



Performance of the ablation index during pulmonary vein isolation: periprocedural data from a multicenter registry

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Abstract

Purpose Our study aimed to assess the achievement of target ablation index (AI) values and their impact on first-pass pulmonary vein isolation (FPI) as well as to identify FPI predictors.

Methods Atrial fibrillation (AF) ablation was performed according to the local practice, and target AIs were evaluated. The actual AI was calculated as the median value of all ablation points for the anterior and posterior left atrial (LA) walls.

Results A total of 450 patients from nine centers were enrolled. Patients with first-time ablation ($n = 408$) were divided into the FPI and non-FPI groups. In the FPI group, a higher median target AI was reported for both the anterior and posterior LA walls than those in the non-FPI group. A higher actual AI was observed for the anterior LA wall in the FPI group. The actual AI was equal to or higher than the target AI for the posterior, anterior, and both LA walls in 54%, 47%, and 35% ($n = 158$) cases, respectively. Parameters such as hypertension, stroke, ablation power, actual AI value on the anterior wall, target AI values on both LA walls, AI achievement on the posterior wall, carina ablation, and operator experience were all associated with FPI in a univariate logistic regression model; only carina ablation was an independent predictor of FPI.

Conclusions According to our multicenter study, FPI and a target AI were not achieved in a significant proportion of AF ablation procedures. Higher actual and target AI values were associated with FPI, but only carina ablation can independently predict FPI.

Keywords Atrial fibrillation · Catheter ablation · Ablation index · Registry · Pulmonary vein · Radiofrequency ablation

Abbreviations

AF Atrial fibrillation
AI Ablation index
CF Contact force
CI Confidence interval
FPI First-pass isolation
HPSD High-power short duration
LA Left atrium

NOAC Non-vitamin K antagonist oral anticoagulants
PVI Pulmonary vein isolation
RF Radiofrequency

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1 Introduction

Pulmonary vein (PV) source sleeves are well-known focal triggers for atrial fibrillation (AF). Since the first description of PV isolation (PVI) [1, 2], which is a form of cardiac ablation used for AF management, catheter approaches for AF management have evolved substantially, with multiple approaches being developed for PV ablation using different types of catheters and energy sources [3]. One of the most common and widely performed techniques is point-by-point radiofrequency (RF) ablation for PVI using open-irrigated catheters [4]. The success of RF PVI depends on the achievement of a reliable transmural myocardial lesion around the PV ostia. Nontransmural and/or noncontiguous RF lesions are associated with PV re-conduction and arrhythmia recurrence, whereas excessive and deeper ablation may lead to side effects (steam-pops with cardiac perforation) and collateral damage [3, 5].

The need for prediction of RF lesion depth and size has led to research into an integral parameter that may estimate the amount of energy delivered to the tissue and subsequent lesion formation. Among the parameters developed recently, the ablation index (AI; Biosense Webster, CA, USA) has been proposed to standardize each ablation point delivered around PVs. The AI incorporates the RF ablation power, application duration, and contact force (CF). Additionally, automatic ablation point tagging suggests that catheter position stability should be considered during each application.

AI has been evaluated in prospective studies to identify the AI value associated with the least number of PV reconductions [6–8]. However, according to the developer algorithm, when operators begin using the AI module, they first perform several PVI procedures using their regular approach. Subsequently, at least 10 cases with first-pass PVI (FPI) are selected to calculate the median value of the AI, which is then considered the target value for future procedures because PV FPI as a strict acute result endpoint has a potential to be an important predictor of the long-term success rate of AF ablation [9, 10].

In this prospective multicenter observational study, we sought to assess the achievement of individualized target ablation index values and their impact on FPI as well as to identify FPI predictors.

2 Methods

The study presented the intraprocedural results of the Prospective Registry of Atrial Fibrillation Ablation with the Ablation Index Technology (NCT03634592) (Fig. 1).

