Robot-assisted epicardial ablation of the pulmonary veins: is a completed isolation necessary?

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Aims To study the feasibility and electrophysiological efficacy of minimally invasive beating heart ablation of the pulmonary veins (PVs) via a robot-assisted single-sided approach.

Background PV isolation by minimally invasive epicardial ablation may offer a new treatment for patients with lone atrial fibrillation (AF). However, complete PV isolation has been shown to be difficult to obtain.

Methods and results In 14 mongrel dogs, robot-assisted epicardial microwave ablation was performed on the beating heart by a single-sided right chest approach. Isolation of all PVs was performed in two steps to study the effect of an incomplete and a complete isolation on AF. AF was studied by random and burst pacing. Incremental pacing was performed to study conduction characteristics across the lesions. Opening of the pericardial reflections, introduction of the catheter and ablation were robotically feasible by a single-sided approach in 11 dogs. The AF duration decreased from 6.6 ± 4.1 to 1.3 ± 0.8 s (P = 0.03) and 1.6 ± 1.6 s (P = 0.04 compared with control) after incomplete and completed isolation of the PVs. The AF cycle length increased from 134 ± 5 to 141 ± 5 and 145 ± 8 ms (P = 0.03) after incomplete and complete isolation, respectively. Several incomplete lesions showed 2:1 exit and/or entrance block during incremental pacing. After complete isolation, AF was no longer inducible from the PVs.

Conclusion Epicardial PV isolation can be successfully performed by a single-sided robot-assisted approach. The effect of PV ablation on AF is not an all or none phenomenon. Incomplete isolation already decreases AF duration and lengthens the AF cycle length. However, complete isolation is necessary to prevent AF induction by triggering from the isolated area.

Introduction

Pulmonary vein (PV) isolation is a cornerstone in current surgical treatment of atrial fibrillation (AF). Generally, surgical AF treatment is performed during conventional open heart surgery by endocardial ablation lesions including encircling of the PVs. This treatment, however, can only be offered to patients with concomitant AF undergoing surgery on the arrested heart. Off-pump surgery on the other hand has received much attention in the past decade and new approaches have been developed to perform isolation of the PVs on the beating heart.1–3 This offers the possibility of treating AF patients undergoing surgery without cardiopulmonary bypass. Moreover, lone AF patients can thus be treated surgically using beating heart approaches with endoscopic or robot techniques to minimize the invasiveness and reduce the procedure time.4,5

A critical step, however, in epicardial PV isolation is the positioning of the catheter lateral to the left atrial appendage, since ventral positioning may result in ablation of the circumflex artery. Current minimally invasive techniques to isolate the PVs still need a double-sided approach to the chest to prevent the risk of blind and incorrect positioning of the catheter. Visualization of the left atrial appendage from the right side of the chest through the transverse sinus by use of robot-assisted videoscopy would offer the possibility of performing the procedure from only one side of the chest. This could eventually lead to a procedure which genuinely deserves the tag of ‘minimal invasiveness’.

Although epicardial PV isolation has been shown to be safe and effective,1,3 it can be difficult to achieve a completed isolation due to atrial pathology, blood cooling, epicardial fat, poor catheter–tissue contact, or ‘late’ recovery of conduction.6 That lesions need to be complete in order to be effective is an axiom in surgical PV ablation. Therefore, different evaluation methods such as histological, electrical, and impedance measurements are currently under investigation.

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to assess lesion completeness. Less attention, however, has been paid to the efficacy of incomplete isolation of the PVs. It therefore remains unclear whether complete isolation is required and whether incomplete PV isolation should be considered as a treatment failure.

The present study was designed to investigate whether robot-assisted epicardial beating heart PV ablation in dogs can be performed from only one side of the chest. In addition, we addressed the question of whether incomplete isolation of the PVs already influences the AF duration and electrophysiological characteristics of the atria and whether a complete isolation is needed to halt induction of AF by foci from the PV area.

