Overdrive Pacing From Downstream Sites on Multielectrode Catheters to Rapidly Detect Fusion and to Diagnose Macroequontent Atrial Arrhythmias

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Background—Entrainment criteria for macroreentrant arrhythmias are based on detecting fusion between tachycardia and paced wavefronts, but this is often difficult for atrial tachycardias (AT) after ablation of atrial fibrillation.

Methods and Results—With the use of a multipolar catheter, pacing was performed from electrodes within the coronary sinus showing activation later than adjacent electrodes (downstream overdrive pacing) during 66 ATs in 62 patients: 20 cavotricuspid isthmus–dependent ATs, 20 perimitral ATs, 13 focal ATs with sequential coronary sinus activation, and 13 other macroreentrant left atrial ATs. The paced cycle length was 10 to 30 milliseconds below the tachycardia cycle length (TCL), and activation at the neighboring upstream electrodes was assessed. Downstream overdrive pacing at 48 sites close to a macroreentrant circuit (PPI−TCL <40 milliseconds, where PPI is postspacing interval) produced constant fusion demonstrated by a long stimulus to upstream atrial electrogram interval (S-Au) >75% TCL and was consistent with orthodromic activation of the upstream site despite its close proximity to the pacing site. In contrast, downstream overdrive pacing at 18 sites during focal AT or remote from the macroreentrant AT circuit (PPI−TCL >40 milliseconds) always demonstrated a comparatively short S-Au <25% of TCL (12±4% versus 89±4% of TCL; P<0.001), consistent with direct activation.

Conclusions—Selection of a downstream activation site for overdrive pacing can facilitate rapid recognition of macroreentry and proximity to the reentry circuit using a single multielectrode catheter by recognizing a PPI–TCL <40 milliseconds and S-Au >75% of TCL. Recognition of intracardiac constant fusion by this method is a novel criterion for transient entrainment. (Circulation. 2014;129:2503-2510.)

Key Words: arrhythmias, cardiac ➤ atrial fibrillation ➤ atrial flutter ➤ catheter ablation ➤ electrophysiology

Organized atrial tachycardias (AT) are a common occurrence after catheter ablation of atrial fibrillation (AF), especially wide antral pulmonary vein isolation or linear lesion sets.1–4 These ATs can be either macroreentrant related to gaps in ablation lines or focal-origin ATs with sequential coronary sinus activation, and 13 other macroreentrant left atrial ATs. The paced cycle length was 10 to 30 milliseconds below the tachycardia cycle length (TCL), and activation at the neighboring upstream electrodes was assessed. Downstream overdrive pacing at 48 sites close to a macroreentrant circuit (PPI−TCL <40 milliseconds, where PPI is postspacing interval) produced constant fusion demonstrated by a long stimulus to upstream atrial electrogram interval (S-Au) >75% TCL and was consistent with orthodromic activation of the upstream site despite its close proximity to the pacing site. In contrast, downstream overdrive pacing at 18 sites during focal AT or remote from the macroreentrant AT circuit (PPI−TCL >40 milliseconds) always demonstrated a comparatively short S-Au <25% of TCL (12±4% versus 89±4% of TCL; P<0.001), consistent with direct activation.

Conclusions—Selection of a downstream activation site for overdrive pacing can facilitate rapid recognition of macroreentry and proximity to the reentry circuit using a single multielectrode catheter by recognizing a PPI–TCL <40 milliseconds and S-Au >75% of TCL. Recognition of intracardiac constant fusion by this method is a novel criterion for transient entrainment. (Circulation. 2014;129:2503-2510.)

