

## Characterization of the Excitable Gap in Human Type I Atrial Flutter

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**Objectives.** We sought to characterize the excitable gap of the reentrant circuit in atrial flutter.

**Background.** The electrophysiologic substrate of typical atrial flutter has not been well characterized. Specifically, it is not known whether the properties of the tricuspid valve isthmus differ from those of the remainder of the circuit.

**Methods.** Resetting was performed from two sites within the circuit: proximal (site A) and distal (site B) to the isthmus in 14 patients with type I atrial flutter. Resetting response patterns and the location where interval-dependent conduction slowing occurred were assessed.

**Results.** Some duration of a flat resetting response (mean  $\pm$  SD  $40.1 \pm 20.9$  ms,  $16 \pm 8\%$  of the cycle length) was observed in 13 of 14 patients; 1 patient had a purely increasing response. During

the increasing portion of the resetting curve, interval-dependent conduction delay most commonly occurred in the isthmus. In most cases, the resetting response was similar at both sites. In three patients, the resetting response differed significantly between the two sites; this finding suggests that paced beats may transiently change conduction within the circuit or the circuit path, or both.

**Conclusions.** Some duration of a flat resetting response was observed in most cases of type I atrial flutter, signifying a fully excitable gap in all portions of the circuit. The isthmus represents the portion of the circuit most vulnerable to interval-dependent conduction delay at short coupling intervals.

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Atrial flutter is caused by macroreentry within the right atrium, and a portion of the circuit is constrained to the narrow isthmus of tissue between the inferior vena cava and the tricuspid valve (1-11). The isthmus corresponds to an area of slow conduction during atrial flutter (4,5,7,12,13), but it is not known whether slow conduction is caused by tissue anisotropy, changes in wave front curvature imposed by anatomic constraints (14) or incomplete recovery from refractoriness. The purpose of this study was to characterize the excitable gap of the atrial flutter circuit and to determine whether isthmus conduction is limited by incomplete recovery from refractoriness.

### Methods

**Patient characteristics.** Fourteen patients with spontaneous episodes of atrial flutter were studied. There were 3 women and 11 men with a mean age of  $60 \pm 14$  years (range 37 to 80). None had undergone previous attempts at catheter ablation. Eleven of the 14 patients were studied in the absence of antiarrhythmic medications; in 3, drugs were

administered for concurrent atrial fibrillation (procainamide in 2, propafenone in 1). Structural heart disease was present in all but two patients. Written informed consent was obtained from all patients.

Typical atrial flutter (cycle length  $247 \pm 24$  ms) was identified by 1) "saw-tooth" flutter waves with a negative configuration in the inferior leads, 2) counterclockwise activation of the right atrium, and 3) demonstration of concealed entrainment during pacing from sites within the tricuspid valve isthmus with a postpacing interval within 10 ms of the tachycardia cycle length (9).

**Electrophysiologic study.** Catheters were positioned at standard right atrial sites. In addition, a 7F catheter with 10 bipolar electrode pairs (2-10-2-mm interelectrode spacing [Halo, Cordis/Webster]) was positioned adjacent to the tricuspid annulus (Fig. 1). Catheter positions are given with reference to the left anterior oblique view with the tricuspid valve depicted as a clock face. The distal bipolar electrode pair (Halo 1) was positioned near the coronary sinus (CS) (4:30 position on the clock face). The remaining Halo electrodes extended adjacent to the tricuspid valve, along the lateral wall (Halo 5 = 8:00 position), to the anterior right atrium (Halo 10 = 12:00 position). A 7F mapping catheter with an 8-mm distal tip (EP Technologies) was positioned sequentially at two locations adjacent to the tricuspid annulus (Fig. 1): 1) the low lateral right atrium, anterior to the Eustachian ridge, near Halo 5 (site A, 8:00 position); and 2) the low septal right atrium, anterior to the Eustachian ridge, inferior to the CS os

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**Abbreviations and Acronyms**

CS = coronary sinus  
MAP = monophasic action potential

(site B, 4:30 position). In one patient (Patient 11), stimulation was performed by using a deflectable catheter with a 2-mm distal electrode. The catheter positions were frequently reassessed with biplane fluoroscopy to exclude significant movement. Bipolar electrograms were acquired simultaneously at 1 kHz, filtered at 30 to 500 Hz and stored on optical disk. All measurements were performed at an equivalent sweep speed of 200 mm/s.

