Rapid pulmonary vein isolation utilizing the third-generation laserballoon – The PhoeniX registry

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Abstract

Background: Balloon-based ablation systems for pulmonary vein isolation (PVI) are providing procedural safety and efficacy as well as favourable clinical outcome. Although second-generation laser balloon (LB2) based PVI has been shown safety and efficacy relatively long procedural duration was a strong limitation. The third-generation laser balloon (LB3) offers and automized ablation for rapid PVI. We determined safety, efficacy and procedural characteristics of this new promising ablation system.

Methods and results: A total of 15 consecutive patients were prospectively enrolled. All patients underwent PVI using the LB3. A total 59/59 PVs (100%) were successfully isolated. Procedural data was compared to the last 15 consecutive patients treated by the LB2. The median procedure time significantly declined from LB2 (91 (86, 105) min) to LB3 (77 (68, 87) min), p < 0.001. Similarly, the median left atrial dwelling time significantly decreased from LB2 (72 (62, 84) min) to LB3 (45 (38, 52) min), p < 0.0001. The total laser time decreased from LB2 (1920 (1765, 2193) sec) to LB3 (1077 (896, 1165) sec), p < 0.00001. A pure single shot PVI was performed in 18/59 PVs (31%). For major adverse events no differences were detected between the groups (LB2 1/15 (6.7%) and LB3 1/15 (6.7%), p = 0.999).

Conclusion: The LB3 was safe and effective for PVI. Procedure time, LA dwelling time and total laser time significantly decreased compared to LB2.

1. Introduction:

Pulmonary vein isolation (PVI) forms the cornerstone of invasive atrial fibrillation (AF) treatment [1]. 3D-Mapping-System guided radiofrequency (RF) based point-by-point ablation results in favourable clinical outcome, although its complexity demands a long learning curve and multiple procedures are oftentimes required to achieve durable PVI. Balloon-based ablation systems have been developed to possibly solve these limitations, reduce procedure time and increase safety and efficacy [2,3]. The visually guided laser balloon ablation system (HeartLight, CardioFocus, Marlborough, MA, USA) is a balloon-based ablation system which is utilizing laser-energy for lesion formation [4,5]. The first-generation laser balloon (LB1) showed high PVI durability and similar 1-year freedom of AF recurrence compared to RF-based PVI for paroxysmal as well as persistent AF [6–10]. In 2017 an optimized version, the second-generation laser balloon (LB2, HeartLight Excalibur Balloon; CardioFocus) was introduced and found to improve periprocedural handling and procedure duration due to a more compliant balloon, improved tissue contact and visibility during PVI [11]. The latest version of this system (LB3, HeartLight, X3; CardioFocus) offers an automated continuous lesion formation via the rapid mode and an optimized and accelerated inflation and deflation of the LB3. The objective of the PhoeniX registry was to determine the safety, efficacy and periprocedural characteristics of the LB3 compared to the LB2 for the treatment of AF.
2. Methods

2.1. Patients population

This study (PhoeniX Registry: Rapid Pulmonary Vein Isolation utilizing the third-generation Laser Balloon Ablation System: X3) prospectively included consecutive patients with symptomatic drug-refractory paroxysmal or persistent AF who presented for LB3 based PVI at the university heart center of Lübeck, Germany between June 2019 and February 2020. Exclusion criteria were prior left atrial (LA) ablation, LA-diameter > 60 mm, severe valvular heart disease or long-standing persistent AF (PersAF, AF duration > 12 months). All patients gave written informed consent to the procedure. The study was part of the prospective Lübeck ablation registry and was approved by the local ethic's board and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The procedures were performed by two experienced EP physicians (C. H.H. and R.R.T.) only.

