

# Contemporary technologies used for atrial fibrillation treatment

Przemysław Zająć<sup>1</sup>, Maciej Rycyk<sup>1</sup>, Natalia Zająć<sup>2</sup>,  
Karolina Wójcik<sup>3</sup>, Łukasz Konarski<sup>4</sup>, Maciej Wójcik<sup>4</sup>

<sup>1</sup> Abbott Medical Poland

<sup>2</sup> Independent Provincial Public Hospital in Zamość, Poland

<sup>3</sup> Student, Medical University of Lublin, Poland

<sup>4</sup> Department of Cardiology, Medical University of Lublin, Poland

**European Journal  
of Medical Technologies**

2018; 2(19): 1-11

Copyright © 2018 by ISASDMT  
All rights reserved

www.medical-technologies.eu  
Published online 14.08.2018

## Corresponding address:

dr hab. n. med.

Maciej Wójcik

Department of Cardiology,  
Medical University  
of Lublin, Poland

SPSK Nr 4,

ul. Jaczewskiego 8

20-954 Lublin, Poland

e-mail: m.wojcik@

am.lublin.pl

## Abstract

Currently, atrial fibrillation is the most common arrhythmia with prevalence estimated about 2% of the general population and is characterized by chaotic contraction of the atria. This arrhythmia may be associated with structural heart disease and other co-occurring chronic conditions and also related to an increased risk of stroke. The pulmonary vein isolation is the most commonly employed strategy performed during medical procedure called ablation with several techniques as point-by-point catheter radio frequency ablation, circular radio frequency catheter ablation, cryoballoon ablation, ultrasound ablation, laser ablation and surgical ablation.

## Key words:

atrial fibrillation, radiofrequency ablation, cryoablation, cryoballoon, ultrasound ablation, laser ablation, surgical ablation, cardiology, electrophysiology, heart, arrhythmia

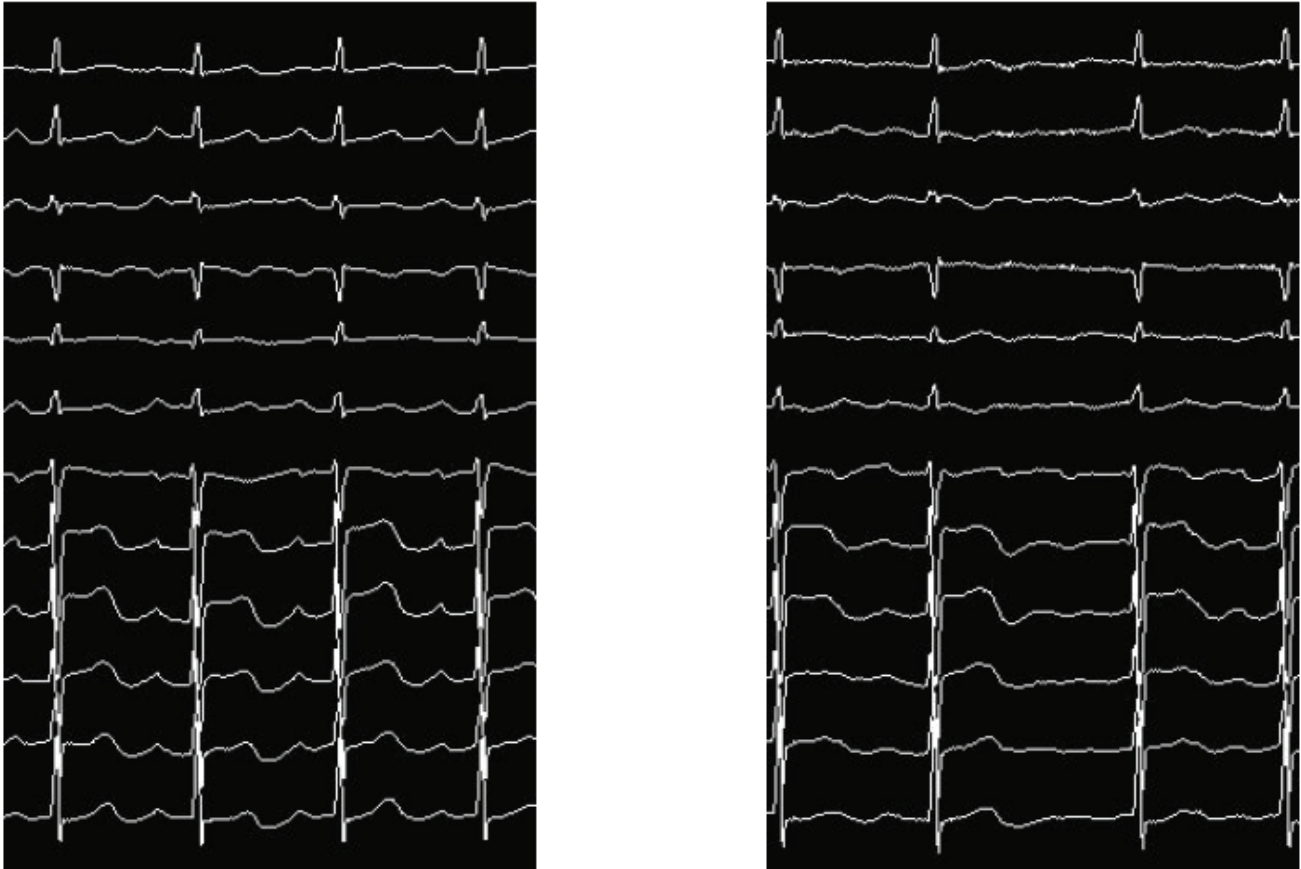
## Introduction

Atrial fibrillation (AF) is the most diagnosed rhythm disturbance that increases in occurrence with advancing age and concerns about 2% of human population. Approximately 1% of patients with AF are younger than 60 years. Prevalence of AF in older patients (75 to 84 years) is up to 12% and above 30% when >80 years old. [1,2]. In some cases, e.g. for individuals of European descent, the lifetime risk of developing AF after 40 years old estimates 26% for men and 23% for women [3]. AF is also associated with structural heart disease and other co-occurring chronic conditions. Fast and precise diagnosis of AF helps to provide individual and successful path of treatment. The clinical symptoms are characterized by dyspnea, palpitations, and more rarely, loss of consciousness. The suspicion of AF is based on the patient's clinical history and physical examination when the presence of an irregular pulse and/or jugular venous pulsations is confirmed. AF can be

