**Background:** Prompt diagnosis and management of atrial tachyarrhythmias (ATAs) during catheter ablation of atrial fibrillation (AF) is still challenging.

**Methods and Results:** In 88 patients undergoing catheter ablation of AF, 128 regular ATAs were induced or converted from AF. The coronary sinus activation time (CSAT) around the mitral annulus (MA) was measured as the difference in activation time between the most proximal and distal poles of the coronary sinus (CS) electrodes. Entrainment pacing was performed around the MA, roof area, or cavotricuspid isthmus (CTI) depending on the CSAT result. Mechanisms of tachycardias included macro-reentry around the MA (perimitral atrial flutter [PM-AFL], n=63), roof-dependent AFL (Roof-AFL, n=14), CTI-dependent AFL (CTI-AFL, n=25), and atrial tachycardia (AT, n=26). When the CSAT was ≥45 ms, the MA activation sequence was sequential, either proximal to distal or distal to proximal. When the CSAT was <45 ms, the MA activation sequence was mainly non-sequential with converging or diverging patterns. CSAT <45 ms was highly sensitive in ruling out PM-AFL from other left ATAs. When combined with PPI data from the MA, roof area or CTI, PM-, Roof-, CTI-AFL and AT was successfully differentiated with a high predictive accuracy.

**Conclusions:** A diagnostic algorithm combining CSAT and entrainment pacing is helpful to assess the mechanism of ATAs during catheter ablation of AF.  

**Key Words:** Atrial fibrillation; Atrial tachycardia; Catheter ablation

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Regular atrial tachyarrhythmias (ATAs) can occur after pulmonary vein isolation (PVI) for atrial fibrillation (AF), and they seem to be more common after anatomically wide area circumferential PVI.1-6 In the differential diagnosis of these ATAs, surface ECGs are not always accurate in predicting the site of origin and mechanisms, and may even be misleading.7,8 Entrainment mapping is useful for localization of ATA sites, but repeat attempts to entrain tachycardia can terminate or transform it to a different tachycardia or AF, and an activation mapping procedure may be time consuming. Therefore fewer entrainment pacing to differentiate organized ATAs would be helpful.9,10 We hypothesized that conduction around the perimitral (PM) annulus would occur sequentially in PM or right atrial (RA) flutter, whereas the conduction time during other types of left atrial flutter (AFL) would be more abbreviated. Previous investigations reported that the mean RA free wall conduction velocity was 88±9 cm/s, and that the PM conduction time was within 30 ms longer than the peritricuspid time.11-13 Our preliminary study for left ATAs showed a coronary sinus activation time (CSAT) >45 ms was the best cut-off value for PM isthmus-dependent AFL from other left ATAs (Figure 1). Based on this observation, we developed a diagnostic algorithm using CSAT and selected entrainment pacing for differential diagnosis of organized ATAs.
Circulation Journal Vol.77, March 2013

Definitions

Macro-reentrant atrial tachycardia (AT) was defined as a regular AT with matching postspacing interval (PPI) (PPI-tachycardia cycle length (TCL) ≤30 ms) in at least 2 different atrial segments. Focal AT was confirmed using the following criteria: (1) failure to meet the entrainment result in ≥2 other atrial regions, (2) centrifugal propagation of activation, and (3) termination by focal ablation. However, the term “focal” did not differentiate between true focal automatic tachycardia and focal micro-reentry.

Methods

Study Population

We prospectively analyzed patients who had regular, sustained ATAs during catheter ablation of AF. Among a total of 380 AF patients, 128 regular ATAs were induced by pacing or converted from AF in 88 patients (1 ATA in 59 patients, 2 ATAs in 21 patients, 3 ATAs in 5 patients, and 4 ATAs in 3 patients). Baseline characteristics of the study patients are listed in Table 1. The mean age of the 88 patients was 55±10 years, and 60 (68%) were men. Forms of arrhythmias included paroxysmal AF in 58 patients (66%), persistent AF in 22 (25%), and AFL after previous AF ablation in 8 (9%). In total, 6 patients (7%) had undergone valve operations, 4 (5%) had undergone Maze procedures (3 paroxysmal and 1 persistent AF), and 18 (20%) had undergone prior catheter ablation, including 16 who underwent AF ablation and 2 who underwent atypical AFL ablation related to prior valve surgery. These 88 patients had a mean left ventricular ejection fraction of 57±9%, and a mean left atrial (LA) diameter in the parasternal window of 43±6 mm.

The study protocol was reviewed and approved by the Institutional Committee on Human Research at Asan Medical Center and each patient provided written informed consent.

