Chapter

New Results in Catheter Ablation for Atrial Fibrillation

Nándor Szegedi and László Gellér

Abstract

Pulmonary vein isolation (PVI) is the cornerstone of rhythm-control therapy for atrial fibrillation (AF). A few years ago, contact force-sensing ablation catheters (CFSAC) were introduced. Nowadays the use of CFSAC became a part of the everyday practice. The durability of PVI depends much on the accurate lesion creation. The recently developed techniques (ablation index, CLOSE protocol) may facilitate the procedure in terms of achieving durable PVI which has already been confirmed by randomized trials. In this chapter, we would like to introduce the theoretical background of PVI and compare different techniques (radiofrequency point-by-point, cryoballoon, additional ablation lines for persistent AF) with special highlight on the importance of durable PVI.

Keywords: pulmonary vein isolation, atrial fibrillation, ablation, point-by-point, CLOSE protocol, cryoballoon

1. Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia. AF is associated with a higher risk of mortality than the general population [1]. It is one of the major causes of stroke, heart failure, sudden death, and cardiovascular morbidity in the world [2]. Thus, appropriate management of this arrhythmia and underlying diseases is of high importance. Besides stroke prevention with therapeutic anticoagulation, the rate-control or rhythm-control treatment is the basis of AF management.

Pulmonary vein isolation (PVI) is the cornerstone of rhythm-control therapy for atrial fibrillation [2, 3]. A few years ago, contact force-sensing ablation catheters (CFSAC) were introduced. Nowadays the use of CFSAC became a part of the everyday practice [4–8]. The durability of PVI depends much on the accurate lesion creation. The recently developed techniques (ablation index, CLOSE protocol) may facilitate the procedure in terms of achieving durable PVI which has already been confirmed by prospective trials [9–12]. In this chapter, we will introduce the theoretical background of PVI and compare different ablation techniques (radiofrequency point-by-point, cryoballoon, additional ablation lines for persistent AF) with special highlight on the importance of durable PVI.

2. Pulmonary vein isolation

2.1 Theoretical background of pulmonary vein isolation

The exact mechanism of atrial fibrillation for the individual patients is not well understood, and it is still a topic of intensive research nowadays. It seems that in most of the patients, the pulmonary veins and surrounding structures play an important role in the pathophysiology. The first cornerstone research was presented by Haissaguerre et al., where they found that electrical firing from the pulmonary veins (PVs) may have an important role in the initiation of atrial fibrillation paroxysms [13] (**Figure 1**).

Jais et al. showed distinctive electrophysiological properties of pulmonary veins in patients with AF compared with healthy patients' PVs. The main difference is the short or extremely short refractory period of the PVs which is likely to play a major role in the arrhythmogenesis [14]. Moreover, episodes of AF may shorten the effective refractory period of the atria and the PVs, which may promote recurrent and longer episodes of AF ("AF begets AF") [15, 16]. These studies are supplemented by another important finding by De Ponti et al. as they showed with high-density mapping of the PVs that majority of ectopic beats have a multifocal pattern and relatively proximal origin [17].

Besides the pulmonary veins, multiple pathophysiological factors may play a role in the mechanism of atrial fibrillation, like ligament of Marshall, vagal ganglia, micro-reentrant circuits, and spiral/rotational activities [18–21].

