Sinus node sequences after atrial stimulation: similarities of effects of different methods

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SUMMARY Sinoatrial conduction is commonly assessed from features of the initial cycle after a single atrial extrastimulus or eight beats atrial pacing. In contrast, sinus node automaticity is assessed by the duration of the first interval after prolonged atrial pacing. The return cycle and initial sequences after these different methods were compared in 10 subjects with normal sinus node function and 30 patients with sick sinus syndrome. Typically, sequences after all three methods showed a maximally prolonged first interval with a progressive decrease over five or more cycles. A model of recovery from overdrive suppression was used to compute the elements of conduction time and automaticity in the first interval. The sequences which followed a single extrastimulus and pacing were similar, the only index which increased significantly with prolonged pacing was associated with the degree of suppression of automaticity. The computed component of sinoatrial conduction in the return cycle was similar for all three methods. Thus all three conventional methods which consider only the initial post-stimulation interval measure both sinoatrial conduction and sinus node automaticity. The separate components of automaticity and conduction may be assessed by analysis of the total sequence.

Assessment of sinus node function is important in those patients presenting with symptoms suggestive of the sick sinus syndrome¹ in whom diagnostic electrocardiographic features are either absent or equivocal. Investigations which may provide valuable additional information include prolonged ambulatory electrocardiographic monitoring,^{2,3} assessment of the heart rate response to autonomic interventions such as exercise and drugs,^{4,5} and intracardiac electrophysiology study.

Two basic procedures are used in the electrophysiological assessment of sinus node function. In the first the response to prolonged overdrive right atrial pacing for periods of between 30 s and 5 min is assessed.⁵⁻⁹ The interval between the last pacing stimulus and the first spontaneous atrial electrogram, "the sinus node recovery time", has been widely used as a measure of sinus node automaticity. A variant of this index is the "corrected sinus node recovery time", which is the recovery time minus

the pre-pacing cycle length.⁹ A second group of tests is used to assess sinoatrial conduction time; these are usually based on the responses of the sinus node to a single atrial extrastimulus.¹⁰ The response of the sinus node to fixed rate pacing for eight beats at a cycle length just short enough to achieve atrial capture¹¹ or more recently direct electrode recording of prepotentials from the sinus node region are alternative approaches.¹²⁻¹⁴ In recent years electrophysiological study has fallen out of favour, partly because of the considerable overlap of conventional indices between subjects with clinically normal sinus node function and those with abnormal sinus node function.

A mathematical model of recovery of the sinus node after overdrive suppression has been developed.¹⁵ When this is applied to the sequences that follow one minute of overdrive atrial pacing, separate indices of sinoatrial conduction and sinus node automaticity can be derived. Preliminary observations have suggested that the sequences that follow single atrial extrastimuli qualitatively resemble those that follow fixed rate pacing.

We have applied this mathematical model to different pacing modalities to compare their effects on sinus node function. We hoped that this might

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lead to the development of better methods for evaluation of sinus node function.

Patients and methods

PATIENT SELECTION

Thirty patients, aged 18–93 years (mean (SD) 71(14) years) were diagnosed as having the sick sinus syndrome on the basis of having symptoms of presyncope or syncope, and evidence of inappropriate sinus bradycardia, sinoatrial exit block, or sinus arrest. Many also had palpitation and evidence of atrial tachyarrhythmias, but these symptoms by themselves were regarded as not being sufficient for diagnosis of the syndrome.

Another 10 patients, aged 21–66 years (mean 37(15) years), had clinically normal sinus node function without a history of syncope of presyncope or bradyarrhythmias. These patients had electrophysiological study for investigation of regular, narrow QRS complex tachycardias.

ELECTROPHYSIOLOGICAL STUDY

Multiple 6 French electrode catheters were positioned under fluoroscopic control in fasting and non-sedated patients in whom cardioactive drugs has been discontinued for at least five elimination half-lives, and who had given their informed consent. A quadripolar electrode was positioned in the high right atrium for recording (proximal pair) and stimulating (distal pair), a tripolar electrode across the tricuspid valve to record the His bundle electrogram, and a bipolar electrode in the right ventricular apex for stimulation. Intravenous heparin 5000 units was given on completion of electrode placement. Programmed stimulation was performed with a Devices Neurolog isolated source stimulator. Surface electrocardiographic leads and three or four concurrent intracavitary electrograms were recorded at 100 mm/s chart speed on a Minograph Model 62 recorder.