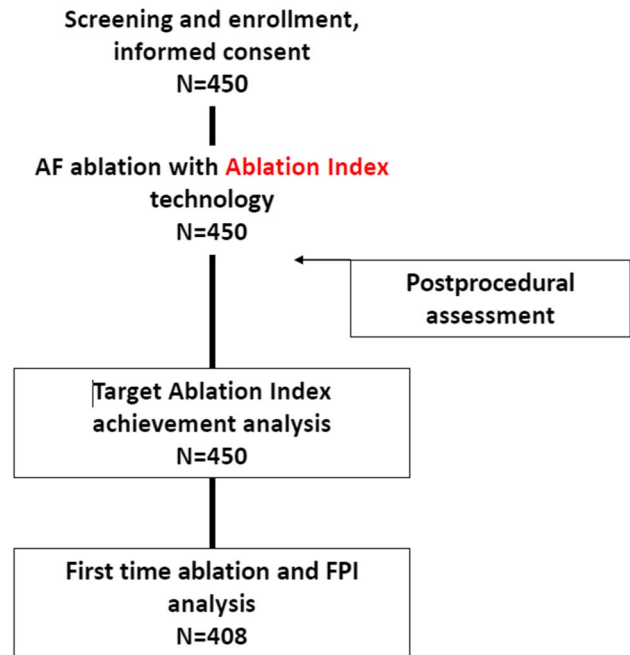


Fig. 1 Study population selection design. FPI, first-pass isolation

The registry was a prospective, multicenter, observational study. The Almazov National Medical Research Center (Saint-Petersburg, Russia) was responsible for data quality control. The study design and rationale have been described in detail previously [11]. Briefly, the inclusion criteria were as follows: age over 18 years, documented paroxysmal or persistent AF refractory to ≥ 1 antiarrhythmic drug (beta-blockers, class I or III), planned AF RF ablation with AI technology, and signed informed consent. The exclusion criteria were as follows: reversible AF causes, left atrial thrombus, indications for myocardial revascularization, New York Heart Association class IV heart failure or recent heart failure decompensation (< 30 days), pregnancy or lactation, and life expectancy < 1 year. AF ablation procedures were performed according to local practice, and ablation techniques, including carina ablation, interlesion distance targeting, and all ablation parameters were left at the discretion of an operator. Importantly, operators were instructed not to perform carina ablation as an additional lesion aiming for PV isolation after failed FPI. Carina ablation was considered a factor for FPI only in cases when an operator performed this ablation routinely and before FPI assessment. The following ablation and VisiTag parameters were recommended: minimum power value of 25 W, maximum 40 W, keep up the distance from the PV ostia to the ablation line of 10 mm, for the location stability maximum distance range was recommended 3 mm, minimum time 3 s, minimum force 3 g.

Demographic and clinical data of the patients were collected during the inclusion visit. Intraprocedural data were obtained as described previously [11], including procedure and fluoroscopy times; RF ablation settings; target, median actual, minimum, and maximum AI values; automatic ablation point acquisition settings (VisiTag module, Biosense Webster, CA, USA); CF values per point; mean and maximum interlesion distances; and first-pass isolation (FPI) achievement. All the obtained data were collated using a specially designed Web-based system (TaskData, UniData, Saint-Petersburg, Russia) that had measures for patient personal data protection.

The study was approved by the Almazov National Medical Research Centre ethics committee; the local ethics committees of all the participating centers approved the required documentation and granted permission to conduct the study. Written informed consent was obtained from all patients. The study was conducted in accordance with the principles stated in the Declaration of Helsinki.

2.1 Definition of outcome measures

As suggested by the manufacturer (Biosense Webster), the target AI was determined based on ten AI- “blinded” paroxysmal atrial fibrillation ablation procedures, with operator-standard ablation parameters (power, contact force, ablation time per point, etc.), with FPI, separately for the anterior and posterior left atrium (LA) walls. These cases were not part of the current study. The target AI was specified for every PVI procedure registered in the study because this parameter could change over time.

A median actual AI was defined post-procedurally; all automatically acquired ablation points around the PVs were sorted by increase in AI value, and the median was considered the actual value. We chose to use a median value in accordance with the original definition of the target AI.

The first AF ablation procedure that incorporated PVI in a patient was considered the first ablation.

FPI was determined as a combination of two indices: (1) bidirectional PVI achieved after first-attempt circular ablation around the PVs without additional applications, as confirmed by registration and stimulation from a diagnostic multipolar circular catheter with cycle length of 500 ms, output of 10 mA, and width length of 2 ms; and (2) persistence of a bidirectional block over a 20-min waiting period.

The primary outcome of the present study was the achievement of FPI in both circles around the right and left PVs. Secondary endpoints included the proportion of patients for whom the actual AI was equivalent to the target AI on the anterior and/or posterior LA walls. Additional outcome measures included procedure and fluoroscopy time, and procedure-related complications (hemopericardium/

tamponade, esophageal injury, acute cerebrovascular accident, and groin hematoma).

2.2 Statistical analysis

All data were extracted using a Web-based system. The data are presented as the mean and standard deviation (symmetric distribution) and as a median and first and third quartiles (asymmetric distribution). Categorical values were presented as absolute and relative values. A comparative analysis of nominal indicators was performed using the chi-square test. For ordinal data, the Mann–Whitney *U*-test was applied. Univariate and multivariate analyses were performed using logistic regression to identify the independent predictors of FPI. A two-sided *p* value of <0.05 was considered statistically significant when assessing the differences in parameters between the groups. The IBM SPSS Statistics 23 software (IBM Corp., Armonk, NY, USA) was used for the statistical analysis.

3 Results

3.1 Study population

From January 2019 to March 2021, 450 patients who underwent AF ablation using the AI module were enrolled in nine centers: the mean age was 61 ± 9 years, with 249 (55%) men, and 330 (73%) participants had paroxysmal AF. The initial enrollment period was planned between January 2019 and December 2020 but was prolonged due to the COVID-19 outbreak, which resulted in a slower inclusion process. The patients' characteristics were as follows: mean body mass index, 30 ± 6 kg/m²; mean left ventricle ejection fraction, $58 \pm 7\%$; mean left atrial diameter, 44 ± 8 mm; 344 patients (76%), hypertension; 48 (10.7%), type 2 diabetes mellitus; 12 (2.7%), chronic obstructive pulmonary disease; 29 (6.4%), history of stroke. The mean number of ineffective antiarrhythmic drugs per patient before ablation was 1.7 ± 0.9 , and 114 (25%) patients had a history of cardioversion (electrical or pharmacological). All patients received periprocedural anticoagulation therapy, and 384 patients (85%) were on non-vitamin K antagonist oral anticoagulants (NOAC).

