ISSN 2706-6819 Vol.6, Issue 9: 1-6, DOI: 10.25236/IJFM.2024.060901

Pulsed Field Ablation as a New Option for the Treatment of Atrial Fibrillation

Baoping Li[1,a], Tingting Zhao[2,b]

[1]Department of Cardiology, Shandong University of Traditional Chinese Medicine Affiliated Hospital, Heze Hospital of Traditional Chinese Medicine, Heze, China
[2]Heze Peony People's Hospital, Heze, China
[a]li_bp89@163.com, [b]z_tt89@sina.com

Abstract: *Atrial fibrillation (AF) is a common cardiac arrhythmia that poses significant health risks and impairs quality of life for affected patients. Traditional treatment methods, such as radiofrequency ablation, have limitations. In recent years, Pulsed field ablation (PFA) has emerged as a new therapeutic option and has attracted widespread research interest. The review aims to evaluate the potential and efficacy of PFA as a treatment for AF. Compared to traditional ablation methods, PFA offers lower risk of complications and less thermal damage to surrounding tissues. However, further studies are needed to verify its long-term efficacy and superiority. Additionally, personalized treatment strategies, technological advancements, and broader clinical applications are important areas for future investigation.*

Keywords: *Atrial fibrillation; Pulsed field ablation; Thermal ablation; Safety; Non-thermal therapy*

1. Introduction

Atrial fibrillation (AF) has become a challenging medical emergency worldwide because of its epidemic proportions leading to a significant increase in morbidity and mortality. Moreover, this clinical scenario poses critical logistical and economic challenges for healthcare systems across several countries[1]. It is the most common sustained cardiac arrhythmia[2],It is estimated that up to 16 million people in the US will have AF by 2050, 14 million in Europe by 2060,and over 70 million in Asia by 2050 [3]. It is estimated that one in four adults over the age of 40 will present with AF at some point during their lifetime [4]. AF can lead to serious complications, including blood clots, stroke, and heart failure[5]. Though also occurs in young adults and adolescent [6]. In younger adults, AF is usually precipitated by many underlying factors such as hypertension, hyperthyroidism [7],alcohol consumption, smoking [8]. Therefore, it is crucial to take preventive measures and maintain sinus rhythm.

Novel technologies and therapies are evolving rapidly in the field of electrophysiology and cardiac ablation, particularly with the aim of improving the management of AF where pharmacologic treatment fails[9]. A novel, potentially disruptive non-thermal energy source, namely, electroporation or pulsed field ablation (PFA) was recently introduced[10]. Also known as pulsed electric field (PEF) ablation[11].PFA is a novel and unique tissue selective ablation method [12] that delivers high-energy pulses in an extremely short duration, providing the advantage of causing less risk of injury to the adjacent myocardial tissue and phrenic nerve [13,14]. Ablation of cardiac tissue with pulsed electric fields is a promising alternative to current thermal ablation methods, and it critically depends on the electric field distribution in the heart[15].This emerging treatment option offers hope for patients with atrial fibrillation, injecting new vitality into improving patients' quality of life and cardiovascular health.

2. Principles of Pulsed Field Ablation

PFA is a novel, unique and tissue-selective ablation method that utilizes non-thermal modalities for tissue ablation [16].It involves the delivery of short nanosecond/microsecond high voltage pulses that generate a large number of water-soluble pores, thereby altering the cell permeability. The induced electric field changes the cellular transmembrane potential by accumulating alters on physical boundaries such as the cell membrane. This triggers multiple changes in the cellular macroenvironment

ISSN 2706-6819 Vol.6, Issue 9: 1-6, DOI: 10.25236/IJFM.2024.060901

and microenvironment. These changes include the redistribution of extracellular and intracellular charged species and disruption of the physical integrity of the cell membrane. These alterations affect the cells ability to maintain critical molecular concentration gradients necessary for maintaining homeostasis. Additionally, it locally alters tissue pH, generates reactive oxygen species, releases mitochondrial cytochrome c, and induces cell death [17-20], forming irreversible electroporation (IRE) [21]. Studies have shown that IRE occurs in myocardial tissue when the electric field intensity reaches 400 V/cm [22-23].