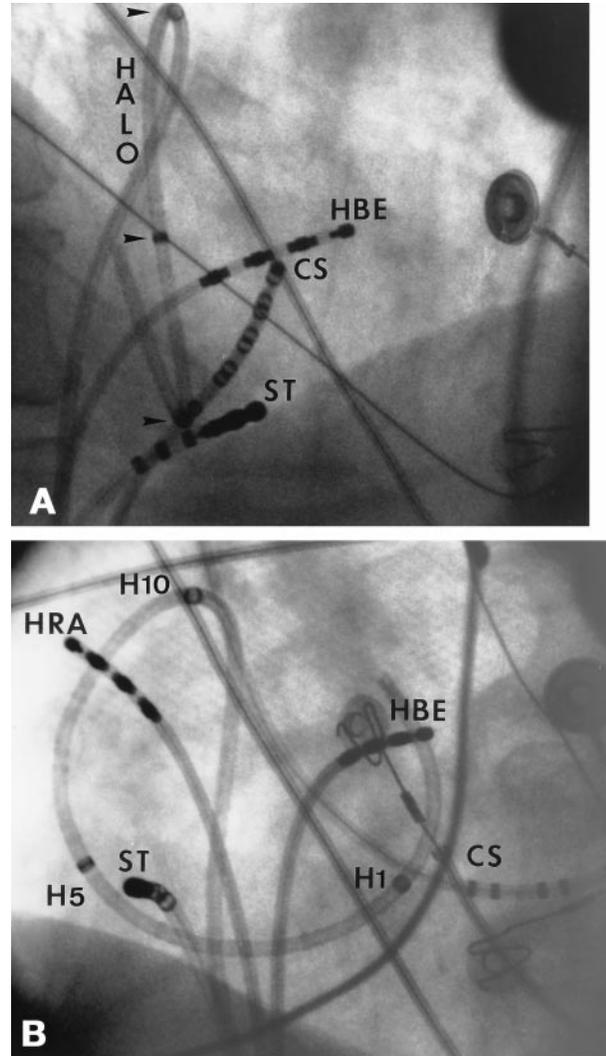
**Stimulation during atrial flutter.** The protocol for resetting has been described previously (15,16). Briefly, single atrial extrastimuli were introduced during atrial flutter from sites A and B over a range of coupling intervals, synchronized to a local electrogram. Bipolar pacing stimuli were delivered at twice diastolic threshold with a 2-ms pulse width; the pacing output was increased to 10 mA as necessary to capture at close coupling intervals. The initial coupling interval was set to 10 ms less than the cycle length and was decreased in steps of 5 to 10 ms. Resetting was defined as advancement of the tachycardia with a less than compensatory pause. Measurements were made in duplicate at each coupling interval.

The entire resetting response was considered defined if atrial flutter terminated during resetting; the entire flat portion of the response was considered determined if conduction delay developed in response to closely coupled extrastimuli (16). Refractoriness at the stimulation site could prevent achievement of either of these end points. Because of concern about stimulus latency confounding measurements in this study, the coupling interval (A1-A2) and the return cycle (A2-A3) were measured at the first electrogram orthodromically distal to the pacing site (Fig. 2). Owing to small, presumably ventriculophasic variations in the flutter cycle length (10 to 15 ms), a flat resetting response was defined by the range of coupling intervals that produced return cycles shorter than the longest cycle length observed in unperturbed atrial flutter.

**Statistical analysis.** The excitable gap (duration of the flat portion and total duration) measurements determined from sites A and B were compared by using paired *t* tests. Results are expressed as mean value  $\pm$  SD. A *p* value  $<$  0.05 was considered significant.

## Results

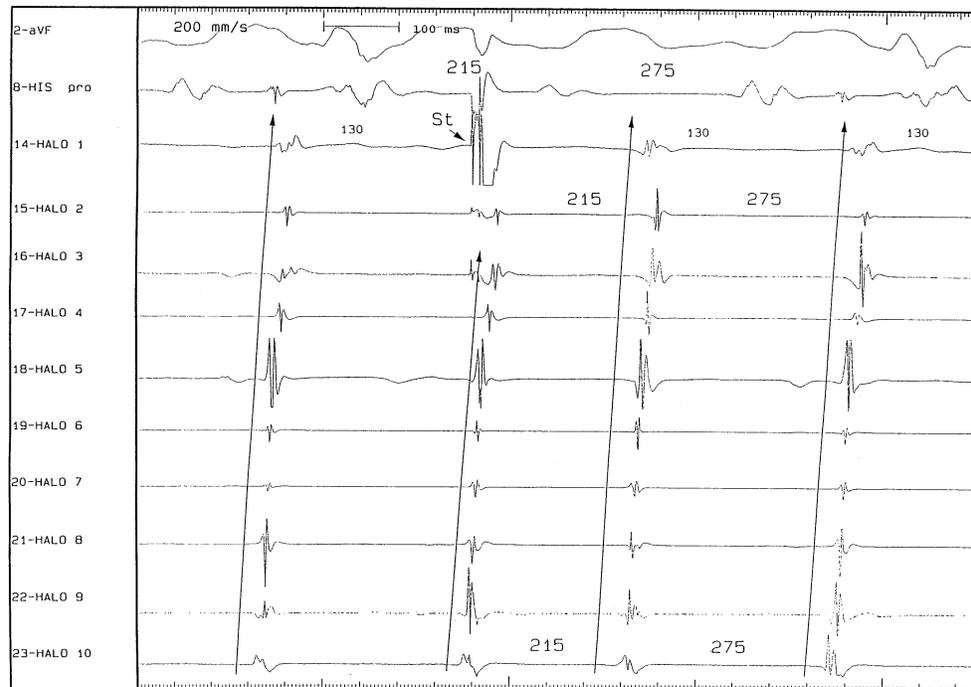
**Flat portion of the resetting response.** Some duration of a flat resetting response was observed in 13 of 14 patients (Table 1). The duration of the flat response (i.e., the longest duration of this response measured at either stimulation site) averaged  $40.1 \pm 20.9$  ms ( $16 \pm 8\%$  of the cycle length). Conduction velocity remained constant in all portions of the circuit during