After a ten minute rest period, cycle length was recorded for one minute. Programmed stimulation was then undertaken to obtain the following data:

(a) Responses after fixed rate stimulation for one minute. Responses were assessed after three to five trials of one minute of overdrive high right atrial pacing at 100 beats per minute and at 130 beats per minute. A two minute rest period was allowed between each pacing trial.

(b) Responses after fixed rate stimulation for eight beats. Pacing trials were repeated 10 times in each patient, sinoatrial conduction time being calculated as the increment in the immediate post-stimulation interval above the mean of 20 prepacing cycle lengths.

(c) Responses to single atrial premature stimuli. Stimuli with coupling interval A_1 were introduced after every eighth beat during sensed sinus rhythm. The first stimuli were placed at the end of diastole and the coupling interval was reduced by 10–20 ms until atrial refractoriness was detected. The sinus cycle lengths immediately preceding and following the premature stimulus were designated A_1 and A_2 respectively.

The sequences following atrial stimulation were digitised by means of a Hewlett Packard Model 9874A digitiser, 9872A plotter, and 9825A calculator with programs specifically written for this purpose. The first post-pacing interval was measured from the pacing spike to the initial rapid deflection of the first spontaneous high right atrial electrogram. For all the sequences that followed these different methods of stimulation we plotted cycle length against beat number. In addition, from the responses to single extrastimuli we plotted the normalised return cycle (A_2/A_1) against the normalised test cycle (A_1/A_1). Sinoatrial conduction time was estimated from this plot as described by Strauss¹⁰ as the mean value of A_2 in the last third of the zone of reset minus the mean value of A_1 .

MATHEMATICAL MODEL

The mathematical model we used was developed by Dr Arie Helfgott in this laboratory.¹⁵ In brief, if responses after overdrive suppression are the consequence of a single elimination or degradation process (such as clearance of extracellular potassium), and if constant action potential duration, constant difference between maximum diastolic and threshold potentials, capture and reset of the sinus node by all atrial extrastimuli, and absence of pacemaker shifts are assumed, recovery may be regarded as depending solely on the increase in the slope of phase 4 depolarisation.¹⁵ From this it can be shown that recovery and decrease in cycle length conforms to an exponential equation (Fig. 1):

$$T_j = T_\infty + (T_1 - T_\infty) \cdot q^{j-1}$$

In this relation, j is an arbitrary notation for any beat in the sequence, T_j its cycle length, T_∞ the asymptotic cycle length to which recovery tends, and q is simply a measure of the rate of recovery (the common ratio) during the sequence.

COMPUTATIONS

Sequences were regarded as being suitable for fitting to the model if the following criteria were satisfied: (a) progressive decrease in post-pacing cycle length until at least the fifth interval, suggesting at least a degree of suppression of automaticity by atrial stimulation; (b) there were no ectopic or escape beats in

Fig. 1 Schema illustrating sinus node recovery after atrial stimulation. Post-pacing cycle length is plotted against post-pacing beat number. Closed circles represent measured intervals and open circle the first interval extrapolated from the curve of best fit to the rest of the sequence. The first interval, the conventional sinus node recovery (SNRT) has components relating to composite sinoatrial conduction time (SACT) and an automatic sinus node interval with an increment (ΔT_1) due to suppression of automaticity by atrial stimulation. As the sinus node recovers the subsequent sequence takes the form of an exponential (decaying geometric progression with common ratio, q) tending towards an asymptotic cycle length (T_∞). Reproduced with permission from PACE, 1984;7:735–48.

the sequence; (c) no change in P wave morphology or atrial activation sequence to suggest pacemaker shift to a focus other than the sinus node.