also suggests by discordant in the heart sounds (intensity of the first heart sound or absence of a fourth sound previously heard during sinus rhythm). Finally, AF episodes occurrence is proven by rhythm monitoring (e.g. telemetry, Holter monitor, event recorders), implanted loop recorders, pacemakers or defibrillators, or, in rare cases, by electrophysiological study [4]. AF is noticeable in 12-lead electrocardiogram (ECG) as an irregular rhythm with no visible P waves, replaced by an incoherent baseline wave, also termed as f wave, which refers to chaotic electric atrial activity (Fig. 1).

From the hemodynamic point of view, many disfunctions such a variable combination of suboptimal ventricular rate control, loss of coordinated atrial contraction, beat-to-beat variability in ventricular filling, and sympathetic activation are impacted by AF [5-7]. Loss of atrial contraction often results in decrease of cardiac output [8-9].

AF also confers an increased risk of stroke and/or peripheral thromboembolism owing to the formation



**Fig. 1.** 12-lead ECG of sinus rhythm (left panel) and atrial fibrillation (right panel)

of atrial thrombi, usually in the left atrial appendage (LAA) [4].

The origin of AF is still unclear. Several hypotheses have been proposed throughout the years to explain the electrophysiological mechanisms that initiate and maintain AF [10]. In terms of above, situation is complex, and it is likely that multiple mechanisms coexist in an individual patient.

AF is connected with structural and/or electrophysiological abnormalities occurrence that leads to formation of abnormal impulse and/or propagation. These abnormalities are caused by diverse pathophysiological mechanisms [11-12]. Also, any disturbance of atrial architecture potentially increases susceptibility to AF [13]. Similarly, diverse diseases such as amyloidosis, hemochromatosis, and sarcoidosis can also promote AF. Moreover, AF can be advanced as well by extracardiac factors for instance hypertension, sleep apnea, obesity, use of alcohol/drugs, and hyperthyroidism. Even in patients suffered from paroxysmal AF without recognized structural heart disease, atrial biopsies have revealed inflammatory infiltrates consistent with myocarditis and fibrosis [14].

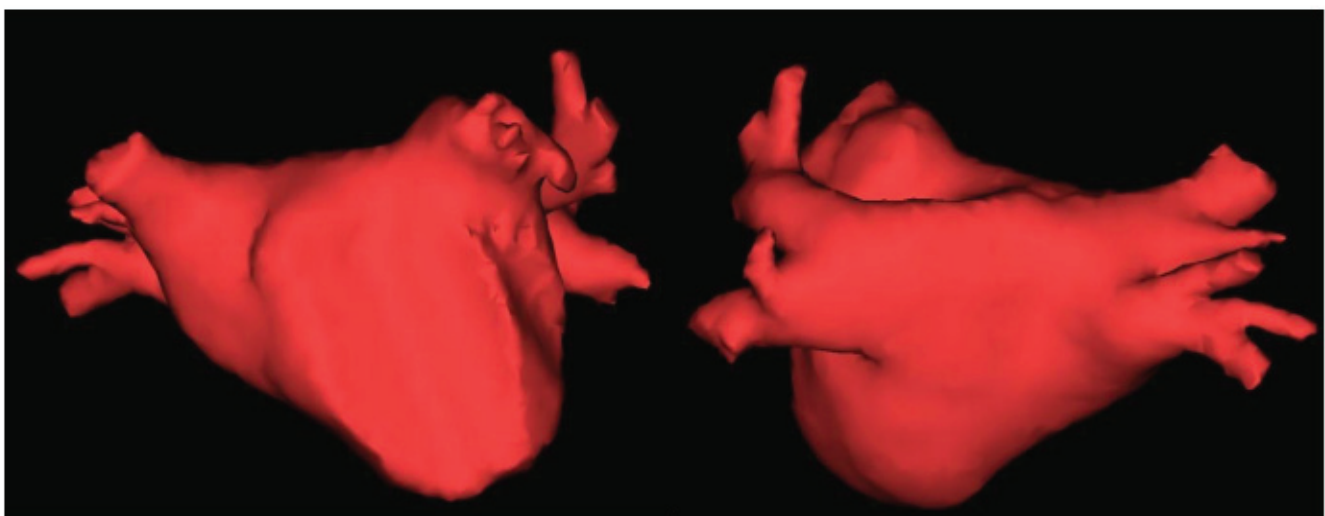
In large number of cases, ectopic focal discharges often initiate AF with its origin in left atrium (LA) (Fig. 2). These triggers, in about 94% of patients, are located in the pulmonary veins (PVs) ostia [15-17]. In comparison to left atrium, pulmonary veins ostia are characterized by dissimilar structure and

propagation features due to different embryological origin. Unique anatomic and electrophysiological features of the PVs and atriopulmonary vein junctions may account for their arrhythmogenic nature, so catheter ablation of left arrhythmogenic triggers has become a valid option for the treatment of AF. These observations led to the development of pulmonary vein isolation (PVI) as the cornerstone for radiofrequency catheter ablation strategies [10]. Although, the PVs are the most common places for ectopic focal discharges, triggers can also somewhere else, for instance LA posterior wall, ligament of Marshall, coronary sinus, venae cavae, septum and appendages [18].

There are four types of AF depending on the duration of the episode (Table 1) [4].

AF often progresses from paroxysmal to persistent over a variable period of time. Cardioversion of AF and subsequent maintenance of sinus rhythm are more likely to be successful when AF duration is <6 months [19]. Another type of AF is called "lone AF" that is a historical descriptor applied to younger people without clinical or echocardiographic evidence of cardiopulmonary disease, hypertension, or diabetes mellitus [20,21]. AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve or mitral valve repair is called nonvalvular AF [10].