Methods

Fourteen mongrel dogs, each weighing 25–35 kg were used in this study. All animals received humane care in compliance with the ‘Guide for the Care and Use of Laboratory Animals’ (NIH publication 86-23, 1985 revision; National Institutes of Health, USA). Experiments were approved by the local ethics committee for the use of experimental animals. The dogs were anaesthetized with 22 mg/kg sodium pentobarbital intravenously, and ventilated by isoflurane (1–2%) and a 1:2 mixture of O2 and N2O. Arterial invasive blood pressure, ECG, and saturation (pulse oximeter) were monitored throughout the experiment. Oesophageal body temperature was monitored and kept constant using a heating lamp.

Atrial instrumentation and robot-assisted beating heart PV ablation

The dogs were placed in supine position with the right front leg positioned cranially towards the shoulder. A right mini thoracotomy was performed (40-mm incision) in the fourth intercostal space at the anterior axillary line. The pericardium was opened inferiorly to the phrenic nerve to expose the right and left atria. On the right atrium (RA), two bipolar electrodes were sutured. Another two bipolar electrodes were sutured to the atrial tissue close to the right PVs. A third pair of bipolar electrodes was placed on the roof of the left atrium (LA). In each area of interest (PV, RA, and LA), one of the two bipolar electrodes was always used for pacing and the other for sensing. Electrodes were made from two silver buttons (diameter 1.5 mm, distance 5 mm) for bipolar recording and pacing. The da Vinci Robotic Surgical System (Intuitive Surgical, Mountainview, CA, USA) was positioned at the left side of the dog allowing the three robotic arms to advance the thorax from the right side. The microwave ablation catheter (Afx Inc., Flex 10, Fermont, CA, USA) is a flexible catheter that can be positioned around the PVs in a lasso-like fashion (see Figure 1). Inside the catheter a 40-mm ablation antenna can be moved to produce a contiguous box lesion. Ablation was performed with 65 W for 90 s. Isolation of the PVs was performed in two steps, to study the effects of an incomplete lesion and a closed box on electrophysiology and AF. The first ablation lesion completed the box around all PVs, except for a 10–20-mm opening at the anterolateral side of the upper right PV. After electrophysiological measurements, the box was completed with a single ablation application on the anterolateral side of the upper right PV. If complete isolation was not obtained, the circular lesion around the PVs was repeated with the same antenna settings (65 W, 90 s). A complete lesion around all PVs was defined as: (i) a present exit block (pacing from the PVs with capture inside the box but without conduction to the area outside the box), and (ii) a present entrance block (pacing from the right atrium with capture outside the box but without conduction to the box area). Pacing was performed at four times the threshold. Figure 1 shows the flex 10 ablation catheter together with a sketch of the incomplete and complete lesion around the PVs.

AF and electrophysiological measurements

To study the effects of incomplete and complete PV isolation on acute AF, two different pacing protocols were used. In addition, the atrial effective refractory period and the maximal atrial pace frequency were determined. All pace protocols and electrophysiological measurements were performed before ablation (control) and after incomplete and complete isolation of the PVs. The pacing protocols were performed from all three electrodes (PV, RA, and LA) at four times the threshold (mA). Data were recorded and analysed with an electrophysiological measurement system with integrated stimulator (EPTracer38, CardioTek, Maastricht Airport, NL).

A random pace model was used to study AF duration and AF cycle length (AFCL). Random pacing was performed by an algorithm that generated irregular stimuli within a chosen range of intervals. To obtain AF, interval settings were adjusted for each pacing site. These control settings were used for the entire experiment. Random pacing was continued for at least 3 min first from the PVs, then from the RA, and finally from the LA. AF during random pacing was determined by three parameters: (i) an irregular interval between the pace artefact and the atrial activation, (ii) non-capture morphology of the atria activation, and (iii) persisting AF after random pacing was stopped. The AF susceptibility during random pacing was defined as the mean of 20 AF episodes. The AFCL was measured during AF. In a second protocol, AF was induced by a 1-s burst of 50 stimuli (interval 20 ms) to study AF duration and AFCL from the different atrial electrodes. Durations of AF after 1-s bursts were calculated from at least 10 AF episodes.

