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Balloon technology for catheter ablation of atrial fibrillation

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ABSTRACT

Unlike the initial balloon ablation catheters which were designed to deliver ablation lesions within the pulmonary veins (PVs), the current balloon catheters are fashioned to deliver lesions out of the PV ostia. Using the current generation of balloon ablation catheters, electrical isolation occurs at the level of the PV ostia, but the antral regions are largely unablated. Because of its initial technical feasibility and presumed safety benefits, balloon cryoablation was being increasingly employed for pulmonary vein (PV) isolation. Other balloon technology – endoscopically navigated laser balloon – was introduced as the first real catheter "one fits all" with adjustable size of balloon inflation.

While high percentage of acute isolation has been demonstrated in most patients with both balloon catheters, little data are available on the chronic durability of cryoballoon or laser balloon lesions. Our own data show that cryoballoon ablation and laser balloon ablation allow for durable PV isolation with the use of a single balloon. With maintained chronic isolation in most PVs, it may represent a significant step toward consistent and lasting ablation procedures.

Klíčová slova:
Balonkový katetr
Elektroanatomické mapování
Fibrilace síní
Katetrizační ablace
Kryoablace
Laser

SOUHRN

Na rozdíl od původních balonkových katetrů, které byly vyvíjeny s cílem aplikovat energii uvnitř plicních žil (PŽ), jsou současné balonkové katetry vyvíjeny tak, aby vytvářely léze vně ústí PŽ. Současná generace balonkových katetrů docílí elektrickou izolaci v úrovni PŽ, nicméně působení v antru plicních žil prakticky není možné. Přesto jsou pro technickou jednoduchost a prokázanou bezpečnost kryobalonkové katetry v poslední době používány stále častěji. Jiná balonková technologie – endoskopicky navigovaný laserový balonek – byla zavedena do klinické praxe jako skutečně první balonková metoda typu „one fits all" včetně nastavitelné velikosti balonku.

Vysoká efektivita dosažení okamžité elektrické izolace plicních žil byla již prokázána u poměrně rozsáhlých souborů nemocných, a to s oběma typy balonkových katetrů; stále je však k dispozici málo dat prokazujících trvalý účinek dosažené elektrické izolace, a to jak kryobalonkovým, tak laserovým katetrem.

Několik prvních prací, ale i naše vlastní data naznačují, že kryobalonková ablace a laserová ablace umožňují dosažení i dlouhodobého efektu elektrické izolace PŽ s použitím jediného balonkového katetru, což ve svém důsledku může znamenat významný krok vpřed k docílení dlouhodobého efektu při provádění katetrizační ablace.

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Introduction

Currently, electrical pulmonary vein (PV) isolation is the cornerstone of the catheter ablation treatment for paroxysmal atrial fibrillation (PAF) [1–8]. Many electrophysiologists also believed that most of the AF triggers come from multiple PV sites, which need to be ablated to stop AF recurrences. Subsequent research has suggested that all PVs were also capable of perpetuating AF. This led to the notion that all 4 PVs needed to be ablated to maximize the efficacy of radiofrequency (RF) ablation. Haissaguerre et al. described mapping of the PV potentials using a specially designed circular catheter that could be positioned at the PV ostia, enabling one to evaluate electrical connection between PV muscle sleeves and the left atrial muscle, making isolation of the electrical impulse between the PV and left atrium (LA) easily and reproducibly ascertained [3,4]. The PV isolation (PVI) technique gave electrophysiologists a new tool to treat AF with a catheter-based approach and instantly became almost synonymous with AF ablation. Given the number of all patients with AF, it is clear that we need to simplify the procedure with respect to the acute effect and, most importantly, durability of electrical isolation. That's why the principle of "single shot" therapy needs to be extended by long-lasting efficacy of the initial procedure. Perhaps also long-lasting forms of AF such as persistent AF should be considered as a target for the balloon technology.

Unlike the initial balloon ablation catheters, which were designed to deliver ablation lesions within the PVs, the current balloon prototypes are fashioned to deliver lesions not at the PV ostia, but extraostially. However, the actual location of the ablation lesions using these devices is not known.