As it has been mentioned, PVI is the first step that leads to abolish or suppress AF. In fact, considering



**Fig. 2.**  
Left atrium anatomy (CT scan)

**Table 1.**  
Types of AF

Term	Definition
paroxysmal AF	<ul style="list-style-type: none"> <li>lasts less than 7 days</li> <li>terminates spontaneously</li> </ul>
early persistent AF	<ul style="list-style-type: none"> <li>&lt;1 year from first diagnosis of persistent AF</li> <li>lasts more than 7 days</li> <li>requires pharmacological cardioversion</li> </ul>
persistent AF	<ul style="list-style-type: none"> <li>lasts more than 7 days</li> <li>requires pharmacological cardioversion</li> </ul>
longstanding persistent AF	<ul style="list-style-type: none"> <li>lasts more than 1 year</li> </ul>
permanent	<ul style="list-style-type: none"> <li>accepted by cardiologist</li> <li>no attempts to restore sinus rhythm</li> <li>no cardioversion considered</li> </ul>

paroxysmal AF, alone correctly performed PVI indicates up to 90% of success rate [22-23]. This approach is generally sufficient in paroxysmal AF treatment but often not enough in patient with persistent or paroxysmal AF and requires more advanced action. In this case, creation of linear lesions within LA (roof, mitral isthmus) results in a compartmentalization of this chamber and could help prevent of AF episodes [4, 24-25]. Success rate of ablation of persistent AF estimates up to 75%, however retreatment is necessary in more than 25% [22].

## Radiofrequency ablation

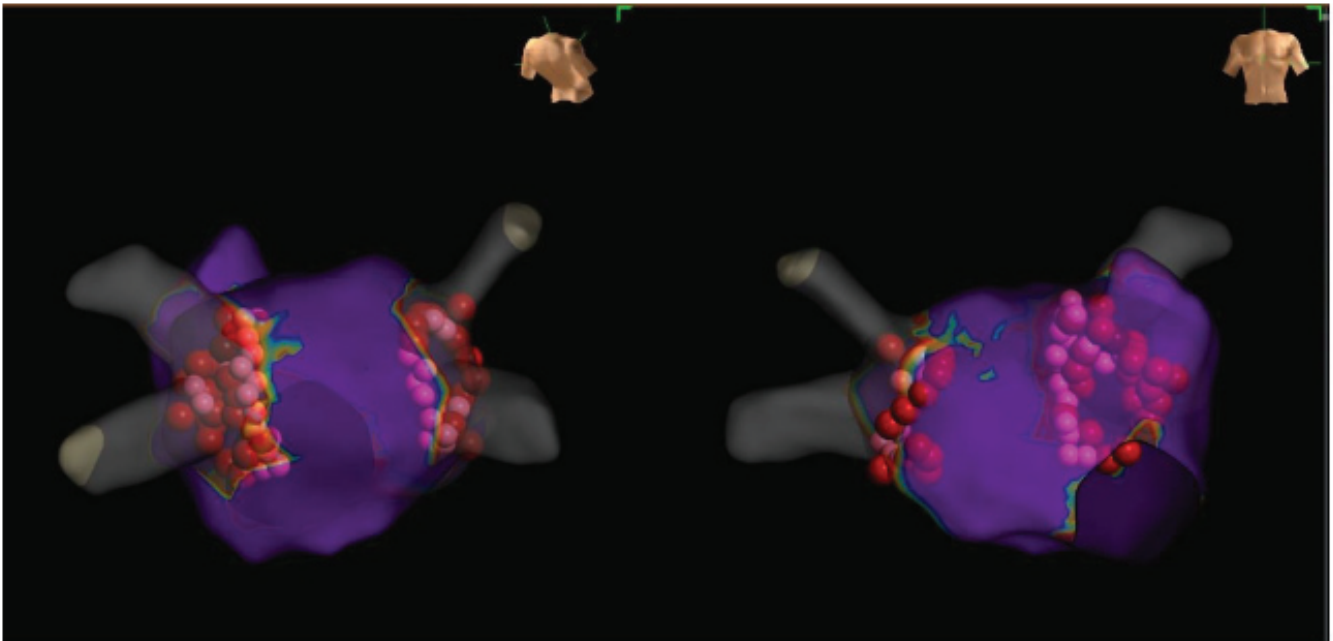
Radiofrequency (RF) energy is the most common and important way for cardiac tachyarrhythmias curative treatment. One of the first experimental studies, that showed the effect of RF ablation, was presented in 1986 [26]. In RF ablation, high frequency electrical current is passed through the myocardium between the catheter electrode and dispersive electrode placed on the patient's body. The tissue resistivity results in dissipation of RF energy as heat that conducts passively to deeper tissue layers. Lesion formation is achieved by penetration of power generated in two processes called resistive and conductive heating. Firstly, electrical current that flows through a cardiac tissue, with a certain electrical resistance, dissipates

power in the tissue. Resistive heating begins immediately with the delivery of RF current but has limited penetration. Secondly, conduction of the heat is relatively slow, especially in biological tissue. Deep tissue destruction and transmural lesion formation is reached as an effect of both described processes [27].

