–10 ml as a bolus injection followed by 0.5 ml/kg/hr as a maintenance dose. A ventilator (HAMILTON C-1®; Hamilton Medical, Bonaduz, Switzerland) in synchronized intermittent mandatory ventilation mode with a respiratory rate of 12 breaths per min and tidal volume of 400 or 500 ml was used together with a supraglottic airway device (i-gel®; Intersurgical Limited, Berkshire, UK). An esophageal temperature probe (SensiTherm®; Abbott, St. Paul MN, USA) was inserted to monitor esophageal temperature during RFA at the left atrial posterior wall.

A 6-Fr decapolar electrode was inserted into the coronary sinus, while a second 6-Fr decapolar electrode was placed in the right atrium. Following a transseptal puncture at the fossa ovalis, one steerable long sheath (Agilis® M curve; Abbott) was introduced into the LA using a transseptal puncture technique.

Mapping in the left atrium and 4 PVs was then performed using RHYTHMIA® (Boston Scientific) under right atrial pacing rhythm (100 ppm) using the small basket catheter (Orion®; Boston Scientific) via the steerable long sheath. Criteria used for beat acceptance included stable cycle length, stable timing difference between two reference electrodes placed in the coronary sinus, respiratory gating, stable catheter location, and stable catheter signal compared to adjacent points.

Ablation procedure

A 4-mm-tip open-irrigated ablation catheter with three 1-mm minielectodes located laterally at the tip (IntellaNav MiFi OI®; Boston Scientific) was used. The catheter can measure real-time LI calculated from a local electric field generated at the tip of the ablation catheter. During the procedure, the operators were blinded to LI measurements.

Circumferential ablation around an ipsilateral PV was performed using a point-by-point technique. Radiofrequency energy was applied for > 20 sec at each site using a maximum temperature of 42 °C and maximum power of 35 W. The irrigation rate was 17 mL/min. RFA was stopped when the catheter moved, esophageal temperature rose to 40 °C, or bradycardia was induced. The ablation point was marked with a 4-mm-diameter point tag. After completing a >20-sec RFA, the catheter tip was moved to the next ablation point, located approximately 4.0 mm from the adjacent point (Figure 1).

After completing circumferential PV ablation, left and right ipsilateral PV were mapped using the basket catheter, and electrical conduction inside the ipsilateral PV was analyzed. If left atrium to PV conduction was present, RFAs targeting conduction gaps on the circumferential line were delivered until left atrium to PV conduction was eliminated.[9] Creation of sufficient ablation lesions was assessed by the absence of a conduction gap.

LI measurements

An electric field was created by altering the current (5.0 micro-A at 14.5 KHz) between each tip of the three miniature electrodes and the proximal ring of the ablation catheter (Figure 2). Voltage was measured between the miniature electrodes and the distal ring. Impedance was calculated by dividing the voltage by the stimulatory current. Among three impedance measurements from the three miniature electrodes, the highest impedance was used as the LI. LI measurements were defined as follows: pre-RFA LI, LI just before the start of RFA; post-RFA LI, LI just after the end of RFA; LI drop, post-RFA LI – pre-RFA LI.

During the procedure, the operator was blinded to LI information. Dedicated medical engineers recorded the pre- and post-RFA LI and GI at each ablation point.

Statistical analysis

Continuous data are expressed as mean ± standard deviation or median (interquartile range). Categorical data are presented as absolute values and percentages. Tests for significance were conducted using the unpaired t -test for continuous variables, and the chi-squared test or Fisher's exact test for categorical variables. To predict sufficient ablation lesion formation, receiver-operating characteristic curves were constructed for different impedance parameter cut-off values. The area under each curve and 95% confidence interval were determined using the bootstrap method. Pearson's correlation coefficient analysis was performed to assess correlations between continuous variables. All analyses were performed using SPSS version 22.0 software (SPSS, Inc., Chicago IL, USA).

Results

Patient characteristics

Patient characteristics among 15 paroxysmal AF patients are shown in Table 1. They had slight left atrial remodeling (small left atrium) and few comorbidities (low CHA_2DS_2VASc score). No patients had significant anatomical abnormalities with regard to the left atrium and 4 PVs.

