Overdrive Pacing from Downstream Sites on Multielectrode Catheters to Rapidly Detect Fusion and Diagnose Macroreentrant Atrial Arrhythmias

Running title: Barbhaiya et al.; Downstream Overdrive Pacing for Detection of Fusion

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Abstract

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—Using a multipolar catheter, pacing was performed from electrodes within the coronary sinus showing activation later than adjacent electrodes (downstream overdrive pacing (DOP)) during 66 ATs in 62 patients: 20 cavotricuspid isthmus (CTI) dependent ATs, 20 perimitral ATs, 13 focal ATs with sequential coronary sinus (CS) activation, and 13 other macroreentrant left atrial ATs. The paced-CL (PCL) was 10-30 ms below the tachycardia cycle length (TCL) and activation at the neighboring upstream electrodes was assessed. DOP at 48 sites close to a macroreentrant circuit (PPI – TCL < 40 ms) produced constant fusion demonstrated by 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, DOP at 18 sites during focal AT or remote from the macroreentrant AT circuit (PPI – TCL > 40 ms) always demonstrated a comparatively short S-Au < 25% of TCL (12 ± 4% vs. 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 ms and S-Au > 75% of TCL. Recognition of intracardiac constant fusion using this method is a novel criterion for transient entrainment.

Key words: arrhythmia (heart rhythm disorders), atrial fibrillation arrhythmia, atrial flutter, ablation, mapping
Introduction

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. These ATs can be either macroreentrant related to gaps in ablation lines or focal origin tachycardia that may be due to microreentrant circuits or automaticity. Differentiation of macroreentry from focal tachycardias is a major challenge in defining the appropriate ablation target for these arrhythmias and the optimal approach for mapping arrhythmias is not defined. Activation mapping can be time consuming and may yield ambiguous results, particularly in previously ablated or scarred atria. Entrainment mapping is also helpful, particularly for macroreentrant tachycardias, but correct interpretation of entrainment findings assumes that the rhythm is known to be macroreentrant. The first two of the four classic findings for transient entrainment are dependent on detecting fusion between the tachycardia and pacing wavefronts from analysis of the p-wave. This is often challenging or impossible for these atrial arrhythmias. The third criterion is based on comparing activation wavefronts while pacing before and after termination of tachycardia. The fourth criterion is the demonstration of progressive fusion detected in intracardiac electrograms during pacing at progressively faster cycle lengths. The need to pace at progressively faster cycle lengths increases the possibility that pacing will alter or terminate tachycardia, which is a major limitation of entrainment mapping techniques.

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 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 following a single pacing train at a cycle length just shorter than the tachycardia cycle length. Specifically, when pacing is
performed during macroreentrant AT from a site that demonstrates later activation relative to its neighbors, electrograms at the earlier “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 paced cycle length (S-A<sub>u</sub> time) that approximates the tachycardia cycle length (TCL) due to 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 paced cycle length, since local activation does not reach equilibrium with a separate wavefront. Likewise, overdrive pacing at sites remote from a macroreentrant wavefront would produce a short conduction time to upstream sites, since all local sites would be activated directly, or antidromically, from the paced wavefront. During overdrive pacing in patients with either 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:

(i) CTI-dependent AT (n=20, all retrospectively collected);
(ii) Perimitral AT (n=20, 5 retrospectively collected and 15 prospectively collected);
(iii) Patients with other Focal AT having proximal-to-distal or distal-to-proximal activation within the coronary sinus (8 retrospectively collected and 5 prospectively collected), and;
(iv) Patients with other macroreentrant left atrial ATs (OMAT) (6 retrospectively collected, 7 prospectively collected – 11 roof dependent ATs, 1 left atrial appendage reentry, and one left superior pulmonary vein reentry) in which downstream overdrive pacing (DOP) was performed using the CS catheter. Six prospective cases with variable CS activation patterns had additional DOP with a five-spline mapping catheter (Pentaray, Biosense-Webster, Diamond Bar, California) placed within the tachycardia circuit.