## Point-by-point RF catheter ablation

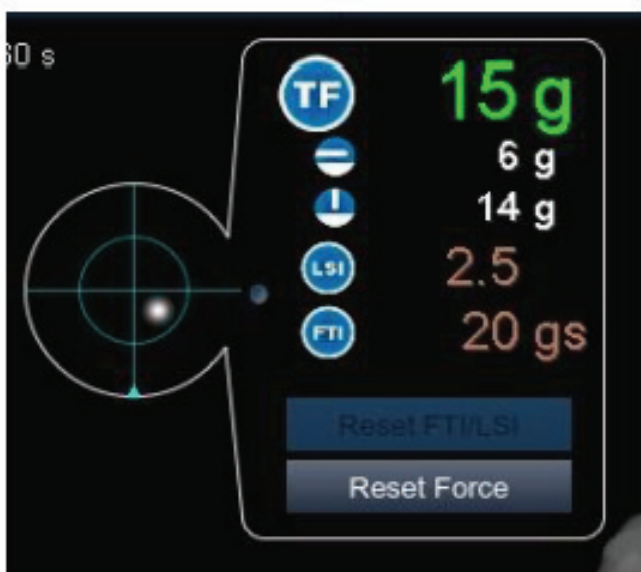
Point-by-point RF catheter ablation technology is a prevailing and the best known type of ablation technique worldwide. The concept of PVI using catheter is based on creation of multiple lesions around the PVs ostia. The successful PVI requires no gap formation along the linear scar (Fig. 3) which is further proved by the presence of the bi-directional conductive block between PVs and LA.

The depth of the individual lesion depends on the size of the distal electrode, electrode cooling and electrode-tissue contact. Nowadays, the technology used in some novel catheters (e.g. TactiCath™ Contact Force Catheter- Abbott (St. Jude Medical), ThermoCool® SmartTouch™ – Biosense Webster) [28] allows to measure and display as numeric value of contact between the tip of the catheter and cardiac tissue (Fig. 4). This unique feature, in combination with other physical values e.g. impedance changes,



**Fig. 3.**

Visualization of left atrium and pulmonary vein isolation (represented by pink/red spheres) with color-coded voltage map (settings:  $<0.1\text{ mV}$  (grey) – scar,  $0.1\text{ mV}$ - $0.5\text{ mV}$  (red, yellow, blue)- low-voltage area,  $>0.5\text{ mV}$  (purple) – normal tissue) (EnSite Precision™)



**Fig. 4.**

Catheter (TactiCath™ Contact Force Catheter) tip-tissue contact visualization (EnSite Precision™)

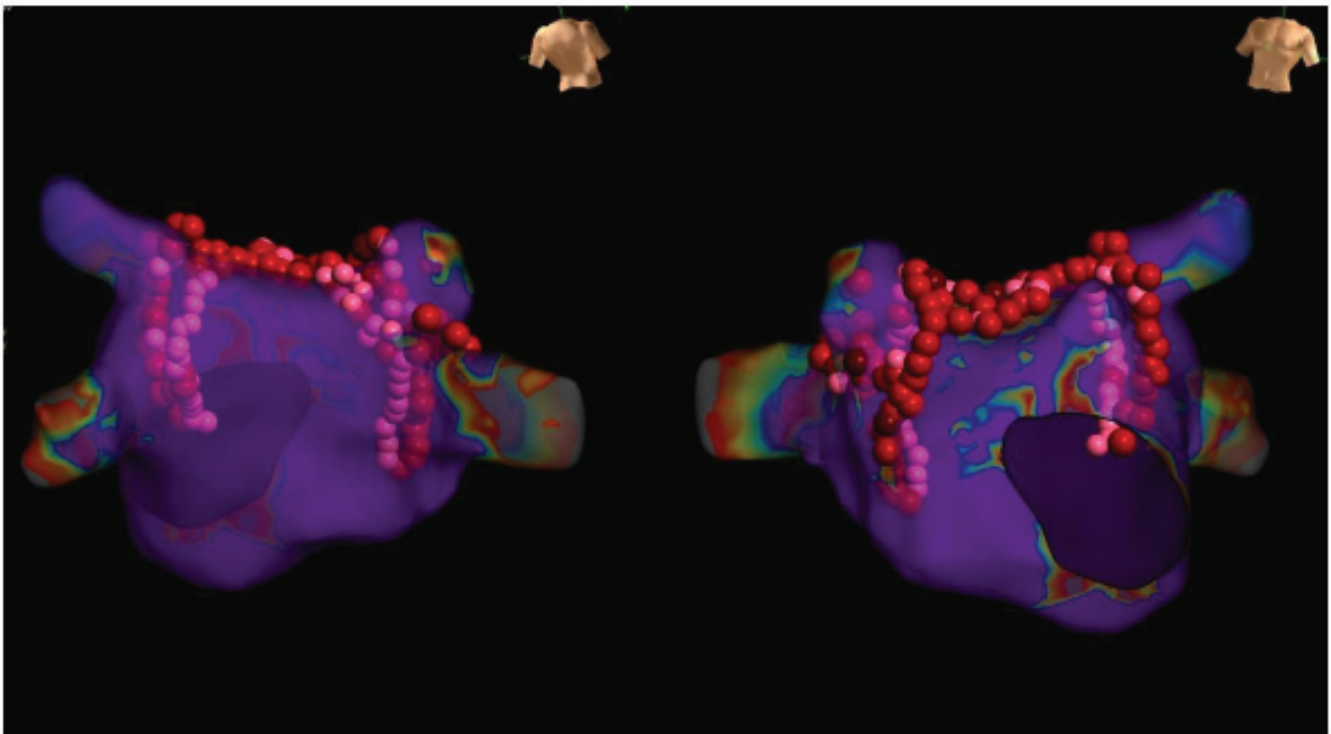
provides information if energy is successfully transmitted directly to the tissue. Electrode-tissue contact is crucial in terms of effective lesion formation what significantly improves procedural success rate [29]. Also monitoring electrode-tissue contact reduces the number of complications, particularly cardiac

tamponade [30]. In addition, RF catheter can be visualized by electroanatomic cardiac mapping system (e.g. EnSite Precision™ – Abbott (St. Jude Medical), Carto™- Biosense Webster) what positively impacts on procedural time, safety and allows to acquire electrical information of LA [31-32].

In some percentage of studies, alone PVI is not enough to eliminate AF episodes. Additional and precise high-density voltage mapping facilitates exact tissue electrical features recognition [33]. In this case point-by-point catheter ablation allows to create further scar lines in LA that can help to abolish AF occurrence (Fig. 5) [34].