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Clinical Perspective on p 2510

It would be useful to have a pacing technique that establishes the presence of fusion at a constant paced cycle length (PCL) minimally shorter than the tachycardia cycle length (TCL). We hypothesized that overdrive pacing of AT from a multielectrode catheter at a site of activation downstream from neighboring electrodes would establish the presence of constant fusion after a single pacing train at a cycle length just shorter than the TCL. Specifically, when pacing is performed during macroreentrant AT from a site that demonstrates later activation relative to its neighbors, electrograms at the earlier

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“upstream” sites will continue to show evidence of orthodromic activation (Figure 1). We hypothesized that constant fusion would be verified by measuring a time between the pacing stimulus and the last upstream atrial electrogram accelerated to the PCL (S–Au time) that approximates the TCL as a result of continued orthodromic activation of the upstream site through most of the reentry circuit. We reasoned that the long conduction time over a relatively short distance should be present only during macroreentrant AT, unless a line of block or very slow conduction existed between the upstream and downstream electrodes. In contrast, overdrive pacing during focal tachycardia should demonstrate a short conduction time between the pacing stimulus and last upstream electrode site accelerated to the PCL because local activation does not reach equilibrium with a separate wave front. Likewise, overdrive pacing at sites remote from a macroreentrant wavefront would produce a short conduction time to upstream sites because all local sites would be activated directly, or antidromically, from the paced wave front. During overdrive pacing in patients with focal AT or at sites remote from the macroreentry circuit, the short stimulus to upstream atrial electrogram interval would approximate the interval by which the upstream site precedes the downstream site during tachycardia and should be identical to the sequence observed when pacing in sinus rhythm.

We sought to define and assess the potential utility of this approach in a series of patients presenting with cavotricuspid isthmus (CTI)–dependent AT, perimitral AT, and other macroreentrant and focal ATs after AF ablation.

Methods

Study Population

This study included 36 retrospectively analyzed and 30 prospectively studied atrial arrhythmias in 62 consecutive patients who underwent an electrophysiology study and catheter ablation procedure at our center between March 1, 2012, and October 1, 2013, and had ATs that met the inclusion criteria below.
The following arrhythmias were studied:

1. CTI-dependent AT (n=20, all retrospectively collected).
2. Perimital AT (n=20, 5 retrospectively collected and 15 prospectively collected).
3. Other focal AT having proximal-to-distal or distal-to-proximal activation within the coronary sinus (CS; 8 retrospectively collected and 5 prospectively collected).
4. Other macroreentrant left atrial (LA) ATs (6 retrospectively collected, 7 prospectively collected: 11 roof-dependent ATs, 1 LA appendage reentry, and 1 left superior pulmonary vein reentry) in which downstream overdrive pacing (DOP) was performed with the CS catheter. Six prospective cases with variable CS activation patterns had additional DOP with a 5-spline mapping catheter (Pentaray, Biosense-Webster, Diamond Bar, CA) placed within the tachycardia circuit.

These patients were selected for inclusion on the basis of the following criteria:

1. Overdrive pacing attempts were made from a catheter with multiple neighboring electrodes, and the atrial rate was clearly accelerated to the pacing rate.
2. The overdrive pacing attempt was made from an electrode with later timing relative to a neighboring electrode, that is, the pacing site was “downstream” from neighboring electrode. Examples of downstream pacing sites in CTI flutter and perimital flutter are shown in Figure 1.
3. Neither TCL nor the activation pattern was altered after cessation of pacing, and tachycardia continued after pacing.
4. Tachycardia cycle length variability was <50 milliseconds.
5. Pacing was performed from a multielectrode catheter within the CS for all left ATs.

Antiarrhythmic drugs were stopped a minimum of 5 half-lives before the procedure in all except 5 patients (3 taking amiodarone, 1 on disopyramide, 1 taking sotalol) at the time of ablation.

Electrophysiology Study

All patients provided written informed consent. Data collection and analysis were done according to protocols approved by the Partners Human Subject Protection Committee. Surface and intracardiac electrocardiograms were digitally recorded and stored (Prucka CardioLab EP system, GE Healthcare, Waukesha, WI). Nonfluoroscopic 3-dimensional mapping was performed with the Carto (Biosense-Webster) or Ensite NavX (St. Jude Medical, St. Paul, MN) system at the operator’s discretion.