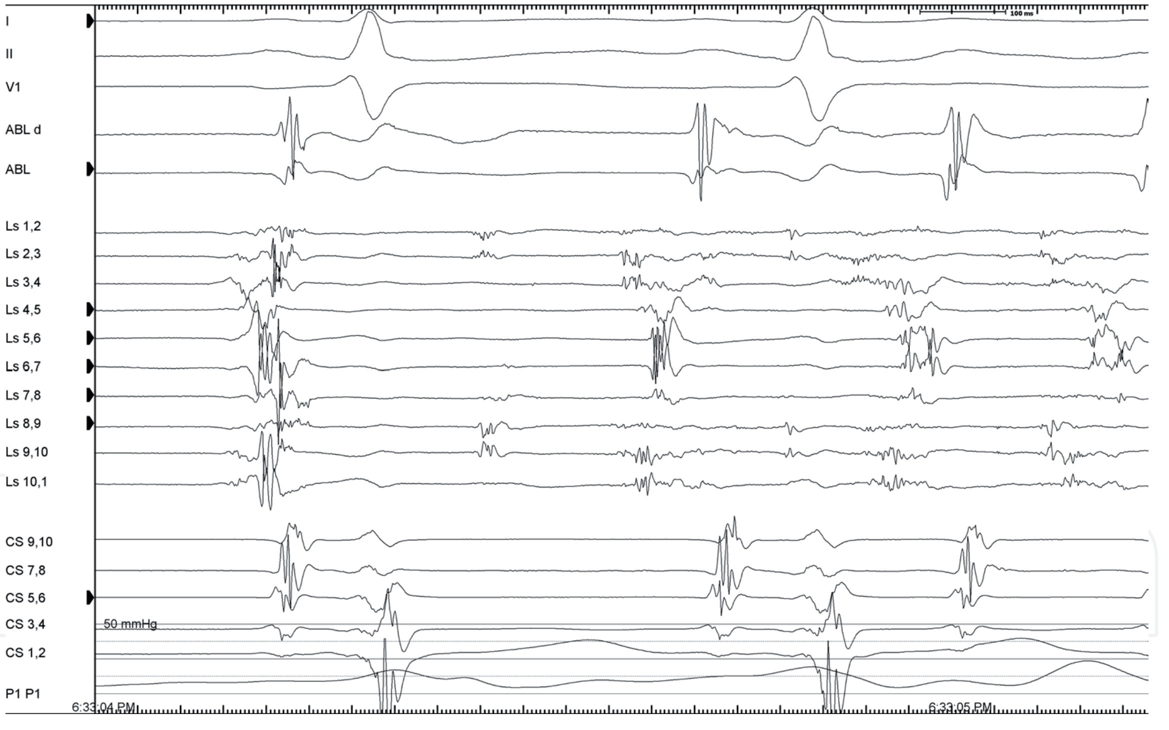

Figure 1.
High-frequency electrical activity in the right superior pulmonary vein registered on the Lasso (Ls) catheter.

2.2 Pulmonary vein isolation procedures

The two most frequently used ablation technologies for pulmonary vein isolation are radiofrequency point-by-point method which leads to coagulation necrosis by heating and single-shot cryoballoon ablation which leads to tissue necrosis by freezing.

PVI with radiofrequency ablation requires limited use of fluoroscopy, because catheter guidance is achieved with the use of an electroanatomical mapping system, but the approach requires extensive training due to the need for a more sophisticated catheter manipulation.

PVI with cryoballoon requires more extensive fluoroscopic guidance to position the balloon catheter at the pulmonary veins. On the other hand, the cryoballoon was developed to create a circular lesion around each pulmonary vein in a relatively simple manner, and thus it is less operator dependent.

Circumferential ablation around the PVs may have ablation-related benefits beyond pulmonary vein isolation, including concomitant ganglionated plexus modification and modification of other substrates located near the PVs [22].

2.2.1 Cryoballoon ablation

Pulmonary vein isolation can be reached with a balloon catheter by the occlusion of the pulmonary veins, causing tissue necrosis via cryothermal energy around antral orifice of the vessels. Occlusion of the pulmonary vein by the cryoballoon is tested by means of contrast injection and fluoroscopic examination (**Figure 2**). If the injection of contrast agent verifies the accurate occlusion of the pulmonary vein ostium, the freezing can be started. The need for fluoroscopic imaging for each PVs may contribute to a prolonged fluoroscopic time and dose.