Atrial electrograms do not directly measure sinus node activity. In particular, after atrial stimulation which captures the sinus node, the first interval must contain two components; an automatic interval and an additional component of sinoatrial conduction into and out of the sinus node from the electrode (Fig. 2). If anterograde (sinoatrial) conduction time is regarded as being constant, then electrograms after the first cycle accurately measure the recovery of automaticity. Accordingly, we used a computer program based on non-linear least squares techniques to obtain the curve of best fit to the second and subsequent cycles of all “acceptable” sequences, and from these we extrapolated a theoretical first automatic cycle. Computed sinoatrial conduction time was then derived as the difference between the measured first post-pacing cycle length and this extrapolated theoretical first cycle length (see Results). In the relation described, potential indices of sinus node automaticity are q , T_∞ , and the increment in the first interval (T_1) due to suppression of automaticity ($\Delta T_1 = T_1 - T_\infty$).

For successful fitting of sequences to the model

Fig. 2 Ladder diagram representing the sinus node (SN) and high right atrium (RA), and recording of high right atrial electrograms (A). R and S are the recording and stimulating pairs of the atrial electrode catheter. After the last atrial extrastimulus which captures the SN (either with fixed rate pacing or a single extrastimulus), retrograde conduction (CTa_{in}), the SN automatic interval (Ta), and anterograde conduction time (CTa_{out}) make up the first interval (T_1) as recorded in the RA. If subsequent sinoatrial conduction times are constant, the measured intervals T_2 , T_3 , etc., reflect subsequent SN automatic intervals Tb , Tc , etc. Reproduced with permission from PACE, 1984;7:735–48.

the following were regarded as necessary: (a) ΔT_1 , computed sinoatrial conduction time and $T_\infty > 0$; (b) $1 > q > 0$; (c) residual mean square < 1000 . The multiple correlation coefficient R^2 was used as a measure of goodness of fit and was usually > 0.98 .

STATISTICAL ANALYSIS

Data are presented as means (1 SD). Indices in each group after single extrastimuli were compared with indices after atrial pacing by means of Student's paired t test. A given index in the two patient groups was compared by means of an unpaired Student's t test. A p value < 0.05 was regarded as significant.

Results

CLINICAL INDICES

Tables 1 and 2 show basic electrophysiological data in the groups with normal and abnormal sinus node function respectively. Both mean age and resting cycle length were significantly greater in those with the sick sinus syndrome ($p < 0.0001$ for both).

SINOATRIAL CONDUCTION TIME CALCULATED FROM ATRIAL EXTRASTIMULI

In nine of 10 patients with normal sinus node function and in 23 of 30 patients with the sick sinus syn-

Sequences after atrial stimulation

Table 1 Basic electrophysiological data in 10 patients with normal sinus node function

Case No	CL (ms)	T ₁ Strauss (reset) (ms)	T ₁ Narula (ms)	SNRT 100 bpm (ms)	SNRT 130 bpm (ms)	SACT APB (ms)	SACT		SACT computed after		
							8 beats pacing (ms)	APB (ms)	8 beats pacing (ms)	FRP 100 bpm (ms)	FRP 130 bpm (ms)
1	865	1108	1160	1242	1216	173	225	116	69	45	18
2	815	1103	1093	1177	1210	168	145	nc	84	61	46
3	430	629	625	—	626	124	94	nc	52	—	59
4	820	883	1121	1154	1114	206	371	127	216	211	nc
5	850	1090	1114	1189	1098	166	189	84	64	53	82
6	690	868	873	921	886	124	175	nc	88	140	119
7	580	696	—	—	654	93	—	84	—	—	92
8	900	1069	—	1185	1124	nc	—	89	—	10	nc
9	830	1003	989	1047	979	160	194	108	115	144	149
10	745	944	947	869	956	281	237	111	91	68	208
Mean	753	939	990	1085	986	166	204	103	97	92	96
(1 SD)	148	171	178	126	211	55	81	17	52	67	61

CL, resting cycle length; T₁ Strauss and T₁ Narula, mean first interval after single atrial extrastimulus or eight beats atrial pacing during Strauss and Narula conduction time determinations; SNRT, sinus node recovery time; SACT APB, sinoatrial conduction time after single extrastimuli; FRP, fixed rate pacing; SACT 8 beats pacing, sinoatrial conduction time after eight paced beats; —, not done; nc, unable to derive or compute sinoatrial conduction time after single extrastimulus from post-stimulation sequence by application of the model.