**Figure 1.** Fluoroscopic images of the catheters in the right anterior oblique 30° (panel A) and left anterior oblique 60° (panel B) projections. Radiopaque markers (arrowheads in panel A) on the Halo catheter coincide with the most distal (Halo 1), middle (Halo 5) and most proximal (Halo 10) bipolar electrode pairs. In the right anterior oblique view, note the proximity of the Halo catheter to the tricuspid annulus. The left anterior oblique view demonstrates that the Halo catheter provides recordings from the 12:00 to the 4:30 position within the flutter circuit; the catheter used to deliver atrial extrastimuli (ST) is positioned at site A (8:00 position). CS = coronary sinus; HBE = His bundle electrogram; H1, H5, H10 = recording sites on the Halo catheter; HRA = high right atrium; ST = pacing catheter.

the flat portion of the resetting response. Sites that were captured antidromically recovered before the return of the next orthodromic wave front, and they did not exhibit conduction slowing (Fig. 3). Although there was some individual variation (see later), in aggregate there was no difference between the durations of the flat response measured at sites A and B ( $31.9 \pm 20.0$  vs.  $37.9 \pm 22.6$  ms, *p* = 0.178). In six patients, the entire portion of the flat curve was considered determined; in seven patients, refractoriness at the pacing site

**Figure 2.** Measurements performed during resetting. Analog tracings from surface electrocardiographic lead aVF and intracardiac recordings from the proximal His bundle (HIS pro) and the Halo catheter are shown. An extrastimulus (St) delivered from site B at a coupling interval of 215 ms (at HIS pro) produces a return cycle of 275 ms. Conduction through the circuit continues in the orthodromic direction without delay. This is apparent from the constant coupling interval at subsequent sites, activation timing identical to that of the unperturbed atrial flutter and a return cycle equal to the flutter cycle length. Conduction time from Halo 1 to HIS pro remains unchanged on the stimulated impulse (130 ms). A similar format is used for Figures 3 through 6.



occurred before conduction delay within the circuit, and the entire duration of the flat response was not determined.

