Temperature-Controlled Cooled-Tip Radiofrequency Linear Ablation of the Atria Guided by a Realtime Position Management System

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Summary

Due to the difficulty in producing a transmural linear lesion and the possibility of complications such as thrombus formation leading to thromboembolism, the catheter-based maze procedure remains problematic.

We tested, in pigs, the possibility of using a temperature-controlled cooled-tip radiofrequency (RF) ablation system together with a realtime position management (RPM) system to create a transmural linear lesion uncomplicated by thrombus formation.

Nine pigs underwent insertion of two electrode catheters (each with two ultrasound electrodes), one into the coronary sinus (CS) and one into the right ventricular apex (references for ultrasound-based non-fluoroscopic three-dimensional mapping). A cooled-tip catheter (with two ultrasound electrodes) was introduced into the right atrium. Linear right atrial ablation was performed with a custom radiofrequency (RF) generator. The catheter was perfused with 0.66 mL/second of saline. RF was delivered for 60 seconds at a target temperature of 40°C. A linear ablation line was created between the superior vena cava and inferior vena cava. Three-dimensional isochronal maps were created during CS pacing before and after ablation.

In 4 of the 9 pigs, a transmural linear ablation line was confirmed by three-dimensional mapping and postmortem macroscopic examination. No endocardial thrombus formation was noted.

Temperature-controlled cooled-tip RF linear ablation guided by an RPM system appears to have potential for creating linear lesions in the atria. Further studies are needed to determine whether such an ablation technique and the parameters used will facilitate successful completion of the catheter-based maze procedure. (Int Heart J 2011; 52: 50-55)

Key words: Cooled-tip ablation, Atrium, Three-dimensional mapping, Linear ablation

Pulmonary vein (PV) isolation is an established treatment for paroxysmal atrial fibrillation (AF), and the success rate is relatively high. However, persistent AF often requires atrial linear ablation. Irrigated-tip catheter ablation has been shown to facilitate bidirectional conduction block in the atria. However, there is greater discrepancy between measured electrode tip temperature and actual tissue temperature than with a standard ablation catheter; thus, there is greater potential for excessive but unrecognized heating within the myocardium. This overheating results in the boiling of any water in the tissues and the creation of steam, which erupts through the tissue surface and is heard as a pop. We have shown the feasibility of temperature-controlled cooled-tip radiofrequency (RF) ablation in vivo experiments. However, precise positioning of the ablation catheter by fluoroscopy only is difficult and time consuming, resulting in long fluoroscopy times. RF catheter ablation procedures may be facilitated using additional endocardial mapping techniques; however, current available techniques are limited. Single electrode mapping or the use of multiple catheters is time consuming, and geometric reconstruction is difficult. To circumvent some of these problems, three-dimensional (3D) mapping systems, such as the electroanatomic CARTO system (Biosense-Webster, Tidar Hacarmel, Israel) and EnSite NavX system (St. Jude Medical, St. Paul, MN, USA) have been developed. Although the use of these systems may overcome some of the disadvantages of the other techniques, these 3D mapping systems still have some problems, ie, the catheter position on the CARTO system can become inaccurate due to movement of the position of the patient on the fluoroscopy table. Also, the catheter position on the NavX system is influenced by respiration, body fluid volume, and sweating between the skin and patches. Another system enabling 3D real time, non-fluoroscopic visualization is a newly developed guiding RF ablation system called real-time position management (RMP). The system uses ultrasound ranging techniques to (1) construct a 3D representation of catheters (including electrodes and transducers), anatomic structures, and ablation sites and (2) display real-time movement of the tip and shaft of the catheters. Our next step was to conduct an animal study in which we attempted to create linear atrial le-
sions using a temperature-controlled cooled-tip RF ablation system guided by a three-dimensional RPM system.

**METHODS**

The care of all animals in this study conformed to the Position of the American Heart Association on Research Animal Use and was carried out in accordance with accepted guidelines for the care and treatment of experimental animals at Nihaon University School of Medicine.