3. Clinical Application

In the clinical realm, the PULSED AF pilot study demonstrated 100% PVI with no serious adverse events, including no change in oesophageal temperature or phrenic nerve injury in 38 patients using the Medtronic Pulsed Select Field Ablation System[24,27]. In the IMPULSE (ClinicalTrials.gov identifier: NCT03700385) and PEFCAT (ClinicalTrials.gov identifier: NCT03714178) trials, the Farapulse Irreversible Electroporation System was used for the treatment of paroxysmal AF and cavotricuspid isthmus-dependent atrial flutter[25].Primary safety endpoints were achieved with no adverse events other than tamponade in one patient in the IMPULSE cohort[25].There was no oesophageal lesions or phrenic nerve damage.27 For persistent AF, the PersAFOn study (Feasibility study of the FARAPULSE endocardial multi-ablation system in the treatment of persistent atrial fibrillation; ClinicalTrials.gov identifier: NCT04170621) also tested the Farapulse PFA system in 25 patients with persistent AF who received PVI + posterior wall isolation + cavotricuspid isthmus[26]. First-pass PVI was achieved in all patients (100%, 96/96 pulmonary veins),with a median of 22 minutes elapsing between the first and last ablations. Invasive remapping performed in 22 patients at 82 days (interquartile range 76-90 days) confirmed PVI durability in 82 of 85 pulmonary veins (96%) and 19 of 22 patients (86%). There were no instances of pulmonary vein stenosis, stroke or transient ischaemic attack, phrenic nerve injury or atriooesophageal fistula. Oesophagogastroduodenoscopy was performed in 21 patients at a median of 3 days (interquartile range 1-5 days) post-procedure, and no oesophageal injury was observed[27]. Another study, The system developed by Farapulse is currently the first CE approved commercially available PAF system, and the results during development of the final clinical prototype were recently published by Reddy et al.[28-29]for 121 patients in the IMPULS, PEFCAT, and PEFCATII trials. The system consists of a small basket-type over-the-wire catheter (delivered to the LA by a 13F sheath) that can be transformed into a flower petal shape to perform PVI in around7–9 applications (4–10 pulses per application) per vein in a mean procedure time of 97 min with 13–14 min of fluoroscopy under generalanaesthesia. The system changed from using monophasic (900–1000 V) to biphasic waveform (1800–2000 V) during its development, which increased durability of PVI in 110 remapped patients from 45% to 98%. The 12-months freedom of atrial arrhythmias for the entire cohort was 79%, while for the later-optimized procedurecohort it was 85%. Regarding safety ,most patients were checked forphrenic nerve palsy or PV stenosis (74 patients with repeat CT/MRI) which was not observed,while around one-third of the cohort did not show signs of oesophageal damage, and 2/18 patients with DWMRI showed signs of asymptomatic cerebral embolism. Looking at these first outcomes, PFA by the FARAPULSE system appears to fulfil many of the promises that were suggested by the animal experimental data of IRE.

The first-in-man study[30-31]describes 76 patients treated with PFA alone (n = 36) or PFA alternating with iRF (n= 40) for variouscombinations of PVI (all),roof lines (n = 34),mitral lines (n= 14), CTIlines (n= 44) with a total ablation time of around 23 min. Both PVI and roof lines could be successfully achieved with a mean of, respectively,53 and 6 applications of PFA, but in some patients mitral or CTI lines were achieved by combining PFA with iRF. There were some, mostly minor, vascular events and in 3/60 patients oesophagealerythema was observed but none in the cohort that was only treated with PFA.

4. Comparison Between Pulsed Field Ablation and Traditional (Radiofrequency, Cryoablation)Ablation Histology

PFA demonstrates distinct characteristics of myocardial injury compared to radiofrequency ablation(RFA) in terms of both macroscopic observation and histological examination, indicating the unique effects of the non-thermal nature of PFA. Moreover, Koruth et al. [32] and Stewart et al. [33]have shown clear boundaries between the post-PFA myocardium and adjacent normal tissues. Although there are variations in the existing literature regarding the description of post-PFA