Catheter Ablation of AF

Briefly, after discontinuation of all antiarrhythmic agents for at least 5 half-lives, an electrophysiological study was performed in the fasting state, typically under sedation with a continuous infusion of propofol (200–600 mg/h). Patients taking amiodarone were instructed to discontinue medication 1 month prior to the procedure. A 6F quadrupolar and a 7F decapolar catheter (St. Jude Medical Inc [St. Paul, MN, USA], inter-electrode distance, 2–8–2–8 mm) were introduced percutaneously through the femoral veins and placed in the His-bundle and CS/high RA regions, respectively. Two 8F sheaths (SL1, St. Jude Medical Inc) were introduced into the LA using a modified Brockenbrough technique. After trans-septal puncture, intravenous heparin was injected as a bolus (80 IU/kg) and intermittently (1,000–2,000 IU/h) to maintain an activated clotting time >300 s. In addition, heparinized saline was continuously infused through the trans-septal sheath (3 ml/min) to avoid formation of thrombi and air emboli. The infusion rate was increased to 17 ml/min (≤30 W) or 30 ml/min (>30 W) during radiofrequency (RF) application. Multiple ECG leads (leads I, aVF and V1, filtered between 0.05 and 100 Hz) and intracardiac bipolar electrograms (filtered between 30 and 500 Hz) were simultaneously displayed and recorded on a digital electrophysiological recording system (CardioLab®, Prucka Eng., Houston, TX, USA). The stimuli were delivered using a programmable digital stimulator (DTU-215, Bloom & Associates, Reading, PA, USA) at twice the diastolic threshold and with a 2-ms pulse width for conventional pacing, and at 10–20 mA for high output pacing. Three-dimensional mapping systems (Carto, Biosense-Webster Inc, Diamond Bar, CA, USA or NavX, ver 6.0 or 7.0, St Jude Medical Inc) were used for all ablations. PVI was performed 5–10 mm outside the PV ostia, with isolation of 2 ipsilateral veins in 1 circumferential lesion. Ablation in the LA was performed using an irrigated catheter with a target temperature of 43°C, a maximal power of 30 W, and an infusion rate of 17 ml/min. Power was temporarily increased to 35 W in the anterior circumference resistant to RF application. The endpoint of the PVI was elimination or dissociation of the PV potentials. An ostial or carinal touch-up

Table 1. Baseline Characteristics of the Patients

<table>
<thead>
<tr>
<th>Patients (n=88)</th>
<th>Age (years)</th>
<th>Male sex (%)</th>
<th>Form of arrhythmia</th>
<th>LVEF (%)</th>
<th>Left atrial diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>55±10</td>
<td>60 (68)</td>
<td>Paroxysmal AF (%)</td>
<td>57±9</td>
<td>43±6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Persistent AF (%)</td>
<td></td>
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<td></td>
<td>AFL (%)</td>
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<td></td>
<td>Heart failure (%)</td>
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<td></td>
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<td></td>
<td>Prior valve operation (%)</td>
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<td></td>
<td>Prior Maze operation (%)</td>
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<td></td>
<td></td>
<td></td>
<td>Prior catheter ablation (%)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Prior ablation of AF (%)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Prior ablation of AFL (%)</td>
<td>2 (2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Diastolic arrest time (ms)</td>
<td>45±10</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Coronary sinus activation time (ms)</td>
<td>60±10</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Left atrial diameter (mm)</td>
<td>43±6</td>
<td></td>
</tr>
</tbody>
</table>

AF, atrial fibrillation; AFL, atrial flutter; LVEF, left ventricular ejection fraction.
Coronary Sinus Activation in ATA

was additionally performed if PV potential remained after PVI without an obvious gap along the line. Ablation at the PV ostia and within the CS was performed at 15–25W and 43°C. Energy was applied for 40–60s at each point until the loss of antral potential or the sharp component of the bipolar electrogram. After PVI, induction of ATA was routinely performed at baseline and during isoproterenol infusion (up to 20 μg/min), and non-PV triggers of AF were targeted for ablation. When the ATA was successfully terminated by RF and bidirectional block was confirmed, induction of the ATA was repeated until regular ATAs were no longer induced.