2.2. Preprocedural management

Transesophageal echocardiography was performed prior to ablation to assess the LA-diameter and to rule out intracardiac thrombi. Apart from echocardiography, no additional preprocedural imaging was performed. In patients on vitamin K antagonists, anticoagulation was continued throughout the procedure aiming at an INR of 2–3. In patients treated with novel oral anticoagulants (NOACs), the drug was in the morning of the procedure on and re-initiated six hours post-ablation at half the regular dose, and at full dose the following day [12,13].

2.3. Third-generation laser-balloon based PVI

All procedures were performed under deep sedation using midazolam, fentanyl, and propofol as earlier described [13,14]. Following ultrasound scan guided femoral venous puncture one diagnostic catheter was introduced via the right femoral vein and positioned within the coronary sinus. A double transseptal puncture was performed via the right femoral vein under fluoroscopic guidance, using a modified Brockenbrough technique and an 8.5 French transseptal sheath. Heparin was administered after transseptal puncture to maintain an activated clotting time of ≥300 s. One transseptal sheath was exchanged over a guidewire for a 12-F steerable sheath (CardioFocus), and the LB3 was advanced into the LA. A 15 mm circular mapping catheter (Lasso, Biosense Webster) was introduced via the second transseptal sheath and placed at the individual PV ostia. In order to identify all PV ostia, selective PV angiography was performed. In all patients, an esophageal temperature probe (CIRCA S-CATH™) was inserted and positioned according to the individual LB3 position to facilitate esophageal temperature monitoring during energy delivery. The intraluminal esophageal temperature cutoff was set at 40.5 °C. If esophageal temperature exceeded the cutoff energy delivery was terminated and ablation was continued using reduced energy and/or at a more proximal or distal location. During ablation of right superior PV (RSPV) and right inferior PV (RIPV) phrenic-nerve pacing (maximum output, maximum duration) via a diagnostic catheter placed in the superior vena cava was performed. A loss of capture resulted in instant termination of energy delivery. Before PVI, a circular mapping catheter as placed at the PV ostium to record baseline electrograms. Periprocedural handling of the LB2 have been published before [13].

For LB3 based PVI the balloon was inflated at the antrum of the individual PV and expanded aiming an optimal PV occlusion and 360° visibility by utilizing the remote-control unit. We aimed to perform a 360° circumferential ablation strategy via the rapid mode without rotating (zero-rotation) the LB3 (Fig. 1) [11,13]. Therefore, ablation behind the catheter shaft (i.e. blind spot) was performed utilizing the arc marks if possible. For performing a safe, effective and continuous ablation line in the area behind the blind spot complete PV occlusion was confirmed pulling the laser generator to a proximal position and utilization of the arc markers for orientation during the ablation [13]. If no complete PV occlusion was possible a rotation of the LB3 was performed like earlier described [5,11]. Although 13 W and 15 W are available utilizing the rapid mode only 13 W was utilized to improve safety and prevent pinhole ruptures. If necessary rapid mode was interrupted and restarted with an overlapping of 100% to ensure a continuous lesion formation. The manuell mode (5.5–8.5 W) was used if it was required to perform energy titration near the blood due to poor PV occlusion and consecutive imperfect view. As described for the LB2 laser energy in the manual mode was deployed in a point-by-point fashion, overlapping each lesion by 30–50% [11,13].

After complete circular ablation, PVs were re-mapped using a circular mapping catheter. If PV potentials remained, additional laser balloon ablation was performed with a circumferential mapping catheter guidance [13]. For this purpose, a circumferential mapping catheter was placed inside the target PV. The PV segment with the earliest activation of PV potentials was targeted for reablated by the LB3. All PVs were checked by the circular mapping catheter to confirm acute electrical PVI at the end of the procedure. Due to our in-house protocol no non-PVI foci were targeted during the first PVI procedure and no adenosin testing was performed after PVI. No rapid pacing has been performed during the procedures [13]. Patients presenting in AF received an electrical cardioversion at the end of the procedure.