ISSN 2706-6819 Vol.6, Issue 9: 1-6, DOI: 10.25236/IJFM.2024.060901

myocardium and adjacent tissues, it is consistently noted that the boundaries of ablation damage are clearly visible. Further study by Stewart et al. [34] found that PFA performed in the superior vena cava, right atrial appendage, and right pulmonary veins resulted in transmural injury and complete circumferential scarring and fibrosis at four weeks post-ablation. In addition, PFA did not damage to the remaining myocardial tissue, as pathological examination of post-operative pig tissue showed no surviving myocardial fibers. Compared with the adjacent pre-ablation tissues, post-ablation tissue exhibited disrupted cell membrane, preserved structural extracellular matrix, and residual fibrosis or fibroblasts [35]. Unlike RFA, the damage caused by PFA is not coagulation necrosis but rather muscle fiber disruption and inflammation [36].Post-RFA, Pulmonary veins exhibit endoluminal hyperplasia, irreversible myocardial damage, scar tissue and stenosis, whereas pulmonary veins treated with PFA are surrounded by healthy connective tissue [37]. Tissue damage resulting from PFA presents as uniform fibrosis, without endocardial rupture, minimal retained myocardial and septal muscle cells, and minimal arterial remodeling [34]. In 2020, Bradley et al. [38] conducted energy delivery using catheters in the left and right atrial appendages and right upper pulmonary veins of pigs, and the results showed that PFA, compared to RFA, is less likely to induce of epicardial fat inflammation and promotes more uniform fibrosis remodeling of the myocardial wall. This further confirms the feasibility of implementing pulsed field therapy for atrial fibrillation in the heart.

4.1 Effective apposition-based ablation

During radiofrequency ablation or cryoballoon ablation procedures, the success or failure of the therapeutic outcome depends on the effective apposition-based ablation of the catheter to the tissue. Insufficient apposition can lead to the formation of incomplete transmural lesions, which may pose a risk for atrial fibrillation recurrence and create conditions for its recurrence. In Comparison to radiofrequency ablation, PFA acts on the tissue in close proximity rather than through direct apposition. The damage inflicted on the target tissue is caused by a high-voltage electric field, with the extent of damage depending on the intensity and proximity of the voltage delivered by the pulse field. Greater voltage intensity and closer proximity result in larger tissue damage [39]. The non-appositional nature of PFA effect on the tissue also increases the success rate of the procedure.

4.2 Ablation time

During the thermal or cryoablation, which involves heating or freezing, it typically takes several seconds to several minutes to achieve irreversible damage to the target tissue. Although research advancements have allowed for the delivery of radiofrequency ablation energy at higher power levels in shorter durations, period of time, it still requires a significant amount of time to achieve the desired ablation target [40-41]. In contrast, the energy supply in PFA is almost instantaneous, and the required energy level can be reached in a very short time. Reddy et al. [42] achieved rapid pulmonary vein isolation using biphasic PFA, with typically only one ablation per pulmonary vein requiring approximately three minutes of energy supply per patient. The average total operation time was 92.2 min, which was shorter than the average operation time of radiofrequency ablation and cryoballoon ablation reported by Kuck et al. [43] (141 min, 124 min) . The average catheter dwell time in PFA (34 min) was also shorter than that of radiofrequency ablation and cryoballoon ablation (109 min, 92 min) [42-43]. As research on PFA progresses, the required procedure time is likely to become even shorter, making it a realistic possible.

5. Factors Influencing the Efficacy of PFA

The effectiveness of PFA in the treatment of AF is influenced by multiple factors. Patient characteristics are one important factor, including age, gender, medical history and underlying health conditions. Older patients, those with other significant heart conditions, or comorbidities, may have a suboptimal response to the treatment. In addition, the severity of AF itself may also affect the effectiveness. Patients with milder disease may get better treatment outcomes, while patients with more severe or longer duration of the disease may require additional treatment to achieve desired results.

Operational technology is another key factor. The success rate and safety of pulse field ablation are influenced by the experience and expertise of the physician, as well as the quality and performance of the equipment. Precise and skilled manipulation is crucial to the outcome of treatment.

In addition, post-operative follow-up and management are also crucial for ensuring long-term

ISSN 2706-6819 Vol.6, Issue 9: 1-6, DOI: 10.25236/IJFM.2024.060901

efficacy of treatment. Regular electrocardiograms, cardiac monitoring, and clinical evaluations can help monitor the patient's rhythm status and make timely adjustments to the treatment plan. In actual clinical practice, it is necessary to comprehensively consider the individual characteristics and specific circumstances of the patients in order to formulate the optimal treatment approach.