The index ablation was a first-time AF ablation procedure in 408 of 450 cases (90.7%). Half of the procedures (53%) were performed under general anesthesia, and one-third (32%) were under conscious sedation, and local anesthesia was used in the remaining procedures (15%); and heparin administration was performed before transseptal access in 43% of cases. The mean minimal activated clotting time was 312 ± 21 s.

3.2 Radiofrequency ablation settings and automatic ablation point acquisition

The following VisiTag parameters were used: the median minimal CF for point acquisition was 3 g [3; 4], the median minimal time per point was 4 s [3; 15], and the median catheter stability parameter (characterizing the maximum allowed movement of the ablation catheter during RF ablation) was 3 mm [3; 3]. In 365 (81%) procedures, operators used a 3-mm tag point size, and in 19% of cases, operators preferred a 2-mm ablation point size. The median RF ablation power on the anterior and posterior LA walls was 40 W [35; 45] and 35 W [30; 45], respectively. The median CF on both LA walls was 12 g [10; 15]. The median RF application duration per point was 20 s [13; 25] on the anterior wall and 17 s [12; 23] on the posterior wall.

3.3 First-pass isolation

The primary outcome, FPI, was achieved in 63% of cases (FPI group: 260 out of 408 procedures); it was not achieved in 148 cases (non-FPI group). Baseline characteristics and procedural data differences between groups are summarized in Table 1. In the FPI group, higher target AI values were observed for both the anterior and posterior LA walls (Table 1). The actual AI was significantly higher for the anterior LA (409 units) in the FPI group than in the non-FPI group (405 units) with odds ratio of 1.8 [95% CI 1.2–2.7], while no difference was found in the actual AI values between groups for the posterior LA wall (Fig. 2). We did not find any differences in the VisiTag parameters between the FPI and non-FPI groups: $p=0.88$ for catheter stability, $p=0.57$ for minimum force, and $p=0.64$ for the minimum duration.

Carina ablation between ipsilateral PV was performed empirically before FPI checking on both sides in 48 (11%) cases. In the case of carina ablation, the proportion of FPI was significantly higher ($p=0.002$). Left and right carina ablation was associated with FPI on each side ($p=0.002$ for FPI on the left PV, $p=0.04$ for FPI on the right PV).

In the FPI group, the operators used a higher RF ablation power on the LA anterior wall. A shorter interlesion distance was observed in the non-FPI group. Operators who performed more than 100 ablation procedures a year were more likely to achieve FPI.

High-power short duration (HPSD) ablation at 50 W was performed in 32 out of the 408 cases (7.8%) with first-time AF ablation procedures. The median target AI on the anterior wall was 450 [400; 500], which was significantly higher than that in the standard ablation procedures ($p=0.01$). However, the median actual AI for the HPSD procedures was similar to that of other procedures: 408 [396; 431] vs. 409 [394; 428] ($p=0.8$). The median posterior wall target

AI for HPSD ablation was similar to that of standard procedures (400 [350; 400]), while the median actual AI was significantly lower than that of standard procedures (379 [360; 405] vs. 390 [375; 407]) ($p=0.008$). Bilateral FPI using the HPSD approach was achieved in 10 (31%) procedures. The HPSD approach was not associated with a shortening of the total procedure and fluoroscopy times (103 ± 27 min and 11 ± 8 min vs. 98 ± 41 and 11 ± 8 min, $p=0.7$ and $p=0.9$, respectively).

Comorbidities such as hypertension and a history of stroke were highly prevalent in the non-FPI group. The mean fluoroscopy and total procedure times were higher in the non-FPI group.

All clinical and ablation parameters, including the mean and the maximum interlesion distances and type of anesthesia, were assessed in the correlation matrix and logistic regression model. The correlation matrix revealed no significant associations between the FPI and ablation parameters (r coefficient ranged between -0.2 and -0.06). The univariate logistic regression analysis demonstrated that hypertension ($p=0.002$), the history of stroke ($p=0.02$), ablation power ($p=0.024$) and actual AI ($p=0.006$) values on the anterior wall, target AI value on both LA walls ($p=0.01$, anterior wall; $p=0.001$ for posterior wall), target AI achievement on the posterior wall ($p=0.03$), carina ablation ($p=0.03$), and operator experience ($p=0.032$) were associated with FPI achievement. However, the multivariate regression analysis showed only carina ablation as a predictor independently associated with FPI (Table 2).

3.4 Achievement of the target ablation index

The adherence to the target AI is shown in Table 3. For the anterior LA wall, the median actual AI was not lower than the target AI in 213 (47%) cases and exceeded the target value in 198 cases with a mean delta of 13 ± 10 units. For the posterior LA wall, the median actual AI was not lower than a predefined value in 244 (54%) cases and exceeded this value in 225 procedures, with a mean difference of 19 ± 18 units.