All the aspects of the use of balloon catheters need to be taken account of including: procedure efficacy, procedure and fluoro exposure time, collateral damage, and other related complications. In this paper, we describe in detail cryoballoon and laser-balloon technologies, as development of the high-intensity focused ultrasound (HIFU) balloon (Prorhythm Inc., Ronkonkoma, NY, USA) was stopped after several serious complications, the duty-cycled system (Ablation Frontiers Medtronic, Carlsbad, California, USA) has been associated with significant numbers of silent strokes, and the Mesh ablator catheter (Bard Inc., Lowell, MA, USA) is now in the process of redesigning.

Because of the technical difficulties associated with point-to-point ablation using a standard spot ablation catheter with the LA, there has been a significant effort in developing alternative ablation catheter designs to quickly and easily isolate PVs. The first such device tested clinically was an ultrasound balloon ablation catheter that delivered energy in a radial fashion at the level of the diameter of the balloon – hence necessitating that the balloon catheter be placed within the PV when delivering energy [9]. This balloon design was suboptimal since the level of electrical isolation typically excluded the proximal portions of the vein, so PV triggers of AF located at this region would not be included in the ablation lesion [10]. From a safety perspective, the intra-venous location of the energy delivery resulted in PV stenosis.

The initially very promising HIFU balloon [9], which was designed as the only one contactless catheter, was withdrawn from the market as, due to uncontrolled energy delivery, it had resulted in life-threatening complications, i.e., atrial-esophageal fistulas.

Since this first-generation device, balloon ablation catheters have evolved considerably [11]. There are now two major balloon-based ablation devices used in clinical practice but still at various stages of clinical evaluation for: i) cryoballoon ablation, and ii) endoscopic laser-balloon ablation. Each of these has been fashioned to be placed at the PV ostia, so as to theoretically isolate the veins outside their tubular portion.

Cryoballoon technology

To date, the largest global experience with such technology involves the Arctic Front cryoballoon (Medtronic Cryocath LP, Pointe-Claire, Quebec, Canada) – a balloon catheter designed for inflation at the PV ostium, thereby allowing for temporary occlusion of PV blood flow and circumferential ostial contact [12]. Balloon-based ablation systems potentially offer a simpler and faster means of achieving PVI that, theoretically, is less reliant on operator skills. At the same time, cryothermal energy offers advantages over RF energy including increased catheter stability, less endothelial disruption with lower thromboembolic risk, and minimal tissue contraction with healing, an observation thought to result in less esophageal damage and PV stenosis. With optimal positioning, it has been demonstrated that electrical isolation can be obtained acutely with the delivery of a single, 240-second lesion. The system consists of a deflectable catheter with a balloon-within-a-balloon design (two layers because of safety reasons), wherein a cryo-refrigerant (N_2O) is delivered into the inner balloon. There are currently two sizes of the cryoballoon, 23 and 28 mm, but there is expanding literature evidence the bigger size (28 mm) is much more effective [13]. While deflated, the balloon catheter is deployed through a 12-French deflectable sheath. The placement

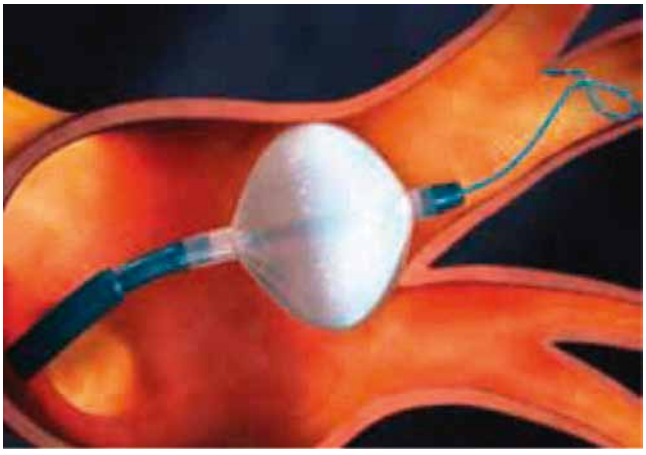

Fig. 1 – Cartoon of left superior pulmonary vein occlusion with Arctic Front balloon, stabilised electrically active wire (Achieve) registered electrical potentials from each treated vein.