These patients were selected for inclusion based on 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 i.e. the pacing site was “downstream” from neighboring electrode. Examples of downstream pacing sites in CTI flutter and perimitral flutter are shown in Figure 1.
3. Neither TCL nor activation pattern was altered after cessation of pacing and
tachycardia continued after pacing.

4. Tachycardia cycle length variability was < 30 ms.

5. Pacing was performed from a multielectrode catheter within the coronary sinus for all left atrial tachycardias.

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

**Electrophysiology Study**

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

A 7-F multipolar (20-pole)catheter (Daig DuoDeca 2-10-2, St. Jude Medical, or Ismus, Biosense Webster) was used with the distal poles (poles 1 to 10) placed within the coronary sinus and the proximal electrodes (poles 11 to 20) located along the tricuspid annulus in the lateral and inferior right atrium. For left atrial mapping and recording, a 10- or 20-pole circumferential PV mapping catheter (Optima, Irvine Biomedical, Irvine, California, or Lasso, Biosense-Webster), or a five-spline mapping catheter with splines in star configuration and 1mm electrodes (PentaRay Nav, Biosense-Webster) was utilized.

Ablation was performed with an open-irrigated 3.5-mm tip ablation catheter paired with a 3-dimensional mapping (Navistar Thermocool, Biosense-Webster, Diamond Bar, California). 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 cavo-tricuspid isthmus) and the electrical isolation of the PVs were evaluated during sinus rhythm when possible. Macroleventrants ATs were diagnosed when a PPI exceeded the TCL by no more than 30 ms 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 ms 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 msec 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 measured from the last stimulus to the last electrogram accelerated to the pacing cycle length at all neighboring electrodes. For CTI-dependent AT and perimitral AT the closest upstream electrodes with activation immediately preceding the pacing stimulus (Figure 1a and 1b) typically 8 mm from the pacing site was 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-Au that was much less than the TCL. Orthodromic activation was defined as acceleration to the pacing cycle length with a long S-Au interval approaching the TCL. Retrospectively collected data from CTI-dependent AT and perimitral AT was used to develop cutoff values for short S-Au intervals.
indicating antidromic or direct activation and long S-Au intervals indicating orthodromic activation and constant fusion. In the Focal AT group (Figure 2), the S-Au interval was measured using an electrode approximately 20mm upstream from the pacing site for comparison to simulate the maximal distance to the analyzed upstream electrode in CTI and perimitral ATs. For prospectively collected ATs, the mapping strategy included DOP from CS followed by DOP from common sites of macroreentry, including, LA roof, anterior and posterior walls, left atrial appendage when appropriate.

**Statistical Methods**

Continuous variables are expressed as the mean value ± SD. Continuous variables were analyzed using the Student t test. Scatterplots were constructed by using Prism (version 5.0d, GraphPad Software, Inc, La Jolla, CA). A 2-tailed P value < .05 was considered 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 perimitral flutter patients, 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 Perimitral AT**

A PPI-TCL < 30ms and long S-Au 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 (Figures 1a and 1b). Overdrive pacing from a downstream electrode resulted in long S-Au intervals at the upstream electrodes (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-Au time approached the TCL (90 ± 4% of TCL) for the closest orthodromically activated site that could be clearly identified.

Focal AT

A PPI-TCL > 40ms (range 50 ms to 190 ms) and a centrifugal activation pattern during overdrive pacing from the CS was 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.

OMAT

With overdrive pacing from a downstream CS electrode a PPI-TCL > 30 msec 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 or distal-to-proximal, and the latest activated CS electrode was selected for DOP. Downstream overdrive pacing from the CS resulted in two categories of upstream responses: 1) When the PPI-TCL exceeded 40 ms (range 45 ms to 144 ms) S-Au times were short relative to the TCL (12 ± 4% of TCL) consistent with antidromic activation (Figure 2, panel a). 2) When the PPI-TCL was less than 40 ms (range 5 ms to 35 ms) S-Au times greater than the PCL were observed, which resulted in upstream EGMs appearing after the next pacing stimulus prior to termination of pacing (99 ± 3% of TCL) consistent with orthodromic activation after a long interval (Figure 2b).