To study the conduction characteristics over the incomplete and complete lesion, incremental pacing was performed from different pacing sites (PV, LA, and RA) at four times the threshold, 50 beats per frequency. Pacing rate was started at 400 ms and decreased in steps of 50 ms until a 250-ms interval was reached followed by steps of 10 ms until AF was induced or 2:1 capture was observed. The atrial effective refractory period (AERP) was measured at a basic cycle length of 400 ms. AERP was performed from all three electrodes (PV, RA, and LA) at four times the threshold (mA). Data were recorded and analysed with an electrophysiological measurement system with integrated stimulator (EPTracer38, CardioTek, Maastricht Airport, NL).

Statistical analysis

Statistical comparison was performed by the paired Student’s t-test. Bonferroni correction was applied for the multiple pairwise comparisons between the three conditions of interest: control vs. incomplete isolation, control vs. complete isolation, and incomplete vs. complete isolation. Results are expressed as mean ± standard
deviation (SD) or as median ± SD for the AF duration and AFCL. The calculated number of dogs required was based on an 80% decrease in AF duration with a sampling weight of 90%. Five extra animals were added to the calculated sample size for development of the robotic procedure. A two-tailed P-value of less than 0.05 was considered to be statistically significant.

Results

Robot-assisted ablation of the PVs

Opening of the transverse and oblique sinus was performed robotically. Opening of the pericardial reflections between the superior right PV and the superior caval vein, and between the inferior right PV and the inferior caval vein, and development of the inter-atrial groove were also performed robotically. Figure 2 shows an intra-operative photograph of blunt robotic preparation of the inter-atrial groove.

Positioning of the catheter at the left atrial side along the lateral border of the appendage could be achieved under direct vision by introducing the robotic camera into the transverse sinus. The catheter was then moved downwards in the direction of the spine and the catheter naturally encircled the lower PVs. By further moving the catheter, the tip appeared at the border of the right PV and the inferior caval vein. Figure 3 shows a schedule and two photographs of the single right-sided approach with direct vision through the transverse sinus on the left atrial appendage.

The single-sided robotic isolation of the PVs was feasible in 11 of the 14 dogs. In the first three dogs, the procedure was performed only partly robot-assisted and should be counted as technical incompleteness of the robotic procedure. There was one atrial injury with bleeding complications immediately after introduction of the ablation catheter. This was the result of catheter insertion under limited vision and limited space around the PVs in that dog.

Electrophysiological effects of incomplete and complete isolation of the PVs

The pacing thresholds from the right atrial and PV electrodes (1.1 ± 0.8 and 1.0 ± 0.5 mA, respectively), did not change after incomplete (0.9 ± 0.4 and 1.4 ± 0.6 mA, respectively) and complete isolation (1.5 ± 1 and 2 ± 1.4 mA, respectively). Completed isolation after closure of the intentional gap was obtained in 8 animals (57%) and in 13 animals after repeated ablation (93%). In the remaining animal, a second repeat of the ablation was needed to obtain a completed lesion.

The ability to induce and maintain AF by random pacing depended on the interval settings. Too-short random pacing intervals resulted in a 2 to 1 capture relation, and too-long pacing intervals in a 1 to 1 capture relation. When settings of the random pacing intervals were chosen around the maximal atrial pace frequency, AF could be induced and maintained. The minimal interval was chosen 20–30 ms below the maximal atrial pace frequency, and the maximal interval 20–30 ms above the maximal atrial pace frequency. The intervals ranged between 90 ± 15 and 120 ± 20 ms. The AF duration during random pacing decreased from 4.1 ± 4 to 0.6 ± 0.4 s (P = 0.001) after the incomplete isolation of the PV when pacing was performed from within the PVs. After completion of the box, AF was no longer inducible when pacing was performed from the PV electrodes (P = 0.0001 compared with control and P = 0.003 compared with incomplete isolation). The AF duration induced from the RA decreased from 7.1 ± 2 to 2 ± 0.6 s (P = 0.003) and 2.6 ± 1 s (P = 0.01) after incomplete and completed ablation, respectively, as illustrated in Figure 4. After burst pacing from the RA, the AF duration decreased from 6.6 ± 4.1 to 1.3 ± 0.8 s (P = 0.03) and 1.6 ± 1.6 s (P = 0.04 compared with control), respectively.