RF catheter ablation is associated with important risks of major complications. An international survey of radiofrequency catheter ablation procedures conducted in 2010 reported a 4.5% incidence of major complications, including a 1.3% rate of cardiac tamponade, a 0.94% of stroke, a 0.04% rate of atrial-esophageal fistula, and a 0.15% rate of death [35].

Due to complexity of maneuverability and potential severe complications there is still field to emerge novel and alternative techniques which can be used in AF treatment [36].



**Fig. 5.**

Visualization of left atrium and pulmonary vein isolation with additional roof line (represented by pink/red spheres) with color-coded voltage map (settings:  $<0.1\text{mV}$  (grey)- scar,  $0.1\text{mV}$ - $0.5\text{mV}$  (red, yellow, blue) – low-voltage area,  $>0.5\text{mV}$  (purple) – normal tissue) (EnSite Precision™)

## Multielectrode circumferential ablation catheters

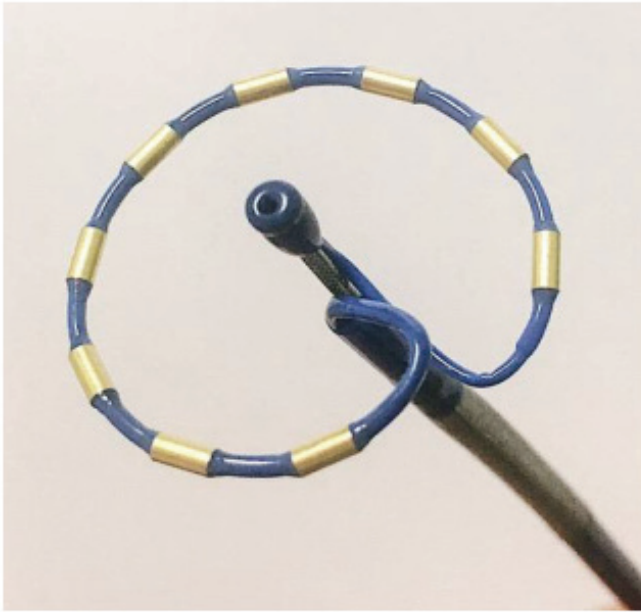
Multielectrode circumferential ablation catheters were developed in order to create linear lesions around the PVs in short time and single shot process. Two circular multielectrode catheters are available on the market. PVAC® (Medtronic) (Fig. 6) is based on the phased RF ablation technology, while – nMARQ™ (Biosense Webster) (Fig. 7) – is based on the irrigated multielectrode electroanatomically guided RF catheter. If the circular multielectrode catheter is correctly placed in the region of PV ostium, complete PVI is reached in just one or two applications. Energy is transmitted to the tissue from all electrodes simultaneously leading to scar formation. PVAC® consists of 10 electrodes placed on 25 mm diameter spiral array, with the capability of straightening the circular end over the wire into the vein. The nMARQ™ consists of 10 irrigated electrodes with an adjustable circular array of 20-35 mm diameter. The second

presented catheter can be recognized by the CARTO® (Biosense Webster) electroanatomical mapping system [37]. Nowadays, nMARQ™ catheter has been deleted from the market due to multiple PVs stenosis and esophageal injuries occurrence [38].

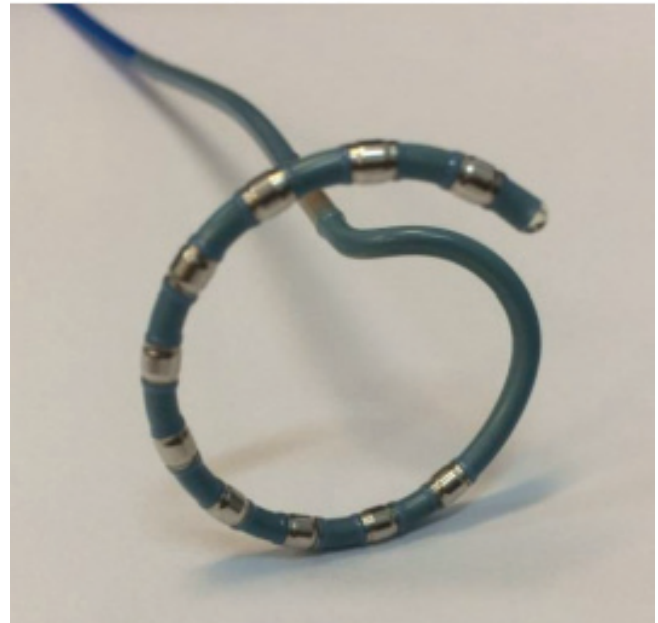
The success rate of usage of the multielectrode circumferential ablation catheters strongly depends on LA anatomy. In case of any anatomical abnormalities (e.g. atypical diameter or number of PVs) the successful PVI is rarely achievable [39].

## Cryothermal energy

Cryothermal ablation is an alternative source to RF that can be used for treatment of cardiac arrhythmias. Recently, a number of point-by-point and balloon-based cryoablation systems have been developed for endocardial use [40]. The mechanism of tissue injury is achieved by creation of ice crystals within the cell that disrupts cell membranes and interrupts both cellular metabolism and any electrical activity in that cell [31].