PV isolation

After first-pass encircling PV antrum ablation, electrical conduction between the left atrium and PV remained in 12 of 30 (40%) ipsilateral PVs. Mapping using the mini-basket catheter identified 48 ablation points through which the propagation wave entered the PV (ablation points with a gap). At the remaining 742 ablation points, the propagation wave was blocked along the PV isolation line (ablation points without a gap). Additional ablation targeting ablation points with a gap successfully eliminated conduction between the left atrium and PV. In the end, PV isolation was achieved without complications in any patients.

RFA was unexpectedly suspended at 84 of 790 (11%) ablation points due to a rise in esophageal temperature (42 points), bradycardia (4 points), or catheter dislodgement (38 points). RFA duration was significantly shorter at points with unexpected suspension than those without (14 ± 5 vs. 28 ± 8 sec, $p<0.0001$). However, the presence of gaps was comparable between the two groups (5% vs. 6%, $p=0.51$).

Impedance measurements

LI of the ablation catheter floating in the left atrial blood pool was 93 ± 11 ohm. Pre- and post-RFA LI values are shown in Figure 3. Pre-RFA LI was significantly lower at ablation points with than without a gap (106 ± 13 vs. 116 ± 17 ohm, $p<0.0001$; Figure 3A). Regional analyses revealed higher pre-RFA LI only at non-anterior regions. There was no difference in post-RFA LI between ablation points with and without a gap (94 ± 12 vs. 93 ± 12, $p=0.61$; Figure 3B). At ablation points with a gap, the LI drop during RFA was half that at points without a gap, irrespective of whether or not measurements were conducted at anterior walls (12 ± 7 vs. 23 ± 12 ohm, $p<0.001$; Figure 3C). A representative case is shown in Figure 1.

With regard to GI, the degree of impedance drop was significantly smaller using GI than LI at ablation points without a gap (14 ± 10 vs. 23 ± 11, $p<0.0001$). In contrast, there was no difference in impedance drop at ablation points with a gap (12 ± 7 vs. 12 ± 7, $p=0.87$). In addition, LI and GI were poorly correlated (correlation coefficient of pre-RFA measurements=0.40, $p<0.0001$; post-RFA=0.51, $p<0.0001$; impedance drop during RFA=0.12, $p<0.01$).

Impedance measurements as predictors of ablation lesion formation without a gap

Predictive values of impedance measurements for ablation lesion formation without a gap are compared in Figure 4. Receiver-operator characteristics curve analyses revealed that an LI drop during RFA best predicted lesion formation without a gap. A cut-off value of [?]15 ohm predicted ablation lesion formation without a gap with a sensitivity of 0.71, specificity of 0.81, and predictive accuracy of 0.75.

Ablation points with an LI drop <15 ohm had shorter RFA time (25 +- 9 vs. 27 +- 9 sec, p=0.020), higher frequency of unexpected RFA suspension (15% vs. 10%, p=0.046), and lower pre-RFA LI (104 +- 12 vs. 119 +- 15 ohm) than those with an LI drop [?]15 ohm.

Discussion

This prospective observational study aimed to explore target LI measurements at each RFA for creating sufficient ablation lesions during PV isolation. The main findings were: (1) a large LI drop ([?]15 ohm) best predicted the absence of a conduction gap; (2) ablation points with an LI drop <15 ohm demonstrated short RFA time, low pre-RFA LI, and unexpected RFA suspension; (3) an LI drop was more prominent than an GI drop at ablation points without a gap; (4) GI was not correlated with LI. To our knowledge, this is the first study to report a target LI drop at each RFA for creating sufficient ablation lesions assessed by the absence of a conduction gap during PV isolation.