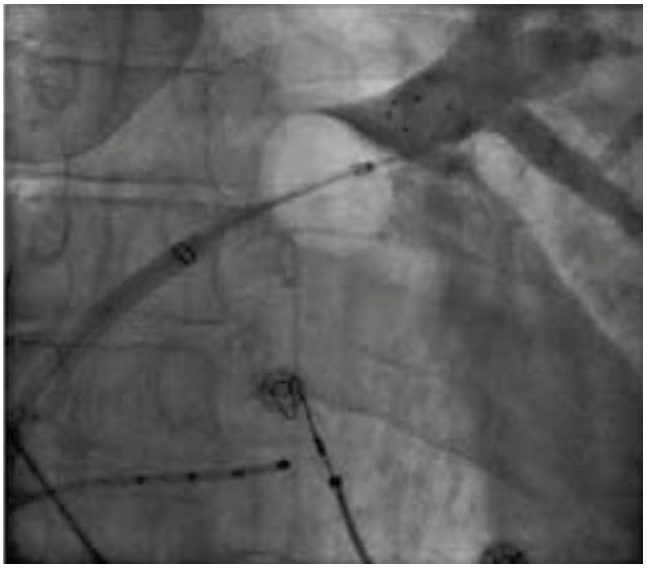

Fig. 2 – Identical Arctic Front balloon – on fluoro in the position of left superior pulmonary vein occlusion with circular Achieve wire. In both examples deflectable sheath (ID 12 Fr) is used.

into the PV is supported by the wire inserted into the lumen of the catheter to stabilize the balloon while being inflated in the PV. Once in the LA and individual PV, the balloon is inflated and positioned at the PV ostium to temporarily occlude blood flow from the targeted PV (Fig. 1, 2). After placement and occlusion have been verified with the distal injection of contrast on fluoroscopy, cryothermal energy delivery is initiated, and all tissue in contact with the balloon is ablated. When adequate tissue apposition cannot be achieved, as indicated by a leak observed on intracardiac echo (ICE; AcuNav, Siemens-Ultrasound, Inc., Mountain View, CA, USA) or contrast fluoroscopy, a "pull-down" technique can be employed. Users in many centers now employ only the single-transseptal technique with evaluation of PVI after all lesions. The current strategy of cryoballoon use for catheter ablation still varies among the centers, most of the users apply 300-second lesions plus one "bonus" lesion. Each PV must be treated individually, in the right superior PV, cryoenergy must be delivered together with phrenic nerve stimulation to avoid phrenic nerve palsy, which is the most important complication (which is important for all balloon technologies). Besides, there is evidence of collateral damage, specifically two reports of atrio-esophageal fistula formation, so esophageal temperature during the ablation should be also considered [14]. There are two main developments of the cryoballoon system available: (i) the Arctic Front Achieve, and (ii) the Arctic Front Advance. The first one is designed as a stiff wire with a circular shape available to record the potentials from the each targeted PV even during freezing. The second one is a new balloon freezing system design with a much homogeneous freezing effect covering a larger surface of the balloon (Fig. 3). The Arctic Front Advance features EvenCool Cryo Technology providing improved cooling uniformity. To improve the cooling uniformity on the balloon surface, the number of injection ports was increased from four to eight, resulting in two refrigerant jets per quadrant; the injection coil was moved distally from its current location near the equator; the refrigerant spray pattern was optimized; and the flow rate for the 28-mm balloon size was increased by 16%. These product changes have resulted in reducing the observed variability in temperatures on the cryoballoon surface.

Centers with extensive experience have reported a progressive decrease in procedural time, fluoroscopy time, number of cryoballoon applications, and need for additional focal ablation with increasing operator familiarity [15,16]. Likewise, single procedural success rates have increased progressively with increasing familiarity with the procedure (77.5% for the latest quartile of patients treated vs 39.5% for the earliest quartile of patients treated).