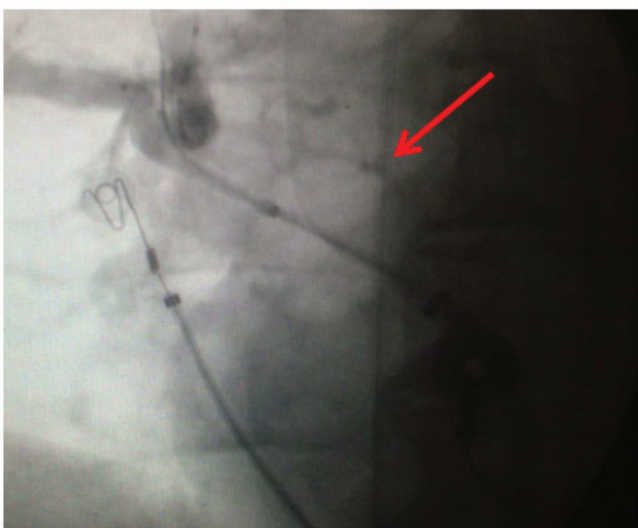
**Fig. 6.**  
Multielectrode circumferential ablation catheter PVAC®  
(Medtronic)



**Fig. 7.**  
Multielectrode circumferential ablation catheter nMARQ™  
(Biosense Webster)

## Cryoballoon ablation

In the beginning, cryothermal technology was implemented to point-by-point catheter ablation and used during supraventricular tachyarrhythmias treatment, especially with the origin near atrioventricular node area. Currently, cryoablation had emerged as a promising alternative approach to traditional point-by-point RF ablation, and was characterized by creating circumferential lesions with cryoballoon (Medtronic) (Fig. 7) (23 or 28 mm diameter) in a relatively



**Fig. 8.**  
Inflated cryoballoon (Medtronic) seen under fluoroscopy

simple manner. Similarly to ablation with multi-electrode circumferential catheter, the principle of operation is based on fast and not complicated technique. After the balloon is placed in the PV ostium, liquid nitrous oxide is delivered under pressure through the catheter within the balloon, where it changes to gas, resulting in cooling surrounding tissue [31].

Cryoballoon technology indicates similar success rate to RF point-by-point catheter ablation in patients with paroxysmal AF [41] although, the usage is limited to typical LA anatomy. Using big cryoballoon (23/28 mm) in small atria (<40 mm) is currently debated as such a cryoballoon may lead to atrium stiffness. Among complications associated with cryoablation systems (e.g. esophageal injuries, PVs ostia stenosis) [42], phrenic nerve palsy is the most common with incidence report about 3.5% [43].

Learning curve is much shorter in comparison to point-by-point catheter ablation and may be less influenced by individual difference in experience and aptitude [44-45].

## Laser ablation

Both described approaches, RF and cryoablation, are the most common technologies used for AF

treatment. Another tool that has been developed for AF ablation is the visually guided laser ablation balloon (CardioFocus). The system consists of the following major components: delivery sheath, balloon ablation catheter, endoscope, lesion generator, and cooling console [46]. In this case, 980 nm laser wave generated by a diode is responsible for lesion formation. Inserted balloon-catheter, that can be inflated and deflated in accordance with PV diameter to the range of 9–35 mm [47], is filled with deuterium oxide, which allows the laser energy to pass through it with minimal absorption [48]. The laser energy is delivered around the PV ostium and each PV is isolated individually [49].

Endoscopic laser balloon ablation system is a relatively novel and complicated technique used for PVI with no significant worldwide attention.

## Ultrasound ablation

A high-intensity focused ultrasound balloon catheter (ProRhythm) has been developed to simplify PVI with less ostial and more antral lesion creation with lower risk of thrombus formation, pulmonary vein stenosis, as well as left atrial perforation [50]. The ultrasound concept consists of two attached non-compliant balloons where one is filled with water and contrast media, second with carbon dioxide. The distal balloon contains additionally a 9 MHz ultrasound crystal. The proximal balloon forms a parabolic surface at the base of the distal balloon, which reflects the ultrasound in the forward direction. Three different balloon sizes are available depending on the PVs diameter (24, 27 and a 32 mm) [51-52].

Although this balloon-based ultrasound ablation system was demonstrated to be effective, it was removed from the market because of a high incidence of atrial esophageal fistulas, some of which resulted in patient death [10,53].

## Surgical ablation

Surgical techniques initially aimed at isolating the abnormal tissue from a particular area of the atria.

The technique used in surgical epicardial ablation of AF is called Cox maze procedure and was firstly introduced in 1987 by James Cox surgery [54]. This method is typically performed in conjunction with surgery of another heart surgery for CABG or valve implantation. The procedure involves complex bi-atrial incisions (along mitral isthmus, across fossa ovalis, PVs encirclement) designed to stop abnormal electrical activity. The procedure resulted in high rate of pacemaker implantation. The Cox maze procedure was evolved throughout the years by variety of additional concepts, e.g. excision of the left atrial appendage [55]. The Cox maze procedure had not been widely adopted by the surgical community because of its complexity. Introduced clinically in 2002, the Cox maze IV procedure consists of a combination of bipolar radiofrequency and cryothermal ablation lines that replace most of the surgical incisions [56].

The surgical maze procedure for AF shows some success [57], however is not very often due procedural complexity, invasiveness and potential severe complications [58].

## Conclusions

The development of medical technologies has a significant impact on treatment of patients with atrial fibrillation disease. Several approaches can be used for deleting isolating triggers of that arrhythmia. Pulmonary veins isolation indicates distinct success rate. Ablation, despite its limitation, is the most efficient method in terms of atrial fibrillation abolishment. Continuous evolution of technologies is still required to make the procedure as fast, safe and effective as possible.

## References

1. Wolf P, Benjamin E, Belanger A, et al. Secular trends in the prevalence of atrial fibrillation: the Framingham Study. *Am Heart J* 1996; 131: 790-5.
2. Camm A, Kirchhof P, Lip G, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European society of Cardiology (ESC). *Eur Heart J* 2010; 31: 2369-429.