Estimation of radiofrequency ablation lesion formation

Radiofrequency ablation lesion formation is dependent on tissue exposure to heat generated by radiofrequency current. Since the early use of radiofrequency ablation, tissue temperature has been indirectly measured using a thermostat located at the catheter tip.[10]However, myocardial surface temperature does not correctly reflect intramural heating, and fails to estimate lesion size.[11]

Instead, GI has been measured using the radiofrequency energy generated during ablation.[3-5] However, GI is not commonly recognized as a marker of sufficient ablation lesion formation. The problem with GI is that it is influenced by the electrical properties of not only the myocardium but also skin, subcutaneous tissue, lungs and other structures in the mediastinum and breast wall, making it a bulk measurement. Conversely, LI measurement is based on the near electric field generated at the catheter tip, and is therefore theoretically more specific to the near-field myocardium beneath the catheter than GI. The present study and a prior study consistently demonstrated a poor correlation between GI and LI, and a larger impedance drop during RFA in LI than in GI at ablation points without gaps.[8] These clinical data also suggest that LI represents near-field electrical properties, and support the hypothesis that LI is superior for impedance monitoring compared with GI during radiofrequency ablation.

Efficacy of LI monitoring for sufficient ablation lesion formation during PV isolation

The present study showed that ablation points with a gap had a significantly smaller LI drop. In addition, a smaller LI drop most effectively predicted the presence of a conduction gap among impedance parameters. Radiofrequency ablation lesion formation is dependent on the temperature of the tissue heated by radiofrequency current,[12] and the myocardial impedance drop during RFA is explained by increased ion movement as a result of heat-promoted ion channel activity on the myocardial cell membrane.[13] Therefore, an LI drop specifically represents a myocardial impedance drop due to tissue heating, and can thereby act as an intramural thermometer. An LI drop is thus expected to provide accurate information on thermal lesion formation.

The association between a conduction gap and low pre-RFA LI may have been observed because the low pre-RFA LI acted as an indicator of catheter-tip contact with the myocardium, given that LI is a synthesized impedance of catheter-myocardium and catheter-blood impedance. LI has previously been reported to correlate with the proximity and contact area between the catheter tip and myocardium.[6]

Post-RFA LI was not different between ablation points with and without a gap, although post-RFA LI may reflect myocardial heating at the end of RFA. The problem with impedance measurements at specific time points is that they are highly dependent on the baseline blood pool and myocardial electrical properties, which differ considerably among individuals. Prior studies reported that the LI of a catheter tip floating in the left atrial blood pool varies from 80 to 120 ohm,[8] and myocardial properties such as the proportion of fibrotic tissue influence LI.[8,14] Therefore, it would be difficult to identify a specific post-RFA LI cut-off value for predicting sufficient lesion formation.

Clinical implication and future perspectives

The main clinical implication of this study is the recommendation of a target LI drop of 15 ohm at each RFA with a 4-mm distance between adjacent ablation points for impedance-guided PV isolation. Factors associated with an LI drop of <15 ohm in this operator-blinded study were short RFA time, low pre-RFA LI, and unexpected RFA suspension due to a rise in esophageal temperature and catheter dislodgement. These data suggest that insufficient catheter stability, catheter contact with tissue and RFA time contribute to an insufficient LI drop. Robust catheter-tissue contact using a contact-force-sensing catheter and prolongation of RFA time until achievement of an LI drop of [?]15 ohm may overcome the issue of insufficient ablation lesion formation. Multifaceted evaluation such as that using pre-existing lesion formation indexes based on contact force is expected to contribute to the creation of optimal lesions by radiofrequency ablation. [15, 16]

In addition, to extend the potential benefits of impedance monitoring to improving the safety of the ablation procedure, future studies should clarify the LI predictor of steam pop. Furthermore, identification of target LI drop values for optimal lesion formation is needed for a variety of arrhythmias.

Limitations

Several limitations of this study warrant mention. First, while operators attempted to maintain a 4-mm distance between ablation points, the actual distances were variable. Unevenness in the distribution of ablation points may influence conductivity along the linear ablation line irrespective of ablation lesion formation at each point. Second, although LI measurement is significantly influenced by catheter orientation in relation to the myocardial surface, this study did not consider this issue. Third, myocardial thickness should be considered when creating a transmural ablation lesion. Target LI drop values may differ among regions with different myocardial thickness. Although regional analyses were performed to attempt to overcome this issue, the small sample size made it difficult to interpret the results. Fourth, we used the absence of a conduction gap as a surrogate for sufficient lesion formation. However, because electrical connection between the left atrium and PV is derived from prolonged myocardial sleeves extending into PVs, contiguous lesion formation is not necessarily required to achieve PV isolation.[17] As a consequence, ablation points without a gap do not always have transmural lesion formation. Finally, the results of statistical analyses may have been influenced by the relatively small size of the study population.