Twenty-three studies have reported the procedural success of cryoballoon ablation for AF. Acute procedural success was achieved in 91.67% to 100% of patients (19 studies; 924 patients) and 94.87% to 100% of targeted veins (18 studies; 3,803 veins). Overall, 98.81% of patients achieved complete PVI (95% CI 97.88–99.40%), and 98.47% of targeted veins were successfully isolated (95% CI 98.03–98.84%). Ablation with the cryoballoon catheter alone (i.e., excluding concomitant focal ablation) resulted in PVI in 92.64% of targeted veins (95% CI 91.76–93.45%) and complete PVI in 77.81% of patients (95% CI 74.99–80.45%). Studies using a prespecified exclusive cryoballoon ablation strategy achieved complete PVI in 98.74% of patients (8 studies, 317 patients; 95% CI 96.80–99.66%) and 99.23% of targeted veins (6 studies, 912 targeted veins; 95% CI 98.42–99.69%). Chierchia et al. [17,18] observed acute procedural reconnection in 2.8% (3/104) of veins within a 60-minute post-ablation observation period. In all cases, reconnection occurred in the right inferior pulmonary vein (RIPV), two in the

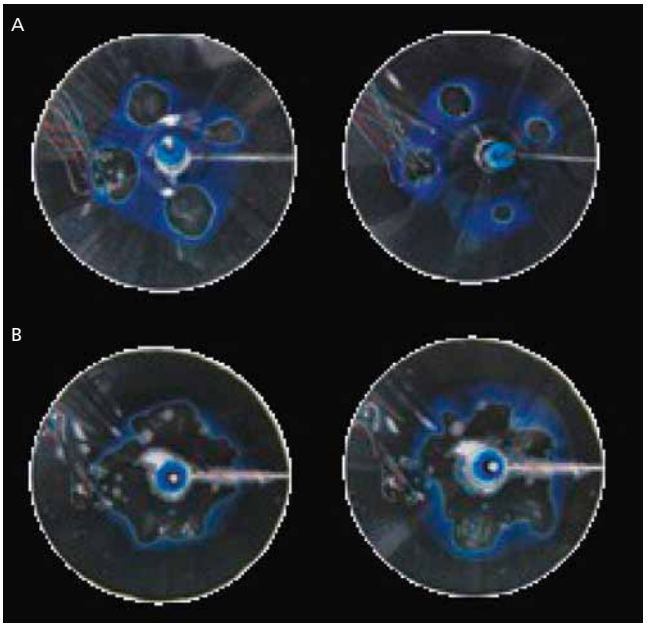

Fig. 3 – On cross section shown the freezing process using the original Arctic Front balloon – 23 and 28 mm size (A); bottom (B) is the same cross section freezing process using newer balloon Arctic Front Advance with more homogenous cryotherapy application.

inferior portion, and one in the posterior portion. Another study did not report any acute reconnection after a postablation observation period of up to 30 minutes [19]. Two studies reported a comparison of cryoballoon ablation with conventional RF for paroxysmal AF. Linhart et al. [20] compared 20 patients with paroxysmal AF who underwent their first PV ablation with the cryoballoon and matched them to 20 patients undergoing RF ablation. Six-month freedom from documented AF did not differ between the groups (55% with cryoballoon vs 45% with RF), although there was a non-significant trend toward decreased AF burden in those with a recurrence after cryoballoon ablation.

Similarly, Kojodjojo et al. [21] reported no difference in 12-month freedom from recurrent AF between those who underwent cryoballoon ablation for paroxysmal AF (90 patients) and those undergoing RF ablation (53 patients) (77% and 72%, respectively).

Cryoballoon ablation was studied in STOP-AF, one of the most important randomized trials, involving a comparison of cryoballoon ablation with AADs for patients with paroxysmal AF who had previously failed at least one AAD [21]. This US study proved the efficacy of the cryoballoon technology and, despite some important limitations (the study contained the learning curve of most of the centers; only the 23-mm balloon size was available with related complications – moderate PV stenosis and phrenic nerve palsy – 14%).