2.4. Postprocedural management

Following ablation, all patients underwent transthoracic echocardiography to rule out pericardial effusion. Low molecular-weight heparin was administered in patients on vitamin K antagonists and an INR < 2.0 until a therapeutic INR of 2–3 was achieved. New oral anticoagulants were re-initiated at full dose 6 h post ablation. Anticoagulation was recommended for at least 3 months.
Table 1
Baseline characteristics.

|                  | LB2 | LB3 | p     |
|------------------|-----|-----|-------|
| Number of patients | 15  | 15  |       |
| Age (years)       | 65 (58, 72) | 68 (63, 70) | 0.453 |
| Left atrial diameter (ml/m²) | 30 (20, 35) | 25 (25, 30) | 0.252 |
| Persistent AF     | 15 (100) | 9 (60) | 0.064 |
| Duration of AF (month) | 24 (1, 36) | 12 (6, 24) | 0.0001 |
| Female gender     | 3 (20) | 7 (47) | 0.121 |
| Arterial hypertension | 7 (47) | 9 (60) | 0.464 |
| Coronary artery disease | 2 (13) | 2 (13) | 0.999 |
| Congestive heart failure | 0 (0) | 2 (13) | 0.549 |
| Diabetes mellitus type II | 0 (0) | 2 (13) | 0.549 |
| Coronary artery disease | 2 (13) | 2 (13) | 0.999 |
| Arterial hypertension | 7 (47) | 9 (60) | 0.464 |
| Coronary artery disease | 2 (13) | 2 (13) | 0.999 |
| Congestive heart failure | 0 (0) | 2 (13) | 0.549 |
| Diabetes mellitus type II | 0 (0) | 2 (13) | 0.549 |
| Prior TIA/stroke   | 1 (7) | 1 (7) | 0.999 |
| CHA2DS2-VASc score | 2 (1, 4) | 2 (2, 2.5) | 0.418 |

Continuous data are summarized as medians [25th and 75th percentiles]. Categorical data are presented as N (%). AF = atrial fibrillation, TIA = transient ischemic attack.

Table 2 (continued)

|                  | LB2 | LB3 | p     |
|------------------|-----|-----|-------|
| Total Laser time (RIVP) | 506 (484, 539) | 350 (255, 389) | <0.00001 |
| Total Laser time (RIPV) | 600 | 294 |       |
| Total Laser time (LIPV) | 500 (410, 633) | 220 (199, 288) | <0.00001 |
| Periprocedural complications |
| Major complications | 0 (0) | 1 (6.7) | 0.163 |
| Phrenic nerve palsy | 1 (6.7) | 0 (0) | 0.163 |
| Severe hematoma | 0 (0) | 0 (0) | 0.999 |
| Pericardial tamponade | 0 (0) | 1 (6.7) | 0.163 |
| Periprostural Stroke | 0 (0) | 0 (0) | 0.999 |

Continuous data are summarized as medians [25th and 75th percentiles]. Categorical data are presented as N (%). PV = pulmonary vein. LSPV = left superior PV, RIPV = right inferior PV, LCPV = left common PV, RMPV = right middle PV.

and thereafter according to the individual CHA2DS2-VASc score. Previously ineffective antiarrhythmic drugs were continued for 3 months post ablation. All patients were treated with proton-pump inhibitors for 6 weeks [14].

2.5. Clinical follow-up

Our in-house protocol aims to follow-up the patients via outpatient clinic visits at 3, 6 and 12 months and in 6-month intervals thereafter including ECGs and 24 h-Holter ECGs.

2.6. Statistical analysis

Continuous data were summarized as means ± standard deviations or as medians [25th and 75th percentiles] as appropriate. Categorical data were presented as N (%). Differences in procedural data between the groups were analyzed with an unpaired t-test and the Wilcoxon-Mann Whitney test as appropriate. Differences in complications between the groups were analyzed using the Chi-squared test. All p-values were two-sided and a p-value < 0.05 was considered significant. All calculations were performed with the statistical analysis software R (R Core Team, 2018).