Conclusion

An LI drop of 15 ohm at each RFA with a 4-mm distance between adjacent ablation points may facilitate creation of sufficient lesions during PV isolation.

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Figure legends

Figure 1. A representative case

(A) Ablation points for ipsilateral encircling PV isolation on a three-dimensionally-constructed computed tomography image. Each point has a 4-mm diameter. Operators attempted to deliver radiofrequency application at 4 mm from adjacent points. (B) Propagation map depicting the conduction gap and LI drop at each point (white numbers in red tags). Ablation points with a gap (yellow arrows) had a small LI drop ($<$15 ohm).

Figure 2. Technology used for LI measurement

IntellaNav MiFi OI^{TM} catheter (A; Boston Scientific) and an image of an electric field generated by the catheter (B). An electric field was created by altering the current (5.0 micro-A at 14.5 KHz) between each tip of the three miniature electrodes and the proximal ring of the ablation catheter. Voltage is measured between the miniature electrode and the distal ring. Impedance was calculated by dividing the voltage by the stimulatory current. Among three impedance measurements from the three miniature electrodes, the highest impedance was used as the LI. Illustrations were provided by Boston Scientific.

A representative graph showing the impedance change with a large impedance drop during RFA (C), and that with a small impedance drop (D).

LI indicates local impedance; RFA, radiofrequency application.

Figure 3. Comparison of impedance parameters between ablation points with and without gaps.

Graphs showing pre-RFA LI (A), post-RFA LI (B), LI drop (C), pre-RFA GI (D), post-RFA GI (E), and GI drop (G) values measured in all cases and at anterior and non-anterior walls. Ablation points with a gap had lower pre-ablation LI, LI drop, and pre-ablation GI. In particular, at ablation points with a gap, the LI drop was nearly half that at points without a gap, irrespective of whether measurements were conducted at anterior or non-anterior walls. +p<0.05 and ++ p<0.005 for comparison between ablation points with and without a gap. LI indicates local impedance; GI, general impedance; RFA, radiofrequency application.

Figure 4. ROC analyses for the prediction of lesion formation without a gap

ROC curves incorporating various impedance parameters revealed that LI drop had the largest area under the curve for prediction of lesion formation without a gap. An LI drop of 15 ohm demonstrated the best predictive value, with a sensitivity of 0.71, specificity of 0.81, and predictive accuracy of 0.75.

ROC indicates receiver-operator curve; Se, sensitivity; Sp, specificity; Ac, predictive accuracy

Table 1. Patient characteristics

Variable	*n=15*
Age, years	62 ± 16
Female, n (%)	9 (29)
Body mass index, kg/m^2	237 ± 5.6
Hypertension, n (%)	4 (40)
Diabetes mellitus, n (%)	2 (20)
Heart failure, n (%)	1 (10)
Stroke, n (%)	1 (10)
Vascular disease, n (%)	0 (0)
CHA2DS2VASc score	2.2 ± 2.0
Left atrial volume, mm	38 ± 5