A 7F multipolar (20-pole) catheter (Daig DuoDeca 2-10-2, St. Jude Medical, or Ismus, Biosense Webster) was used, with the distal poles (poles 1–10) placed within the CS and the proximal electrodes (poles 11–20) located along the tricuspid annulus in the lateral and inferior right atrium. For LA mapping and recording, a 10- or 20-pole circumferential pulmonary vein mapping catheter (Optima, Irvine Biomedical, Irvine, CA, or Lasso, Biosense-Webster) or a 5-spline mapping catheter with splines in the star configuration and 1-mm electrodes (PentaRay Nav, Biosense-Webster) was used.

Ablation was performed with an open-irrigated 3.5-mm-tip ablation catheter paired with a 3-dimensional mapping (Navistar Thermocool, Biosense-Webster). Ablation lesions were generated in a power-controlled mode applying 20 to 35 W for 30 to 60 seconds per lesion during irrigation at a rate of 8 to 30 mL/min. In patients undergoing repeat procedures, previously placed linear lesions (mitral isthmus and CTI) and the electric isolation of the pulmonary veins were evaluated during sinus rhythm when possible. Macroreentrant ATs were diagnosed when a PPI exceeded the TCL by no more than 30 milliseconds for overdrive pacing from 2 widely separated segments within the presumptive circuit and the tachycardia terminated with ablation in the isthmus for that arrhythmia. Focal AT was diagnosed when no evidence of intracardiac fusion was present, PPI–TCL values <30 milliseconds were limited to a narrow area around the focus, and an activation map revealed a centrifugal activation pattern.

Downstream Pacing for Attempted Entrainment

Overdrive pacing was performed at cycle lengths within 10 to 30 milliseconds of the TCL from a local downstream site. Neighboring upstream atrial electrograms were analyzed for changes in activation sequence during pacing, and the stimulus to electrogram interval was measured from the last stimulus to the last electrogram accelerated to the pacing cycle length at all neighboring electrodes. For CTI-dependent AT and perimital AT, the closest upstream electrodes with activation immediately preceding the pacing stimulus (Figure 1A and 1B), typically 8 mm from the pacing site, were selected for analysis. If no electrogram was discernable at this site or there was antidromic capture (see below), then the next electrode pair (typically 20 mm from the pacing site) was examined. In addition, activation was also assessed at electrodes further from the pacing site. Antidromic or direct activation was defined as acceleration to the pacing rate with an obvious change in electrogram morphology and a relatively short S-A interval that was much less than the TCL. Orthodromic activation was defined as acceleration to the pacing cycle length with a long S-A interval approaching the TCL. Retrospectively collected data from CTI-dependent AT and perimital AT were used to develop cutoff values for short S-A intervals, indicating antidromic or direct activation, and long S-A intervals, indicating orthodromic activation and constant fusion. In the focal AT group (Figure 2), the S-A interval was measured with an electrode ≈20 mm upstream from the pacing site for comparison to simulate the maximal distance to the analyzed upstream electrode in CTI and perimital ATs. For prospectively collected ATs, the mapping strategy included DOP from CS followed by DOP from common sites of macroreentry, including the LA roof, anterior and posterior walls, and LA appendage when appropriate.

Statistical Methods

Continuous variables are expressed as mean±SD. Continuous variables were analyzed with the Student t test. Scatterplots were constructed with Prism (version 5.0d, GraphPad Software, Inc, La Jolla, CA). A 2-tailed value of P<0.05 was considered to be statistically significant.

Results

A total of 66 sustained ATs were analyzed in 62 patients who underwent 59 procedures. The mean age was 67.4±8.1 years, and 67% were male. The mean LA diameter was 44±5 mm in the parasternal window. Mean left ventricular ejection fraction was 56±8%, and 25% had structural heart disease. AT occurred either during the index ablation procedure (42%) or late after AF ablation (58%). Of the 20 patients with perimital flutter, 17 had prior AF ablations, of which 11 included linear LA lesions in addition to pulmonary vein isolation, with 5 having conduction across prior mitral isthmus lines. Each arrhythmia was successfully ablated.

