Circumferential pulmonary vein isolation: the role of key target sites

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Aims Circumferential pulmonary vein isolation (CPVI) had been proved effective for treating atrial fibrillation (AF). However, the achievement of pulmonary vein (PV) isolation was sometimes challenging. PVs could not be isolated until some key target sites (KTSs) were ablated thoroughly. The aim of our study was to explore the distribution of KTSs.

Methods and results Four hundred and fifty-two cases (271 males, mean age 62.5 ± 12.6 years) with drug-refractory AF were enrolled for catheter ablation. CARTOTM-guided CPVI was performed in all cases with one circular catheter for verification of PVs isolation. Target sites where PV potentials delayed, conduction sequence changed, slowed down, or isolated were defined as KTSs. From 452 CPVI procedures, 1520 KTSs were identified; 813 of which were located at left PV antrums and 707 were at right PV antrums. KTSs at left PV antrums were most commonly situated at anterior wall (63%), while KTSs at right PV antrums were most commonly situated at posterior wall (66.2%). Additional gaps ablation was performed for left PVs in 344 cases and for right PVs in 248 cases owing to incomplete PVs isolation by a single attempt of CPVI. One thousand one hundred and fifty-eight KTSs were identified, 662 of which were located at left PV antrums and 496 were at right PV antrums. At the anterior wall, 66.1% of left PV KTSs were located, and 67.9% of right PV KTSs were located at the posterior wall. Out of 1158, 961 (82.99%) KTSs were predicted correctly by circular mapping. PV isolation could not be achieved until some KTSs were ablated by applying higher power, longer duration, and higher irrigation rate than usual.

Conclusion KTSs during CPVI were most commonly situated at the anterior wall of left PVs and at the posterior wall of right PVs. Circular mapping within ipsilateral PVs’ ostia could accurately predict the location of KTSs. Some KTSs must be ablated thoroughly by applying higher power, longer duration, and higher irrigation rate than usual to achieve PV isolation.

KEYWORDS
Atrial fibrillation; Ablation; Pulmonary vein

Introduction
A magnitude of studies have proved the efficacy of circumferential pulmonary vein isolation (CPVI) for the treatment of atrial fibrillation (AF), and this procedure has been adopted as the mainstream of ablation approach for eliminating paroxysmal and persistent AF by more and more investigators.1–6 However, pulmonary vein (PV) isolation can only be obtained in 20–55% of PVs by circumferential PV ablation with empirical settings of voltage abatement by more than 80% or ablation duration of 40–60 s for each lesion.7–9 which means isolation cannot be achieved for the remaining PVs until conduction gaps along initial lesion lines have been ablated thoroughly. We then hypothesized the presence of key target sites (KTSs) along initial circumferential lesion lines and carried out this study to explore the distribution of KTSs of CPVI and to investigate the mapping and ablation for KTSs.

Methods
Patients’ population
From June 2005 to June 2006, altogether 452 cases with symptomatic, drug-refractory AF were enrolled for catheter ablation. Of them, 271 were males with the mean age 62.5 ± 12.6 years (range 54–75 years). AF was paroxysmal in 326 cases and persistent in 126 cases with the mean AF duration of 5.2 ± 4.6 years (range 0.5–14 years). Two hundred and fifty cases were with no evidence of structural heart disease, 163 cases with hypertension, 15 cases with coronary artery disease, 23 cases with valvular heart disease, nine cases with dilated cardiomyopathy, 11 cases with the history of ischaemic stroke, 32 cases with diabetes mellitus, and 12 cases with pacemaker implantation. Forty-three cases had undergone
previous ablation for AF, including eight of them who received segmental PV ostia ablation and 35 cases received CPVI. By trans-thoracic echocardiography, mean left atrium (LA) diameter was measured to be 36.8 ± 9.7 mm (range 23–57 mm). Transoesophageal echocardiography was performed to exclude thrombus in LA. The baseline characteristics of the patients in this study were shown in Table 1. All cases provided written informed consent.