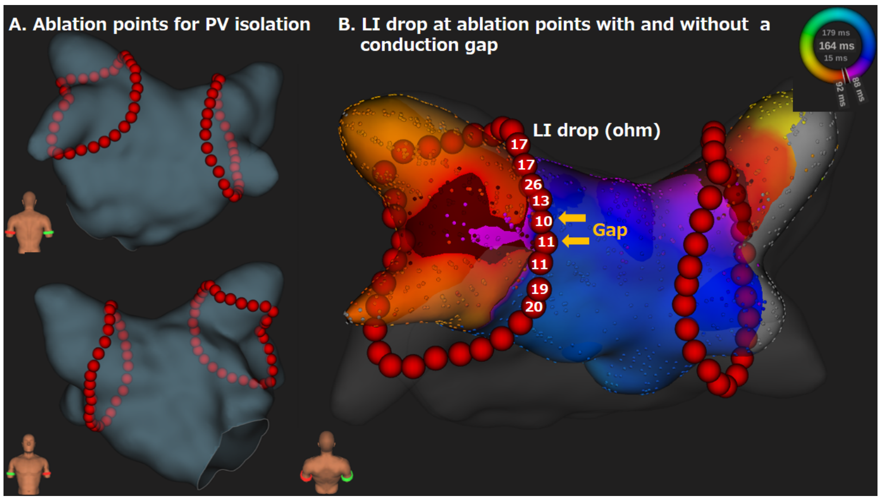
Values indicate mean ± standard deviation unless otherwise indicated

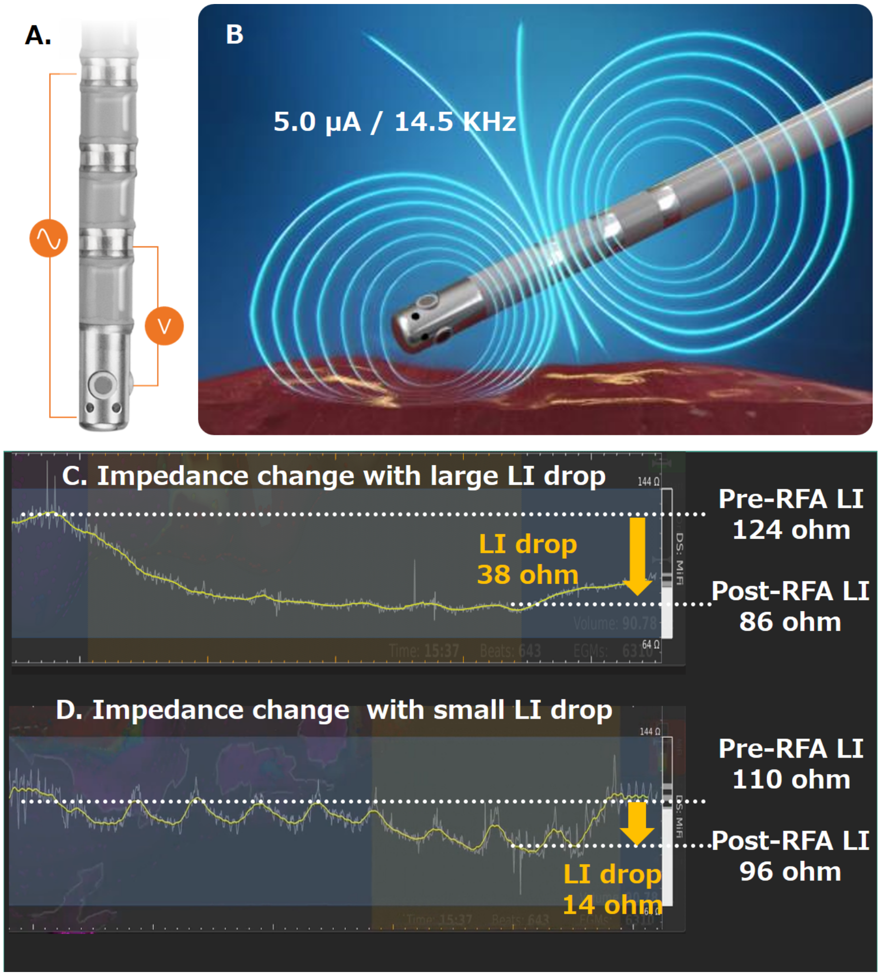
Table 2. Impedance parameters pre- and post-ablation

	Gap	**Gap**	
	With *n=48*	**Without** *n=742*	*p*
Local impedance			
Pre-ablation (absolute value), ohm	106 ± 13	116 ± 17	<0.001
Pre-ablation (difference from blood pool), ohm	17 ± 12	22 ± 16	0.023
Post-ablation (absolute value)	94 ± 12	93 ± 12	0.61
Post-ablation (difference from blood value)	5 ± 10	0 ± 11	<0.001