The median actual AI equalizing or exceeding a target AI on both the anterior and posterior LA was achieved in only 158 (35%) procedures.

There was a significant difference between the target and actual AI, with a greater difference between these values for the anterior wall ($\Delta -21$ [95% CI [16; 25], $p=0.0001$) than those for the posterior wall ($\Delta -2$ [95% CI [-1.4; 5], $p=0.3$).

Other VisiTag components were also analyzed. In patients with achieved prespecified (target) AI, the minimum force 3 g was kept in 79% (126/159) of procedures, while the minimum force 3 g was kept in 62% (183/291) of cases in subjects with non-achieved target AI ($p=0.021$). The median maximum stability range differed between subjects

Table 1 Clinical characteristics and procedural data in procedures with FPI and non-FPI ($n=408$) and with achieved and non-achieved target AI ($n=450$)

Parameter	Total ($n=408$)	FPI ($n=260$)	Non-FPI ($n=148$)	p	Total ($n=450$)	Target AI achieved ($n=158$)	Target AI not achieved ($n=292$)	p
Age, y/o	61 ± 9	61 ± 11	61 ± 8	0.9	61 ± 10	61 ± 9	61 ± 11	0.2
Males, n (%)	231 (56%)	145 (55)	86 (58)	0.7	249 (55)	114 (56)	135 (52)	0.6
Paroxysmal AF, n (%)	312 (76%)	200 (77)	112 (75)	0.9	330 (73)	148 (73)	182 (73)	0.4
BMI, kg/m ²	30 ± 6	30 ± 5	31 ± 5	0.1	30 ± 6	30 ± 5	30 ± 6	0.5
LVEF, %	58 ± 7	58 ± 8	59 ± 6	0.2	58 ± 7	59 ± 6.6	58 ± 8	0.1
LAD, mm	43 ± 8	44 ± 8	44 ± 7	0.9	44 ± 8	43 ± 8	44 ± 8	0.3
Hypertension, n (%)	306	127 (68)	179 (85)	0.002	344 (76)	156 (77)	188 (75)	0.5
COPD, n (%)	12	7 (2)	5 (3)	0.7	12 (2)	4 (1.9)	8 (3)	0.4
Stroke, n (%)	25	10 (3.8)	15 (10)	0.02	29 (6.4)	15 (7.4)	14 (5.6)	0.5
Diabetes mellitus, n (%)	44	22 (8.4)	22 (14)	0.1	48 (11)	21 (10)	27 (10.8)	0.8
Cardioversion before ablation, n	93	60	33	0.5	114 (25)	47 (23)	67 (27)	0.001
Number of ineffective AAD, n	1.6 ± 0.4	1.6 ± 0.8	1.7 ± 0.8	0.3	1.7 ± 0.9	1.9 ± 1	1.5 ± 0.8	0.0001
Procedure time, min	102 ± 37	95 ± 43	105 ± 35	0.02	98 ± 41	96 ± 49	100 ± 32	0.001
Fluoro time, min	11 ± 8	10 ± 8	12 ± 8	0.04	11 ± 8	11 ± 7	11 ± 8	0.26
Target ablation index								
Anterior wall	425 [400; 500]	440 [400; 500]	400 [400; 500]	0.005	420 [400; 500]	400 [380; 420]	438 [400; 500]	0.0001
Posterior wall	400 [380; 400]	400 [380; 400]	392 [380; 400]	0.0001	400 [380; 400]	380 [380; 400]	400 [380; 400]	0.0001
Actual ablation index								
Anterior wall	409 [394; 425]	409 [396; 437]	405 [393; 414]	0.004	409 [394; 428]	409 [398; 430]	409 [390; 422]	0.072
Posterior wall	390 [376; 407]	390 [376; 497]	390 [373; 407]	0.6	390 [375; 407]	401 [385; 413]	390 [373; 400]	0.0001
Power, W								
Anterior wall	40 [35; 45]	40 [35; 45]	35 [35; 45]	0.02	40 [35; 45]	35 [32; 47]	40 [35; 45]	0.07
Posterior wall	35 [30; 45]	40 [35; 45]	35 [35; 45]	0.07	35 [30; 45]	35 [30; 47]	40 [32; 45]	0.2
Contact force, g								
Anterior wall	12 [10; 15]	13 [13; 15]	12 [10; 15]	0.8	12 [10; 15]	12 [10; 14]	13 [11; 16]	0.003
Posterior wall	13 [10; 15]	12 [10; 15]	13 [11; 17]	0.06	12 [10; 15]	12 [10; 14]	14 [10; 17]	0.006
Ablation time per point, s								
Anterior wall	20 [14; 25]	20 [13; 24]	21 [16; 26]	0.4	20 [13; 25]	21 [11; 27]	20 [17; 23]	0.9
Posterior wall	17 [13; 23]	16 [12; 22]	19 [13; 23]	0.3	17 [12; 23]	18 [11; 25]	17 [13; 20]	0.3
Interlesion distance, mm								
Mean	4 ± 0.7	4.1 ± 0.8	3.9 ± 0.8	0.02	4.3 ± 0.8	4.2 ± 1.1	4.4 ± 1.7	0.01
Maximum	6.9 ± 0.9	6.8 ± 1.3	7.0 ± 1.5	0.1	7.1 ± 2	7.1 ± 1.7	7.1 ± 3	0.5
Procedures performed by experienced operators, n (%) (≥ 100 AF ablation per year)	352 (86)	229 (88)	123 (83)	0.03	391 (86)	128 (81)	265 (91)	0.01