After a 3-month blanking period, 69.9% (114/163) of the cryoballoon group were free of recurrent AF at 1 year versus 7.3% (6/82) of the AAD group. At 12 months, there was a statistically significant improvement in symptoms and every aspect of quality of life as measured by the SF-36 questionnaire in the cryoablation group. For all metrics, symptomatic improvement was greater in the cryoablation group compared with the AAD group.

It is clear that the cryoablation is associated with minimal rates of silent strokes, as shown by several reports. The incidence of thromboembolic complications including periprocedural stroke, transient ischemic attack, or myocardial infarction was 0.57%. Compared to conventional RF catheters, the observed microembolic signals in middle cerebral arteries were significantly lower with the cryoballoon and irrigated RF catheters (3,908 ± 2,816 vs 935 ± 463 and 1,404 ± 981 total microembolic signals, respectively).

In several systematic reviews, an acute procedural success rate greater than 98% was observed. Not unexpectedly, the most challenging PV to isolate was the RIPV, although special techniques ("hockey-stick", "pull-down" or "large loop") and focal cryoablation were helpful in achieving PVI in the majority of cases [23]. For patients with paroxysmal AF, the 1-year freedom from recurrent AF off AAD (73% with a 3-month blanking period and 60% with no blanking period) compares favorably with results reported in the global RF literature. In the systematic review and meta-analysis by Calkins et al. [24], the single procedural success rate of RF catheter ablation off AAD therapy after a mean follow-up of 14 months was 57% (50–64%) when a 2- to 14-week blanking period was included in a sizeable proportion of patients. In a prospective long-term cohort study of RF ablation, the actuarial arrhythmia-free survival rate after a single procedure was 39.8% ± 5.1% with no blanking period [24,25].

The laser balloon technology

The Light Ring laser balloon catheter (CardioFocus Inc., Marlborough, MA, USA) is a novel complex endoscopic ablation system (EAS) using adjustable balloon to adapt various PV sizes to get ideal contact with the tissue and also allows to titrate the power of each individual laser therapy application. Size of the balloon is adjustable from 9 mm up to 35 mm in 9 steps, it is continuously flushed by heavy water (deuterium D_2O), a 980 nm wavelength laser beam represents a 30° arc which could be placed by rotation circumferentially around all the PV ostia, a 2-Fr endoscopic wire is implemented so optimal or suboptimal contact could be controlled by the operator [16,26]. In principle, the laser generates a very similar tissue effect compared with the RF energy source, with some photon reflection, scattering but there is also the "hot spot" as in the case of RF application and conduction heating effect. Histological findings represent fibrous tissue with much sharper edges compared with RF. Hence, EAS offers a fully tailored approach to the ablation, allowing customized lesion design and nearly individualized energy delivery that takes into account the proximity of the PVs to the collateral anatomical structures – mainly the esophagus and phrenic nerve.

The catheter itself is not deflectable, but it is used with a single-direction deflectable transseptal sheath (12 Fr ID, 16 Fr OD). Laser energy is applied for not more than 30 seconds with preselected power (range from 5.5 to 12 W). The laser arc could be rotated independently to the balloon under visual control of the operator to get continuous lesion set with overlapping the laser beam by 10–50% (Fig. 4, 5). The majority of laser applications are visible by whitening of the tissue while creating transmural lesion (which could be only suspected). To confirm the lesion overlap, a second (memory) screen could be used. Rotating, advancing, and retracting the laser beam could facilitate continuous lesion application in respect to the amount of energy we need