Electrophysiological study
Prior to ablation, all anti-arrhythmic drugs except amiodarone were withdrawn for five or more half-lives. The procedure was performed under conscious sedation with continuous infusion of propofol. One decapolar mapping catheter (Biosense Webster, Diamond Bar, CA, USA) was positioned in coronary sinus via left or right subclavian vein access. Two L1-type Swartz sheathes (St Jude Medical, Minnetonka, MN, USA) were advanced into the LA after two successful transseptal punctures. Heparin 80–100 U/kg of body weight was infused via the sheath and followed 1000 U/h to maintain an activated clotting time of 300–350 s. Selective PV venography was performed to identify all PV ostia. One decapolar circular mapping catheter (Lasso, Biosense Webster) was positioned at the ostium of each PV for recording PV potentials (PVPs). Surface echocardiogram (ECG) and bipolar endocardial electrograms were stored continuously for further analysis. Bipolar signals were filtered at the range of 300–500 Hz.

Circumferential pulmonary vein ablation
The circumferential pulmonary vein ablation (CPVA) procedure was performed under the guidance of CARTO™ system (Biosense Webster, Diamond Bar, CA, USA). The circumferential pulmonary vein ablation (CPVA) procedure was advanced into the LA after two successful transseptal punctures. Two L1-type Swartz sheathes (St Jude Medical, Minnetonka, MN, USA) were advanced into the LA after two successful transseptal punctures. Heparin 80–100 U/kg of body weight was infused via the sheath and followed 1000 U/h to maintain an activated clotting time of 300–350 s. Selective PV venography was performed to identify all PV ostia. One decapolar circular mapping catheter (Lasso, Biosense Webster) was positioned at the ostium of each PV for recording PV potentials (PVPs). Surface echocardiogram (ECG) and bipolar endocardial electrograms were stored continuously for further analysis. Bipolar signals were filtered at the range of 300–500 Hz.

Table 1  Baseline characteristics

| Male/female | 271/181 |
| Age (years) | 62.5 ± 12.6 | 54–75 |
| Paroxysmal/persistent | 326/126 |
| Duration of AF (years) | 5.2 ± 4.6 | 0.5–14 |
| Structural heart disease | 202 |
| Hypertension | 163 |
| Coronary artery disease | 15 |
| Dilated cardiomyopathy | 9 |
| Valvular heart disease | 23 |
| Previous history of AF ablation | 43 |
| LA diameter (mm) | 36.8 ± 9.7 | 23–57 |

AF, atrial fibrillation; LA, left atrium.

The division algorithm for circumferential lesion lines around ipsilateral right and left pulmonary veins
The circumferential lesion lines around right and left PVs were divided equally into eight segments empirically: the antero-superior segment, the antero-median segment, the antero-inferior segment, the postero-superior segment, the postero-median segment, the postero-inferior segment, the roof segment, and the inferior segment. KTSs were classified according to this division algorithm (Figure 3).

Mapping and ablation of key target sites along initial lesion lines
The decapolar Lasso catheter was utilized as a roadmap for predicting the localization of KTSs, which was positioned at the ostia of each PV with the electrode pairs 10-1 pointing at 12 o'clock with fluoroscopic projection of right anterior oblique 30° for right-sided PVs (RPVs) and projection of left anterior oblique 45° for left-sided PVs (LPVs). The Lasso catheter was positioned at the ostium of the ipsilateral superior and inferior PV sequentially to identify the earliest atrium-PV conduction. For RPVs, Lasso 1-5 represented the posterior wall, and Lasso 6–10 represented the anterior wall. For LPVs, on the contrary, Lasso 1-5 represented the anterior wall and Lasso 6–10 represented the posterior wall. The correlation of Lasso electrode pairs and segment of circumferential lines were illustrated in Figure 3. The lesion manifesting the earliest atrium-PV conduction predicted the possible location of KTSs and was then allocated into one segment of circumferential lines (Figure 4). KTSs were also mapped by ablation catheter by roving the catheter along initial ablation lines, and the endocardogram of possible KTS often had the characteristics of fractionated or fusion potentials downwardly at the posterior wall, then from the antero-superior wall to the antero-inferior wall to close the circular line (Figure 1). The endpoint of the procedure was PV isolation, which was characterized as PVPs disappearance or dissociation with atrial electrograms. The KTSs were defined as the lesions where atrium-PV conduction was delayed, or its sequence was changed (during sinus rhythm), or the cycle length of PVPs prolonged (during AF), or PV isolation was achieved (Figure 2).
Figure 2 The illustration of key target sites (KTSs) during circumferential pulmonary vein isolation. Panels A–C showed various KTSs identified during the procedure. Tracings were surface ECG lead I, V1, Lasso 1-2 to Lasso 9-10, coronary sinus (CS) 9-10 to CS 1-2, ABLd, and ABLp. Note that in Panel A, during ablation, the conduction from atrium (A) to pulmonary vein potential (PVP) was delayed, and finally blocked; in Panel B, during ablation, the conduction sequence of A-PVP changed abruptly from the earliest A-PVP conduction Lasso 1-2 to Lasso 2-3 and Lasso 8–9 to Lasso 9-10, and the conduction of A-PVP was delayed as well; in Panel C, during AF persistence by ablation PVPs slowed down gradually and disappeared.
The predicting accuracy of Lasso mapping was evaluated by calculating the proportion of correct ones out of all predictions. RF energy was delivered with greater power or longer duration than usual for ablating some KTSs. A maximum of 40 W, 45°C, and 90–120 s were applied for some KTSs at anterior wall, and a maximum of 35 W, 43°C, and 40–60 s were applied for some KTS at posterior wall and roof. The saline irrigation speed increased to 25–30 mL/min. Ablation was repeated several times when necessary.