Management of Regular ATAs During Catheter Ablation of AF

If a regular ATA was induced or converted during catheter ablation of AF, CSAT was measured and selected entrainment pacing depending on the CSAT result were performed to identify the mechanism and location of the tachycardia. CSAT around the mitral annulus (MA) was measured as the difference in activation time between the earliest atrial potential at the most proximal (CS 9, 10) and distal (CS 1, 2) poles of the CS electrodes (St. Jude Medical Inc, inter-electrode distance, 2–8–2–8 mm). A train of atrial stimuli at a CL 10–30 ms shorter than the TCL was applied for a sufficient duration to accelerate all recorded electrograms to the pacing CL. PPI was measured from the last stimulus to the first peak of the next electrogram recorded from the pacing site. The difference between the PPI and TCL was calculated at each site, and sites at which the PPI was within 30 ms of the TCL were considered to be within the reentry circuit. Activation sequence mapping was aided by an electroanatomic mapping system to help determine whether the circuit was focal or macro-reentrant. The location of the ATA was further supported by successful ablation, defined as the termination and suppression of re-initiation by ablation. Catheter ablation was performed in a linear fashion from a site within the reentry circuit to an anatomical barrier or an area with the conduction block. If the entrainment mapping results were not compatible with the reentrant AFL
Table 2. Relationship Between Predicted Site of Atrial Tachyarrhythmia and Actual Site Based on Ablation Site

<table>
<thead>
<tr>
<th>Actual site (n=128)</th>
<th>CSAT (ms)</th>
<th>PPI-TCL (ms)</th>
<th>Predicted site</th>
<th>SN (%)</th>
<th>SP (%)</th>
<th>PV (%)</th>
<th>NV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM (n=63)</td>
<td>55±11</td>
<td>8±11</td>
<td>59 2 0 2</td>
<td>94</td>
<td>95</td>
<td>95</td>
<td>94</td>
</tr>
<tr>
<td>Roof (n=14)</td>
<td>29±14</td>
<td>14±11</td>
<td>1 13 0 0</td>
<td>93</td>
<td>96</td>
<td>72</td>
<td>99</td>
</tr>
<tr>
<td>CTI (n=25)</td>
<td>46±15</td>
<td>8±9</td>
<td>0 0 25 0</td>
<td>100</td>
<td>99</td>
<td>96</td>
<td>100</td>
</tr>
<tr>
<td>AT (n=26)</td>
<td>31±15</td>
<td>60±46</td>
<td>2 3 1 20</td>
<td>77</td>
<td>98</td>
<td>91</td>
<td>94</td>
</tr>
</tbody>
</table>

AT, atrial tachycardia; CSAT, coronary sinus activation time; CTI, cavotricuspid isthmus; NV, negative predictive value; PM, perimital; PPI, postspacing interval; PV, positive predictive value; SN, sensitivity; SP, specificity; TCL, tachycardia cycle length.

and the activation sequence showed a centrifugal propagation, we performed focal ablation targeting the earliest activation. Conduction block across a line was confirmed by conventional methods.

Statistical Analysis
Continuous variables are expressed as mean±SD, and categorical variables as numbers and percentages. Statistical analysis was performed using SPSS 12.0 software (SPSS Inc, Chicago, IL, USA).

Results

Differentiation of ATA
Using CSAT and entrainment pacing, regular ATAs were differentiated as shown in Figure 2. The first site of entrainment pacing was determined by the CSAT result. Mean values of CSAT of each ATA are shown in Figure 3. If the MA activation was sequential either proximal to distal or distal to proximal with CSAT ≥45 ms, a short (≤30 ms) PPI-TCL difference at the PM area was indicative of PM-AFL. If CSAT was <45 ms or MA activation was non-sequential with converging or diverging patterns, a short PPI-TCL difference at the roof or posterior LA wall suggested Roof-AFL. When PPI from these areas did not match the TCL, a short PPI-TCL at the CTI indicated CTI-dependent AFL (CTI-AFL). If entrainment pacing from all of these areas did not match the TCL, a focal mechanism of tachycardia was suggested. After reaching a diagnosis of tachycardia according to the algorithm, we continued with additional entrainment pacing to verify the diagnosis. For example, with PM-AFL, additional pacing was performed at another site around the MA, and with Roof-AFL, additional pacing at the anterior, posterior or roof was added.

Mechanism of Regular ATAs
We assessed a total of 128 regular ATAs induced or converted from AF during catheter ablation in 88 patients. The mechanism of the tachycardias was PM-AFL (n=63), Roof-AFL (n=14), CTI-AFL (n=25), and AT (micro-reentry or focal, n=26) (Table 2). The mean CSAT was significantly longer in patients with PM-AFL or CTI-AFL compared with Roof-AFL or AT (Figure 3). CSAT <45 ms was highly sensitive (CSAT in 61/63 patients with PM-AFL was >45 ms) for excluding PM-AFL in the early stage of differential diagnosis, with high sensitivity (92%) and specificity (69%). Using this diagnostic algorithm, we successfully diagnosed 91% (117/128) of regular ATAs during catheter ablation of AF, including PM-AFL (59/63, sensitivity 94%, specificity 95%), Roof-AFL (13/14, sensitivity 93%, specificity 96%), CTI-AFL (25/25, sensitivity 100%, specificity 99%), and AT (20/26, sensitivity 77%, specificity 98%), respectively. Each representative case is shown in Figure 4.