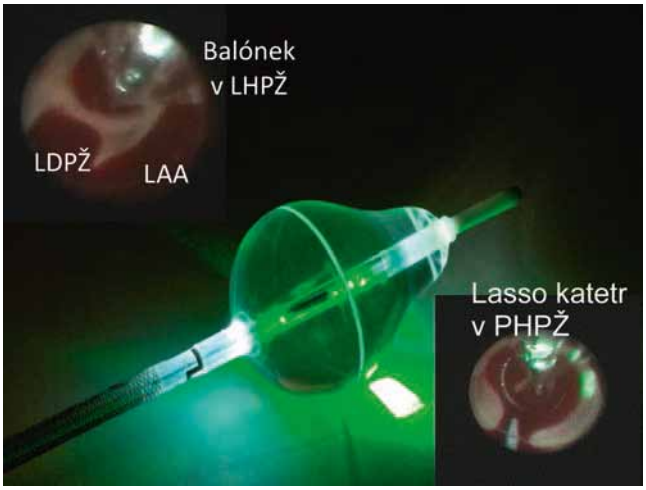

Fig. 4 – Figure of adjustable laser balloon Light Ring with 2 Fr size endoscop and light source allowing direct visualisation and energy application control; width of laser beam is 30°, left upper part – endoscopic view of both left veins visualised with optimal balloon-tissue contact. Right bottom part – endoscopic view of the right upper vein with simultaneous circular mapping catheter placement to adjust electrical isolation.

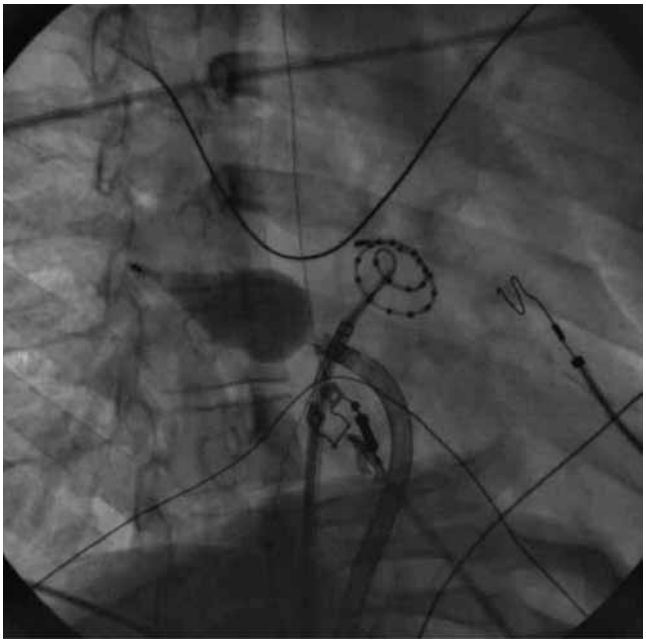

Fig. 5 – Inflated Light Ring Laser balloon (fluoroscopy) in the position of full occlusion of right inferior pulmonary vein.

to apply to guarantee a transmural lesion. This was documented by a study conducted by the Hamburg group and reported recently by Adreas Metzner et al. [27]. The use of higher energy leads to better acute and chronic success rates. The superiority of higher energy levels regarding chronic PVI has been suggested on the basis of the porcine model; however, previous studies did not assess the impact of varying energy on the acute success rate of PVI [28]. In several reports (including the very first preclinical one) [28], around 85–90% of PVs were isolated on the first attempt of the lesion set. In the very first prospective multicenter study including 200 patients, 761 PVs out of 770 (98.8%) were acutely isolated, and 604 PVs (79.4%) were isolated on the first attempt. For complete PVI 1.3 attempts were needed [29]. To assess durability of the PVI, 52 out of 56 patients even asymptomatic, without clinical evidence of AF recurrence were studied by the remapping procedure. Out of initially isolated 189 PVs, 162 were persistently isolated, which represents 86% of long-lasting electrical isolation; 62% of these 52 patients had all their PVs permanently isolated. Interestingly, when PVs had not been isolated, there was always only a very small gap within the original ablation line [30]. If we can document this high-level of PVI in a larger study population, it will be the best chronic result in catheter-based ablation of AF. In an all-updated literature review containing 687 reported patients with EAS used for PVI, there was an average 2% of pericardial effusion/tamponade without any report of PV stenosis, clinical TIA/stroke, and atrio-esophageal fistula. Phrenic nerve palsy was observed in around 3% of the patients [31].