3. Results

3.1. Patient characteristics

A total of 15 consecutive patients were prospectively enrolled in this study. The median age of patients was 65 (58, 73) years. A total of 9/15 (60%) suffered from PersAF. Patients characteristics are summarized in Table 1. No differences in patients baseline characteristics have been observed for the two groups.
### 3.2. Acute procedural efficacy

Periprocedural data is depicted in Table 2. A total of 59 PVs were identified and 59/59 PVs (100%) were successfully isolated solely utilizing the LB3. The median procedure time significantly declined from LB2 (91 (86, 105) min) to LB3 (77 (68, 87) min), p < 0.001 (Fig. 2A). Similarly, the median left atrial dwelling time significantly decreased from LB2 (72 (62, 84) min) to LB3 (45 (38, 52) min), p < 0.0001 (Fig. 2B). The total laser time decreased from LB2 (1920 (1765, 2193) sec) to LB3 (1077 (896, 1165) sec), p < 0.00001. The median number of laser applications to achieve PVI per PV significantly decreased utilizing the LB3 compared to the LB2 for LSPV (p < 0.00001), LIPV (p < 0.00001), LCPV (p < 0.00001), RIPV (p < 0.00001) and RSPV (p < 0.00001). (Fig. 2C). Fifty-six of 59 PVs (95%) proved PVI after the first application of a circular lesion around the PVs (first attempt vein isolated, FAVI). No differences were observed between the two groups. Successful PVI of all PVs after the initial circular ablation (first attempt all veins isolated, FAAVI) was achieved in 14/15 (93%) patients, Fig. 3. Although no difference was detected between the groups, a trend towards higher rates of successful PVI after the initial circular ablation was observed for the LB3. A pure rapid mode ablation (without necessity of manual mode applications) was performed in 41% of PVs while a single shot laser application utilizing solely the rapid mode in one single application was performed in 31% of PVs. Zero rotational maneuvers utilizing the arc marks were similar between the groups for the LSPV, LIPV and RIPV while for the RSPV the significantly higher rates were detected (33% vs. 87%, p = 0.003). For one patient with LCPV a zero rotational maneuver utilizing a combination of rapid mode and manual mode ablations was performed and no sequential isolation of superior and inferior branches was necessary to achieve first pass PVI [13]. To achieve stable sinus rhythm a total of 10/15 (67%) patients received an electrical cardioversion at the end of the procedure.

### 3.3. Pinhole balloon ruptures

A total of two pinhole balloon ruptures occurred during the procedures. A pinhole rupture leads to loss of balloon pressure and decreased view, which therefore required a change of the complete system. As earlier described pinhole ruptures were categorized into three groups (mechanical pinholes, hot pinholes and unknown pinholes) and previously published strategies have been performed to prevent pinhole ruptures [13]. In the two cases pinhole ruptures with 13 W and rapid mode occurred due to laser applications despite imperfect view on the PV and performing of laser applications on blood instead of LA tissue. Therefore, both pinhole ruptures were classified as “hot pinhole”. Compared to the LB2 no differences concerning incidence of pinhole ruptures have been detected (p = 0.543).

### 3.4. Periprocedural complications

The total rate of periprocedural complications for the LB3 was 6.7% (1/15 patients, Table 2) and was similar to the LB2 group. One (6.7%) pericardial tamponade, not related to LB3 handling, requiring epicardial puncture was detected at the end of the procedure after successful PVI. It was drained by percutaneous puncture. No operation was necessary and the patient recovered without any sequelae. No further complications have been observed utilizing the LB3. For major adverse events no differences were detected between the groups (LB2 1/15 (6.7%) and LB3 1/15 (6.7%), p = 0.999).
3.5. Short term Follow-up and clinical success

Short term follow-up within the first 3-months showed comparable rates between the groups. A total of 4/15 patients of the LB2 group and 3/15 patients of the LB3 group experienced AF recurrence within the first 3 months (p = 0.666).