3. Lloyd-Jones D, Wang T, Leip E, et al. Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. *Circulation* 2004; 110: 1042-6.
4. January C, Wann L, et al. 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation. *Journal of the American College of Cardiology*, Elsevier 2014 VOL. 64. NO. 21.
5. Ikeda T, Murai H, Kaneko S, et al. Augmented single-unit muscle sympathetic nerve activity in heart failure with chronic atrial fibrillation. *J Physiol* 2012; 590: 509-18.
6. Hsu L, Jais P, Sanders P, et al. Catheter ablation for atrial fibrillation in congestive heart failure. *N Engl J Med* 2004; 351: 2373-83.
7. Segerson N, Sharma N, Smith M, et al. The effects of rate and irregularity on sympathetic nerve activity in human subjects. *Heart Rhythm* 2007; 4: 20-6.
8. Williams L, Frenneaux M. syncope in hypertrophic cardiomyopathy: mechanisms and consequences for treatment. *Europace* 2007; 9: 817-22.
9. Ammass N, Seward J, Bailey K, et al. Clinical profile and outcome of idiopathic restrictive cardiomyopathy. *Circulation* 2000; 101: 2490-6.
10. Calkins H, Kuck K, Cappato R, et al. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, end-points, and research trial design. *Heart Rhythm* 2012; 9: 632-96.
11. Savaliev I, Kakouros N, Kourliourous A, et al. Upstream therapies for management of atrial fibrillation: review of clinical evidence and implications for European Society of Cardiology guidelines: part I: primary prevention. *Europace* 2011; 13: 308-28.
12. Wakili R, Voigt N, Kaab S, et al. Recent advances in the molecular pathophysiology of atrial fibrillation. *J Clin Invest* 2011; 121: 2955-68.
13. Kistler P, Sanders P, Fynn S, et al. Electrophysiologic and electroanatomic changes in the human atrium associated with age. *J Am Coll Cardiol* 2004; 44: 109-16.
14. Frustaci A, Chimenti C, Bellocci F, et al. Histological substrate of atrial biopsies in patients with lone atrial fibrillation. *Circulation* 1997; 96: 1180-4.
15. Haissaguerre M, Jais P, Shah D, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med* 1998; 339: 659-66.
16. Jais P, Haissaguerre M, Shah D, et al. A focal source of atrial fibrillation treated by discrete radiofrequency ablation. *Circulation* 1997; 95: 572-6.
17. Scherf D, Romano F, Terranova R. Experimental studies on auricular flutter and auricular fibrillation. *Am Heart J* 1948; 36: 241-51.
18. Cuculich P, Wang Y, Lindsay B, et al. Noninvasive characterization of epicardial activation in humans with diverse atrial fibrillation patterns. *Circulation* 2010; 122: 1364-72.
19. Frick M, Frykman V, Jensen-Urstad M, et al. Factors predicting success rate and recurrence of atrial fibrillation after first electrical cardioversion in patients with persistent atrial fibrillation. *Clin Cardiol* 2001; 24: 238-44.
20. Patton K, Zacks E, Chang J, et al. Clinical subtypes of lone atrial fibrillation. *Pacing Clin Electrophysiol* 2005; 28: 630-8.
21. Wójcik M, Berkowitsch A, Zaltsberg S, Hamm CW, Pitschner HF, et al. Cryoballoon ablation in young patients with lone paroxysmal atrial fibrillation. *Rev Esp Cardiol* 2014; 67:558-63- Vol. 67.
22. Khoueiry Z, Albenque J, Providencia R, et al. Outcomes after cryoablation vs. radiofrequency in patients with paroxysmal atrial fibrillation: impact of pulmonary veins anatomy. *Europace* 2016; 18, 1343-1351.
23. Wójcik M, Berkowitsch A, Zaltsberg S, Hamm CW, Pitschner HF, Kuniss M, Neumann T. Cryoballoon ablation of atrial fibrillation: how important is the proper selection of patients? *Cardiol J* 2015; 22 (2): 194-200.
24. Kettering K, Yim D, Albert C, Gramley F. Catheter ablation of persistent atrial fibrillation: Long-term results of circumferential pulmonary vein ablation in combination with a linear lesion at the roof of the left atrium. *Herzschrittmacherther Elektrophysiol*. 2017.
25. Haumer M, Wutzler A, Parwani A, Attanasio P, Matsuda H, et al. Comparison of the anterior and posterior mitral isthmus ablation lines in patients with perimitral annulus flutter or persistent atrial fibrillation. *J Interv Card Electrophysiol* 2015; 44 (2): 119-29.
26. Hoyt R, Stephen Huang S, Marcus F. Factors influencing trans-catheter radiofrequency ablation