Boris Schmidt and Julian Chun recently compared the mid-term effect of PVI, in a randomized fashion, the cryoballon and laser balloon strategy with better results using the laser balloon (73% clinical success) compared with the cryoballoon (original version) with a 63% long--lasting success rate [32]. They also proved much less fluoroscopy time per procedure using laser ablation. The only limitation is that the endoscopic view (due to the catheter shaft) does not permit full circumferential view and the circular linear line needs to be finished after rotation of the catheter. There are also several papers on the way reporting silent stroke rates.

It could be summarized that the EAS system can deliver circumferential lesions set "anatomically", with no real-time electrograms and despite the fact the operator is not able to see any electrogram until the circle is completed by around 80–84%. Another very important parameter of EAS is the ability to directly visualize tissue and the quality of balloon/tissue contact which guarantees constant, real-time confirmation that energy is being delivered into tissue. With optimal contact visual control, a limited respiratory and cardiac movement artifact can also improve the outcome of the whole procedure while the balloon moves in concert with the targeted PV. But what we consider the most important parameter of this very complex balloon ablation system is its ability to carefully "overlap" successive lesions under direct visualization simply because the energy is repositioned without moving the catheter.

Conclusion

Balloon-based technologies offer the advantage of "single-shot" isolation of the PV, thus decreasing dependence on operator dexterity. Compared with other balloon--based ablation technologies (high-intensity focused ul-

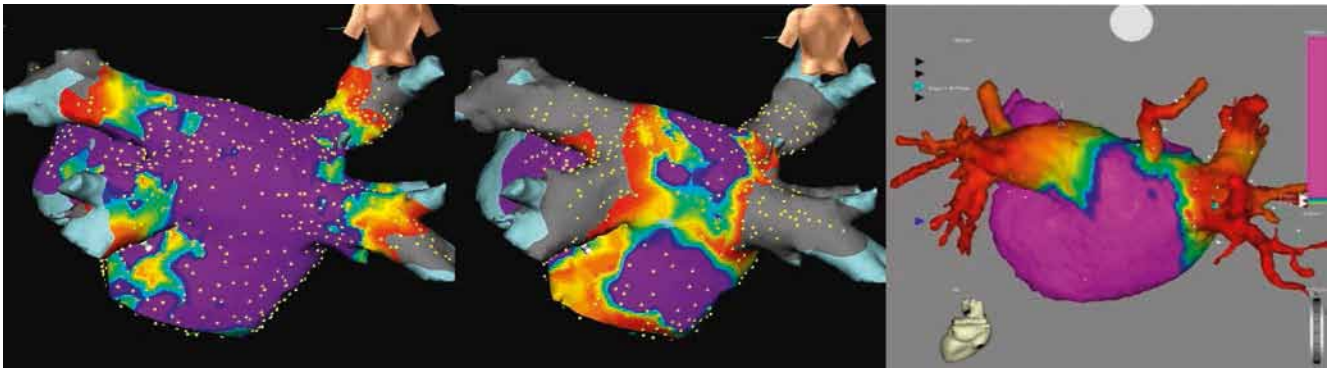

Fig. 6 – Electroanatomical map – EAM (NavX, St. Jude Medical, USA) of the left atrium before and after cryoablation. The third picture shows EAM (CARTO, Biosense Webster, USA) after laser balloon ablation. All maps after application show the level of achieved isolation, in case of laser ballon the lines are close to the LA antrum.

trasound and the endoscopic laser), the cryoballoon is less direction-dependent as the refrigerant jet inside the balloon is directed to produce the lowest ablation temperatures in a large circular zone on the anterior third of the balloon. As such, cryoballoon ablation may be expected to isolate the muscular PV sleeves as well as the PV antrum (Fig. 6). In this systematic review, we observed an acute procedural success rate greater than 98%. This systematic review of the cryoballoon and EAS ablation procedure for paroxysmal AF results in high acute and medium-term efficacy rates. We have no data supporting the success rates when the cryoballoon and EAS are used as stand-alone therapy for persistent AF. The rate of "balloon-technology" procedure complications is relatively low and includes the most prominent incidence of phrenic nerve palsy (3–6%), most of which is transient. Further studies, including direct comparison with conventional RF ablation, are ongoing and will provide important insight into balloon technology long-term efficacy and safety.

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