Table 2 Basic electrophysiological data in 30 patients with sick sinus syndrome

Case No	CL (ms)	T ₁ Strauss (reset) (ms)	T ₁ Narula (ms)	SNRT 100 bpm (ms)	SNRT 130 bpm (ms)	SACT APB (ms)	SACT		SACT computed after		
							8 beats pacing (ms)	APB (ms)	8 beats pacing (ms)	FRP 100 bpm (ms)	FRP 130 bpm (ms)
1	740	1120	860	1390	1250	141	116	115	nc	353	132
2	1040	1307	1323	1267	1052	212	285	147	143	nc	206
3	870	1198	1136	1287	1319	288	286	157	182	96	189
4	905	1084	1080	1288	1615	188	199	217	142	261	523
5	975	1133	1092	1246	1196	212	184	nc	163	244	237
6	1130	1197	—	3699	4345	52	—	nc	—	nc	nc
7	1210	1338	1675	2045	1777	nc	497	269	324	nc	nc
8	1115	1256	1268	1426	1425	130	113	69	110	138	123
9	1090	1236	1323	1227	957	162	114	98	91	nc	159
10	1020	1243	1241	1340	1301	230	211	189	154	296	89
11	730	1015	946	1767	2884	212	224	237	204	nc	nc
12	1140	1324	1346	1087	1079	131	148	61	106	132	23
13	1450	1631	1626	1543	1491	72	84	nc	27	nc	nc
14	1000	1228	1238	1357	1585	192	220	nc	164	258	275
15	1165	1405	1492	1279	1032	198	247	nc	81	137	nc
16	1130	1333	1322	1542	1935	156	157	104	105	205	97
17	1090	1193	1131	924	885	181	194	223	188	35	nc
18	1300	nc	—	1475	1594	nc	—	—	—	nc	nc
19	750	1014	—	1348	1568	nc	—	nc	—	442	nc
20	910	1343	—	1403	1344	nc	—	141	—	222	nc
21	730	886	—	973	1093	157	—	103	—	131	178
22	800	921	—	1082	923	nc	—	nc	—	190	81
23	1155	1066	—	1156	1152	291	—	111	—	94	135
24	1225	1556	1497	1239	—	285	388	271	245	nc	—
25	825	1272	1320	1288	1301	209	240	126	143	143	330
26	1020	1350	1421	939	2373	313	406	253	302	16	nc
27	1040	840	1139	1121	1181	nc	304	nc	nc	58	197
28	1015	1182	1172	1280	1149	155	159	131	127	81	49
29	935	1253	1277	1387	1455	309	270	nc	176	358	nc
30	1165	nc	—	2036	2231	nc	—	—	—	nc	nc
Mean	1022	1212	1269	1415	1541	195	229	159	159	185	178
(1 SD)	179	182	200	506	707	70	103	67	71	114	119

See footnote to Table 1 for abbreviations.

Fig. 3 Electrocardiographic lead (L)II showing prolongation of not only the first but also subsequent cycle lengths (in ms) after a single atrial extrastimulus (S). (Measurements made from intracardiac recordings).

drome, sinoatrial conduction time after single extrastimuli could be derived from the plot of A_r/A_1 against A_1/A_1 (Tables 1 and 2). In those in whom it could not be calculated, either the points were widely scattered or, in the patients with sick sinus syndrome, there was no reset zone (3/7) or probable sinoatrial exit block (2/7). Sinoatrial conduction time in the patients with normal sinus node function (166 (55)ms) was not significantly different from that in the patients with sick sinus syndrome (195 (70)ms).

SINOATRIAL CONDUCTION TIME AFTER FIXED RATE ATRIAL PACING (EIGHT BEATS)

In eight patients with normal sinus node function and in 22 patients with the sick sinus syndrome, sinoatrial conduction time was assessed by the method described by Narula *et al*,¹¹ and mean values were 204(81)ms and 229(103)ms, respectively (difference not significant).

SINUS NODE RECOVERY TIME

After atrial pacing at 100 beats per minute, mean sinus recovery time was significantly greater ($p < 0.0001$) in the patients with sick sinus syndrome (1415 (506)ms) than in those with normal sinus node function (1085 (126)ms). The sinus node recovery time at 100 beats per minute could not be obtained in two patients with normal sinus node function whose resting cycle length was less than 600 ms. Similar differences between those with normal and abnormal sinus node function were found after pacing at 130 beats per minute.