The AFCL increased after incomplete isolation from 134 ± 5 to 141 ± 5 ms (RA), from 129 ± 4 to 137 ± 8 ms (LA), and from 131 ± 5 to 138 ± 9 ms (PV). After closure of the box, the AFCL showed a significant increase in both the RA and LA to 145 ± 8 ms (P = 0.03) and 145 ± 8 ms (P = 0.01), respectively. The AFCL inside the PVs could not...
be measured after complete isolation since AF was no longer inducible inside the box. The AFCL measured before and after the incomplete and complete lesions is shown in Figure 4. After completed isolation, AF was no longer inducible when burst-pacing was performed from the PVs. AF could be activated only during the burst inside the box, without conduction to the LA or RA. Figure 5 shows a typical example of the AF duration after 1-s burst pacing from the PVs after incomplete and complete isolation of the PVs.

The maximal atrial pace frequency did not significantly change after ablation when pacing was performed outside or inside the box. However, in five dogs an increase of the maximal atrial pace frequency was observed in each case, when pacing was performed inside the box (from 126 ± 8 to 155 ± 16 ms) after incomplete isolation. In four dogs, fast pacing (147 ± 6 ms) after incomplete isolation from the RA showed a 1:1 capture outside the box area, whereas a 1:2 capture rate was observed inside the box. In three dogs, fast pacing (143 ± 15 ms) from inside the incomplete box lesion resulted in 1:1 capture inside the box area whereas the LA and RA outside the box only captured at a 2:1 rate. Figure 5 shows a typical example of the exit and entrance 2:1 conduction block after incomplete isolation.

The AERP from the PV electrode did not change after incomplete isolation (150 ± 10 ms control, and 148 ± 21 ms incomplete box). However, after completed isolation, the AERP inside the box increased significantly to 163 ± 27 ms ($P = 0.048$). The right and left atrial AERP did not change after the ablations (RA: from 144 ± 17 to 142 ± 20 to 141 ± 13 ms and LA: from 148 ± 12 to 147 ± 23 to 152 ± 17 ms after incomplete and completed isolation, respectively).

**Discussion**

**Robot-assisted PV ablation**

Interestingly, isolation of the PV was included in the Cox–Maze procedure from the early beginning, based on experimental and clinical experiences. Only 10 years later, Haissaguerre et al. showed that the PVs are a preferential site for atrial ectopic foci, which can induce and even maintain AF. Since then, most centres have focused on surgical and transcatheter PV isolation as a treatment for AF, often combined with linear lines to the mitral
annulus and the left atrial appendage. To further optimize the treatment, several groups have investigated epicardial beating heart approaches using new energy sources such as cryo-, radiofrequency, and microwave ablation. A number of studies have shown that only a single epicardial ablation lesion encircling the PVs is an effective surgical procedure for cardiac surgery patients with concomitant AF. However, since the procedure is still invasive and is only performed in patients with concomitant AF, the search for a total endoscopic minimally invasive beating heart approach remains ongoing.

Standard, minimally invasive methods using thoracoscopy, are characterized by limited manoeuvrability of the instruments with limited two-dimensional vision. The recent developments in robot-assisted surgery may overcome these drawbacks of endoscopic surgery. In the present study, application of robotic techniques using a single-sided approach to open the pericardial reflections, and for introduction of the catheter around the PVs with correct positioning with respect to the left atrial appendage and the circumflex artery, has been shown to be safe and effective. The small and precise movements of the robotic instruments combined with the three-dimensional vision of the robot camera made it possible to create incomplete and complete box lesions around the PVs.