**Figure 3** Division of circumferential pulmonary vein ablation lines and placement of Lasso within each pulmonary vein’s ostium.

**Figure 4** Key target sites (KTS) predicted by Lasso mapping within ipsilateral superior and inferior pulmonary veins (PVs) and the local potential configuration of KTS. Panel A showed the fractionated potential configuration of KTS at the top of left superior pulmonary vein (LSPV). Panel B showed the division of circumferential pulmonary vein isolation lesion lines for left-sided PVs. In Panel C and D, Lasso mapping of LSPV and left inferior pulmonary vein (LIPV) potentials were demonstrated. Tracings were surface electrocardiogram lead I, V1, Lasso 1-2 to Lasso 9-10, coronary sinus (CS) 9-10 to CS 1-2, ABLd, and ABLp. Note that the earliest A-PV conduction in LSPV was Lasso 1-2 to Lasso 9-10 (at the top of LSPV). The earliest A-PV conduction in LIPV was Lasso 1-2 to Lasso 2-3 (at antero-superior wall of LIPV), but was much delayed, based on these results we could conclude that KTS (conduction gap) was at the top of LSPV.

**Figure 4**. The predicting accuracy of Lasso mapping was evaluated by calculating the proportion of correct ones out of all predictions. RF energy was delivered with greater power or longer duration than usual for ablating some KTSs. A maximum of 40 W, 45°C, and 90–120 s were applied for some KTSs at anterior wall, and a maximum of 35 W, 43°C, and 40–60 s were applied for some KTS at posterior wall and roof. The saline irrigation speed increased to 25–30 mL/min. Ablation was repeated several times when necessary.

**Statistical analysis**
Continuous variables were expressed as mean ± SD and categorical variables as counts or proportions (%).
Results

All cases underwent the procedure successfully. PVs isolation was achieved in 434 cases (96.0%) for RPVs and in 423 cases (93.6%) for LPVs. The mean procedural time was $175 \pm 34$ min (range 90–245 min), and the mean fluoroscopic time was $22 \pm 15$ min (range 10–42 min). Procedure-related complications included femoral artery-venous fistula in two cases and femoral artery pseudo-aneurysm in two cases, major stroke with left limb hemiplegia in two cases, all cases were treated with conservative therapy. Pericardium effusion developed in four cases and was treated with pericardiocentesis.

The distribution of total key target sites along circumferential lesion lines in all cases

During 452 CPVI procedures, 1520 KTS were identified; 813 of which were located at LPVs and 707 were at RPVs. For KTS at LPVs, 201 (24.7%) of them were located at antero-superior wall, 180 (22.1%) of them at antero-median wall, 132 (16.2%) of them at antero-inferior wall, 87 (10.7%) of them at postero-inferior wall, 84 (10.3%) of them at the roof, 60 (7.4%) of them at postero-superior wall, 39 (4.8%) of them at postero-median wall, and 30 (3.7%) of them at the inferior wall. For KTSs at RPVs, 207 (29.3%) of them were located at postero-superior wall, 162 (22.9%) of them at postero-median wall, 99 (14%) of them at postero-inferior wall, 72 (10.2%) of them at antero-median wall, 52 (7.2%) at the roof, 48 (6.8%) of them at antero-inferior wall, 36 (5.1%) of them at antero-superior wall, and 33 (4.7%) of them at the inferior wall (Figure 5).