4. Discussion

This is the first prospective study reporting on the safety, efficacy, and periprocedural characteristics of the LB3 in clinical practice. The main findings are (1) With 100% successful PVI without the necessity of RF touch up the LB3 was highly effective. (2) Procedure time, LA dwelling time and total laser time significantly decreased compared to the LB2. (3) The LB3 offers the opportunity of real single shot applications to achieve PVI in 31% of PVs. (4) The rate of periprocedural major complications was relatively low (6.7%) and comparable to the LB2.

Recently Balloon-based ablation systems, applying RF, cryothermal or laser energy, have been developed to possibly reduce complexity and improve safety and efficacy of 3D-Mapping-system guided point by point RF-based ablation [6,15,16]. The VGLB allows for precise PVI under direct endoscopic view. Compared to 3D-Mapping guided RF based PVI the LB1 has shown similar clinical efficacy [6,8]. Recently, the next generation of this system (LB2) was introduced to clinical practice and some features to optimize the procedure were implemented and has been evaluated [11,13]. Recently an improved version of this promising system has been introduced offering an automated continuous lesion formation via the rapid mode to possibly improve procedural time, lesion formation and efficacy. Our aim was to determine the safety, efficacy and periprocedural characteristics of the LB3 compared to the LB2 for the treatment of AF.

4.1. Acute efficacy

4.1.1. The VGLB offers a PVI by a purely visually guided circular ablation.

Previous studies found acute PVI in 68–85% of cases after the first circular ablation utilizing the LB1 [17–19], and 80–91% utilizing the LB2 [11,13]. This fact is reflecting the earlier suggested improved characteristics of the LB2 with respect to PV occlusion and zero rotational maneuvers [11]. Utilizing the LB3 a rate of 93% acute PVI after first circular ablation was observed and procedure time, LA dwelling time and total laser time were significantly reduced compared to the LB2 by implementing the rapid mode. A promising median procedure time of 77 min was achieved and the total laser time was almost halved compared to LB2 without decreasing efficacy of PVI. With the rapid mode the LB3 offers the opportunity to perform a single shot application to achieve PVI without the necessity to perform point by point applications. In this population a pure single shot application utilizing only the rapid mode was performed in 31% of PVs. Furthermore, rapid mode only was performed in 41% of PVs. We are suggesting to aim a single shot laser application in combination with zero rotational maneuver if possible and subsequent rapid mode applications in case of imperfect view and necessity of rotational maneuvers. With a median procedure time of 77 min the LB3 shows comparable data to cryoballoon based PVI procedures (70–86.7) [20,21].

All PVs have been isolated solely utilizing the LB3, no tough-up by RF ablation was necessary to achieve acute PVI. Together with the above mentioned single shot rate and promising procedures times this system is presenting the opportunity to be a competitor to cryoballoon based PVI procedures.

4.2. Safety

With 6.7% periprocedural complication the rate of complications was relatively low for the LB3 and no significant differences were observed between the groups. Since the total laser time was significantly reduced without reducing the efficacy of acute PVI the LB3 may further decrease the complication rates for characteristic complications of balloon-based procedures like right phrenic nerve injury as well as esophageal injuries. Balloon catheters were suggested to have a reduced risk for cardiac tamponades by cardiac perforation due to larger surface area compared to single-tip ablations catheters. In our population one pericardial tamponade occurred, which was not related to the LB3 and was treated by epicardial puncture and drainage without any sequelae. Since the number of patients was relatively low the reported complication rate can only be hypothesis generating.

