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Balloon Catheters for Pulmonary Vein Isolation

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Abstract

The mainstay of catheter ablation for atrial fibrillation (AF) is pulmonary vein isolation (PVI). The shortcomings of a point-by-point ablation approach using radiofrequency current steadily kindle the interest in new energy sources and catheter designs. The most promising currently available techniques are balloon catheters using cryothermal energy (CRYO) or high-intensity focused ultrasound (HIFU).

Both technologies have proven to be efficacious. However, for both technologies treatment strategies

have to be developed to overcome the relatively high incidence of collateral damage such as phrenic nerve palsy or atrial-to-esophageal fistula.

The results for patients with persistent AF in whom substrate modification is considered beneficial are poor and limit the use of balloon-based PVI to patients with paroxysmal atrial fibrillation (PAF). Moreover, based on the individual anatomy more than one balloon size may be required or may even make balloon-based PVI impossible in certain patients.

Ballonkatheter zur Pulmonalvenenisolation

Zusammenfassung

Die Katheterablation von Vorhofflimmern (VHF) ist mittlerweile eine anerkannte Therapie. Durch Anlage zirkumferentieller Ablationslinien mittels Hochfrequenzstromenergie um die jeweils ipsilateralen Pulmonalvenen (PV) wird eine komplette elektrische Isolation angestrebt. Wegen der technischen Schwierigkeiten und der damit verbundenen Komplikationen (PV-Stenose, atrioösophageale Fistel) wurden alternative Technologien entwickelt. Am vielversprechendsten sind derzeit Ballonkatheter, die durch singuläre Applikation von hochfokussiertem Ultraschall (HIFU) oder kryothermaler Energie (CRYO) zirkuläre transmuskuläre Ablationsläsionen erzeugen können.

Erste Berichte konnten für beide Energieformen gute klinische Ergebnisse aufzeigen. In zwei klini-

schen Studien mit HIFU konnten 87–89% der PV isoliert werden, während der Nachuntersuchung traten nur bei 25–41% der Patienten Rezidive auf.

Demgegenüber wurden kürzlich die Ergebnisse einer trizentrischen Studie mit CRYO publiziert. Hierin wird eine akute (chronische) Erfolgsrate von 97% (74% für paroxysmales VHF und 42% für persistierendes VHF) berichtet.

Hauptproblem bei der Anwendung von Ballonkathetern ist das Auftreten von Phrenikuspareisen durch Verletzung des N. phrenicus dexter (Inzidenz ca. 5–10%).

Bei der technischen Anwendung kann die individuelle Anatomie der PV (z.B. große gemeinsame PV-Ostien) den Einsatz von Ballonkathetern verhindern.

Introduction

The mainstay of catheter ablation for atrial fibrillation (AF) is pulmonary vein isolation (PVI) [16]. This procedural endpoint is achieved by destroying the muscular sleeves extending from the left atrium into the pulmonary veins (PVs) by either a segmental or a circumferential ablation approach [21, 23]. Early reports demonstrated the difficulty of achieving complete contiguous ablation lesions in the left atrium [10]. Consequently, electrical reconnection through gaps in the circumferential ablation lines has been shown to be the dominant factor for clinical recurrences of AF or atrial tachycardias following PVI procedures [22].

Moreover, radiofrequency (RF) current ablation of AF is associated with a small but definite risk of serious complications such as PV stenosis, stroke and atrial-to-esophageal fistula [5, 24].

The aforementioned shortcomings of a point-by-point ablation approach using RF current steadily kindle the interest in new energy sources and catheter designs. Ideally, the new energy should be safe and create transmuskuläre circumferential lesions with a single application. The most promising currently available techniques are balloon catheters using cryothermal energy (CRYO; CryoCath® Technologies, Inc, Canada) or high-intensity focused ultrasound (HIFU, ProRhythm®, Inc, USA). This review

article will summarize the basic principles and early clinical results of these technologies.

Basic Principles of HIFU

HIFU relies on the basic concepts of conventional ultrasound. By focusing highly energetic ultrasound waves to a well-defined volume, local heat rise (usually $> 56^{\circ}\text{C}$ and up to 80°C) occurs and causes rapid tissue necrosis by coagulative necrosis [6]. Another mechanism by which HIFU destroys tissue is called acoustic cavitation [14]. This process is based on vibration of cellular structures causing local hyperthermia and mechanical stress by bubble formation due to rapid changes in local pressure leading to cell death.