The distribution of key target sites along circumferential lesion lines in cases with additional gaps ablation

During circumferential PV ablation, the target sites which were ablated finally usually were the KTSs to achieve PV isolation, accordingly different ablation sequence might yield different KTSs distribution. In order to exclude such biases, we further analysed KTSs distribution in cases with additional gaps ablation after single circumferential PV ablation had failed to achieve PV isolation. Altogether, PV isolation was not achieved for LPVs in 344 cases and for RPVs in 248 cases by a single attempt of CPVA.

Additional gaps ablation revealed 1158 KTSs. Of which 662 were located at LPVs, and 496 were at RPVs. For KTS at LPVs, 165 (24.9%) of them were located at antero-superior wall, 151 (22.8%) of them at antero-median wall, 122 (18.4%) of them at antero-inferior wall, 74 (11.2%) of them at the roof, 49 (7.4%) of them at postero-inferior wall, 48 (7.3%) of them at postero-superior wall, 32 (4.8%) of them at postero-median wall, and 21 (3.2%) of them at the inferior wall. For KTS at RPVs, 140 (28.2%) of them were located at postero-superior wall, 120 (24.2%) of them at postero-median wall, 77 (15.5%) of them at postero-inferior wall, 33 (6.7%) of them at antero-inferior wall, 31 (6.3%) of them at antero-superior wall, 44 (6.2%) at the roof, 30 (6.0%) of them at antero-median wall, and 21 (4.2%) of them at the inferior wall (Figure 6).

Results from mapping of key target sites guided by Lasso catheter during gaps ablation

According to the foregoing results, additional gaps ablation revealed 1158 KTSs, and each one was predicted in advance by Lasso mapping. KTSs were also mapped and ablated by ablation catheter by roving the catheter along initial ablation lines. The predicting accuracy of Lasso mapping was evaluated by calculating the proportion of correct ones out of all prediction. The total prediction by Lasso mapping and the correct ones at eight segments of CPVA lines were illustrated in Figure 7. The real location of the corresponding KTSs, which was predicted incorrectly by Lasso were shown in Figure 8. In summary, the overall predicting accuracy was 82.99%; however, the predicting...
accuracy was low when KTSs were situated at the postero-superior wall, postero-median wall for LPVs, antero-median wall and antero-inferior wall for RPVs. Usually, KTSs predicted incorrectly by Lasso were located close to initial Lasso-predicted segments. However, some KTSs which were predicted at postero-superior and postero-median wall of LPVs were actually located at antero-inferior and antero-median wall of LPVs. Similarly, some KTSs which were predicted at antero-median and antero-inferior wall of RPVs were actually located at postero-superior and postero-median wall of RPVs.

**Results from key target sites ablation for cases with additional gaps ablation**

For 438 KTSs situated at anterior wall of LPVs, the mean RF power was $38.3 \pm 2.5$ W, the mean temperature was $44.3 \pm 1.8$ °C. The mean RF duration for each KTS was $100 \pm 23$ s.
For 224 KTSs situated at posterior, inferior wall, and roof, the mean RF power was $31.4 \pm 2.5$ W, the mean temperature was $41.3 \pm 1.8$ °C. The mean RF duration for each KTS was $50 \pm 14$ s. For 94 KTSs situated at anterior wall of right PVs, the mean RF power was $34.3 \pm 4.6$ W, the mean temperature was $43.1 \pm 2.2$ °C. The mean RF duration for each KTS was $50 \pm 11$ s. For 402 KTSs situated at posterior, inferior wall, and roof, the mean RF power was $32.1 \pm 1.7$ W, the mean temperature was $42.3 \pm 1.6$ °C. The mean RF duration for each KTS was $35 \pm 7$ s. After further ablation of additional KTSs, LPVs were isolated in 315 out of 344 cases and RPVs were isolated in 230 out of 248 cases. However, the remaining 29 LPVs and 18 RPVs could not be isolated despite deliberate KTSs ablation.

Discussion

This study was carried out according to our hypothesis of KTSs during CPVI procedure for AF therapy. The results of the study demonstrated that KTSs were present when performing CPVI, which could be predicted accurately by circular mapping, and that some KTSs should be ablated intensively to achieve PVs isolation.

CPVI has become the main ablative strategy for the therapy of AF, which was proposed by Ouyang et al. who reported that PVs isolation could be achieved by continuous ablation encircling the ipsilateral PVs at PVs antrum, where atrium-PV connected each other circumferentially. However, several investigators reported that PVs isolation could not be achieved in 45–80% of PVs during initial CPVI procedure until some gaps along circumferential lines were ablated. We then hypothesized that KTSs were present along ablation lines, although atrium-PV connection was circumferential at the antrum of ipsilateral PVs.