Overdrive Pacing From Downstream Electrodes

CTI-Dependent AT and Perimital AT

A PPI–TCL <30 milliseconds and long S-A times suggestive of constant fusion were observed in all patients with CTI-dependent AT during DOP within the CTI and all with perimital AT during DOP within the CS (Figure 1A and 1B). Overdrive pacing from a downstream electrode resulted in long S-A intervals at the upstream electrodes (right atrium [RA] 19,20 and RA 17,18 in Figure 1A and Figure 1B). Evidence of antidromic penetration to neighboring electrodes was usually confined to <20 mm from the pacing site (RA 14,15 in Figure 1A; not seen in in Figure 1B). S-A time approached the TCL (90±4% of TCL) for the closest orthodromically activated site that could be clearly identified.
Focal AT
A PPI−TCL >40 milliseconds (range, 50–90 milliseconds) and a centrifugal activation pattern during overdrive pacing from the CS were observed in all patients with focal AT during DOP from the CS. S-Au times were <25% of the TCL in all cases (12±3% of TCL), indicating direct activation.

Other Macroreentrant LA ATs
With overdrive pacing from a downstream CS electrode, a PPI−TCL >30 milliseconds was seen in 8 of 13 patients. Of the 7 prospectively collected patients, 4 had a CS activation pattern that was neither clearly proximal to distal nor distal to proximal, and the latest activated CS electrode was selected for DOP. DOP from the CS resulted in 2 categories of upstream responses. First, when the PPI−TCL exceeded 40 milliseconds (range, 45–144 milliseconds), S-Au times were short relative to the TCL (12±4% of TCL), consistent with antidromic activation (Figure 2A). Second, when the PPI−TCL was <40 milliseconds (range, 5–35 milliseconds), S-Au times greater than the PCL were observed, which resulted in upstream electrograms appearing after the next pacing stimulus before termination of pacing (99±3% of TCL), consistent with orthodromic activation after a long interval (Figure 2B).

To prospectively test whether DOP would produce similar findings for pacing near macroreentrant AT circuits that were not perivalvular, we performed DOP from within the tachycardia circuit with a 5-spline catheter in 6 of the 13 cases of other macroreentrant LA ATs. In 4 patients with roof-dependent macroreentry, the pacing electrodes were placed on the LA roof between the right upper and left upper pulmonary veins (Figure 3A). In 1 patient with macroreentry around the LA appendage, the mapping catheter was placed within the LA appendage (Figure 3B). One patient had macroreentry around the left superior pulmonary vein related to lung transplant anastomosis, and the mapping catheter was placed at the left superior pulmonary vein ostium. A PPI−TCL <30 milliseconds and S-Au time approaching the TCL (89±3% of TCL) and less than the PCL were observed in all 6 patients.
In each of these cases, the tachycardia circuit was confirmed by 3-dimensional mapping using the multipolar catheter and terminated with ablation on the roof or within zones of slow conduction in the 2 patients with LA appendage or left superior pulmonary vein reentry.

As shown in Figure 4, DOP at sites close to a macroreentry circuit (CTI-dependent AT with pacing in the CTI, perimitral AT with pacing from the CS, and other macroreentrant LA ATs with pacing at sites within or near the circuit as judged by a PPI−TCL <40 milliseconds) resulted in S-Au intervals approaching the TCL, consistent with orthodromic capture of upstream sites and evidence of constant fusion (S-Au/TCL >75%). In contrast, DOP for focal ATs and at sites remote from macroreentry circuits demonstrated a short S-Au (S-Au/TCL <25%), consistent with direct activation. For all ATs, the electrode selected for overdrive pacing was 32±13 milliseconds (range, 19-61 milliseconds) downstream from the analyzed upstream electrode. The mean values for S-Au/TCL for perianular ATs were significantly higher than for focal ATs (89±4% of TCL versus 12±4% of TCL; P<0.001). Of note, no included patients had both perianular AT and focal AT in the present analysis.