The basic principle of these balloon catheters is an ultrasound crystal housed in a fluid-filled balloon. The only currently available HIFU balloon catheter consists of a noncompliant distal balloon, which is filled with a mixture of water and contrast media (6 : 1 ratio) and an integrated 9-MHz ultrasound crystal. Proximally, a second noncompliant balloon, filled with carbon dioxide, forms a parabolic surface at the base of the distal balloon. The emitted ultrasound waves are reflected in the forward direction, focusing a ring of ultrasound energy (sonicating ring) ~ 4 mm distally to the balloon surface. The catheters are steerable through a pull wire mechanism integrated in the handle of the catheter. Three different balloon sizes are available: a 24-mm diameter balloon (20 mm sonicating ring diameter), a 27-mm diameter balloon (25 mm sonicating ring diameter), and a 32-mm diameter balloon (30 mm sonicating ring diameter). The catheter has a central lumen used for insertion of a spiral mapping catheter (ProMap[®], ProRhythm[®], Inc) to assess the presence or absence of PV potentials.

A major advantage of HIFU is that no direct tissue contact is needed for the generation of the ablation lesion. Lesion volume depends on sonication time and on the initial tissue temperature as well as on the amount of acoustic power [9, 12]. According to the balloon shape, it creates circular ablation lesions by a single HIFU application within 40–90 s depending on the balloon size (Figure 1).

Basic Principles of CRYO

Lesions created by CRYO differ in several respects from those created by conventional RF current ablation. CRYO lesions show intact endothelial lining and hence are associated with less thrombus formation as compared to RF lesions [15, 27]. This may reduce the likelihood of thromboembolic events. While RF lesions show progressive contraction, CRYO lesions are associated with minimal collagen formation and tissue shrinkage [3]. This in agreement with experimental animal

data not reporting PV stenosis even after deployment of multiple CRYO applications at a single PV [2, 11].

The CRYO balloon catheter (Arctic Front[®], available in diameters of 23 and 28 mm) consists of a double-walled balloon, where the refrigerant N_2O is delivered into the inner lumen, undergoing a liquid-to-gas phase change resulting in cooling down to approximately -80°C . The catheter is equipped with a central lumen for the insertion of a guide wire and injection of contrast medium for PV angiograms. Both, sheath (12 F) and balloon, are steerable through a pull wire mechanism. In contrast to the HIFU balloon, the CRYO balloon system requires perfect local balloon/tissue contact as a prerequisite for a transmural lesion which is assessed by PV occlusion angiogram (Figure 2).

Clinical Results with Balloon Ablation

In the early stage of developing balloon catheters for PVI, a balloon applying RF current was investigated with promising results [28, 32].

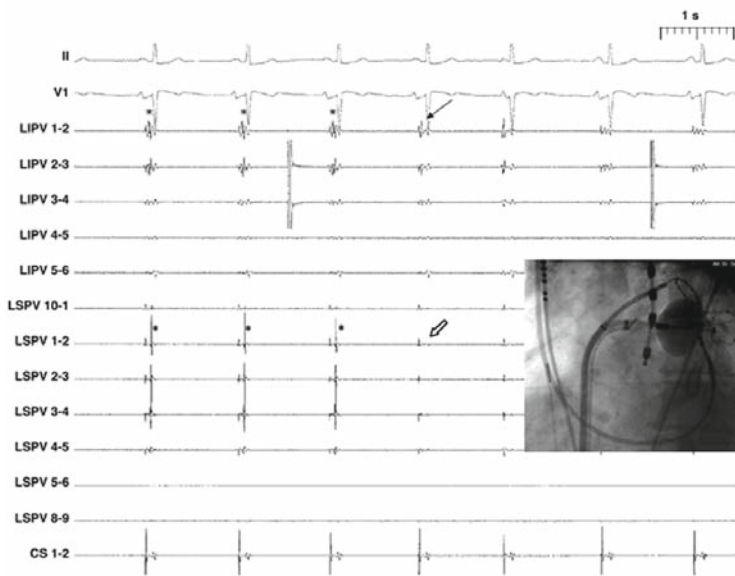
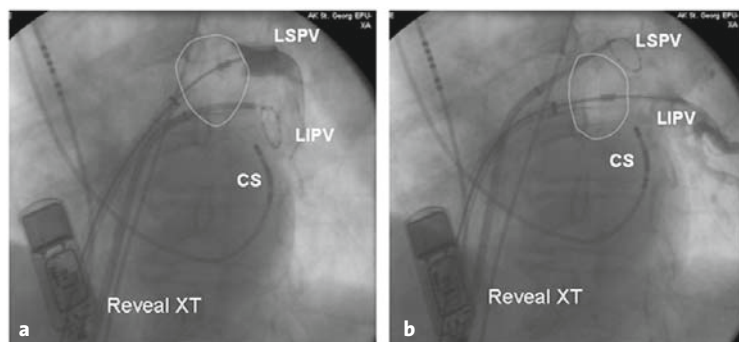