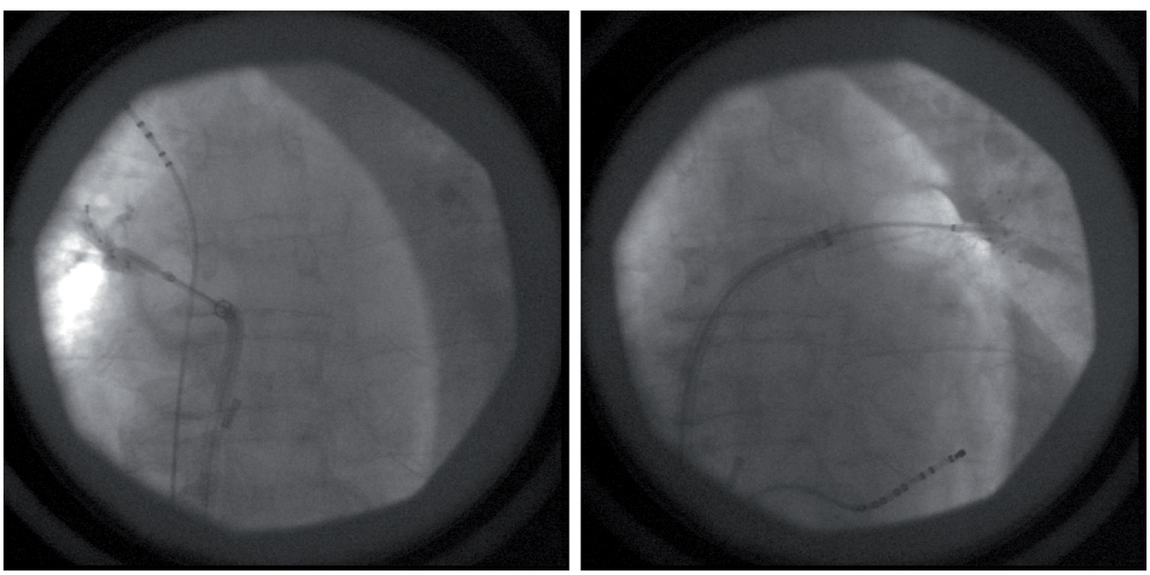

Figure2.
Right side: contrast injection in the right inferior pulmonary vein; decapolar catheter is placed in the superior vena cava to perform phrenic nerve pacing. Left side: contrast injection in the left superior pulmonary vein; decapolar catheter is placed in the coronary sinus.

First-generation cryoballoons deliver ablation only via the equator of the balloon. Freeze AF randomized trial found that first-generation cryoballoon was non-inferior as compared with the radiofrequency ablation. There was a higher rate of adverse events driven by the higher incidence of transient phrenic nerve palsy [23].

Second-generation cryoballoons were introduced to overcome some of these disadvantages. The number of injection ports has been doubled (from four to eight), and have been positioned more distally on the catheters' shaft resulting in a larger and more uniform zone of freezing on the balloons' surface [24] (**Figure 3**). The improved thermodynamic characteristics of the second-generation cryoballoon lead to a higher rate of single shot-PVI and a better chronic lesion durability. This high rate of durable PV isolation is anticipated to translate to improved clinical outcome [25].

Second-generation cryoballoon was found to be non-inferior to radiofrequency ablation in the FIRE and ICE randomized trial with respect to efficacy for the