GROSS ANALYSIS OF SEQUENCES AFTER ATRIAL STIMULATION

Figure 3 shows an electrocardiographic recording of the typical events after an atrial extrastimulus in the zone of reset. Figure 4 illustrates this result as a plot of cycle length against beat number. After the return cycle there was a progressive decrease in cycle length, indicating suppression and then progressive recovery of automaticity.

Fig. 4 Plot of cycle length against beat number during estimation of sinoatrial conduction time by single atrial extrastimulus (A_1). For purposes of illustration, responses to many extrastimuli are excluded; all followed the same pattern. The extrastimuli are shown in the lower half of the figure. After these extrastimuli, sequences had a maximally prolonged first interval in the return cycle (A_r) and then a progressive decrease in subsequent cycles (A_{r+1} , A_{r+2} , etc). Reproduced with permission from PACE, 1984;7:735-48.

Cycle length decreased until after the fourth post-stimulation interval in seven of the 10 patients with normal sinus node function and 19 of the 30 with abnormal sinus node function, when test extrastimuli were introduced during the zone of reset. This decrease often continued until the next extrastimulus was given eight cycles later.

In all eight patients with normal sinus node function and in 20 of 22 with abnormal sinus node function, sequences after atrial pacing for eight beats had the same form—that is with maximally prolonged first post-pacing interval and a decrease in subsequent cycles. Sinoatrial exit block and widely scattered cycle lengths made sequences in the other two patients with sick sinus syndrome unsuitable for detailed analysis by the model. Sequences of post-pacing intervals were similar in most of the trials after one minute of atrial pacing. Cycle length tended to decline, irrespective of the pacing mode (after

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pacing at 100 beats per minute in 27/30 trials in the patients with normal sinus node function and in 56/95 trials in the patients with sick sinus syndrome). Thus, the mathematical model could be used to compare the effects of the different methods.

COMPUTED INDICES AND ANALYSIS OF SEQUENCES

After single extrastimuli

Thirty nine of the 45 sequences suitable for computation in those with normal sinus node function and 170 of 208 in patients with sick sinus syndrome were successfully fitted. With the exception of one patient with normal sinus node function and one with sick sinus syndrome, all 25 patients in whom indices could be computed were from the 32 in whom sinoatrial conduction time could be derived as described by Strauss *et al.*¹⁰ In the other patients, scatter of cycle lengths, sinoatrial exit block, or frequent spontaneous extrasystoles prevented the derivation of either the conventional or the computed sinoatrial conduction time. When the Strauss conduction time could be derived but the sequences were unsuitable for computation, the post-pacing sequences did not show decay of cycle length for more than four intervals.

A comparison of results in the six patients with normal sinus node function and in the 17 with the sick sinus syndrome in whom sinoatrial conduction time after single extrastimuli could be derived conventionally and computed from the model showed that the computed sinoatrial conduction time was significantly less than the conventional sinoatrial conduction time in both patient groups ($p < 0.025$ for both). This is of course to be expected because computed sinoatrial conduction time is simply conventional sinoatrial conduction time minus an element ΔT_1 that we attribute to depression of sinus node automaticity. Of considerable importance, however, is the improved ability of computed sinoatrial conduction time to differentiate between patients with a sick sinus and those without. Mean computed sinoatrial conduction time in the controls was 103 ms with a standard deviation of 17 ms, giving a "range" (mean (2 SD)) of 69–137 ms. Nine of the 18 patients with sick sinus syndrome (50%) fell outside this range. Mean sinoatrial conduction time derived by the method of Strauss was 166 ms with a standard deviation of 55 ms, giving a "normal" range of 56–276 ms, which includes all but four of the sick sinus group.

Of the indices of automaticity after an atrial premature beat, T_∞ was significantly greater in those with sick sinus syndrome ($p < 0.025$), while q and ΔT_1 were not significantly different from values in patients with normal sinus node function.

After eight beats fixed rate pacing

Computed indices in both groups of patients strongly resembled indices derived after single extrastimuli and overdrive pacing for one minute. The mean values of ΔT_1 were intermediate between those after single atrial extrastimuli and atrial pacing at 100 beats per minute and were not significantly different (178 (51) ms in controls and 172 (112) ms in those with sick sinus syndrome) in the two patient groups.