6. Future Development Trends

First of all, with ongoing technological advancements and accumulated clinical practice, pulsed field ablation techniques will further enhance treatment accuracy and safety. By optimizing electrical field parameters, improving electrode designs, and enhancing image guidance, abnormal cardiac electrical signals can be located and ablated more accurately, thereby improving the therapeutic effect.

Secondly, pulsed field ablation technology will be better integrated with other treatment modalities, forming a multi-modal treatment strategy. By combining approaches such as pharmacotherapy, radiofrequency ablation, or surgical interventions, personalized treatment plans can be tailored to the specific needs of patients, and further improving the success rate of treating paroxysmal atrial fibrillation.

In addition, with the development of technologies such as artificial intelligence and machine learning, pulsed field ablation technology will be better integrated with intelligent-assisted systems. Through automated electrode positioning, real-time signal analysis, and predictive models, more accurate treatment decisions and personalized treatment plans can be provided, further enhancing treatment outcomes and improving patients' quality of life. Clinical studies and large-scale multicenter research will further validate the long-term efficacy and safety of pulsed field ablation techniques. A deeper understanding of the impact of pulsed field ablation on the mechanism of atrial fibrillation will help to better optimize treatment strategies and provide more precise and individualized treatment for specific patient populations.

7. Challenges

The first challenge lies in the consistency of treatment effect and the durability of long-term efficacy. Although pulsed field ablation technology has shown promising treatment effects, there are still variations in the success rate and long-term efficacy among different patients. Some patients may require multiple treatments or a combination of different therapeutic approaches to achieve sustained restoration of normal heart rhythm. Therefore, further research and technical improvements are still enhance the consistency and long-term stability of treatment.

The second challenge is the cost and accessibility of pulsed field ablation technology. The equipment and facilities required for this technology can be expensive, and it is not yet widely available in all healthcare facilities. This may limit the range of options for patients and the accessibility of the treatment. However, as the further development of technology and costs decrease, it is expected that this challenge will gradually be alleviated.

8. Conclusion

Pulsed field ablation technology, as a new treatment method for atrial fibrillation, holds significant potential and development prospects. Despite facing challenges and unsolved issues, there is an optimistic outlook for its future development, with ongoing technological improvements and accumulated clinical practice. It is expected to further improve the accuracy and safety of treatment. By combining with other treatment methods to form a multi-modal treatment strategy, personalized management of paroxysmal atrial fibrillation can be achieved, leading to better treatment results and improved quality of life for patients. Clinical studies and large-scale multi-center research will further validate the long-term efficacy and safety of pulsed field ablation technology, and provide more evidence for the optimization of treatment strategies. Gradually addressing the issues of cost and accessibility will ensure that more patients can benefit from this technology.

References

[1] Tondo C. How the new technologies and tools will change the electrophysiology of the future. Eur

ISSN 2706-6819 Vol.6, Issue 9: 1-6, DOI: 10.25236/IJFM.2024.060901

Heart J Suppl. 2023;25(Suppl C):C249-C252.

[2] Hindricks G, et al. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European association for cardio-thoracic surgery (EACTS). Eur Heart J. 2021;42(5):373–498

[3] Kornej J, Borschel C, Benjamin E, Schnabel R. Epidemiology of Atrial Fibrillation in the 21st Century: Novel Methods and New Insights. Circ. Res. 2020; 127, 4–20.

[4] Kirchhof P, et al. 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J. 2016;37(38):2893–2962.

[5] Chen L. Y, and Shen WK.Epidemiology of atrial fibrillation: Acurrent perspective. Heart rhythm. 2007; 4 (3), S1–S6.

[6] Tini G, Scagliola R, Monacelli F, La Malfa G, Porto I, Brunelli C, Ros G.M. Alzheimers Disease and Cardiovascular Disease: A Particular Association. Cardiol. Res. Pract. 2020; 2020, 2617970.

[7] Frost L, Vestergaard P, Mosekilde L. Hyperthyroidism and risk of atrial fibrillation or flutter: A population-based study. ACC Curr. J. Rev. 2004; 164, 1675–1678.

[8] Chamberlain A.M, Agarwal S.K, Folsom A.R, Duval S, Soliman E.Z, Ambrose M, Eberly L, Alonso A. Smoking and incidence of atrial fibrillation: Results from the Atherosclerosis Risk in Communities (ARIC) Study. Hear. Rhythm. 2011;8, 1160–1166.