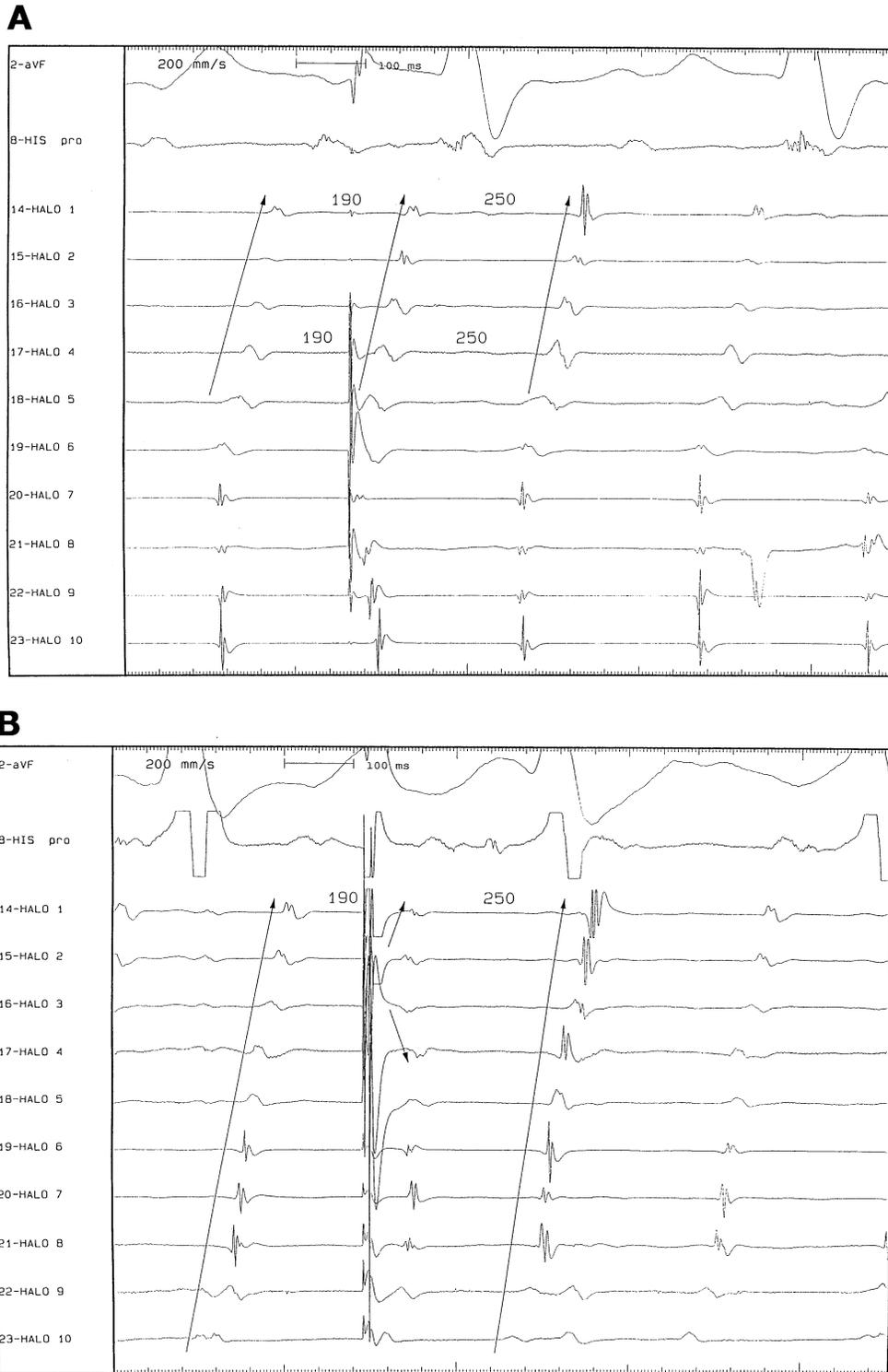
**Increasing portion of the resetting response.** In seven patients (Table 1) some portion of the resetting response was an increasing response; that is, it was marked by progressive interval-dependent conduction delay, with the delivery of progressively premature extrastimuli. In one patient (Patient 13), the response was increasing at all coupling intervals; in six

patients, a flat plus increasing response was observed. The extent of the increasing portion averaged  $11.0 \pm 16.8$  ms; it was limited by local refractoriness rather than by conduction block and thus was potentially underestimated. The total duration of the excitable gap was  $50.7 \pm 17.0$  ms; there was no difference between durations of the total excitable gap measured at sites A and B ( $48.1 \pm 13.9$  vs.  $45.0 \pm 22.0$  ms,  $p = 0.55$ ). The increase in return cycle during stimulation from either site was

**Table 1.** Resetting Responses in the 14 Study Patients

Pt No.	Drug Therapy	AFI CL (ms)	Duration of Site A Resetting Response (ms)		Duration of Site B Resetting Response (ms)		Resetting Response
			Flat	Total	Flat	Total	
1	None	250-255	$\geq 55^*$	$\geq 55^*$	>65	>65	F
2	None	260-265	$\geq 40^*$	$\geq 40^*$	45	$\geq 52^*$	F + I
3	Propaf	265-275	5	$\geq 70^*$	35	>45	F + I
4	None	225-235	$\geq 35^*$	$\geq 35^*$	$\geq 23^*$	$\geq 23^*$	F
5	Proc (iv)	270-275	$\geq 40^*$	$\geq 40^*$	>45	>45	F
6	None	245-255	65	$\geq 70^*$	60	$\geq 70^*$	F + I
7	None	215-220	10	$\geq 45^*$	>45	>45	F
8	None	195-205	15	$\geq 45^*$	$\geq 12^*$	$\geq 12^*$	F + I
9	None	260-275	50	$\geq 70^*$	60	$\geq 75^*$	F + I
10	None	250	$\geq 40^*$	$\geq 40^*$			F
11	None	265-275	$\geq 37^*$	$\geq 37^*$	$\geq 70^*$	$\geq 70^*$	F
12	None	225-245			$\geq 18^*$	$\geq 18^*$	F
13	None	220	0	$\geq 48^*$	0	$\geq 50^*$	I
14	Proc (po)	270	23	$\geq 30^*$	$\geq 15^*$	$\geq 15^*$	F + I
Mean		247	31.9	48.1	37.9	45.0	
SD		24	20.0	13.9	22.6	22.0	

\*The entire duration was not assessed because local refractoriness was attained before conduction block. AFI = atrial flutter; CL = cycle length; F = flat; I = increasing; iv = intravenously; po = orally; Proc = procainamide; Propaf = propafenone; Pt = patient.