Analysis of Misclassified ATAs
The described method failed to predict the tachycardia mechanism in 11 of 128 ATAs, including 4 PM-AFLs, 1 Roof-AFL, and 6 ATs (Table 3). Two PM-AFLs were classified as Roof-AFLs because of the short CSAT (<45 ms), and were correctly diagnosed after entrainment pacing at other regions and by the 3D activation map. In 2 cases, PM-AFL was classified as AT because of long PPIs in the PM area even though the CSAT was >45 ms. These long PPIs around the lateral MA presumably resulted from slow conduction created by RF lesions between the left PVs and MA during antral isolation. In 1 case, Roof-AFL was misclassified as a PM-AFL, because the CSAT was >45 ms and tachycardia was entrained in the lateral PM area. In this case, the reentry loop was around the lateral PV, matching the PPI at the lateral MA. In 6 cases, AT was misclassified: 2 as PM-AFL, 3 as Roof-AFL, and 1 as CTI-AFL. The actual AT sites were the anterior region of the left superior PV (1 PM-AFL and 3 Roof-AFL), the anterior LA free wall (1 PM-AFL), and the CS ostium area (1 CTI-AFL). These ATs were entrained with matching PPI near the target area close to the AT foci.

Results of Catheter Ablation of ATAs
Results of catheter ablation of ATAs are shown in Table 3. Catheter ablation was successful in 104/128 (81%) cases. For ATAs in which the mechanism was correctly predicted (n=117), successful ablation was performed in 45/59 (76%) PM-AFL, 9/13 (69%) Roof-AFL, 25/25 (100%) CTI-AFL, and 18/20 (90%) ATs. Bidirectional block could not be achieved by linear ablation in 14 PM-AFL and 4 Roof-AFL. Because of prolonged procedure time and concern over complications, we failed to terminate 2 cases of AT. For ATA that we failed to predict the mechanism (n=11), successful ablation was possible in 3/4 (75%) PM-AFL, 0/1 (0%) Roof-AFL, and 4/6 (67%) AT. In 2 cases (1 PM- and 1 Roof-AFL), the ATA remained inducible because of an incomplete line; 2 cases of AT (1 originating from the region anterior to the left superior PV and 1 from the CS ostium) persisted after focal ablation.

Discussion
The main findings of this study were: (1) a short CSAT is an important indicator for ruling out PM-AFL and differentiating it from AFL arising from other mechanisms, and (2) when combined with PPI data, we successfully differentiated PM-, Roof-, and CTI-AFL and AT with high predictive accuracy. One of the most difficult aspects of the AF ablation proce-
Figure 4. Representative cases of the differential diagnosis of each atrial tachyarrhythmia using the algorithm. (A) PM-AFL. Entrainment was performed at the 3 o’clock position of the mitral annulus. The CSAT was 67 ms, and the difference between PPI (238 ms) and TCL (223 ms) was 15 ms. (B) Roof-dependent AFL. The CSAT was 32 ms. After entrainment pacing at the roof of the left atrium, the PPI was 242 ms and the TCL was 243 ms (ΔPPI-TCL=−1 ms). Electroanatomic activation mapping was consistent with reentry around the pulmonary veins. (C) CTI-dependent AFL. After entrainment at the CTI, the PPI was 222 ms and the TCL was 215 ms (ΔPPI-TCL=−7 ms). (D) AT. Entrainment pacing at the posterior left atrial wall (ΔPPI-TCL=−50 ms) and CTI, the PPI was 304 ms and the TCL was 254 ms (ΔPPI-TCL=−50 ms). Electroanatomic activation mapping was consistent with AT in the left inferior pulmonary vein ostium area, which was propagated in different directions throughout the left atrium in the left antero-oblique view of the 3D map. Shown from top to bottom are surface ECG leads II, III, aVF, and V1, ablation proximal (ABL p), ablation distal (ABL d), and CS (CS 9, 10: proximal, 1, 2: distal). AFL, atrial flutter; AT, atrial tachycardia; CS, coronary sinus; CSAT, coronary sinus activation time; CTI, cavotricuspid isthmus; PM, perimitral; PPI, postpacing interval; TCL, tachycardia cycle length.
The development of regular ATAs after linear LA lesions, because of either PV reconnection or to macro-reentry around the isolated PV antral area as the central or lateral border. Addition of linear lesions further increases the incidence of macro-reentrant ATAs because of either re-conduction or failure to achieve block during the initial procedure. These ATAs have been reported in 2.6–31% of patients and may be problematic because they are often incessant and can lead to a rapid ventricular response. Symptoms may be worse than those from AF prior to ablation.