As was found after a single extrastimulus, computed sinoatrial conduction times (97 (52) ms in controls and 159 (71) ms in the sick sinus syndrome) were significantly different ($p < 0.025$) in the two patient groups. T_∞ was significantly longer in the group with sick sinus syndrome (1003 (187) ms) than in the controls (721 (111) ms, $p < 0.0005$).

After one minute of fixed rate pacing

The longer sinus node recovery time in patients with the sick sinus syndrome was associated with a significantly greater asymptotic cycle length T_∞ ($p < 0.005$) and computed sinoatrial conduction time ($p < 0.05$). ΔT_1 , an index of the extent of suppression of the sinus node, was no different in controls and those with abnormal sinus node function. The common ratio q was also similar between the two groups.

COMPARISON OF RESULTS AFTER SINGLE EXTRASTIMULI AND AFTER FIXED RATE PACING

Indices indicating effects of a single extrastimulus, eight beats, and one minute of atrial pacing are compared in Table 3. The mean value of the first post-stimulation cycle length was not significantly different in either group of patients after a single extrastimulus or atrial pacing for eight beats or one minute.

Of all the computed indices, only ΔT_1 was significantly greater ($p < 0.05$) after fixed rate pacing (100 beats per minute) than after a single atrial extrastimulus. This held whether sinus node function was normal or abnormal. The common ratio q increased significantly ($p < 0.05$) with fixed rate pacing in those with the sick sinus syndrome but not in controls. The indices T_∞ and computed sinoatrial conduction time were not significantly different after the different methods of stimulation.

Discussion

We examined in detail sequences that followed all pacing modalities used in conventional assessment of sinus node function. The "normal" patients were not strictly a control group for patients with sick

Table 3 Comparison of computed indices after single extrastimuli and overdrive atrial pacing

	Single extrastimuli	8 beats pacing	Overdrive pacing (1 min, 100 bpm)	Overdrive pacing (1 min, 130 bpm)
Normal:				
T ₁ (ms)	939 (171)	990 (178)	1085 (126)	986 (211)
q	0.675 (0.155)	0.698 (0.136)	0.685 (0.090)	0.687 (0.100)
ΔT ₁ (ms)	136 (78)	178 (51)	249 (131)	188 (144)
T _∞ (ms)	736 (175)	721 (111)	733 (75)	677 (111)
Computed SACT (ms)	103 (17)	97 (52)	92 (67)	96 (61)
Sick sinus syndrome				
T ₁ (ms)	1212 (182)*	1269 (200)*	1415 (506)	1541 (707)
q	0.643 (0.155)	0.706 (0.101)	0.731 (0.087)	0.652 (0.174)
ΔT ₁ (ms)	145 (143)	172 (112)	254 (130)	249 (131)
T _∞ (ms)	919 (175)*	1003 (187)*	887 (137)*	867 (148)*
Computed SACT (ms)	159 (67)*	159 (71)*	185 (114)*	178 (119)*

T₁, first post-stimulation cycle length; q, ΔT₁, and T_∞, computed indices of automaticity; SACT, sinoatrial conduction time (computed from T₁ using model of sinus node recovery); *p < 0.05 by t test for comparison of grouped mean indices in those with normal sinus node function and those with sick sinus syndrome.

sinus syndrome, because they were significantly younger and aging itself affects sinus node function¹⁶; thus a case/control study with age matching is needed.

Although the methods proposed for indirect assessment of sinoatrial conduction time,^{10,11} are based on only the lengthening of the first post-stimulus interval after atrial extrastimulus and fixed rate atrial pacing for eight beats, they usually also reduce the prolongation of second and subsequent intervals. The time course of this ongoing depression closely resembles that seen after prolonged atrial pacing and may be attributed to depressed automaticity of the sinus node. This suggests that sinoatrial conduction time as calculated by these methods is in fact a compound measurement composed partly of sinoatrial conduction time and partly of depressed sinus node automaticity. We used a mathematical model of overdrive suppression to identify the two separate components in the overall sequence of post-pacing intervals. The model allows us to compare the extent to which each of the pacing methods individually influences sinoatrial conduction and sinus node automaticity. The model is not applicable to all patients since a few post-pacing sequences cannot be fitted to the model because of strong autonomic effects on the sinus node, spontaneous atrial activity, and sinoatrial exit block.