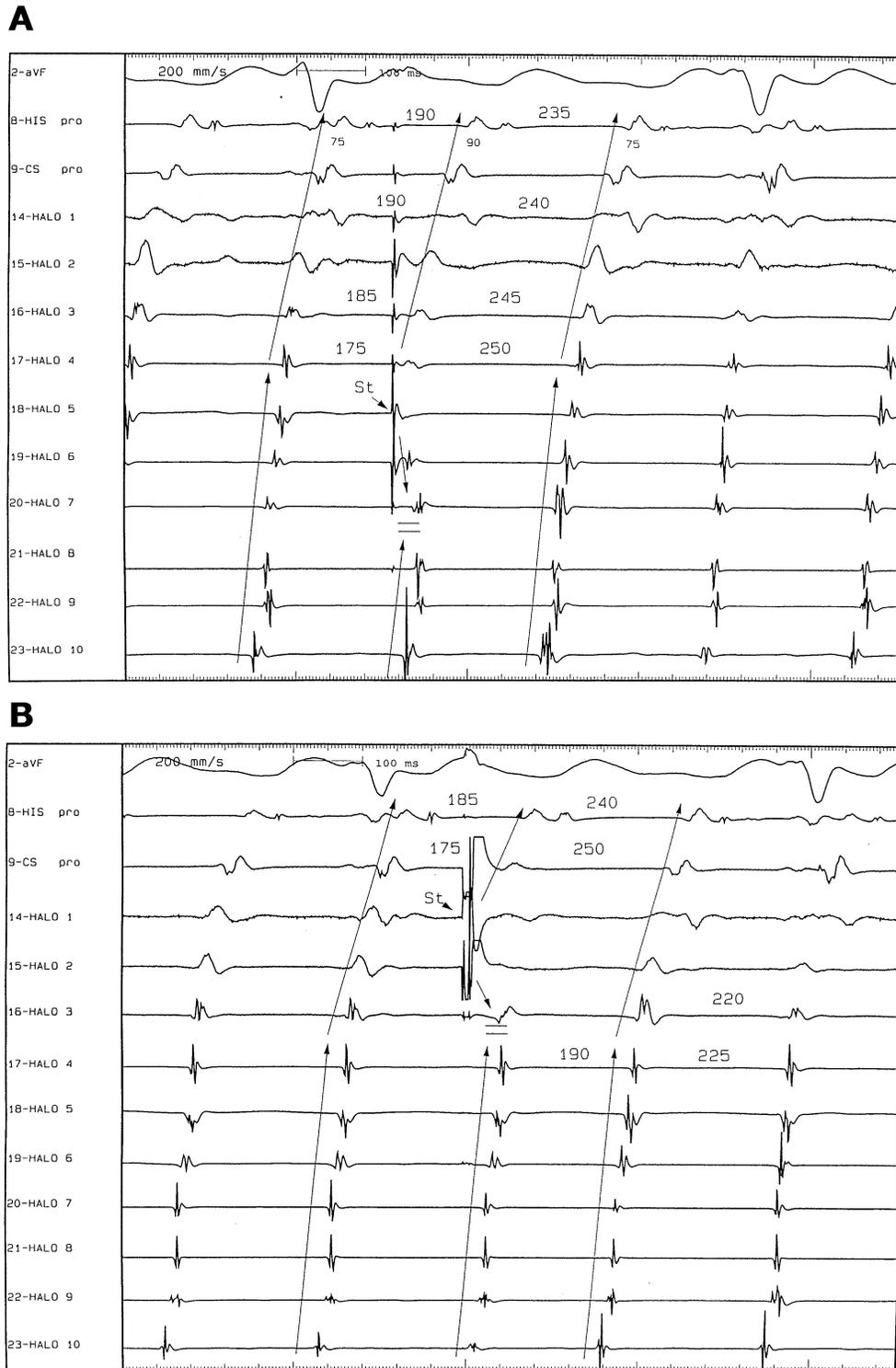


**Figure 3.** Flat resetting response during stimulation from both sites. An extrastimulus delivered at a coupling interval of 190 ms from site A (**panel A**) and from site B (**panel B**) conducts through the circuit without conduction delay. The electrograms and the activation sequence are essentially identical to those of the unperturbed flutter despite antidromic capture of several sites (Halos 7 to 9 at site A and Halos 3 and 4 at site B). HIS pro = proximal His bundle.

typically caused by interval-dependent conduction delay in the isthmus (Fig. 4A); in some cases, conduction delay occurred between the CS os and the His bundle (Fig. 4B).