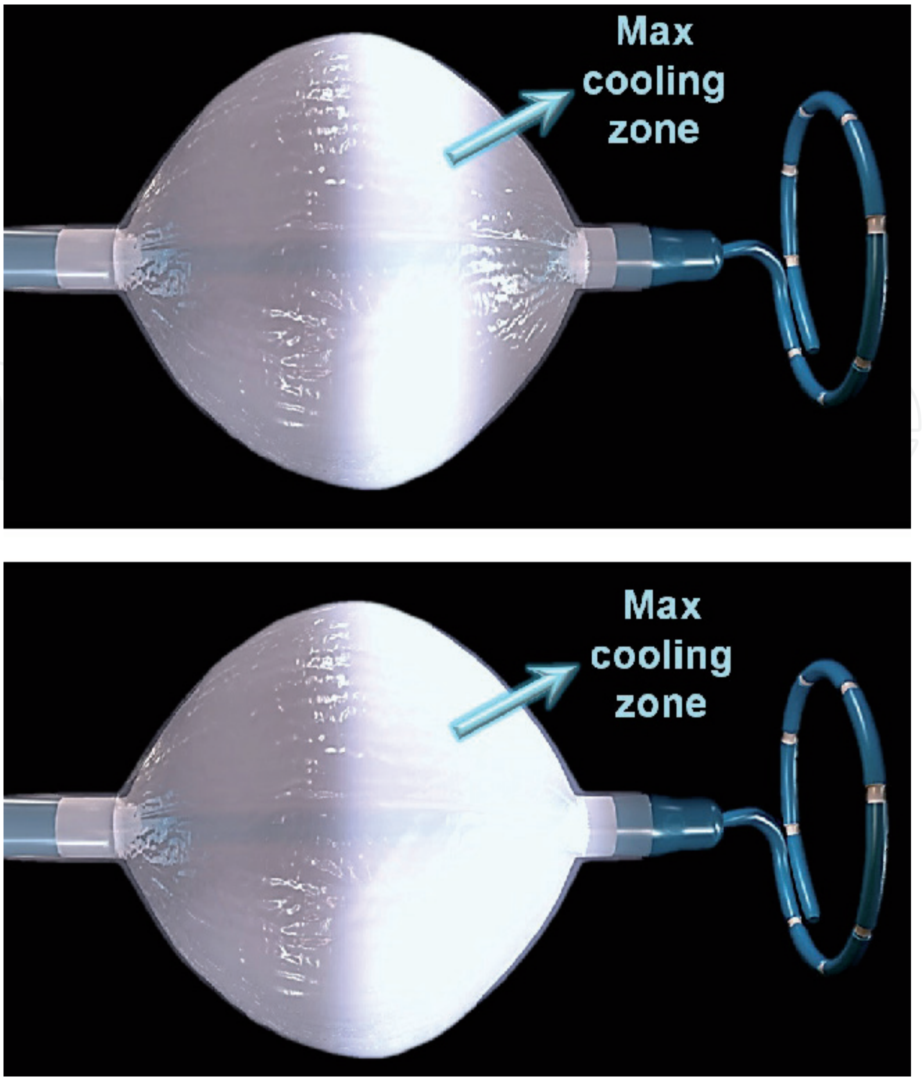

Figure 3.
First (upper part) and second (lower part) generation cryoballoons. First-generation cryoballoon produces an annular freezing zone at the balloon's equator. Second-generation cryoballoon has broader and more homogenous freezing zone, thus providing freezing at the whole distal hemisphere of the balloon.

treatment of patients with drug-refractory paroxysmal atrial fibrillation. There was also no significant difference between the two methods with regard to overall safety. Phrenic nerve injury was the most common safety event in the cryoballoon group [26]. The enlarged volume of tissue freezing may cause a trend toward higher incidence of phrenic nerve palsy in the case of the second-generation cryoballoons. However, these events are transient in most of the cases [27, 28].

A growing evidence suggests that second-generation cryoballoon is also safe and effective in patients with persistent AF [29, 30]. In persistent AF the isolation of the left atrial appendage as an adjunct to PVI may improve 1-year outcomes compared with the PVI-only strategy using cryoballoon [31].

However, the cryoballoon may be less effective in some anatomical variations of the pulmonary veins such as long left common trunk, additional pulmonary veins, or in the case of a more oval PV orifice [32, 33]. In some cases the complication rates may also differ in pulmonary venous anatomical variations [34].

2.2.2 Radiofrequency point-by-point ablation

Circumferential pulmonary vein isolation with radiofrequency ablation was the first type of ablation that was proven to be superior compared with the antiarrhythmic drug treatment [35]. It requires limited use of fluoroscopy, because catheter guidance is achieved with the use of an electroanatomical mapping system. The disadvantage of the technology is that the approach requires extensive training due to the need for a more accurate catheter manipulation. It is both proven to be effective in paroxysmal and persistent AF in terms of reducing symptoms related to AF [36, 37]. Moreover it may have a positive effect on mortality in heart failure patients [38–40].