Figure 1. Simultaneous isolation of the lateral pulmonary veins (PVs) with an HIFU balloon. The balloon catheter is located at the left inferior pulmonary vein (LIPV; LAO 40°). Distal to the balloon is the ProMap[®] catheter, a spiral catheter is positioned in the left superior pulmonary vein (LSPV). Proximal to the balloon, the temperature probe in the esophagus is visualized. ECG tracings show two surface ECGs and recordings from the LIPV and LSPV. Note the disappearance of the PV spike (*) during sonication (arrows). The LSPV had been sonicated before without achieving isolation.

Abbildung 1. Simultane Isolation der lateralen Pulmonalvenen (PV) mit einem HIFU-Ballon. Der Ballonkatheter ist an der linken unteren Pulmonalvene (LIPV) positioniert (LAO 40°). Distal liegt der ProMap[®]-Spiralkatheter, ein zweiter Spiralkatheter ist in der linken oberen Pulmonalvene (LSPV) platziert. Proximal des Ballons sieht man die Temperatursonde im Ösophagus. Die EKGs zeigen zwei Oberflächenableitungen sowie intrakardiale EKGs aus den PV. Man beachte das Verschwinden des PV-Potentials (*) in beiden PV während Bestrahlung mit HIFU (Pfeile). Die LSPV war zuvor mit HIFU bestrahlt worden, ohne sie zu isolieren.



Figures 2a and 2b. Occlusion angiograms of the lateral pulmonary veins (PVs) via the CRYO balloon. Fluoroscopic views (LAO 40°) of a CRYO balloon positioned at the left superior pulmonary vein (LSPV, a) and left inferior pulmonary vein (LIPV, b). Via the central lumen contrast media is injected demonstrating a complete occlusion of the respective PV. A spiral catheter is located in the LIPV and LSPV, respectively. An event recorder (Reveal XT, Medtronic) had been implanted for unexplained syncope.

Abbildungen 2a und 2b. Verschlussangiogramme der lateralen Pulmonalvenen (PV). Fluoroskopie (LAO 40°) mit Abbildung eines CRYO-Balloon an der linken oberen (LSPV, a) und linken unteren Pulmonalvene (LIPV, b). Durch das zentrale Lumen des Katheters wird Kontrastmittel injiziert, um die komplette Okklusion der PV zu demonstrieren. Ein Spiralkatheter ist in der jeweils anderen PV positioniert. Bei diesem Patienten war ein Ereignisrekorder (Reveal XT, Medtronic) wegen unklarer Synkopen implantiert worden.

The first-generation ultrasound balloons (Atrionix, Inc, USA) emitted the ultrasound energy in a transradial fashion. A single clinical trial including 15 patients reported a success rate of 60% [19]. However, in three patients serious adverse events occurred, including phrenic nerve palsy in one. This device disappeared from the market.

To date, the initial results of a balloon catheter emitting laser energy have not been published.

Results from two clinical trials including a total of 42 patients with drug-refractory paroxysmal (PAF) and persistent AF using the first- (nonsteerable) and second-generation HIFU catheters are published [18, 29]. The acute success rates defined as acute PVI

Table 1. Merits and demerits of balloon catheter ablation compared to radiofrequency ablation. PAF: paroxysmal atrial fibrillation; PVI: pulmonary vein isolation.