[9] Casciola M, Feaster TK, Caiola MJ, Keck D, Blinova K. Human in vitro assay for irreversible electroporation cardiac ablation. Front Physiol. 2023;13:1064168.

[10] Metzner A, Kuck KH, Chun JKR. What we have learned: is pulmonary vein isolation still the cornerstone of atrial fibrillation ablation? Europace. 2022; 24(Suppl 2):ii8-ii13.

[11] Patterson E, Po SS, Scherlag BJ, Lazzara R. Triggered firing in pulmonary veins initiated by in vitro autonomic nerve stimulation. Heart Rhythm. 2005; 2, 624–631.

[12] Avazzadeh S, O'Brien B, Coffey K, O'Halloran M, Keane D, Quinlan LR. Establishing Irreversible Electroporation Electric Field Potential Threshold in A Suspension In Vitro Model for Cardiac and Neuronal Cells. J Clin Med. 2021 ;10(22):5443.

[13] Aldaas OM, Malladi C, Aldaas AM, Han FT, Hoffmayer KS, Krummen D, Ho G, Raissi F, Birgersdotter-Green U, Feld GK, Hsu JC. Safety and acute efficacy of catheter ablation for atrial fibrillation with pulsed field ablation vs thermal energy ablation: A meta-analysis of single proportions. Heart Rhythm O2. 2023;4(10):599-608.

[14] Stewart MT, et al. Intracardiac pulsed field ablation: proof of feasibility in a chronic porcine model. Heart Rhythm. 2019;16(5):754–764.

[15] Xie F, Zemlin CW. Effect of Twisted Fiber Anisotropy in Cardiac Tissue on Ablation with Pulsed Electric Fields. PLoS One. 2016;11(4):e0152262.

[16] Kotb A, Chin SH, Ng GA. Recent advances in the tools available for atrial fibrillation ablation. Expert Rev Med Devices. 2022;19(2):141-154.

[17] Ruzgys P, Novickij V, Novickij J, Šatkauskas S. Influence of the electrode material on ROS generation and electroporation efficiency in low and high frequency nanosecond pulse range. Bioelectrochemistry. 2019;127:87-93.

[18] Munawar T, Fujimori M, Vista W, Solomon S, Srimathveeravalli G. Abstract No. 368 Changes in ph and not temperature significantly contributes to cell death during IRE performed at low-voltage and high pulse numbers. J Vasc Interv Radiol. 2019; 30: S162-S163.

[19] Rubinsky L, Guenther E, Mikus P, Stehling M, Rubinsky B. Electrolytic effects during tissue ablation by electroporation. Technol Cancer Res Treat. 2016;15:NP95-NP103.

[20] Xie F, Varghese F, Pakhomov AG, Semenov I, Xiao S, Philpott J, Zemlin C. Ablation of myocardial tissue with nanosecond pulsed electric fields. PLoS One. 2015;10:e0144833.

[21] Zhang H, Liu K, Xue Z, Yin H, Dong H, Jin W, et al. High-voltage pulsed electric field plus photodynamic therapy kills breast cancer cells by triggering apoptosis. Am J Transl Res. 2018; 10: 334–51

[22] Howard B, Haines DE, Verma A, Packer D, Kirchhof N, Barka N, Onal B, Fraasch S, Miklav D, Stewart M.T.Reduction in pulmonary vein stenosis and collateral damage with pulsed field ablation compared with radiofrequency ablation in a canine model. Circ. Arrhythmia Electrophysiol. 2020;13, e008337.

[23] Lindemann F, Nedios S, Seewöster T, Hindricks G. Pulmonalvenenisolation bei vorhofflimmern mittels pulsed field ablation.Herz 2021;46, 318-322.

[24] Verma A, Boersma L, Haines DE, et al. First-in-human experience and acute procedural outcomes using a novel pulsed field ablation system: The PULSED AF Pilot Trial. Circ Arrhythm Electrophysiol. 2022; 15:e010168.

[25] Reddy VY, Neuzil P, Koruth JS, et al. Pulsed field ablation for pulmonary vein isolation in atrial fibrillation. J Am Coll Cardiol. 2019; 74: 315-26.