How valid is the model? It assumes that all sinus node cells follow the same process of recovery, that the anterograde sinoatrial conduction time of all cycles in the sequence is constant, and that there are no pacemaker shifts, or if these are present, that they contribute negligibly to the sinoatrial conduction time. There is evidence from animal experimentation that the cycle length changes seen after atrial extrastimuli relate to changes in the primary pacemaker location.¹⁷ Further, the atrial electrical

events do not correlate well with events within the sinus node.¹⁸ Even if the above assumptions are shown to be incorrect in man, certain conclusions can be drawn from this study which are most important in highlighting the limitations of widely used techniques of assessment.

CONVENTIONAL METHODS OF DETERMINATION OF SINOATRIAL CONDUCTION TIME ARE IMPURE

The derivation of sinoatrial conduction time from cycles that follow a single atrial extrastimulus or eight beats of fixed rate pacing assumes that the contribution of depression of automaticity is an insignificant part of the return cycle. The post-pacing sequences observed in this study strongly suggest that this does not hold. The results indicate that depression of automaticity either because of depression of the primary pacemaker, pacemaker shift,¹⁷ or both together, may contribute up to 50% of the prolongation of the return cycle over the pre-pacing cycle length. Although suppression of automaticity by atrial extrastimuli has been shown in both experimental animal preparations and in man¹¹ it has been considered to be of only minor importance.

Other factors affecting automaticity may also operate when sinoatrial conduction time is estimated by atrial pacing. At times, pacing at a cycle length within 30–50 ms of that of the sinus node may result in acceleration due to electronic interaction and shortening of action potential duration¹⁹ and isorhythmic sinoatrial dissociation.²⁰ Furthermore, computed sinoatrial conduction time more reliably differentiates between controls and those with sick sinus syndrome than do conventional indirect methods of estimation of sinoatrial conduction time. The

mean computed values for sinoatrial conduction time showed a 56 ms difference between sick sinus patients and controls. The difference derived conventionally from the same data was 29 ms. This difference is compounded by the much reduced standard deviation of the computed sinoatrial conduction time of the normal group (17 ms) as compared with the conventional sinoatrial conduction time (55 ms). Thus only four sick sinus patients could be identified by conventional methods, whereas nine were identified by the computational method.

SEQUENCES AFTER SINGLE ATRIAL EXTRASTIMULI AND FIXED RATE PACING ARE QUALITATIVELY SIMILAR AND DIFFER ONLY IN THE EXTENT OF SINUS NODE SUPPRESSION

Observations on the sequences that follow both single atrial extrastimuli and atrial pacing showed that most had a maximally extended first interval with a decline in the prolongation in subsequent cycles. The most obvious effect of prolonged pacing was greater suppression of automaticity (reflected by ΔT_1), and this effect occurred whether sinus node function was normal or abnormal. Other indices computed by fit to the model showed pronounced similarity. In particular, the different methods of stimulation gave the same mean computed sinoatrial conduction time. The asymptotic cycle length that followed recovery was no different with the various methods and probably reflects only resting sinus node automaticity.

SUPPRESSION OF THE SINUS NODE BY OVERDRIVE IS THE SAME IN PATIENTS WITH NORMAL AND ABNORMAL SINUS NODE FUNCTION

The only indices of automaticity which differed significantly between the two patients groups were resting cycle length and T_∞ (which as discussed may be primarily dependent on resting cycle length). As not only resting cycle lengths but also mean age were significantly different in those with normal and abnormal sinus node function, indices relating to this cycle length may have been less discriminatory if patients of similar ages had been compared.

In conclusion, this study suggests that previously used stimulation methods for electrophysiological testing of sinus node function (sinus node recovery time and sinoatrial conduction time derived from the first interval after atrial single extrastimuli or atrial pacing) are qualitatively similar and differ only in the extent of pacemaker suppression that they produce. The fact that they measure both sinoatrial conduction and sinus node automaticity may explain

their frequent failure to distinguish between normal and abnormal function, given the heterogeneous nature of bradyarrhythmias with which patients present. It might be expected that sinus node function will be better assessed by pure indices of automaticity or conduction, the latter obtained either directly by electrode recording¹²⁻¹⁴ or from application of simplified versions of the mathematical model.

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