2.2.2.1 Radiofrequency point-by-point ablation with contact force-sensing catheters

The clinical efficacy of catheter ablation of AF remained limited by difficulty in achieving durable pulmonary vein isolation. Suboptimal catheter tip-to-tissue contact force (CF) during lesion delivery may result in a reduced clinical efficacy. Despite the fact that acute PVI is nearly universally achieved, recurrences of atrial arrhythmias after AF ablation are common, and recurrences are usually due to PV reconnection and indicate insufficient lesion formation during the initial ablation.

A few years ago, contact force-sensing ablation catheters (CFSAC) have been introduced in the clinical practice. It has been shown that the contact force between the catheter tip and the target tissue is a key factor to a safe and effective lesion formation. Insufficient CF may result in an ineffective lesion, whereas excessive CF may result in complications such as heart wall perforation, steam pop, thrombus formation, or esophageal injury. High CF values may occur during catheter manipulation and not just during ablation, suggesting that measuring CF may provide additional useful information to the operator for safe catheter manipulation.

Catheter ablation using real-time CF technology was shown to be safe for the treatment of supraventricular tachycardias and AF [5, 6]. Pulmonary vein isolation with the use of contact force information results in a shorter procedure duration and a lower rate of AF recurrence after 12 months than conventional PVI without this information [41]. Analysis of the first trials with CFSACs showed that CF during catheter ablation for AF correlates with clinical outcome. Arrhythmia control is best achieved when ablation lesions are placed with an average CF of >20 g, whereas clinical failure is noted with an average CF of <10 g [8, 42].

The EFFICAS I multicenter study was to demonstrate the correlation between CF parameters during initial procedure and the incidence of isolation gaps at a repeated left atrial procedure at 3 months. To characterize the effect of CF applied over time, the system automatically detects the beginning and end of RF current delivery and calculates the force-time integral (FTI) defined as the total CF integrated over the time of RF delivery. Ablations with minimum FTI <400 g showed increased likelihood for reconnection. Thus, optimal CF parameter recommendations became a target CF of 20 g and a minimum FTI of 400 g for each lesion [7]. These recommendations together with contiguous lesion deployment were then confirmed by the EFFICAS II study as procedures with the abovementioned criteria resulted in more durable PVI [4].

2.2.2.2 Radiofrequency point-by-point ablation guided by ablation index

The routine use of CFSACs improved the arrhythmia-free survival after PVI; however, the recurrence rate remained substantial.

Ablation index (AI) incorporates CF, power, and time in a weighted formula and predicts lesion depth. It works together with SmartTouch catheter and CARTO system (**Figures 4** and 5).

$$\text{Ablation Index} = \left(K * \int_0^t CF^a(\tau) P^b(\tau) d\tau \right)^c$$

Figure 4.
Mathematical formula for the ablation index.