**Discussion**

**Main Findings**

In this study, the response to DOP from various multielectrode catheters at a rate slightly faster than the TCL during AT demonstrated constant fusion when the catheter electrodes were within or near a macroreentry circuit, as judged by a PPI−TCL <40 milliseconds. To detect constant fusion, the pacing site...
reported that 72% of persistent AF ablation–related ATs are macroreentrant from the tachycardia circuit. This finding suggests that macroreentry is present in the region of the pacing electrode but that the upstream electrodes are far from the tachycardia circuit. For DOP with a PPI−TCL <40 milliseconds in which the upstream electrodes were farther from the circuit than the downstream pacing electrode, as seen in CS pacing in selected roof-dependent ATs (Figure 2B), a long S-A, interval resulted in upstream electrograms occurring within or after the subsequent pacing stimulus artifact during DOP, and the last upstream electrogram accelerated to the pacing rate followed the last pacing stimulus after an interval longer than the PCL.

Figure 4. Scatterplot showing stimulus to upstream atrial electrogram (S–A upstream)/tachycardia cycle length (TCL; %) for downstream overdrive pacing (DOP) from cavotricuspid isthmus (CTI) in CTI-dependent atrial tachycardia (AT), the coronary sinus (CS) in perimital AT and focal AT, and DOP from the CS or 5-spline mapping catheter (6 ATs) in other macroreentrant left atrial AT (OMAT). Closed symbols indicate retrospectively collected data points; open symbols, prospective data points. Dashed lines at 25% and 75% illustrate S–A upstream/TCL cutoff values determined by retrospective analysis. Note that all retrospective and prospective cases with DOP at sites close to a macroreentry circuit (CTI-dependent AT, perimital AT, and OMAT with PPI−TCL <40 milliseconds) resulted in S–A upstream/TCL >75% whereas DOP for focal ATs and at sites remote from macroreentry circuits resulted in S–A upstream/TCL <25%.

Clinical Significance
Given that AT after AF ablation is most often macroreentrant, we believe that entrainment mapping is a useful initial mapping strategy. Although the risk of alteration or termination of tachycardia with entrainment is low when pacing just faster than the TCL, reaching a diagnosis in as few pacing maneuvers as possible is desired. The method we describe for detecting constant fusion with multielectrode catheters may simplify mapping of ATs after AF ablation by rapidly detecting macroreentry at common sites for each suspected arrhythmia with relatively few attempts. For instance, in clockwise perimital flutter with distal-to-proximal sequential CS activation, DOP from the proximal CS electrode would demonstrate a short PPI−TCL and constant fusion recognized by a S–A time slightly shorter than the PCL; that is, distal electrograms will appear just before the pacing stimulus during entrainment. Without a transseptal puncture and within 1 pacing maneuver, the arrhythmia diagnosis could be made with reasonable certainty. To confirm the diagnosis, an additional site of pacing on the opposite side of the mitral valve annulus may be sought after transseptal puncture. Theoretically, constant fusion should be detectable in all forms of macroreentry and, importantly, was detected with the use of the same technique in patients with multiple macroreentrant circuits. Because the vast majority of LA macroreentrant ATs are perimital or roof dependent, DOP with a multipolar catheter from within the CS or on the LA roof should provide a diagnosis in most cases, after which usual sites of macroreentry or focal arrhythmia could be sought. Furthermore, because we did not observe antidromic capture >2 cm from the downstream pacing site when near the circuit, the method can be applied with the use of 2 relatively close sites on a single catheter. It is theoretically possible that macroreentry could be identified even if AT is terminated by overdrive pacing if there is a period of constant fusion before termination that allows identification of 2 distinct S–A times, because this would fulfill the third criterion of constant fusion described by Waldo.10