In order 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 OMAT. In four 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 one patient with macroreentry around the left atrial appendage, the mapping catheter was placed within the left atrial appendage (Figure 3b). One patient had macroreentry around the left superior pulmonary vein (LSPV) related to lung transplant anastomosis and the mapping catheter was placed at the LSPV ostium. A PPI-TCL < 30ms, S-Au time approaching the TCL (89 ± 3% of TCL) and less than the PCL were observed in all six patients. In each of these cases the tachycardia circuit was confirmed by 3D mapping using the multipolar catheter and terminated with ablation on the roof or within zones of slow conduction in the two patients with LAA or LSPV reentry.

As shown in figure 4, DOP at sites close to a macroreentry circuit, (CTI-dependent AT with pacing in the CTI, perimiral AT with pacing from the CS, and OMAT with pacing at sites within or near the circuit as judged by a PPI-TCL < 40 ms) 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. The mean values for S-Au /TCL for periannular ATs was significantly higher than for focal AT’s (89 ± 4% of TCL vs. 12 ± 4% of TCL, p < 0.001). Of note, no included patients had both periannular 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 tachycardia cycle length during atrial tachycardia was able to demonstrate constant fusion when the catheter electrodes were within or near a macroreentry circuit, as judged by a PPI-TCL < 40 ms. To detect constant fusion, the pacing site must be downstream in terms of local activation time during AT compared with neighboring electrodes. In tachycardia, the electrode selected for overdrive pacing was 32 ± 13 ms (range of 19 ms to 61 ms) downstream from the analyzed upstream electrode. In all cases of macroreentrant AT with electrodes placed within or near the tachycardia circuit, we found that the S-A interval from the downstream pacing site to a neighboring upstream electrode was at least 75% of the TCL and the PPI–TCL was < 40 ms. Additionally, DOP with PPI-TCL < 30ms and upstream atrial activation that immediately precedes the pacing stimulus prior to cessation of pacing suggests that upstream and downstream electrodes are both within or near the tachycardia circuit and may strongly suggest the specific location of the tachycardia circuit, as we saw in all cases of perivalvular AT with electrodes placed along the valve annulus and OMATs with a multielectrode catheter placed within the tachycardia circuit. For DOP with a PPI-TCL < 40 ms in which the upstream electrodes were further from the circuit than the downstream pacing electrode, as seen in CS pacing in selected roof dependent ATs (Figure 2b), a long S-Au interval was observed that 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. This finding suggests that macroreentry is present in the region of the pacing electrode, but that the upstream electrodes are further from the tachycardia circuit.

**Previous Studies**

Multiple mapping strategies have been suggested in order to efficiently diagnose common atrial
arrhythmias arising during or after catheter ablation of atrial fibrillation\textsuperscript{8,12-15}. Coffey et al.\textsuperscript{8} reported a strategy of detailed activation mapping followed by focused entrainment mapping of AF ablation related ATs. Rostock et al.\textsuperscript{13} report that 72\% of persistent AF ablation related ATs are macroreentrant and have proposed a mapping strategy starting with entrainment mapping from up to 6 LA sites in order to establish the correct AT diagnosis. Steven et al.\textsuperscript{14} proposed a focused mapping strategy based on recognition of a number of biatrial activation patterns. Pascal et al.\textsuperscript{15} report that 56\% of persistent AF ablation related ATs are macroreentrant and propose utilizing CS activation pattern and timing of mid-CS activation relative to the surface p-wave to focus entrainment mapping. Each of these strategies requires multiple steps for confirmation of arrhythmia mechanism.