**Surgical procedure:** Nine domestic pigs weighing 34.3 ± 4.5 kg were used for acute experiments. The pigs were immobilized with ketamine (15 mg/kg, intramuscular administration) and anesthetized with pentobarbital sodium (25 mg/kg, intravenous administration). Anesthesia was maintained with pentobarbital sodium (100 mg) as needed. Each pig was intubated and placed on a volume controlled animal ventilator (Model 613, Harvard Apparatus, South Natick, MA, USA). Intravenous Ringer’s solution was infused as needed to replace lost fluid. Surgical cut-down was performed in the right and left neck areas and of the right and left femoral veins to isolate the right external jugular vein, left external jugular vein, right femoral vein, and left femoral vein, and a 7-French introducer was positioned in each vein.

**Reference and ablation catheters:** Two reference catheters and one mapping/ablation catheter were introduced by either a femoral or grade 3, ie, not continuous (Figure 4); grade 2, ie, endocardial lesion that was continuous but not transmural in at least one section (Figure 3); grade 1, ie, continuous and transmural (Figure 2); grade 2, ie, endocardial lesion that was continuous but not transmural in at least one section (Figure 3); or grade 3, ie, not continuous (Figure 4).

**Histological analysis:** Animals were killed 1 hour after the last RF ablation. RF energy was delivered as an unmodulated RF current of 500 kHz between the tip of the catheter and a skin patch placed under the skin on the animal’s back. Positioning of the ablation catheter was guided non-fluoroscopically by the RPM system. Details of the RPM were reported previously.[10,11] Each RF application site was tagged with a white spot and numbered. Linear ablation was performed between the superior vena cava (SVC) and the inferior vena cava (IVC). Three-dimensional isochronal maps were created before and after ablation during CS ostium pacing at a pacing cycle length of 400 ms.

**Cooled RF ablation system:** The internally cooled ablation catheter was constructed with a pair of inner lumens through which room-temperature saline could be circulated under constant pressure by a motor-driven injector pump at a steady flow of 0.66 mL/minute to cool the catheter tip throughout the delivery of RF current (Figure 1). A custom RF generator was used, which was capable of automatically controlling the catheter-tip temperature at a preset level ≥ 30°C during a slow increase in power (maximum power = 70 W; average time to reach the preselected temperature = 40 seconds, Japan Lifeline Co./Central Kogyo Co., Tokyo).[9] Temperature-controlled cooled-tip RF applications at a target temperature of 40°C were performed for 60 seconds each. RF ablation was repeated at the same site if the local bipolar electrogram amplitude decrease was less than 50% of control.[9]

**Postmortem examination:** Animals were killed under deep anesthesia by injection of saturated potassium chloride. Afterward, the heart was excised, and the ventricle was dissected away at the level of the atrioventricular valves. The epicardial and endocardial aspects of the right atrium were inspected for gross evidence of lesion formation, eschar/char formation, and/or perforation. Lesions were classified as grade 1, ie, continuous and transmural (Figure 2); grade 2, ie, endocardial lesion that was continuous but not transmural in at least one section (Figure 3); or grade 3, ie, not continuous (Figure 4).

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**Cooled RF abl...
ablation. Tissue sections from grossly detectable lesions were fixed in 10% formalin, dehydrated, embedded in paraffin, sectioned at 5-μm thickness, and stained with hematoxylin and eosin.

Figure 3. Hematoxylin-eosin stain of lesion shown in Figure 2 demonstrates transmural lesion formation (hyperemic staining shown by the arrows). Upper side = endocardium.

Figure 4. Endocardial (right panel) and epicardial (left panel) views of a lesion created between the superior vena cava (SVC) and inferior vena cava (IVC) with the cooled-tip radiofrequency (RF) ablation system. Note the continuous lesion with char formation on the endocardial surface. Note also a gap between lesions on the epicardial site (arrows).