**Difference in resetting response between sites.** In three patients, site-dependent differences in the resetting response were observed. In two patients, an increasing response was

seen at site A over the same range of coupling intervals that produced a flat response at site B (Fig. 5). This observation suggests that the stimulated impulse transiently changes conduction within the flutter circuit or changes the circuit path, or both. In the third patient, site A resetting resulted in a return cycle length shorter than the flutter cycle length. The conduc-

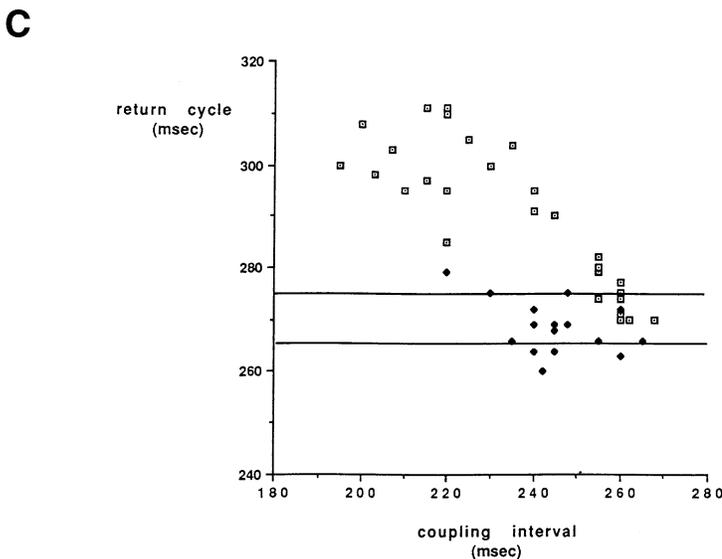
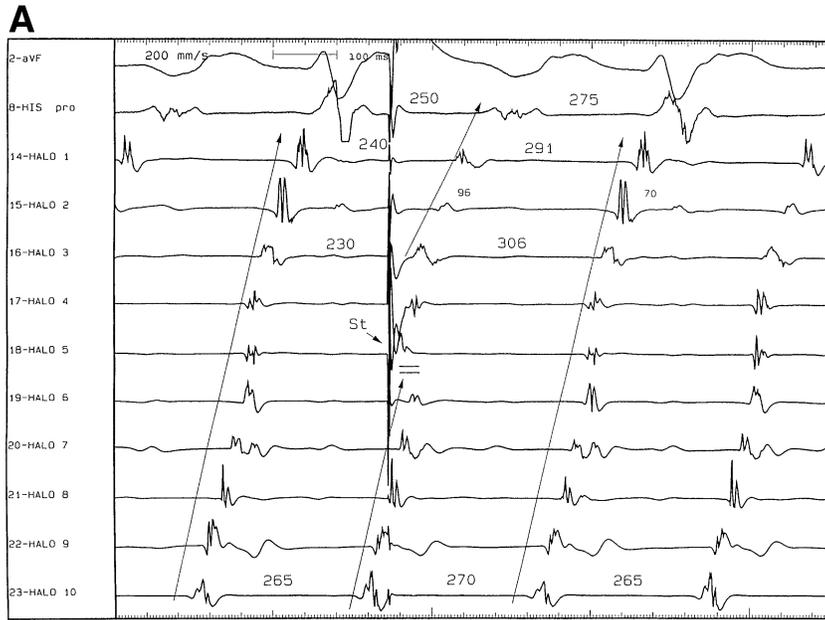


**Figure 4.** Increasing response during stimulation from both sites. **Panel A**, An extrastimulus (St) is delivered at site A with a coupling interval of 175 ms at Halo 4. The stimulated impulse encounters conduction delay in the isthmus and posterior atrial septum (sites from Halo 4 to Halo 1). This is recognized by 1) an increase in the return cycle relative to baseline at Halo sites 4 through 1; 2) an increase in the conduction time at Halo 4 and the proximal His bundle (HIS pro) (90 ms on the stimulated beat vs. 75-ms baseline); and 3) an increase in the coupling interval from Halo 4 to Halo 1. During resetting from site B (**panel B**), an increasing response is also observed, although the conduction delay occurs from the proximal CS (CS pro) to HIS pro, noted by the difference in the coupling interval and the increased conduction time between these two sites.