The left atrial appendage has been shown to be an important potential source of thrombus formation and removal to prevent thrombo-embolic events has been performed in most left atrial surgical lesion sets for AF. Although the robot-assisted video camera could visualize the left atrial appendage for lateral placement of the catheter, exclusion of the appendage was not performed in this study since this remains a technically demanding and risky quest through the transverse sinus. However, since we think that this approach can eventually lead to a generally applicable, minimally invasive, off-pump approach for the treatment of patients with symptomatic lone AF, new tools are currently being designed to exclude the left atrial appendage from the circulation through the transverse sinus, using bending techniques.

Altogether, the technical aspects of the procedure are promising in the development of a valid minimally invasive off-pump approach for the treatment of patients with symptomatic lone AF. However, whether this new robot technology will gain a widespread clinical application will depend on future developments of the procedure including the cost–benefit profile, procedure times, and success of treatment.

Effect of complete and incomplete PV isolation on atrial electrophysiology

Previous studies have extensively indicated the need for complete linear lesions in treating experimental and clinical AF. Shah et al. demonstrated that recurrence of atrial flutter after ablation treatment in patients is associated with an incomplete ablation line. Also in a rapid-pacing canine model for AF, AF persisted in the animals with incomplete linear lesions. The AF data of the current study, derived from pacing inside the PV, show that a completed lesion is needed to completely isolate the AF-inducing foci from the remaining atrial tissue. Also when AF was induced from outside the box, completed isolation decreased the AF duration. This was accompanied by an increase in AFCL, both in the LA and in the RA. This observation has also been shown before in dogs with AF, where the median AFCL increased with the number of linear radiofrequency ablation lesions.

However, a completed lesion has been shown to be difficult to obtain. The present study shows that after a single ablation application, 6 out of 14 lesions were incomplete. Other studies also showed that, particularly, epicardial beating heart ablations often result in incomplete lesions. This indicates that the occurrence of incomplete epicardial isolation of the PVs in patients has to be assumed despite a highly successful AF treatment that is generally reported. Therefore we studied the effect of intentionally incomplete isolations on AF characteristics in an experimental model. Interestingly we found that an incomplete encircling lesion around the PVs already decreases the AF
duration and increases the AFCL. Recently, a clinical study where endocardial isolation of the PVs was performed showed that isolation of all PVs is not necessary for preventing AF recurrence. In this study, only 2 of 41 patients without AF recurrence during follow-up had all the PVs isolated. The authors of this study suggested different hypotheses such as denervation, interruption of re-entry, and damage to the ligament of Marshall or the bundle of Bachmann as an explanation for the clinical success of incomplete isolations. As shown by the incremental pacing data of the current study, a filter function from inside to outside the box and vice versa could be observed in several dogs at fast pacing rates. This finding indicates that conduction delays may be responsible for the prevention of AF by fast triggers, and for excluding the box region from the atria at fast rates but preserving the area for conduction at slow rates. However, since these conduction disturbances were not observed in all lesions, it is likely that other mechanisms such as atrial mass reduction, a strategic lesion shape that interrupts re-entry, elimination of a pro-arrhythmic area, or denervation may also be responsible for the observed effects.

Study limitations

The results in this study were obtained in a canine model with different anatomical properties to humans. This may have implications for the robotic procedure with respect to the larger PV anatomy and the different chest shape of humans. Also, the ablations were studied acutely. There may be acute effects of the ablation that change over time. Therefore, future studies need to be conducted to study the chronic effects of robot-assisted PV ablation on atrial electrophysiology and AF. Furthermore, although not observed in this study, organized atrial arrhythmias induced by incomplete lesions have been reported before, and can be a potential disadvantage of incomplete isolation of the PVs. Lastly, the electrophysiological results were obtained in healthy dog hearts that may not be comparable to human AF. The model we used however, allowed us to study different pacing protocols with short paroxysms of AF as was described earlier and may be partly comparable to paroxysmal focal AF in man.

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