Although the rapid mode allows for an increased energy application (13 and 15 W) compared to the manual mode (maximum of 12 W) the rate of pinhole ruptures did not increase in the observed population. Pinhole ruptures are leading to a complete change of the whole system. In consequence the procedure become a loss-making business in those cases. Therefore, pinhole ruptures should be avoided. In our opinion a combination of rapid mode applications and manual mode applications in case of imperfect view might be the best strategy to prevent pinhole ruptures. Furthermore, we recently published strategies to effectively avoid pinhole ruptures for laser balloon procedures [13].

5. Limitations

The number of patients included in this study was relatively small and was only reflecting the experience of a single center. However, the periprocedural data of a novel device with technological improvements need to be evaluated and reported to current and potential users. Although the patients number is low our data may help to implement the system into clinical practice of centers. The Phoenix registry focused on the acute procedural data of the LB3 compared to the LB2 but differences in the long-term outcome remains unknown.

No definitive conclusion can be established regarding the available data. Therefore, our findings may only be hypothesis generating. Further studies are required to assess the long-term follow up after LB3 based PVI.

6. Conclusion:

The LB3 was effective for PVI. Procedure time, LA dwelling time and total laser time were significantly decreased compared to laser balloon generations. A high rate of successful isolated PVs solely by a single shot laser application was observed. Further investigation is necessary to draw final conclusions and to judge on safety and efficacy of this new promising system.

7. Disclosures

CHH received travel grants and research grants by Medtronic, Boston Scientific, Claret Medical, SentreHeart, Biosense Webster and Cardiofocus and Speaker’s Honoraria from Biosense Webster, Cardiofocus and Boston Scientific. RRT received travel grants from St. Jude Medical, Topera, Biosense Webster, Daichi Sankyo, SentreHeart and Speaker’s Bureau Honoraria from Biosense Webster, Biotronik, Pfizer, Topera, Bristol-Myers Squibb; Bayer, Sano Aventis and research grants by Cardiofocus. CE received travel grants and educational grants by Medtronic. All other authors have no relevant disclosures. KHK received travel grants and research grants
from Biosense Webster, Stereotaxis, Prorhythm, Medtronic, Edwards, Cryocath, and is a consultant to St. Jude Medical, Biosense Webster, Prorhythm, and Stereotaxis. He received speaker’s honoraria from Medtronic.

IRB information: The present study was approved by Ethics committee of the University of Lübeck (Reference number: EK-AZ 15-347).

CRediT authorship contribution statement

Christian-H. Heeger: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing. Christian M. Tiemeyer: Data curation, Writing - review & editing. Huong-Lan Phan: Data curation, Writing - review & editing. Rozia Meyer-Saraei: Writing - review & editing. Spryidon Liosis: Writing - review & editing. Ben Brüggemann: Writing - review & editing. Niels Große: Writing - review & editing. Bezahd Fahimi: Writing - review & editing. Samuel Reincke: Writing - review & editing. Karl-Heinz Kuck: Writing - review & editing. Feifan Ouyang: Writing - review & editing. Charlotte Eitel: Writing - review & editing. Roland R. Tilz: Investigation, Project administration, Supervision, Writing - review & editing.

Declaration of Competing Interest

CHH received travel grants and research grants by Medtronic, Boston Scientific, Claret Medical, SentreHeart, Biosense Webster and Cardiofocus and Speaker’s Honoraria from Biosense Webster, Cardiofocus and Boston Scientific. RRT received travel grants from St. Jude Medical, Topera, Biosense Webster, Daiichi Sankyo, SentreHeart and Speaker’s Bureau Honoraria from Biosense Webster, Biotronik, Pfizer, Topera, Bristol-Myers Squibb; Bayer, Sano Aventis and research grants by Cardiofocus. CE received travel grants and educational grants by Medtronic. All other authors have no relevant disclosures. KHK received travel grants and research grants from Biosense Webster, Stereotaxis, Prorhythm, Medtronic, Edwards, Cryocath, and is a consultant to St. Jude Medical, Biosense Webster, Prorhythm, and Stereotaxis. He received speaker’s honoraria from Medtronic.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2020.100576.

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