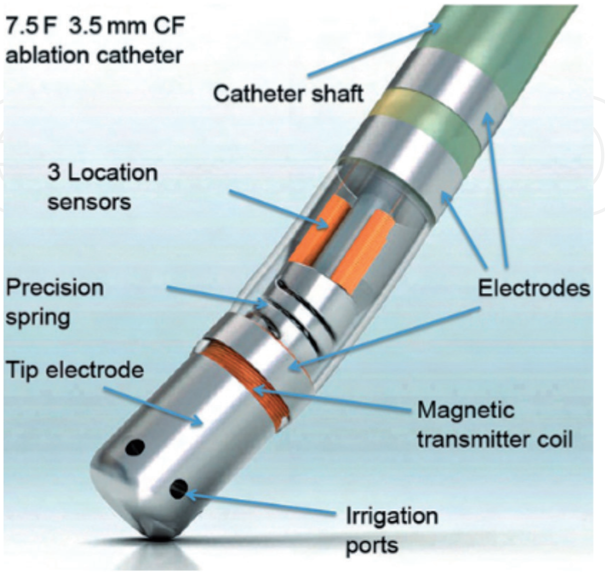

Figure 5.
SmartTouch catheter. This is a 7.5 French, 3.5-mm-irrigated-tip ablation catheter. Catheter tip contact force information and direction is measured by three location sensors within the shaft and the degree of spring bending via a magnetic transmitter at the catheter tip. The catheter and information are integrated into the Carto® 3 mapping system and can be displayed to the operators.

The analysis of PVIs guided by AI resulted in the development of the "CLOSE protocol." The CLOSE protocol is a new approach aiming to enclose the PVs with contiguous and optimized radiofrequency lesions by targeting an inter-lesion distance (ILD) ≤6 mm and AI ≥400 at the posterior wall and ≥550 at the anterior wall [11]. In the case of chest pain or intraesophageal temperature rise >38.5°C during posterior wall ablation, energy delivery may be stopped at an AI of 300. Target AI values can be reached with higher-energy applications as well (**Figures 6** and **7**).

The use of CLOSE protocol was associated with high incidence of first-pass isolation (98%). Overall, single-procedure arrhythmia-free survival was 91% at 1 year without antiarrhythmic drug treatment. These findings are in line with the hypothesis that avoiding weak links within the deployed radiofrequency circle is the key to durable PVI and clinical success. These procedural results do not compromise safety and are associated with relatively short procedure and ablation times [12].

The optimal AI target values are not determined yet, and values recommended by the CLOSE protocol may overshoot. Lee et al. presented that PVIs with AI target values of ≥450 at the anterior/roof segments and of ≥350 at the posterior/inferior/carina segments are optimal AI thresholds for avoiding acute pulmonary vein reconnection [9]. In the left atrium, the AI-impedance relationship plateaus from 430 AI for the SmartTouch catheter, suggesting ablation beyond this value, have minimal additional biophysical benefit [43]. Solimene et al. found that radiofrequency energy targeting inter-lesion distance ≤6 mm and ablation index of 330–350 at posterior wall and 400–450 at anterior wall produces similar good results and low complication rates [44]. Another study found that no reconnection was seen where the minimum AI value was ≥370 for posterior/inferior segments and ≥480 for anterior/roof segments at repeat electrophysiology study [45].

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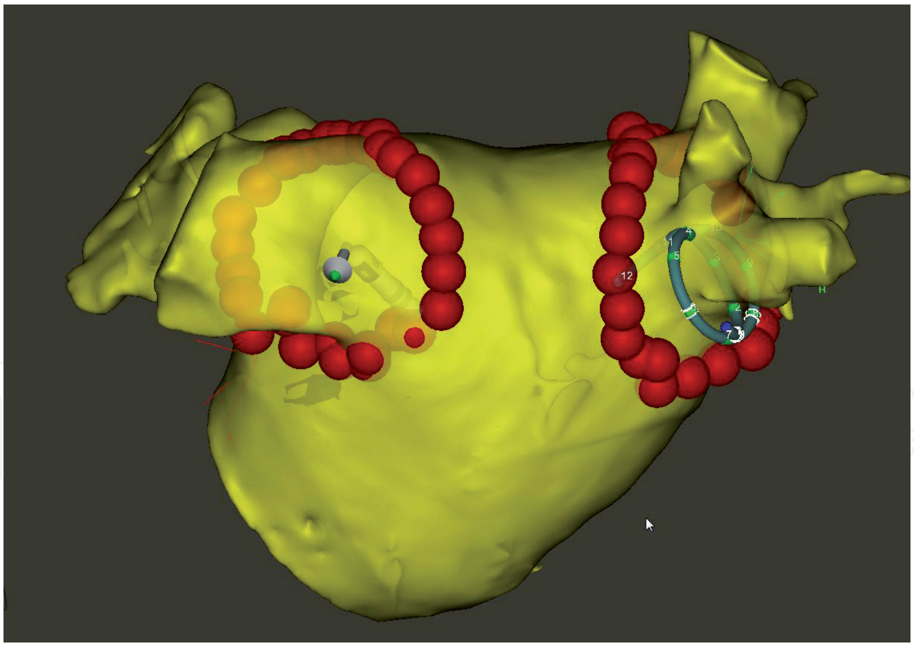