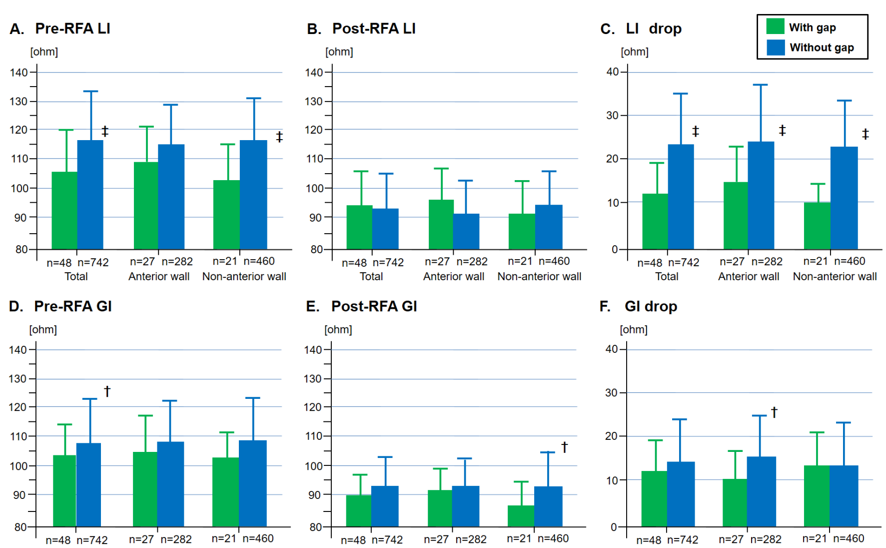
	Gap	**Gap**	
Change	12 ± 7	23 ± 12	<0.001
Generator impedance			
Pre-ablation	104 ± 10	108 ± 15	0.03
Post-ablation	89 ± 8	93 ± 11	0.047
Change	12 ± 7	14 ± 10	0.10

Values indicate mean ± standard deviation unless otherwise indicated

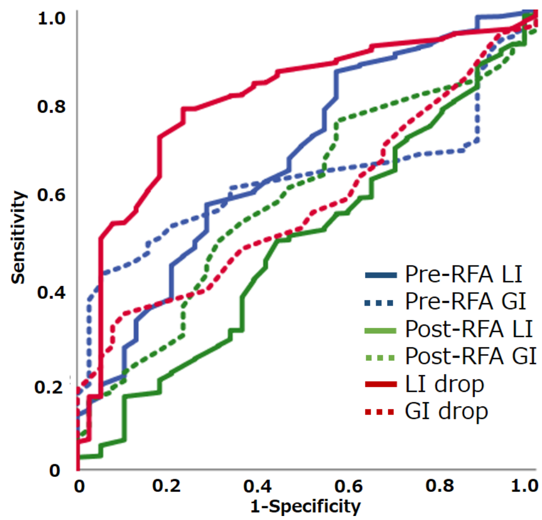




A.
B
5.0 µA / 14.5 KHz
C. Impedance change with large LI drop
Pre-RFA LI 124 ohm
LI drop 38 ohm
Post-RFA LI 86 ohm
D. Impedance change with small LI drop
Pre-RFA LI 110 ohm
Post-RFA LI 96 ohm
LI drop 14 ohm



A. Pre-RFA LI
B. Post-RFA LI
C. LI drop
With gap
Without gap
D. Pre-RFA GI
E. Post-RFA GI
F. GI drop
[ohm]
n=48 n=742 Total
n=27 n=282 Anterior wall
n=21 n=460 Non-anterior wall



Area under the curve

	LI	GI
Pre-RFA	0.68	0.63
Post-RFA	0.50	0.59
Drop	0.80	0.58

Predictive values of various LI drop cut-off levels

LI drop	Se	Sp	Ac
5 ohm	0.96	0.60	0.92
10 ohm	0.87	0.58	0.86
15 ohm	0.71	0.81	0.75
20 ohm	0.51	0.88	0.56
25 ohm	0.37	0.94	0.41