Tabelle 1. Vor- und Nachteile der Ballonkatheterablation im Vergleich zur herkömmlichen Ablation mit Hochfrequenzstromenergie. PAF: paroxysmales Vorhofflimmern; PVI: Pulmonalvenenisolation.

	Balloon catheter	Radiofrequency current ablation
Merits	Single-shot strategy Easy navigation No thrombus formation	PVI and substrate modification Suitable for all anatomic variations Large clinical experience
Demerits	Indication PAF only Anatomy-dependent Only short-term experience	Long ablation lines Complex navigation Potentially thrombogenic

rates were good (87–89% of all PVIs achieved). During long-term follow-up, 25–41% developed a recurrence of atrial tachyarrhythmias. The major drawback of HIFU is safety. In 3/42 patients a phrenic nerve palsy was observed. The use of three-dimensional pace mapping of the phrenic nerve could not help to prevent the occurrence of phrenic nerve palsy [30].

Moreover, during clinical use three patients suffered from atrial-to-esophageal fistula following HIFU treatment, of whom one patient died [4]. Consequently, the HIFU balloon was redesigned and equipped with a defocused energy zone in order to prevent collateral damage. Currently, a new treatment algorithm is being developed and tested at our center with special emphasis on esophageal temperature monitoring followed by endoscopy.

A large triple-center trial including 346 patients with symptomatic PAF or persistent AF was conducted using CRYO [20]. Acutely, 97% of all treated PVs could be isolated CRYO. However, in approximately 10% of all patients, two different balloon sizes or touch-up ablation with the CRYO point ablator (Freezor Max, CryoCath®) had to be used. The overall success rate defined as freedom from symptomatic AF after 12 months was 74% and 42%, respectively. However, phrenic nerve palsy occurred in 7.5% of all patients, particularly if small balloons (23 mm; in 24/26 patients) were used for PVI at the right superior PV. Similar results were reported in two smaller single-center trials that enrolled a total of 138 AF patients [17, 33].

In our center the single big balloon strategy was developed, an approach using exclusively the 28-mm CRYO balloon irrespective of the individual anatomy. By means of this technique 98% of all PVs could be isolated in 26 patients [7].

Merits and Demerits of Balloon Technology

PVI using balloon catheters may be achieved with a single or few energy applications instead of long contiguous circumferential ablation lines (Table 1). However, it lies in the nature of the technology, that the location of energy deployment is less flexible and restricted to the balloon surface or the focus zone.

As compared to the wide circumferential ablation lines established with RF current ablation, the level of PVI is rather distal and does not include the atrial, potentially arrhythmogenic muscle fibers and ganglionic plexuses [25, 26].

Substrate modification by ablating complex fractionated atrial electrograms that have been shown to improve the clinical outcome for patients with persistent AF is not feasible with balloon catheters [13]. This is reflected by the poor results in patients with

persistent AF and may limit the use of balloon-based PVI to patients with PAF. Nonetheless, novel ablation targets such as atrial appendage isolation may evolve [8].

It is well known, that the myocardial ridge between the left PVs and the left atrial appendage is narrow and to achieve a stable catheter position is challenging [31]. Oppositely, navigation to and positioning at the respective PV ostia using balloons is relatively easy. Nonetheless, the large interindividual variation of the PV ostial anatomy and the fairly high incidence of large common PV ostia may limit the use of balloon catheters in certain patients [1]. The use of multiple balloons during a single procedure or additional touch-up ablation may overcome this issue but will certainly raise economic concerns. In this regard, the aforementioned single big balloon strategy is promising.

Conclusion

Balloon catheters were designed to facilitate PVI procedures for patients with AF. Currently, two different technologies using HIFU or CRYO are available. Both technologies have proven to be efficacious. However, for both technologies treatment strategies have to be developed to overcome the relatively high incidence of collateral damage such as phrenic nerve palsy or atrial-to-esophageal fistula.

The results for patients with persistent AF in whom substrate modification is considered beneficial are poor and limit the use of balloon-based PVI to patients with PAF. Moreover, based on the individual anatomy more than one balloon size may be required or may even make balloon-based PVI impossible in certain patients.

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