AAD, antiarrhythmic drug; AF, atrial fibrillation; BMI, body mass index; COPD, chronic obstructive pulmonary disease; LAD, left atrium diameter; LVEF, left ventricle ejection fraction

with achieved and non-achieved target AI ($p=0.007$). In the latter subgroup, a wide range of stability values (from 2 to 7 mm) was observed. The minimum stability time did not differ between those sub-groups (4 [3; 15] vs. 3 [3; 15] s, $p=0.249$). The ablation tag point sizes were 2 or 3 mm and

were not different between patients with achieved and non-achieved target AI ($p=0.52$).

In general, there was no meaningful difference in baseline demographic and comorbidity characteristics between patients for whom the target AI was achieved and those for

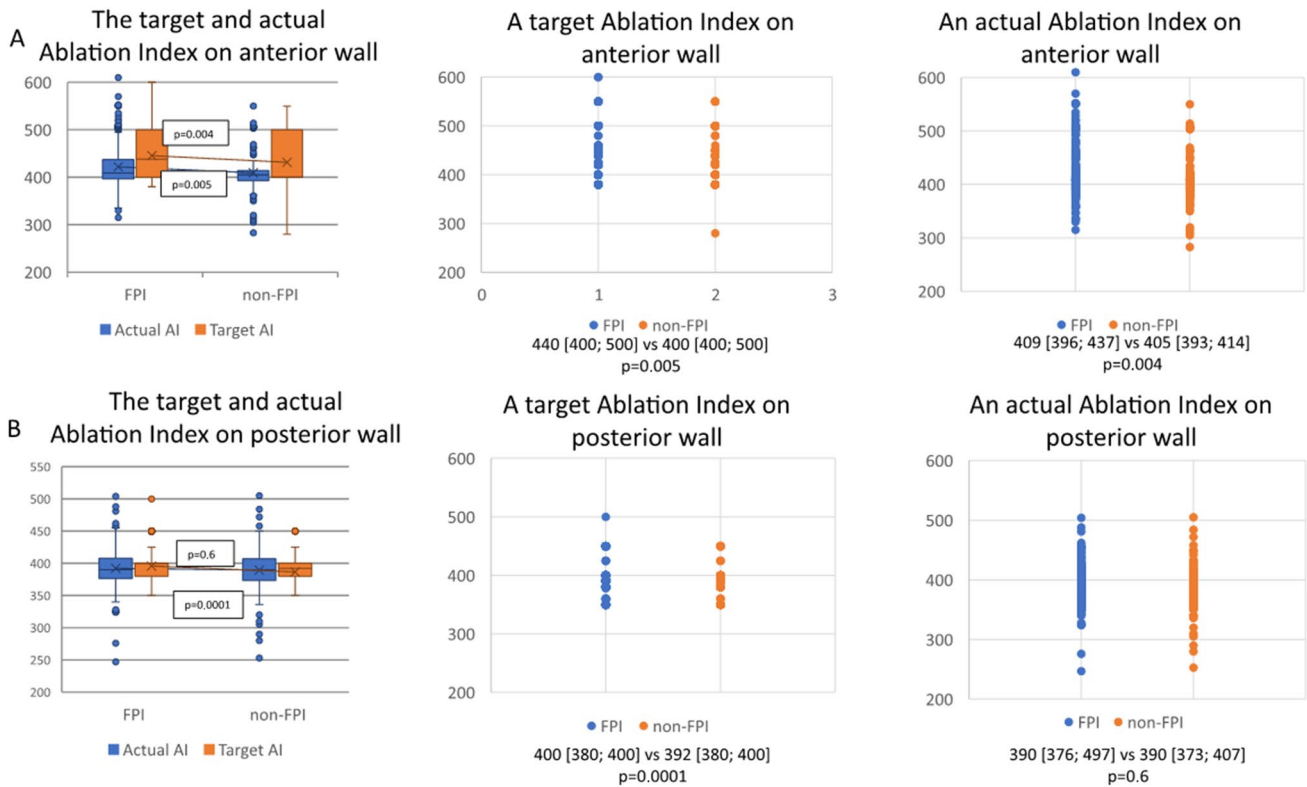


Fig. 2 Dot plots representing the actual and target ablation index values on the anterior and posterior left atrial walls. Panel **A** represents the relationship between the target and actual ablation index and FPI achievement on the anterior wall. Panel **B** represents the relationship between the target and actual ablation index and FPI achievement on the posterior wall. FPI, first-pass isolation