Figure 5. Hematoxylin-eosin stain of lesion shown in Figure 4 demonstrates nontransmural lesion formation (hyperemic staining shown by the arrows and island of viable myocardium in the epicardial site shown by the white arrow). Upper side = endocardium.

Results

Lesion configuration: Upon examination, we found that a grade 1 lesion had been created in 4 of the 9 pigs, a grade 2 lesion had been created in two of the 9 pigs, and a grade 3 lesion had been created in 3 of the 9 pigs. There was no obvious thrombus formation in any animal, but some char formation was noted in all pigs. In two of the 9 pigs, an ablated lesion was also noted in the pericardium.

Activation map: Activation sequences were examined on right atrial activation maps obtained before and after SVC-IVC linear ablation during CS ostium pacing at a pacing cycle length of 400 ms. In the 4 pigs with a grade 1 lesion, there was an apparent change in the activation sequence, ie, the SVC was the site of latest activation before ablation, but the low lateral right atrium was the site of latest activation after ablation (Figure 5). In the two pigs with a grade 2 lesion, there was no apparent change in the activation sequence after ablation, but activation time increased (Figure 6). In the 3 pigs with a grade 3 lesion, there was no apparent change in the activation sequence or activation time (Figure 7).

Figure 6. Endocardial (right panel) and epicardial (left panel) views of a lesion created between the superior vena cava (SVC) and inferior vena cava (IVC) with the cooled-tip radiofrequency (RF) ablation system. There are two apparent gaps between the lesions on the endocardial surface (arrows) and also two apparent gaps between the lesions on the epicardial site (arrows). Note that in this experiment, a linear lesion was created on the free wall side of the right atrium; thus, pectinate muscles cross the lesion.

Figure 7. Hematoxylin-eosin stain of lesion shown in Figure 6 demonstrates viable myocytes present transmurally (between the arrows) bridging the transmural lesions (hyperemic staining). Lower side = endocardium.
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TEMPERATURE-CONTROLLED COOLED-TIP LINEAR ABLATION

In 1959, Moe and Abildskov hypothesized that AF is due to multiple randomly propagating reentry waves in the atrium, suggesting that functional reentry is the mechanism underlying fibrillation. Subsequent work by Wijffels, et al confirmed this hypothesis, ie, AF was shown to require at least 6 to 8 circulating reentrant wavefronts. Maintenance of AF depends on a critical atrial mass and on conduction velocity and refractory periods in the atrial tissue to support functional reentry. Twenty years after publication of the Moe and Abildskov hypothesis, Cox, et al began a series of revolutionary clinical experiments aimed at curing AF surgically. The Cox-Maze III procedure, which incorporates 4 lesion sets and involves; (1) encirclement of the PVs; (2) a lesion joining the circumferential PV lesion to the mitral annulus with amputation of the left atrial appendage; (3) a circumferential lesion in the CS; and (4) ablation of the right atrium, is probably the most widely performed curative surgical intervention for AF. While the long-term success rate is good, 80%-99% with the use of antiarrhythmic drugs, these sur-

**Figure 8a.** Isochronal map of the right atrium created by the real-time management system in the experiment shown in Figure 2. The latest activation during coronary sinus ostium pacing was located in the superior vena cava before ablation (left panel) but shifted to the right atrial posterolateral wall (right panel) after ablation. Right atrial activation time also increased from 42 ms to 60 ms.

**Figure 8b.** Ablation points shown in Figure 8a. The total number of ablation points shown as white dots was 16. Points encircled by a red square represent anatomical landmarks.

**Figure 9a.** Isochronal map of the right atrium created by the real-time management system in the experiment shown in Figure 3. The latest activation during coronary sinus ostium pacing was located in the superior vena cava before ablation (left panel) and at a similar position (right panel) after ablation. Right atrial activation time increased from 76 ms to 86 ms.