\textbf{Clinical Significance}

Given that AT after AF ablation is most often macroreentrant, we believe that entrainment mapping is a useful initial mapping strategy. While 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 using 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 as well as constant fusion recognized by a S-A\textsubscript{u} time slightly shorter than the PCL i.e. distal electrograms will appear just before the pacing stimulus during entrainment. Without a transseptal puncture and within one 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 using the same technique in patients with multiple macroreentrant circuits. Since the vast majority of left atrial macroreentrant AT is perimital or roof dependent, DOP with a multipolar catheter from within the CS and/or on the LA roof should provide a diagnosis in most cases, after which unusual sites of macroreentry or focal arrhythmia could be sought. Furthermore, as we did not observe antidromic capture more than 2 cm from the downstream pacing site when near the circuit, the method can be applied using two 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 prior to termination that allows identification of two distinct S-Au times, as this would fulfill the third criterion of constant fusion described by Waldo10.

Potential Pitfalls and Study Limitations

Overdrive pacing maneuvers may be difficult to interpret when the atrial tachycardia cycle length is variable. We did not include unstable atrial tachycardia in this analysis (AA intervals varied less than 30 msec) but theoretically constant fusion might still be detected by a long SA time even if the PPI-TCL would be less reliable under these circumstances. Faster pacing rates relative to the tachycardia CL will result in greater antidromic penetration of the pacing wavefront 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 and 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
more than 2 cm distant from the pacing site were seen in macroreentrant AT when the PCL was within 30 ms of the TCL, and the PPI-TCL was < 40 ms. 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.\textsuperscript{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 Rostock et al should be considered if that mechanism is suspected\textsuperscript{17}. If the upstream and downstream electrodes are on opposite sides of a line of block, a long SA time to the upstream electrode 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 two sites, with a very long PPI on the side of block further 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 msec. Additionally, recognition of a long S-A\textsubscript{u} in cases where the upstream electrodes were outside the tachycardia circuit, such as DOP from CS in roof dependent AT, required careful analysis due to the frequent presence of an S-A\textsubscript{u} > PCL creating a “pseudo-short S-A\textsubscript{u}” (\textbf{Figure 2b}) that can be confused with a short S-A\textsubscript{u} as seen in the absence of macroreentry. Careful measurement to determine the last electrogram accelerated to the paced cycle length easily differentiates these two situations. Since 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 was ambiguous based on conventional criteria or when the PPI–TCL was misleadingly long\textsuperscript{18}. Demonstration of the utility of this method to detect fusion in five different
macroreentrant atrial tachycardia mechanisms establishes the proof of concept, however
prospective evaluation is required to evaluate 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 perimital 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 atrial fibrillation.

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**Figure Legends:**

**Figure 1. A.** Schematic representation of tricuspid and mitral annuli in LAO projection. DOP from low lateral RA (RA 13,14 indicated by the star) in CTI-dependent AT. PPI equals TCL. Blue dots indicate each upstream electrode clearly captured at the paced cycle length. The S-Au interval at RA 17,18 is 220 ms (88% of TCL) and is suggestive of fusion and macroreentry along the multielectrode catheter. Note that RA 15,16 is also an upstream site captured orthodromically but is partially obscured by the pacing stimulus. Therefore RA 17,18 was chosen for S-Au measurement. Collision of orthodromic (red arrow) and antidromic (green arrow) wavefronts is likely occurring between RA 13,14 and RA 15,16. LAO indicates left
anterior oblique; DOP, downstream overdrive pacing; PPI, post pacing interval; TCL, tachycardia cycle length; and S-Au, stimulus to upstream atrial electrogram interval. **B.** DOP from distal CS in perimitral flutter. Pacing is performed from CS 1,2 (star). PPI equals TCL. Blue dots indicate each electrogram at upstream electrodes clearly captured at the paced cycle length. The S-Au time is 192 ms (91% of TCL) and is suggestive of fusion and macroreentry along the multielectrode catheter. All orthodromically activated electrograms at upstream electrodes immediately precede pacing stimuli. Collision of antidromic (green arrow) and orthodromic (red arrow) wavefronts occurs between CS 1,2 and CS 3,4. DOP indicates downstream overdrive pacing; PPI, post pacing interval; TCL, tachycardia cycle length; and S-Au, stimulus to upstream atrial electrogram interval.