Table 2 Univariate and multivariate analyses for predictors of first-pass isolation

Parameter	Univariate analysis		Multivariate analysis			
	OR	95% confidence interval	p	OR	95% confidence interval	p
Hypertension	0.418	(95% CI 0.239–0.731)	0.002	0.45	(95% CI 0.964–5.122)	0.06
Stroke	0.373	(95% CI 0.163–0.854)	0.02	0.294	(95% CI 0.796–14.543)	0.098
Power on anterior wall	0.963	(95% CI 0.931–0.995)	0.024	0.998	(95% CI 0.941–1.058)	0.943
Actual AI on anterior wall	0.993	(95% CI 0.988–0.998)	0.006	0.996	(95% CI 0.987–1.004)	0.318
Target AI on anterior wall	0.995	(95% CI 0.991–0.999)	0.01	0.996	(95% CI 0.988–1.004)	0.347
Target AI on posterior wall	0.985	(95% CI 0.977–0.994)	0.001	1.009	(95% CI 0.992–1.026)	0.315
AI achieve on posterior wall	0.635	(95% CI 0.421–0.956)	0.03	2.026	(95% CI 0.987–3.125)	0.06
Carina ablation	2.54	(95% CI 1.379–4.677)	0.003	2.139	(95% CI 1.161–6.212)	0.03
Operators' experience	1.951	(95% CI 1.058–3.6)	0.032	0.425	(95% CI 0.145–1.251)	0.12

AI, ablation index; OR, odds ratio

Table 3 Target and actual ablation index on the anterior and posterior LA walls

Ablation index	Anterior wall	Posterior wall
Target	420 [400; 500]	400 [380; 400]
Actual	409 [394; 428]	390 [375; 407]
p	0.0001	0.3
Target achieved, n (%)	213 (47)	244 (54)

whom it was not (Table 1). Thus, the number of cardioversions was higher in the group with non-achieved target AI, but the number of ineffective antiarrhythmic drugs was higher in the group with achieved target AI. Regarding procedural characteristics, a lower actual AI than the target AI value was associated with a longer procedure time (96 ± 49 min vs. 100 ± 32 min, $p = 0.001$). Interestingly, the median ablation power on the anterior wall and the median

CF were higher in procedures without a target AI, and experienced operators did not achieve a target AI more often than those with less experience. A higher target AI was characterized by a trend toward a higher probability of failure. On the posterior wall, the rate of achieved target AI was much higher (Table 1) than that on the anterior wall.

The relationship between the FPI and the achievement of a target AI is shown in Fig. 3. For the anterior wall, the non-FPI procedures were characterized by lower target AI (≤ 400) and prespecified but not achieved higher target AI values (≥ 500); the difference between the two indices had a negative mean delta (-56 ± 30 (from -1) to (-147) units). The FPI procedures were characterized by actual AIs exceeding a target value of 14 ± 10 units (from 1 to 61). No relationship was found between FPI and adherence to target AI on the posterior wall ($p > 0.05$).

3.5 Safety

Nine (2%) adverse events were registered during the 7-day post-ablation period. Six patients developed a groin hematoma: three with bridging anticoagulation, one with uninterrupted NOAC therapy, one with uninterrupted vitamin K antagonist therapy, and one with a skipped dose of NOAC ($p > 0.05$). One patient experienced a femoral artery pseudoaneurysm without the need for surgical repair. Pericardial effusion developed in one patient, a 65-year-old woman, following an audible steam-pop on the anterior LA wall, and no additional intervention was required. The following lesion characteristics were observed: ablation index was 507, power value was 40 W, and the flow rate was 30 ml/min, CF was 17 g, the temperature was 33 °C. One episode of acute

urinary retention was registered in a 72-year-old man; this was treated with pharmacological therapy.

Esophageal endoscopy was performed in 12 (2%) patients 1–4 days after the ablation procedure at the discretion of operators, and in all cases was triggered by severe pain during ablation on the LA posterior wall; one transient lesion was observed (ablation power on the posterior LA wall was 35 W, the actual median AI was 380 units).

4 Discussion

This real-practice prospective multicenter study showed that during AI-guided PV ablation, the median actual AI value equals or exceeds a prespecified (target) value only in one-third of the procedures. Although not independent, this is associated with a lower probability of FPI while ablating around the PV ostia. In contrast, FPI is more frequently achieved in cases of higher target AI values on both the anterior and posterior LA walls, and with a higher median actual AI on the anterior LA. Only carina ablation as a predictor independently associated with FPI. Failure to achieve a target AI is associated with a significant increase in the total procedure and X-ray exposure times. Surprisingly, more experienced operators have a higher rate of FPI even though they are less likely to achieve the preset target AIs. Additionally, our study confirms that AI-guided AF ablation in real practice is safe, with a low number of severe complications.