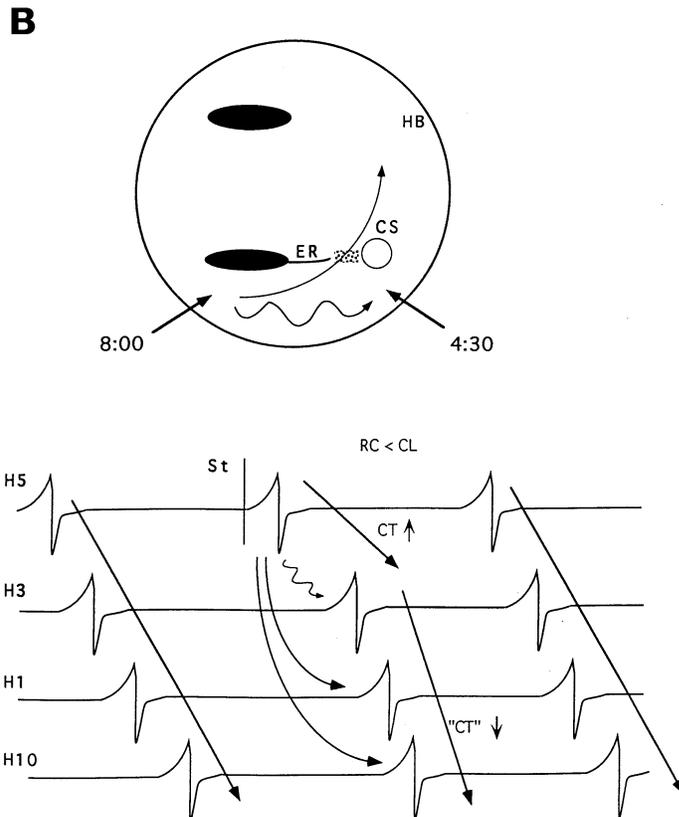
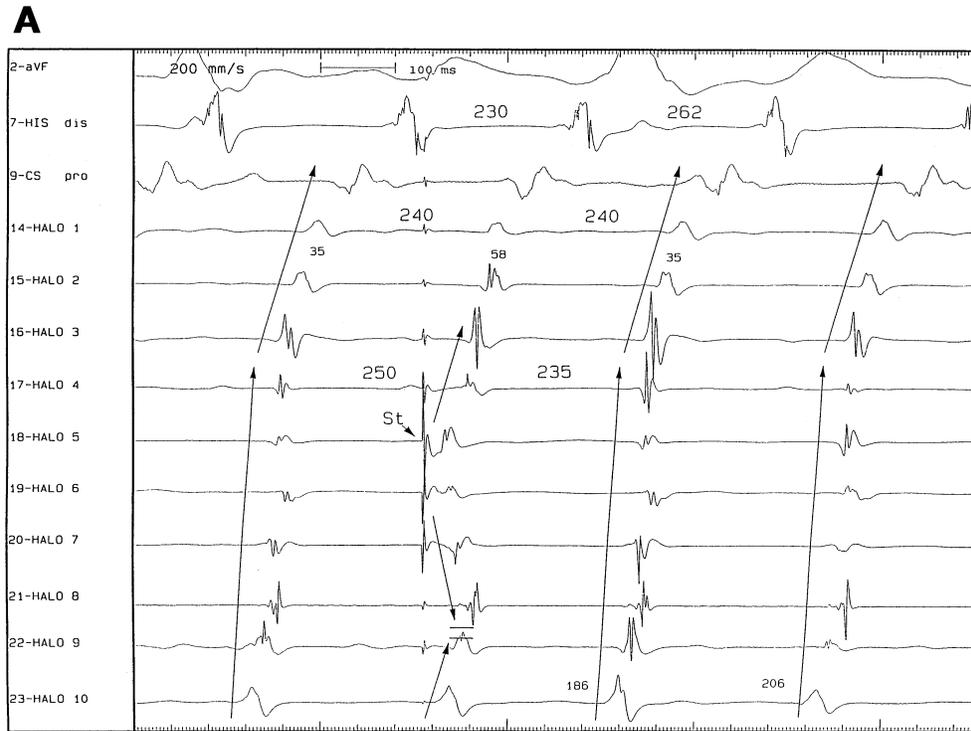
tion time required for the stimulated wave front to pass from Halo 3 to Halo 10 was shorter than that during baseline atrial flutter (Fig. 6). This finding suggests that the stimulated wave front was able to short-circuit a barrier that existed during unperturbed flutter, resulting in a change in the circuit path. Resetting from site B resulted in a flat curve for  $\geq 70$  ms with a return cycle equal to the flutter cycle length.

### Discussion

**Fully excitable gap in atrial flutter.** This study demonstrates that in the majority of cases typical atrial flutter has a fully excitable gap. Over the range of coupling intervals defined by the flat resetting response, interval-dependent conduction delay was absent in all portions of the circuit. When conduc-



**Figure 5.** Site-dependent differences in the resetting response. Delivery of an atrial extrastimulus (St) at a coupling interval of 230 ms (relative to Halo 3) at site A (**panel A**) produced interval-dependent conduction slowing in the isthmus. **Panel B** illustrates the effect of an extrastimulus at the same coupling interval delivered at site B. The extrastimulus occurs distal to Halo 1; thus, the first site that is advanced is the proximal His bundle (HIS pro) (coupling interval 230 ms). This stimulated wave front conducts through the entire circuit, including the isthmus portion, without conduction delay. Resetting response curves for the two sites are shown in **panel C**. Extrastimuli delivered at site A (**squares**) result in an increasing curve over the entire range of coupling intervals. Extrastimuli delivered at site B (**diamonds**) demonstrate a flat (coupling intervals 265 to 230 ms) plus increasing response. These findings imply that the delivery of extrastimuli at site A transiently changes conduction within the flutter circuit or changes the circuit path, or both.