**Figure 2. A.** CS pacing during left atrial roof dependent AT is shown. DOP from distal CS followed by resumption of AT with proximal to distal CS activation. PPI is 316 ms (85 ms greater than TCL). Blue dots indicate each electrogram at upstream electrodes clearly captured at the paced cycle length. The long PPI and short S-A consistent with antidromic activation of upstream sites indicate that the pacing site is remote from the AT circuit or focus. The short S-Au time of 33 ms (15% of TCL) is consistent with antidromic activation of these sites and there is no evidence of fusion along the multielectrode catheter. DOP indicates downstream overdrive pacing; PPI, post pacing interval; TCL, tachycardia cycle length; and S-Au, stimulus to upstream atrial electrogram interval. **B.** DOP from proximal CS (star) in LA roof dependent AT around left pulmonary veins (blue arrow in LA schematic) with distal to proximal CS activation. PPI is 35 ms greater than TCL. Blue dots indicate each electrogram at upstream electrodes clearly captured at the paced cycle length. There are no upstream electrograms noted preceding the
pacing stimulus, however there is a long S-Au time 256 ms (>100% of TCL) suggestive of constant with fusion. DOP indicates downstream overdrive pacing; PPI, post pacing interval; TCL, tachycardia cycle length; and S-Au, stimulus to upstream atrial electrogram interval.

**Figure 3. A.** DOP from five spline mapping catheter (illustrated in blue) at LA roof (star) in LA roof dependent AT. PPI is less than 30 ms greater than TCL. Blue dots indicate each electrogram at upstream electrodes clearly captured at the paced cycle length. The long S-Au time 335 ms (89% of TCL) is suggestive of fusion and macroreentry along the mapping catheter. Although multiple electrograms are obscured by the pacing stimuli, some upstream sites are recognized as immediately preceding the pacing stimuli and are orthodromically activated (A, B and D splines). DOP indicates downstream overdrive pacing; PPI, post pacing interval; TCL, tachycardia cycle length; and S-Au, stimulus to upstream atrial electrogram interval. **B.** DOP from five spline mapping catheter (illustrated in blue) at LA appendage (star) in LA appendage reentry. PPI equals TCL, indicating that the pacing electrode is within the tachycardia circuit. Blue dots indicate each electrogram at upstream electrodes clearly captured at the paced cycle length. The long S-Au time 200 ms (89% of TCL) is suggestive of fusion and macroreentry along the mapping catheter. Upstream sites are orthodromically activated during pacing with a long S-Au such that the orthodromic electrograms that immediately precede the pacing stimuli. DOP indicates downstream overdrive pacing; PPI, post pacing interval; TCL, tachycardia cycle length; and S-Au, stimulus to upstream atrial electrogram interval.

**Figure 4.** Scatterplot showing stimulus to upstream atrial electrogram (S-A upstream) / Tachycardia Cycle Length (%) for DOP from CTI in CTI-dependent AT, the CS in perimtrial
AT, and Focal AT, and DOP from CS or five spline mapping catheter (6 ATs) in OMAT. Closed symbols indicate retrospectively collected data points and open symbols indicate prospective data points. Dashed lines at 25% and 75% illustrate S-A_u/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 ms) resulted in S-A_u/TCL > 75% whereas DOP for focal ATs and at sites remote from macroreentry circuits resulted in S-A_u/TCL < 25%. DOP indicates downstream overdrive pacing; PPI, post pacing interval; TCL, tachycardia cycle length; and S-A_u, stimulus to upstream atrial electrogram interval.
Figure 1B
Figure 2A
Figure 2B
Figure 3A
Figure 3B
Figure 4

S-A upstream / TCL (%)
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