AI-guided AF catheter ablation is superior in efficacy and safety when compared with CF-guided procedures, as supported by the results of a large meta-analysis [12]. Therefore, AI is used in standard clinical practice. In well-designed randomized trials performed in high-volume expert

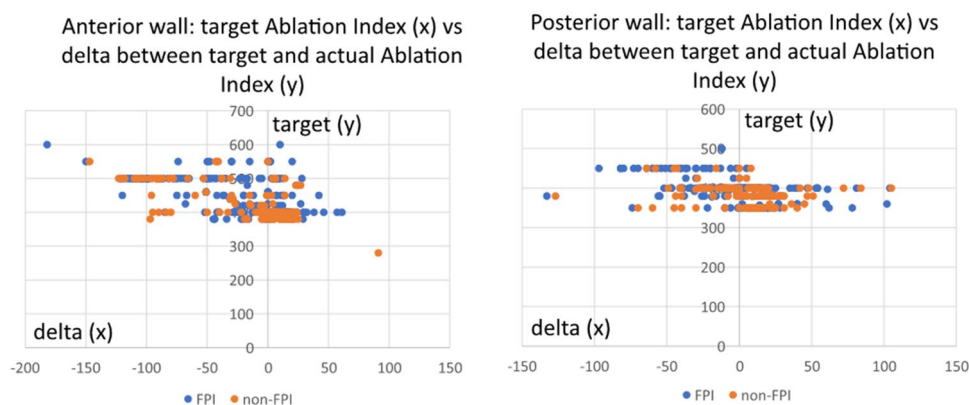


Fig. 3 Target ablation index vs. differences between target and actual ablation index. For the anterior wall (the left panel): a significant number of non-FPI were characterized by the excess of a target AI (orange dots to the right) when a target AI was lower; for the target AI around 500, the non-FPI cases were characterized by an actual AI lower than a target value (orange dots to the left). For the

posterior LA wall (the right panel): a majority of non-FPI cases were characterized by the excess of a target AI (orange dots to the right) when a target AI was ≤ 400 ; when a target AI was > 400 , many FPI cases were characterized by an actual AI less than the target AI (blue dots to the left). AI, ablation index; FPI, first-pass isolation; LA, left atrium

institutions, the acute efficacy of AI-guided AF ablation has shown tremendous improvement and high success [9], while the real-practice analysis presented in this study shows less optimistic results.

Recent studies have suggested that epicardial connections can lead to FPI failure [13]. The epicardial connection was detected in more than 13% of patients with AF, most often between left PV and coronary sinus using the ligament of Marshall and between the right PV and right atrium. We recommended keeping up 10 mm between PV ostia and ablation line, but we have not assessed a mean distance between the ablation line and PV ostia, nor analyzed the rate of presumable epicardial PV connections.

There is evidence that the carina between the ipsilateral PV is an arrhythmogenic zone and can be both a trigger and a substrate for AF [14]. Presumably, if only the PV is isolated, a reconnection along the ablation line in one of the PVs can lead to the reconnection in the second PV as well. Carina ablation reduces the likelihood of acute PV reconnection [15]. Some operators are inclined to believe that if PV isolation is carried out strictly according to the CLOSE protocol, then carina ablation may be redundant [16]. However, the available data are lacking evidence in favor of any strict suggestion. Based on our data, carina ablation between ipsilateral PV can increase FPI twofold. It should be noted that the number of procedures in our study with carina ablation on both sides was low.

One of the remarkable findings of our study was the lower median target AI value used on the anterior LA wall (420 units). However, in the CLOSE protocol, target AI value of 550 units was used which was subsequently studied extensively [17]. Moreover, other studies have suggested higher target AI values for the LA anterior wall [6, 18]. However, other studies have demonstrated that lower AI values can be as effective as those in the CLOSE protocol, resulting in high acute and long-term procedure efficacy [19, 20]. Therefore, our results confirm that lower actual AI indices on the anterior LA wall (median < 409) might be associated with the need for additional applications and a longer procedure time to achieve complete PV isolation.

Another interesting observation is that the prespecified target AI is frequently not achieved by operators, and the higher it is set, the more often it is not achieved. A systematic review of various target AIs suggests a high efficacy rate of AI-guided AF ablation procedures [21]. Previous studies described results after ablation with target AI values only, and outcomes based on its use have been described. The actual AI (which is encountered in real practice) has not been previously reported. Moreover, when the median actual AI is less than a high target AI value (> 500), the probability of FPI is low. The reason for operators not following their individual prespecified AI remains unclear. A specific finding is that higher power is associated with a lower

probability of achieving a target AI. We suggest that higher power/target AIs may raise safety questions in individual operators, but this remains speculative. The results of the VISTAX trial have demonstrated that higher AI values lead to better FPI rates (82–88%) [9], which suggests that FPI failure is less associated with the achievement of a prespecified target AI. At the same time, a higher actual median AI was associated with FPI. Importantly, adherence to the protocol with the recommended parameters of catheter position stability (maximum range 3 mm and minimum force 3 g) was associated with a more frequent achievement in the target AI. In the VISTAX trial, researchers had the opportunity to select options, and the following catheter position stability parameters were recommended: 2–3 mm stability range, 3–5 s stability time, but 3 g force and 3 mm tag size [9]. Stricter VisiTag parameters (2.5 mm/5 s stability, minimum force 7 g) were associated with higher long-term freedom in both paroxysmal and persistent AF [22]. These parameters are not considered in the AI formula and should be emphasized separately and highlighted by operators. Adherence to prespecified AI and ablation protocol parameters and its association with long-term AF freedom merit further investigation in randomized control trials. Certainly, our results demonstrate that adherence to protocol-based VisiTag parameters was associated with target AI achievement, but not with FPI, and links to the importance of a higher actual AI of each application.