The results of CPVI in all cases showed 63% of KTSs from LPVs located at anterior wall, and 66.2% of KTSs from RPVs located at posterior wall. Obviously, these results were possibly influenced by the specific ablation sequence in our study, and we would have different results if different ablation sequence had been applied; since the final lesions to ablate most probably were the KTSs where PVs isolated were achieved. In order to exclude such biases, we analysed the distribution of additional KTSs during gaps ablation. Because all lesions along circumferential lines had been ablated with the uniform RF energy delivery, the ablation sequence biases were supposed to be decreased as much as possible. Interestingly, additional gaps procedure showed similar results: 66.1% of KTSs from LPVs located at anterior wall, and 67.9% of KTSs from RPVs located at the posterior wall. These results indicated that anterior wall of LPVs and posterior wall of RPVs were the key target areas for achieving PVs isolation, irrespective of ablation sequence. These findings could be explained as follows: the ridge between LSPV and appendage was reported to be as narrow as 4 mm; thus, catheter could be poorly stabilized on the ridge when ablating anterior wall of LPVs, making it very difficult to achieve transmural and continuous lesions. The anterior wall of RPVs was close to the septum, and catheter could be well stabilized, but at the posterior wall of RPVs the catheter stabilization was poor, especially at the postero-superior wall of RPVs.

During additional gaps ablation, Lasso catheter was applied as the roadmap to predict the location of KTSs. According to the results, the overall predicting accuracy rate was 82.99%. For the LPVs, the lowest predicting accuracy was at the postero-superior and postero-median wall. For the RPVs, the lowest predicting accuracy was at the antero-median and antero-inferior wall. The electrical connection between ipsilateral superior and inferior PVs may account for the relative low accuracy at these sites. One study focusing on anatomic examination of the ipsilateral

Figure 8 The real location of corresponding key target sites (KTSs) which was predicted incorrectly by Lasso catheter. KTSs from left-sided PVs (LPVs); KTSs from right-sided PVs (RPVs). For each segment of ablation line, the total amount of prediction (denominator) and the correct prediction (numerator) were listed. The incorrect prediction was illustrated on the small diagram showing the real location of them. The projection view of small diagrams was the same as the large ones for both LPVs and RPVs.
PVs demonstrated the close relationship between them with an atrial tissue of only 3–7.3 mm wide connecting each other, forming the anatomic basis for electrical conduction between ipsilateral PVs. Tritto et al. and Takahashi et al. reported the electrical connection between LSPV and LIPV. However, few literatures were available about the electrical connection between right superior pulmonary vein (RSPV) and right inferior pulmonary vein (RIPV). Results from our study implied electrical connection between RSPV and RIPV, but it was not evaluated systemically.

We applied more ‘aggressive’ ablation for some KTSs to close conduction gaps along circumferential lines. Higher RF power delivery and longer duration were needed to achieve PV isolation, which indicated that some KTSs were difficult to ablate completely if routine ablation setting was applied.

**Study limitations**

There were several limitations in our study. First, the division algorithm of circumferential ablation lines was mainly based on our experience, and when placing Lasso catheter, we were not able to ensure the accurate localization of the electrode pairs 10-1 pointing at 12 o’clock. Secondly, unlike the implication of double Lasso technique by Ouyang in his studies, only one Lasso catheter was used and the ipsilateral superior and inferior PVs were sequentially mapped in our study. This could have slightly altered the results on gaps ablation sites prediction and the identification of connections between ipsilateral PVs. Thirdly, this study was not a randomized and control one. The ablation sequence was not randomized and compared with different groups, while the ablation sequence had great impact on the distribution of KTSs. However, KTSs during additional gaps ablation were further analysed. The ablation sequence bias was decreased as much as possible, since two circumferential ablation lines were already accomplished. Finally, aggressive ablation of some KTSs might contribute to achieve PV isolation, yet its potential risks such as perforation and oesophagus injury were not evaluated systemically.

**Conclusions**

KTSs were present during CPVI procedure for AF treatment and had specific distribution. KTSs were most commonly situated at the anterior wall of LPVs and at the posterior wall of RPVs. Circular mapping within ipsilateral PVs’ ostia could accurately predict the location of KTSs. Some KTSs must be ablated thoroughly by applying higher power, longer energy delivery and higher irrigating flow rate than usual to achieve PV isolation.

**Conflict of interest:** none declared.

**References**