ISSN 2706-6819 Vol.6, Issue 9: 1-6, DOI: 10.25236/IJFM.2024.060901

[26] ClinicalTrials.gov. A Safety and Feasibility Study of the FARAPULSE Endocardial Ablation System to Treat Paroxysmal Atrial Fibrillation. ClinicalTrials.gov Identifier: NCT03714178. Available at: https://clinicaltrials.gov/ct2/show/NCT03714178 (accessed 13 December 2022).

[27] Sanchez-Somonte P, Verma A. Globe Pulsed Field System for High-definition Mapping and Ablation for Atrial Fibrillation. Heart Int. 2022; 16(2):85-90.

[28] Reddy V, Dukkipati S, Neuzil P, Anic A, Petru J, Funasako M et al. Pulsed field ablation of paroxysmal atrial fibrillation; 1-year outcomes of IMPULSE, PEFCAT, and PEFCAT II. JACC Clin Electrophysiol 2021; 7: 614–21.

[29] Boersma L. New energy sources and technologies for atrial fibrillation catheter ablation. Europace. 2022; 24(Suppl 2):ii44-ii51.

[30] Reddy V, Anter E, Rackauskas G, Peichl P, Koruth J, Petru J, et al. Lattice-tip focal ablation catheter that toggles between radiofrequency and pulsed field energy to treat atrial fibrillation. Circ Arrhythm Electrophysiol 2020;13:e008718

[31] Simon R, Mehta NK, Shah KB, Haines DE, Linte CA. Toward a Quasi-dynamic Pulsed Field Electroporation Numerical Model for Cardiac Ablation: Predicting Tissue Conductance Changes and Ablation Lesion Patterns. Comput Cardiol (2010). 2022; 2022:10.22489/CinC.2022.233.

[32] Koruth JS, Kuroki K, Iwasawa J, et al. Endocardial ventricular pulsed field ablation: A proof-of-concept preclini-cal evaluation[J]. Europace, 2020, 22(3) : 434 -439.

[33] Stewart MT, Haines DE, Verma A, et al. Intracardiac pulsed field ablation: Proof of feasibility in a chronic porcine model[J].Heart Rhythm, 2019, 16(5) :754 -764.

[34] Stewart MT, Haines DE, Miklav i D, et al. Safety and chronic lesion characterization of pulsed field ablation in a porcine model[J]. J Cardiovasc Electrophysiol, 2021, 32(4) : 958 -969.

[35] Witt CM, Sugrue A, Padmanabhan D, et al. Intrapulmonary vein ablation without stenosis: A novel balloon-based direct current electroporation approach[J]. J Am Heart Assoc, 2018, 7 (14) : e009575.

[36] Hong J, Stewart MT, Cheek DS, et al. Cardiac ablation via electroporation[J]. Annu Int Conf IEEE Eng Med Biol Soc, 2009: 3381-3384.

[37] Koruth J, Kuroki K, Iwasawa J, et al. Preclinical evalua-tion of pulsed field ablation: Electrophysiological and histological assessment of thoracic vein isolation[J]. CircArrhythm Electrophysiol, 2019, 12(12) : e007781.

[38] Bradley CJ, Haines DE.Pulsed field ablation for pul-monary vein isolation in the treatment of atrial fibril-lation [J].J Cardiovasc Electrophysiol, 2020, 31(8):2136-2147.

[39] Livia C, Sugrue A, Witt T, et al. Elimination of Purkinje fibers by electroporation reduces ventricular fibrillation vulnerability[J]. J Am Heart Assoc, 2018, 7 (15) :e009070.

[40] Barkagan M, Contreras-Valdes FM, Leshem E, et al. High-power and short-duration ablation for pulmonary vein isolation: Safety, efficacy, and long-term durability[J]. J Cardiovasc Electrophysiol, 2018, 29(9) : 1287 -1296.

[41] Bourier F, Duchateau J, Vlachos K, et al. High-power short-duration versus standard radiofrequency ablation: In-sights on lesion metrics[J]. J Cardiovasc Electrophysiol, 2018, 29(11) : 1570 -1575.

[42] Reddy VY, Neuzil P, Koruth JS, et al. Pulsed field ablation for pulmonary vein isolation in atrial fibrillation [J]. JAm Coll Cardiol, 2019, 74(3) : 315 -326.

[43] Kuck KH, Brugada J, Fürnkranz A, et al. Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation[J].N Engl J Med, 2016, 374(23) : 2235 -2245.