Recent studies have reported that the HPSD approach is safer, faster, and more effective than the conventional approach [23, 24]. In our study, similar procedure times and FPI rates were observed for HPSD and standard ablation procedures. We suggest that this finding might be explained by the low rate of HPSD ablation among the participants and lack of experience in performing HPSD in the practice of participating operators.

Current AF RF ablation approaches, such as the CLOSE protocol, suggest that an interlesion distance of < 6 mm is optimal for AF ablation. A recently published study by Hoffman et al. demonstrated the high efficacy of ablation index-guided AF ablation using an interlesion distance of 3–4 mm [25]. Similarly, the OPTIMUM trial demonstrated a high acute efficacy rate (the endpoint was the absence of acute PV reconnection) for AF ablation with a mean distance between ablation points of < 4 mm, but the target AI on the anterior LA wall was higher than that observed in our study [18]. On the other hand, differences were found in the maximum interlesion distance values for each of the PVs collectors in FPI: for the right PVs, the maximum effective interlesion distance was < 5.4/4.4 mm (anterior/posterior LA wall), and for the left PVs—< 5.5/5.1 mm (anterior/posterior wall of the LA) [26]. Although in our study a shorter interlesion distance was not associated with a higher rate of FPI, its association with long-term AF freedom should be assessed

in future studies. We suggest that the combination of factors is associated with FPI, and the interlesion distance is only one of them. A shorter distance with lower AI may result in a poorer outcome than a bit longer distance with a higher median AI.

It has been well reported that RF point-by-point AF catheter ablation requires adequate operator experience that influences long-term procedural efficacy [26, 27]. Not surprisingly, more experienced operators (≥ 100 AF ablations per year) demonstrated a higher FPI rate when compared with their counterparts (< 100 AF ablations per year). However, experienced operators achieved their prespecified target AI less frequently. This finding is contrary to the established purpose of the AI itself since a target AI has to be based on “ideal” procedures defined by the operators themselves. Therefore, underachievement of target AI should inevitably lead to poorer acute and presumably long-term outcomes. The reason for prespecified AI values not being achieved in a significant proportion of cases remains unanswered and this finding should serve as a call for the improvement of intraprocedural protocols.

The results of our study confirm previously published data regarding the low incidence of complications associated with AI-guided AF ablation [28, 29]. No procedure-related death or cases of stroke, atrio-esophageal fistula, or major bleeding were observed.

4.1 Study limitations

The main limitation of this multicenter study was an insensitive measure bias. Selective patient inclusion and possible underreporting cannot be fully excluded [11]. The mean body mass index was 30 ± 6 kg/m² and it can result in fluctuating VisiTag parameters between procedures. Carina ablation performed intentionally after a failed FPI was disregarded from the analysis, while routine ablation before FPI was assessed as a factor associated with FPI, and one may suggest this a limitation. However, we believe that carinal ablation may have additional benefits, modulating LA autonomic innervation and decreasing further PV reconnection. We suggest that the analysis of data for numerical indices tested in a thin range should be interpreted with caution; this might specifically apply to AI ranges on the posterior LA wall and interlesion distances.

5 Conclusions

In the clinical practice of AI-guided AF ablation, target AI values and FPI are not achieved in a significant proportion of patients. However, the results of our prospective multicenter registry showed that the achievement of a prespecified AI (a target value) is not the only parameter required for FPI, and

a higher actual median AI on the LA anterior wall might be a more important parameter for acute PV isolation success. Based on our data, only carina ablation can independently predict FPI. Follow-up is ongoing and the impact of FPI on long-term results will be presented when data are available.

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Eduard A. Ivanitsky, MD, PhD—concept and design, approval of article.

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Dmitry S. Lebedev—concept and design, critical revision of article, approval of article.

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Data availability The rationale and study design underlying this research are available in the *Cardiology* journal (<https://doi.org/10.1159/000508888>), in the ClinicalTrials.gov with NCT 03,634,592 (<https://clinicaltrials.gov/ct2/show/NCT03634592>), and clinical and procedural data are available in the UniData Database (85.143.200.73:8080/unidata-frontend/) for researches and cannot be shared due to the privacy of individuals that participated in the study.

Declarations

Ethics approval The study protocol and informed consent form have been approved by the Ethics Committee of the Almazov National Medical Research Center; the local ethics committees of all participating centers approved the required documentation and granted permission to conduct the study.

Conflict of interest ENM reports receiving consultation fee and speaker honoraria from Biosense Webster, Boston Scientific, Abbott, and Boehringer Ingelheim; other authors declare no potential conflicts regarding this work.

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