Journal of Interventional Cardiac Electrophysiology
https://doi.org/10.1007/s10840-024-01793-z

RESEARCH LETTER

Impedance drop during focal monopolar pulsed field ablation in the atrium

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Received: 4 February 2024 / Accepted: 13 March 2024

During radiofrequency (RF) ablation, lesion formation is associated with changes in tissue properties by resistive and conductive heating, which can be documented clinically by a progressive impedance drop (ID). This ID during RF ablation correlates with contact force and applied RF energy and ID has been shown to correlate to durable conduction block in patients undergoing pulmonary vein isolation [1]. Compared to RF ablation, pulsed field ablation (PFA) is considered a non-thermal energy source, which consists of a high voltage train with very short pulses leading to cardiomyocyte-specific electroporation which causes irreversible formation of hydrophilic membrane micropores, cell necrosis, and apoptosis. ID during focal monopolar PFA with a single-tip catheter and the associations with applied PFA current and tissue contact force are unclear.

Twenty-one patients (29% female, mean age 65.14 ± 8.48 years) undergoing focal monopolar PFA ablation (75% atrial fibrillation/20% macro-reentrant atypical atrial flutter/5% focal atrial tachycardia) were included in this study. This study is part of the prospective ISOLATION (ClinicalTrials.gov identifier: NCT04342312) study and was approved by the local ethical review board (NL:70787.068.19/METC:19–052). All participants provided written informed consent. General anesthesia was used in all patients and paralytics were just used for intubation. Electroanatomic mapping was performed with a high-density mapping catheter (PentaRay catheter, Biosense Webster; HD-Grid catheter, Abbott) using the respective mapping systems (Carto, Biosense Webster; EnsiteX, Abbott). Point-by-point focal monopolar PFA ablation using a monopolar biphasic PFA generator (CENTAURI, Galvanize EP) was delivered through an open irrigated contact force-sensing ablation catheter (ThermoCool SmartTouch, Biosense Webster; TactiCath, Abbott). The ablation catheter's irrigation rate was set to 4 mL/min. We delivered PFA energy using a current of 22 A (7 pulse trains) for ablation of the posterior wall (posterior portions of the pulmonary veins, posterior line of the posterior box) and a current of 25 A (10 pulse trains) for ablation of the anterior wall (anterior portions of the pulmonary veins, anterior lines, roof line of the posterior box). For ablation in the right atrium, a current of 22 A (7 pulse train) was used. Focal monopolar PFA applications—annotated by 6-mm diameter tags—were delivered with 20% overlap.

In total, 1178 PFA applications were used in this analysis, including 507 applications with 22 A and 671 applications with 25 A. The average baseline impedance was 97.11 ± 14.65 Ω and the average impedance at the end of the PFA application was 89.36 ± 12.34 Ω with an average ID of 7.69 ± 4.25 Ω. Average contact force was 12.60 ± 7.42 g. The average ID (7.93 ± 4.31 Ω) for 25 A was more pronounced than the average ID (7.28 ± 4.14 Ω) for 22-A PFA applications ($p = 0.0014$) (Fig. 1A). The ID increased on average with the contact force applied by 0.1131 ± 0.0218 Ω/g ($D = 7.41 + 0.04$*F; $R = 0.08$; $p < 0.0001$) for 22 A and by 0.0884 ± 0.0163 Ω/g ($D = 5.88 + 0.09$*F; $R = 0.015$; $p < 0.0001$) for 25-A PFA applications. ID also increased on average with higher initial impedance by 0.1636 ± 0.0115 Ω/Ω ($p < 0.0001$) for 22 A and by 0.1911 ± 0.0096 Ω/Ω ($p < 0.0001$) for 25-A PFA applications. There were also differences in anatomical locations (Fig. 1B). For 22-A PFA applications, ID was lower for posterior portions of the right pulmonary veins than for posterior lines of the posterior box ($p = 0.0062$) and posterior portions of the left

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Published online: 18 March 2024