**Figure 9b.** Ablation points shown in Figure 9a. The total number of ablation points shown as white dots was 31. Points encircled by a red square represent anatomical landmarks.
catheter ablation approaches based on the early surgical approaches were attempted by a number of groups, the overall success rate was disappointing, with an unacceptably high complication rate.\textsuperscript{16,17} The observation that AF could be triggered from ectopic beats originating from the PVs, with ablation at the source of the ectopy eliminating AF, changed the emphasis of catheter ablation away from linear lesions compartmentalizing the area to treating atrial sources, and then to isolating the PVs.\textsuperscript{1,2,18} However, left mitral isthmus ablation, left atrial roof linear ablation, and linear catheter ablation to transect the anterior left atrium were shown to be necessary to maintain sinus rhythm particularly in patients with persistent AF.\textsuperscript{19-21} Furthermore, in patients with persistent and permanent AF, circumferential PV ablation, combined with linear lesions in the right atrium in addition to left atrial and CS ablation, is reported to be feasible and safe, with a significantly high success rate.\textsuperscript{22,23} However, creating transmural linear lesions with a multipolar ablation system or by the pull-back approach is difficult. Success rates of 45% and 37%, respectively, are reported.\textsuperscript{24} Schwartzman, \textit{et al} compared formation of linear lesions in the right and left atria with the use of an irrigated electrode and with the use of the same electrode but without irrigation. They showed that lesions produced by ablation using an irrigated electrode and guided by electrogram amplitude reduction formed complete conduction barriers and were uncomplicated. In contrast, lesions produced by nonirrigated ablation and energy titration guided by electrode thermometry formed complete conduction barriers but were frequently complicated by endocardial charring, barotrauma, and pericardial damage. During healing, 90% of lesions remained complete conduction barriers, and 10% manifested single discrete conduction gaps where variable appearing myocytes bridge the lesion.\textsuperscript{25} Only 44% (4/9) of our animals showed complete conduction block, and 56% (5/9) showed conduction gap. The discrepancy in the incidence of complete conduction block between the Schwartzman, \textit{et al} study and ours might be due to the ablation endpoints: Schwartzman, \textit{et al} used > 90% reduction in the amplitude of local electrograms, and we used the temperature-controlled mode at a fixed RF delivery time, and > 50% reduction in amplitude of local bipolar electrograms. Yokoyama, \textit{et al} reported that tissue temperature at 3 mm and 7 mm depth during irrigated-tip RF ablation could not be predicted from power and peak electrode temperature in an open-irrigated ablation catheter, but contact force was a major determinant of RF lesion size, and that contact force in an open-irrigated ablation catheter may optimize the selection of RF power and application time to maximize lesion formation and reduce the risk of steam pop and thrombus.\textsuperscript{26} Thus, in closed-loop, cooled-tip temperature-controlled ablation, contact force measurement may also facilitate transmural linear lesion formation without increasing complications. The RPM system guided RF ablation cooled-tip, closed system catheter has been reported to be clinically useful for typical and typical atrial flutter, atrionodal reen-
trant tachycardia, AF, atrial tachycardia, ventricular tachycardia, and WPW syndrome. The RPM system has advantages over CARTO or NavX system regarding stable catheter position that is minimally influenced by body, cardiac, respiratory movement, and sweating, and also no need for skin electrodes or patches. However, one major disadvantage is that the RPM system requires a special catheter, i.e., an ablation catheter and two reference catheters equipped with ultrasound transducers which limited steerability of the mapping/ablation catheter, and dislocation of the reference catheters due to roving catheter manipulation.

**Study limitations:** Our study was limited in several ways. First, we did not compare irrigated and nonirrigated lesions. Second, lesions were produced only in the right atrium. We cannot be certain that these lesions can be replicated in the left atrium. Third, we did not assess the lesions electrophysiologically and histologically.

**Conclusion:** Temperature-controlled cooled-tip RF linear ablation guided by an RPM system looks promising for creating linear lesions in the atria. Further studies are needed to determine whether this type of ablation technique and the parameters we followed during ablation will facilitate a successful catheter-based maze procedure.

**References**