**Figure 6.** Short return cycle with resetting at site A. Delivery of a premature beat at a coupling interval of 250 ms resulted in a return cycle at Halo 4 of 235 ms. This finding occurred consistently, despite orthodromic conduction delay in the isthmus (note the increase in conduction time from Halo 5 to Halo 1 on the extrastimulated beat: 58 vs. 35 ms). Note also the shorter apparent conduction time from Halo 3 to Halo 10 on the stimulated beat (186 vs. 206 ms). A shortcut of the stimulated wave front across an area of pseudoblock during unper-

turbed flutter could explain this finding (panel B). Circles and ovals = anatomic structures (CS, SVS, IVC); straight arrows = spread of conductive impulse; curved arrows = slow conduction. CL = cycle length; CS pro = proximal coronary sinus; CT = conduction time; "CT" = apparent conduction time; ER = Eustachian ridge; HB = His bundle; HIS dis = distal His bundle; H1, H3, H5, H10 = Halo 1, 3, 5, 10, respectively; RC = return cycle; St = stimulus.

tion delay did develop with closely coupled extrastimuli, the tricuspid valve isthmus and the area of the triangle of Koch were consistently the first portions of the circuit to manifest this delay.

**Previous studies of the excitable gap in atrial flutter.** Previous studies of resetting in atrial flutter (17-20) primarily focused on the demonstration of a reentrant mechanism and provided little data about the characteristics of the resetting response. Two studies (17,19) described the presence of a flat resetting curve in the majority of patients studied, but their data were limited by difficulties, such as stimulus latency, in interpreting the resetting response at the stimulation site. Entrainment has also been used to investigate the excitable gap in atrial flutter (9,10,21,22). Classic entrainment establishes the presence of reentry with an excitable gap (21). The finding that the postpacing interval approximates the flutter cycle length during concealed entrainment (9,10,22) suggests the presence of a fully excitable gap but does not quantify its duration (23).

Stambler et al. (24) recently proposed, on the basis of monophasic action potential (MAP) recordings, that a fully excitable gap existed in type I flutter in humans. However, this analysis admits to several limitations. Measurements of action potential duration provided by MAP recordings may correlate with but are not identical to measurements of refractoriness. In addition, because MAP recordings were obtained from a single atrial site outside of the flutter circuit, then cannot a priori be considered representative of all locations within the tachycardia circuit.

In contrast, the findings of our study are in conflict with several observations in human and animal models of atrial flutter. Lammers et al. (25) studied the natural variation in the atrial flutter cycle length caused by ventricular contraction. They argued that this cycle length variation implies that conduction within the circuit is refractory dependent, suggesting that recovery from refractoriness is incomplete. An alternative explanation is that changes in atrial conduction or circuit size modulated by atrial stretch produce cycle length variation. In two experimental models that closely approximate the anatomic substrate of atrial flutter in humans, Frame et al. (26,27) demonstrated a purely increasing resetting response. In contrast, Kus et al. (28) demonstrated the presence of a fully excitable gap in the same atrial incision model, although with larger animals and using different anesthesia. Even as they differ from each other, the electrophysiologic characteristics of each experimental model may be distinct from human atrial flutter.

**Difference in resetting response from different stimulation sites.** In three patients, resetting from different sites resulted in markedly different return cycle responses. A similar phenomenon was observed during resetting of ventricular tachycardia (16). This finding could represent a transient change in the anatomic or electrophysiologic properties of the circuit caused by the stimulated impulse, perhaps due to alteration of a refractory-dependent circuit barrier (Fig. 6) (16). The atrial flutter circuit appears to be largely anatomically determined; however, there are areas of the circuit where the path is

incompletely bounded, such as the potential gap between the eustachian ridge and the posterior aspect of the CS os (11).

**Limitations of the study.** Our study has some limitations. 1) Atrial extrastimuli were delivered from a large distal electrode (8 mm), at times with the use of high current outputs. Point stimulation with a smaller electrode at a low multiple of the diastolic pacing threshold might have been preferable. The present methods were used because of the requirement to capture over a broad range of coupling intervals. In one patient (Patient 11), stimuli were delivered with the use of a 2-mm distal electrode; the results in this patient were not disparate from the others. 2) Data analysis in this study was based on the assumption that the Halo and other catheters remained fixed in space. Although small catheter movements cannot be excluded, fluoroscopy and review of the individual electrograms suggested stable catheter positioning. 3) It is not certain that the Halo recordings represented sites within the tachycardia circuit; however, the Halo catheter was positioned anterior to anatomic structures that appear to form the posterior boundaries of the circuit, that is the crista terminalis and the eustachian ridge (9,11).

**Conclusions.** A flat resetting response was observed in most cases of type I atrial flutter, signifying a fully excitable gap. This finding implies that slow conduction within the isthmus is not caused by incomplete recovery from refractoriness and that it may be due to differences in anisotropy or wave front curvature. The tricuspid valve isthmus and the area of the triangle of Koch are the portions of the circuit most vulnerable to the development of interval-dependent conduction delay with closely coupled extrastimuli.

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