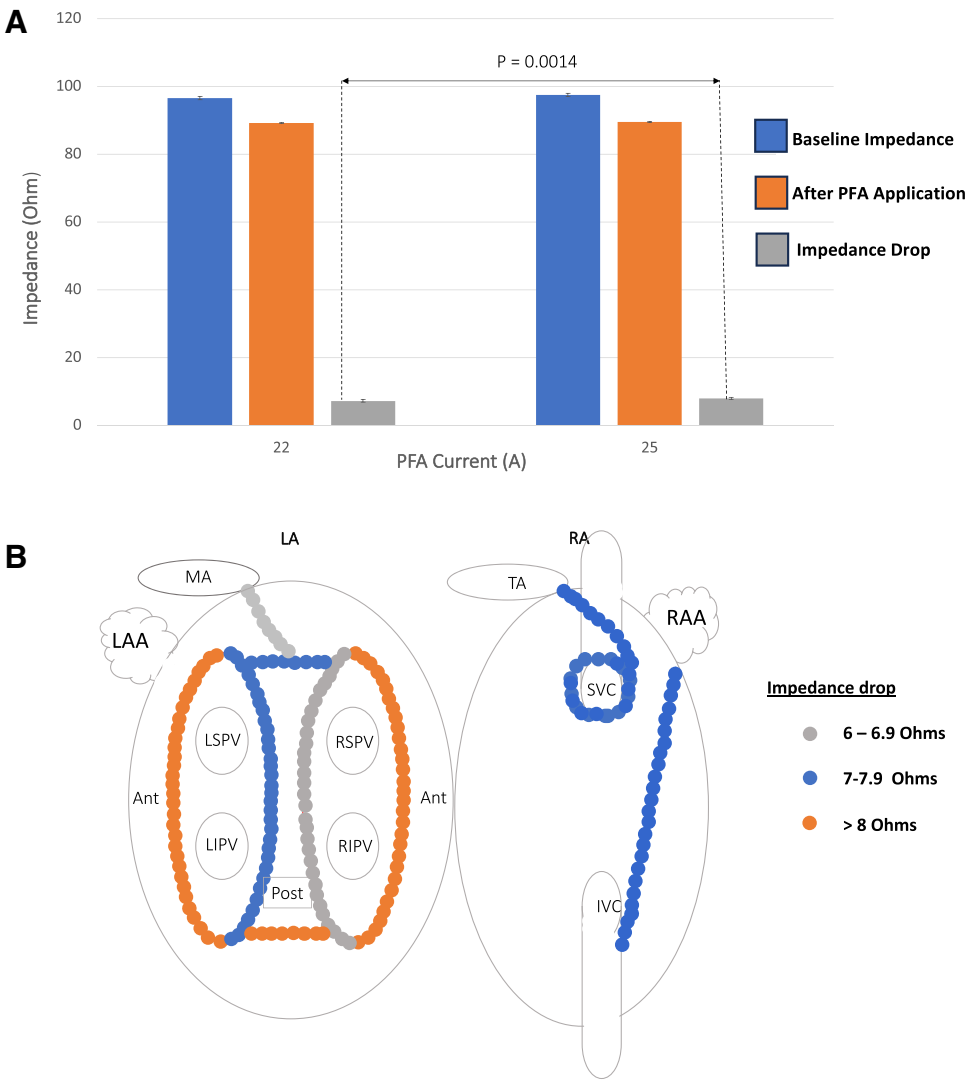

Fig. 1 **A** Baseline impedance, impedance after ablation, and impedance drop both for 22- and 25-A PFA applications. **B** Lesion set with impedance drop according to location. LA, left atrium; LAA, left atrial appendage; RA, right atrium; RAA, right atrial appendage; MA, mitral annulus; TA, tricuspid annulus; SVC, superior vena cava; IVC, inferior vena cava; LSPV, left superior pulmonary vein; LIPV, left inferior pulmonary vein; RSPV, right superior pulmonary vein; RIPV, right inferior pulmonary vein; ant, anterior; post, posterior

pulmonary veins ($p=0.0053$). For 25-A PFA applications, ID was lower for anterior lines than for anterior portions of the right pulmonary veins ($p<0.0001$), anterior portions of the left pulmonary veins ($p<0.0001$), and the roof line of the posterior box ($p<0.0001$).

In this study, we collected impedance data of a large sample of focal monopolar point-by-point PFA applications in the right and left atrium and showed a significant ID during PFA, which was related to the PFA current applied, the contact force, and baseline impedance. The association between increased applied current and ID magnitude may reflect the previously reported greater tissue damage with a higher electric field [2]. Although the temperature changes in muscle tissue during PFA are small, it may partially contribute to the observed ID as well [3]. A recent preclinical study in pigs [4] showed a very weak (in the left ventricle) or no (in the right ventricle) correlation between a relatively small ID and the depth of resulting predominantly non-transmural lesions in the thick-walled ventricular tissue. However, whether the relatively large ID observed in our study always correlates with deep and transmural lesions in the thin-walled atrial tissue warrants further study.

The significant, but weak, relation between contact force and ID with approximately 1-Ω ID per 10-g increase in contact force is in line with earlier studies on RF ablation [5]. On the other hand, acute ID during a PFA application may overestimate irreversible lesion creation, as PFA-induced lesions tend to reduce over time (sideration phenomenon). The regional differences in ID may be related to variable wall thickness and differences in anatomical epicardial (epicardial fat, ganglionated plexi, etc.) and extracardiac (vessels, nerves, esophagus, etc.) structures in the direct proximity to the site of PFA application. Comparable to most previous RF ablation studies, we measured ID through the ablation generator, which may be lower than local ID measured by dedicated mini-electrode catheters, which, however, are not compatible with available PFA systems, yet [6].

In conclusion, focal monopolar point-by-point PFA in the atria using a single-tip catheter was associated with a significant ID, which increased with applied PFA current and tissue

contact force. Whether the ID documented in the current study can be reproduced with other PFA catheters and generators and whether ID can be incorporated in intra-procedurally assessed indices to guide focal PFA for atrial arrhythmias needs to be investigated in future studies.

Data Availability The data that support the findings of this study are available on request from the corresponding author.

Declarations

Conflict of interest The authors declare no competing interests.

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