The mean RA free wall conduction velocity has been reported to be 88±9 cm/s, independent of propagation direction at the epicardial RA free wall in sinus rhythm, and the PM conduction time is within 30 ms longer than the peritricuspid conduction time. These circuit velocities are highly variable among patients and are influenced by other factors, such as atrial dimension, injury to atrial tissue, presence of a low-voltage scar zone, myocardiab fibration orientation, number of depolarizing cells, and the expression and distribution of connexin.

Our preliminary study in patients with left ATAs (40 patients, 56 ATAs: 27 PM-, 8 roof-, 9 CTI-dependent AFL, and 12 AT) showed that a CSAT >45 ms was the most valuable cut-off for sinus and LA conduction delays. Even considering these variables, CSAT of 45 ms is a good initial indicator for differential diagnosis of AFL or could reduce the number of pacing sites for differentiating RA or LA origin, if CTI was not entrained for macro-reentrant AT. Miyazaki et al suggested entrainment mapping to predict the location of macro-reentrant AT. These algorithms use multiple entrainment pacing and provide approximate information on the specific mechanisms for left ATAs. Jais et al suggested a deductive mapping strategy that compares local activation time and entrainment pacing at suspected sites. This stepwise approach provides the arrhythmia mechanism by eliminating the more readily identifiable and prevalent causes first, but it requires experience and adroitness.

The aim of this algorithm is to rapidly diagnose the mechanism of the tachycardia. By measuring the CSAT, the number of pacing sites for entrainment pacing can be minimized or entrainment pacing can be performed at more selected sites relevant to the ATA. We could differentiate PM- or Roof-AFL with 1 step, and CTI-AFL or focal AT with 2 steps, although determination of the focus of focal AT required measurement of local activation time and entrainment pacing at suspected sites.

**Study Limitations**

First, the number of tachyarrhythmias analyzed in this study was relatively small. Second, we measured the CSAT around the MA using the CS electrodes. The activation sequence and PM conduction duration may depend on other factors, such as CS catheter positioning, electrode number, size and spacing, the anatomic relationship of MA to the CS, and intracoronary sinus and LA conduction delays. Even considering these variables, CSAT of 45 ms is a good initial indicator for differentiating PM-AFL from other ATAs, and each ATA could potentially be differentiated with less entrainment pacing. We did not directly compare the number of entrainment pacings with the effectiveness of our algorithm, and further prospective study of whether our method could reduce the time for differential diagnosis of AFL or could reduce the number of entrainment pacings is required.

**Conclusions**

An approach combining CSAT and entrainment pacing is helpful for rapidly assessing the mechanism of ATAs during catheter ablation of AFL. This algorithm may be used in conjunction with other maneuvers to facilitate mapping and ablation of ATAs.
Acknowledgments
We thank Jin Young Jung, Sung Ho Moon, Jong Pil Yun, and Doo Young Han for their technical assistance, and Jung Rae Kwon, Ji Hae Yun, Ji Hyun Kim, Soon Hee Kim, Han Na Kim, and Keun Hae Lee, RN for their help preparing this manuscript. We also thank Dongseum Kim of Dalhousie University, Halifax Canada for his contribution to the interpretation of electrocardiograms.

Disclosures
This study was supported by grants from the Korea Healthcare Technology R&D Project, Ministry of Health & Welfare, Republic of Korea (A100697), from the Asan Institute for Life Science (2012-232), and from Asan R&D Project, Ministry of Health & Welfare, Republic of Korea (A100607). This study was supported by the Korea Healthcare Technology Research and Development Program through the Agency for Healthcare Research and Development, Ministry of Health & Welfare, Republic of Korea (A100607). We thank Jin Young Jung, Sung Ho Moon, Jong Pil Yun, and Doo Young Han for their technical assistance, and Jung Rae Kwon, Ji Hae Yun, Ji Hyun Kim, Soon Hee Kim, Han Na Kim, and Keun Hae Lee, RN for their help preparing this manuscript. We also thank Dongseum Kim of Dalhousie University, Halifax Canada for his contribution to the interpretation of electrocardiograms.