Figure 6.
Pulmonary vein isolation (CT-merged CARTO image) performed with CLOSE protocol. Red ablation tags indicate AI value >400 on the posterior wall and >550 on the anterior wall.

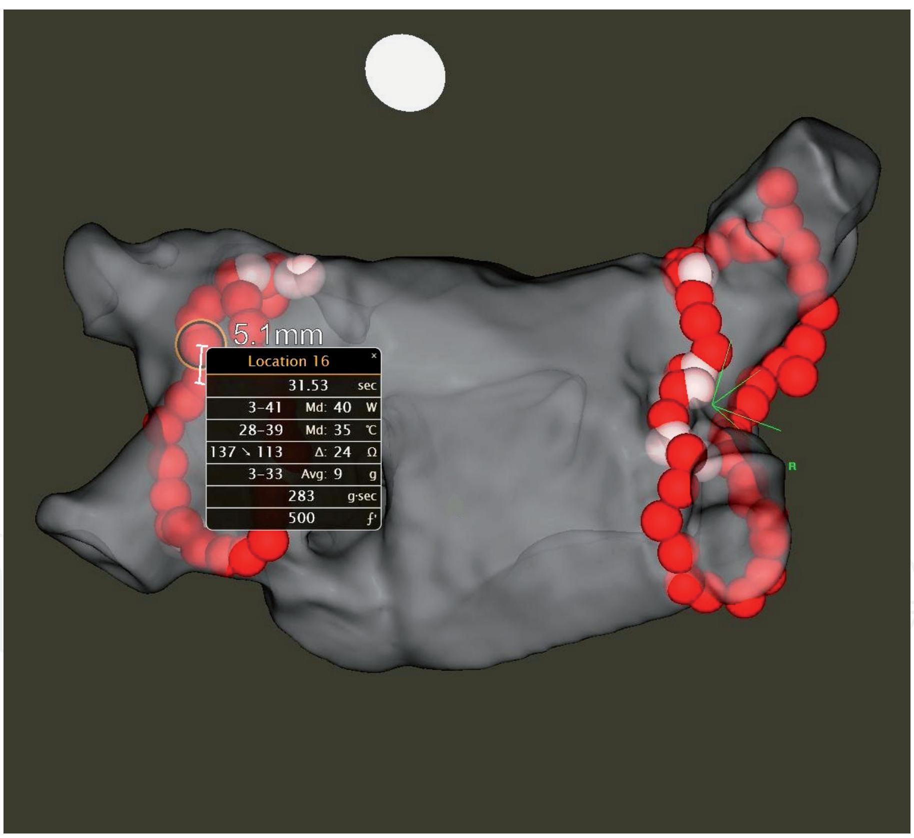

Figure 7.
Pulmonary vein isolation (CARTO, fast anatomical map) performed with CLOSE protocol. Ablation parameters of the highlighted dot (with yellow ring around it) are shown, including application duration, power, temperature, impedance drop, average contact force, force-time integral value, and ablation index value (AI = 500 in this case). The inter-lesion distance between the two marked ablation points (with distance measurement white line between them) is also shown (ILD = 5.1 mm).

The use of AI and small ILD results in a high level of durable PVI and may be also effective in persistent AF. A good clinical outcome can be achieved in the great majority of patients with persistent AF [10].

2.2.2.3 Esophageal temperatures during applications with ablation index

The incidence of endoscopically detected esophageal injury after catheter ablation is high (2–30%), both after PVI guided by cryoballoon and by RF energy [46–49]. High AI target values may further increase the risk of esophageal lesions.