Potential Pitfalls and Study Limitations
Overdrive pacing maneuvers may be difficult to interpret when the AT cycle length is variable. We did not include unstable AT in this analysis (AA intervals varied <30 milliseconds), but theoretically, constant fusion might still be detected by a long S-A even if the PPI−TCL would be less reliable under these circumstances. Faster pacing rates relative to the TCL will result in greater antidromic penetration of the pacing wave front, which may result in activation of all available upstream electrodes antidromically and an inability to detect fusion. Upstream recording electrodes immediately adjacent to the pacing site (eg,
Figure 1A, RA 15,16) may be captured antidromically even at a slow pacing rate; furthermore, stimulus artifact may distort the electrogram. As a result, if there is a short SA interval at the nearest upstream recording electrode, progressively further recording electrodes should be examined (eg, Figure 1A, RA 16,17). No instances of antidromic penetration of sites >2 cm distant from the pacing site were seen in macroreentrant AT when the PCL was within 30 milliseconds of the TCL and the PPI−TCL was <40 milliseconds. In addition, DOP in atria with extensive scarring may be difficult to interpret, and CS DOP depends on intact connections between the LA and CS.16 Lastly, although this technique can diagnose macroreentry readily, it does not distinguish whether multiple loops are present, and additional pacing maneuvers and mapping as described by Linton et al should be considered if that mechanism is suspected.17 If the upstream and downstream electrodes are on opposite sides of a line of block, a long S-A,<sub>2</sub> may occur in the absence of constant fusion. If this condition is suspected, a PPI−TCL value should be sought from both electrodes to exclude this unusual possibility and would be expected to be markedly different at the 2 sites, with a very long PPI on the side of block farther from the AT circuit/focus. Furthermore, if the block is fixed, a long stimulus-to-electrogram interval would also be expected during sinus rhythm. From this relatively small series, it is unclear whether evidence of fusion may be seen under some conditions when the PPI−TCL is >40 milliseconds. Additionally, recognition of a long S-A,<sub>2</sub> in cases when the upstream electrodes were outside the tachycardia circuit such as DOP from the CS in roof-dependent AT required careful analysis because of the frequent presence of an S-A,<sub>1</sub> greater than the PCL, creating a “pseudo-short S-A,<sub>1</sub>” (Figure 2B), which can be confused with a short S-A,<sub>2</sub> as seen in the absence of macroreentry. Careful measurement to determine the last electrogram accelerated to the PCL easily differentiates these 2 situations. Because we included only cases that satisfied certain diagnostic criteria to be sure of the arrhythmia diagnosis, it is not known how well the technique tested in this study would perform prospectively in cases in which the tachycardia mechanism is ambiguous as assessed with conventional criteria or when the PPI−TCL is misleadingly long.15 Demonstration of the utility of this method to detect fusion in 5 different macroreentrant AT mechanisms establishes the proof of concept; however, prospective evaluation is required to evaluate the sensitivity, specificity, and predictive value of this finding.

Conclusions
A single pacing train from a single catheter can demonstrate fusion and provide evidence of the potential reentry circuit location when the pacing site is selected to be downstream from an adjacent activation site. We propose that recognition of intracardiac constant fusion is a novel criterion of transient entrainment. Rapid recognition of perimetal AT, CTI-dependent AT, and additional macroreentrant ATs is possible. A mapping strategy incorporating DOP may facilitate rapid diagnosis of common ATs after catheter ablation of AF.

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References
Mapping atrial tachyarrhythmias arising during catheter ablation of atrial fibrillation remains a clinical challenge. Even distinguishing focal from macroreentrant tachycardias may require extensive activation mapping or entrainment from multiple sites with potential tachycardia termination or alteration. We describe how a single pacing maneuver can demonstrate macroreentry by selecting the later (downstream) site for pacing and assessing paced activation at the upstream site. This new method of downstream overdrive pacing allows recognition of constant fusion and thus macroreentry and can indicate if the pacing site is in or near the reentry circuit. This method can be used to rapidly diagnose common atrial tachycardias that arise during catheter ablation of atrial fibrillation and may be useful for the diagnosis of other macroreentrant tachyarrhythmias.
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