- of the myocardium. *J Appl Cardiol* 1986; 1: 469-486.
27. Wittkamp F, Nakagawa H. RF Catheter Ablation: Lessons on lesions. *Journal Compilation Blackwell Publishing, PACE*, 2006; Vol.29.
  28. Wysocka A, Wójcik M. Contact force technology in catheter ablation of atrial fibrillation. *European Journal of Medical Technologies* 2016; 1 (10): 1-7.
  29. Kuck K, Reddy V, Schmidt B, et al. A novel radiofrequency ablation catheter using contact force sensing. *Tocatta study. Heart Rhythm* 2012; 9:18-23.
  30. Calkins H, Kuck, K, Cappato R, Brugada J, et al. 2012 HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: Recommendations for Patients Selection, Procedural Techniques, Patient Management and Follow-up, Definitions, Endpoints, and Research Trial Design. A report of the Heart Rhythm Society Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. 2011.12.016.
  31. Zając P, Konarski Ł, Wójcik M. EnSite Precision™-3D Cardiac Mapping System. *European Journal of Medical Technologies* 2016; 3 (12): 1-7.
  32. Zając P, Rycyk M, Pić N, Wójcik K, Konarski Ł, Wójcik M. Electroanatomic Mapping System- the useful tool for electrophysiology. *European Journal of Medical Technologies* 2016; 4 (13): 17-26.
  33. Wójcik M, Konarski Ł, Aljabali P, Zając P, Błaszczuk R. Ablation of symptomatic ventricular tachycardia after surgical correction of ventricular septal defect in childhood: using high-density mapping, how precise is EnSite Precision? *Kardiologia Polska*, 2018; 76 (5): 930.
  34. Rolf S, Kircher S, Arya A, Eitel C, Sommer P, Richter S, Gaspar T, Bollmann A, Altmann D, Piedra C, Hindricks G, Piorkowski C. Tailored atrial substrate modification based on low-voltage areas in catheter ablation of atrial fibrillation. *Circ Arrhythm Electrophysiol* 2014; 7 (5): 825-33.
  35. Cappato R, Calkins H, Chen S, et al. Updated worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circ Arrhythm Electrophysiol* 2010; 3: 32-8.
  36. Baman T, Jongnarangsin K, Chugh A, Suwanagool A, Guiot A, Madenci A, et al. Prevalence and predictors of complications of radiofrequency catheter ablation for atrial fibrillation. *J Cardiovasc Electrophysiol* 2011; 22: 626-31.
  37. Laish-Farkash A, Khalameizer V, Fishman E, Cohen O, Yosefy C, et al. Safety, efficacy, and clinical applicability of pulmonary vein isolation with circular multi-electrode ablation systems: PVAC® vs. nMARQTM for atrial fibrillation ablation. *Europace* 2016; 18, 807-814.
  38. Di Monaco A, Quadrini F, Katsouras G, Caccavo V, Troisi F, et al. Ablation of atrial fibrillation and esophageal injury: Role of bipolar and unipolar energy using a novel multipolar irrigated ablation catheter. *Heart Rhythm* 2015; 12 (6): 1120-7.
  39. Mulder AA, Wijffels MC, Wever EF, Boersma LV. Pulmonary vein anatomy and long-term outcome after multi-electrode pulmonary vein isolation with passed radiofrequency energy for paroxysmal atrial fibrillation. *Europace* 2011; 13 (11): 1557-61.
  40. Hoyt R, Wood M, Daoud E, et al. Transvenous catheter cryoablation for treatment of atrial fibrillation: results of a feasibility study. *Pacing Clin Electrophysiol* 2005; 28 Suppl 1: S78-82.
  41. Fuernkranz A, Brugada J, Albenque J, Tondo C, Bestehorn K, et al. Rationale and Design of FIRE and ICE: A multicenter randomized trial comparing efficacy and safety of pulmonary vein isolation using a cryoballoon versus radiofrequency ablation with 3D-reconstruction. *J Cardiovasc Electrophysiol* 2014; 25 (12): 1314-20.
  42. Chen Y, Lu Z, Xiang Y, Hou J, Wand Q, Lin H, Li Y. Cryoablation vs. radiofrequency ablation for treatment of paroxysmal atrial fibrillation: a systematic review and meta-analysis. *Europace* 2017; 19 (5): 784-794.
  43. Herweg B, Ali R, Khan N, Ilcercil A, Barold S. Esophageal contour changes during cryoablation of atrial fibrillation. *Pacing Clin Electrophysiol* 2009; 32 (6): 711-6.
  44. Metzner A, Rausch P, Lemes C, et al. The incidence of phrenic nerve injury during pulmonary vein isolation using the second-generation 28 mm cryoballoon. *J Cardiovasc Electrophysiol* 2014; 25: 466-470.
  45. Wójcik M, Berkowitsch A, Zaltsberg S, Hamm CW, Pitschner HF, et al. Learning curve in cryoballoon ablation of atrial fibrillation: eight-year experience. *Circ J* 2014; 78 (7): 1612-8.
  46. Dukkipati S, Neuzil P, Skoda J, Petru J, D'Avila A, Doshi S, Reddy V. Visual Balloon-Guided

- Point-by-Point Ablation. *Circ Arrhythm and Electro-physiol* 2010; 3: 266-273.
47. Gerstenfeld E, Duggirala S. Atrial Fibrillation Ablation: Indications, Emerging Techniques, and Follow-Up. Elsevier 2015; 58: 202-212.
  48. Kumar N, Blaauw Y, Timmermans C, Pison L, Varnooy K, Crijns H. Adenosine testing after second-generation balloon devices (cryothermal and laser) mediated pulmonary vein ablation for atrial fibrillation. *J Intervent Cardiac Electrophysiol* 2014; 41: 91-97.
  49. Challa P, Mansour M. Atrial Fibrillation: Update on Ablation strategies and Technology. *Curr Cardiol Rep* 2011; 13: 394.
  50. Nakagawa H, Antz M, Wong T, Schmidt B, et al. Initial Using a Forward Directed, High-Intensity Focused Ultrasound Balloon Catheter for Pulmonary Vein Antrum Isolation in Patients with Atrial Fibrillation. *J Cardiovasc Electrophysiol* 2007; 18: 136-144.
  51. Metzner A, Chun J, Neven K, et al. Long-term clinical outcome following pulmonary vein isolation with high-intensity focused ultrasound balloon catheters in patients with paroxysmal atrial fibrillation. *Europace* 2010; 12: 188-193.
  52. Neven K, Schmidt B, Metzner A, Otomo K, et al. Fatal End of a Safety Algorithm for Pulmonary Vein Isolation With Use of High-Intensity Focused Ultrasound. *Circulation: Arrhythmia and Electrophysiology* 2010; 3: 260-265.
  53. Cox J. The surgical treatment of atrial fibrillation. Invasive surgical technique. *J Thorac Cardiovasc Surg* 1991; 101: 584-92.
  54. Fragakis N, Pantos I, Younis J, Hadjipavlou M, Katriotis D. Surgical ablation for atrial fibrillation. *Europace* 2012; 14 (11): 1545-1552.
  55. Prasad S, Maniar H, Camillo C, et al. The Cox maze III procedure for atrial fibrillation: long-term efficacy in patients undergoing lone versus concomitant procedures. *J Thorac Cardiovasc Surg* 2003; 126: 1822-8.
  56. Damiano R Jr., Schwartz F, Bailey M, et al. The Cox maze IV procedure: predictors of late recurrence. *J Thorac Cardiovasc Surg* 2011; 141: 113-21.
  57. Chen M, McCarthy P, Lever H, et al. Effectiveness of atrial fibrillation surgery in patients with hypertrophic cardiomyopathy. *Am J Cardiol* 2004; 93: 373-5.
  58. Kim S, Vingan H, Philpott J. Damaged right internal jugular venous catheter status after Cox Maze IV procedure. *Ann Thorac Surg* 2015; 99 (3): 1053-5.