The incidence of esophageal injury on endoscopy after CLOSE-guided PVI is low (1.2%) despite significant intraesophageal temperature rise during the procedure [50]. The most likely explanation of the low incidence after CLOSE PVI is the ablation protocol itself as AI target value on posterior wall is recommended to be reduced to 300 if pain or esophageal temperature rise occurs. Moreover, the high incidence of first-pass isolation results in smaller amount of applications required to reach the complete PVI.

3. Ablation strategies in persistent atrial fibrillation

Persistent AF is usually a more difficult arrhythmia as compared with the paroxysmal AF. Besides the triggers that induce the arrhythmia, usually a complex substrate is also present due to the atrial enlargement and fibrosis. Thus, pulmonary vein isolation alone is generally less effective than in paroxysmal AF [51]. The success rate of catheter ablation might improve with substrate modification techniques such as additional linear lines, ablation of complex fractionated atrial electrograms, and isolation of the left atrial appendage. The value of these techniques is controversial; however, most of the studies that compared PVI to PVI plus substrate modification were performed before the contact force era and in low-volume centers [29, 31, 52–56]. Substrate modification of persistent AF with the ablation of additional lines may be useful if procedure is performed by experienced operators. Kettering et al. found better arrhythmia-free survival in patients with roofline ablation when added to PVI (72 vs. 63%) [57]. Additional mitral isthmus line ablation may also provide a higher success rate as shown by Jais et al. (87 vs. 69%) [58].

4. Our personal approach for atrial fibrillation ablation

Here we shortly summarize our personal approach for PVI that we use in the Electrophysiology Laboratory of the Heart and Vascular Center, Semmelweis University, Budapest.

In case of symptomatic paroxysmal atrial fibrillation, the primary goal is the durable isolation of all pulmonary veins. Before the procedure cardiac CT or MR angiography is performed to evaluate the presence of potential coronary artery disease and to determine the pulmonary venous anatomy. For patients with typical anatomy (four distinct pulmonary veins), we may choose cryoballoon; however, a vast majority of patients are ablated with point-by-point approach with contact force-sensing ablation catheters. For the latter we may use CARTO or EnSite navigation system. For repeated ablations we first check the pulmonary veins, and if there is reconnection, we re-isolate the PVs with CARTO, EnSite, or Rhythmia system. If all the pulmonary veins are found to be isolated, then we try to find and eliminate non-PV triggers such as superior vena cava or coronary sinus.

In the case of symptomatic persistent atrial fibrillation, the first procedure is also pulmonary vein isolation similar to the paroxysmal cases. For repeated ablations besides re-isolation of PVs, we may use additional ablation lines such as left atrial roofline, posterior line, mitral isthmus line, and in the right atrium the cavo-tricuspidal isthmus line. If the recurrent arrhythmia is a macro-reentrant atrial tachycardia, we perform an electroanatomical activation map to depict the tachycardia circuit and to find the optimal ablation target(s).

5. Conclusion

Pulmonary vein isolation (PVI) is the cornerstone of rhythm-control therapy for atrial fibrillation (AF). A few years ago, new technologies such as cryoballoon and contact force-sensing ablation catheters were introduced. The use of these technologies became the part of the everyday practice. The routine use of CF ablation catheters and cryoballoons improved the arrhythmia-free survival after PVI; however, the recurrence rate remained substantial. The durability of PVI depends much on the accurate lesion creation. The recently developed techniques such as second-generation cryoballoon, ablation index, and CLOSE protocol may result in a higher rate of both acute PVI and thus a more durable lesion creation. The CLOSE protocol is a new approach aiming to enclose the PVs with contiguous and optimized radiofrequency lesions. This high rate of durable PV isolation is anticipated to translate to improved clinical outcome for both paroxysmal and persistent atrial fibrillation. Substrate modification of persistent AF with the ablation of additional lines may be useful if procedure is performed by experienced operators.

Conflict of interest

The authors declare no conflict of interest.

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