The Relationship Between Sinoatrial Conduction Time and Sinus Cycle Length During Spontaneous Sinus Arrhythmia in Adults

By James A. Reiffel, M.D., J. Thomas Bigger, Jr., M.D., and Marvin A. Konstam

SUMMARY
It is well known that atrioventricular conduction varies as a function of atrial rate. However, rate related changes in sinoatrial conduction time (SACT) have not been examined. To determine the relationship between SACT and sinoatrial cycle length (SCL) in man, atrial and His bundle electrograms were recorded during atrial premature stimulation in each of nineteen patients with sinus arrhythmia. Ten of nineteen had asymptomatic, intermittent sinus bradycardia; 3/19 had persistent sinus bradycardia with nonspecific symptoms; 6/19 were felt to represent the sick sinus syndrome. In 18/19 individuals, there was a clearcut, inverse, linear relationship between SACT and SCL, i.e., as SCL increased, SACT decreased. Although this resembles the increase in PR interval that occurs with a decrease in atrial cycle length during atrial pacing, it contrasts sharply with the unchanged or increased PR interval that accompanies spontaneous increases in SCL. Although the range of patients' SACTs at any given SCL was large, the slope of ΔSACT/ΔSCL was remarkably similar in most patients and was quite steep. One patient had episodes of 2:1 S-A block. As predicted, these occurred only at her shortest SCLs. Possible explanations for this behavior are considered and the clinical relevance of these observations is discussed.

Additional Indexing Words: Pacing Sinus node functional testing Conduction system

Although disturbances in sinoatrial conduction have been recognized for over half a century, it is only with the advent of modern techniques that quantitative data concerning sinoatrial conduction in man have become available. For example, Eyster and Evans1 in 1915 and Levine2 in 1916 acknowledged disturbances in sinoatrial conduction but could do little more than comment on the difficulties encountered in assessing their severity from the standard electrocardiogram. Significant progress in delineating the sinoatrial conducting time (SACT) in man did not follow until 1962 when Langendorf et al.3 estimated the SACT in a patient with atrial parasystole by an elegant but necessarily incomplete analysis of the sinoatrial cycles following atrial ectopic beats. Based on the principles used in their analysis, a useful electrophysiological method for evaluating sinoatrial conduction disturbances in patients with sinus node dysfunction4,8 and for evaluating changes in the SACT produced by the administration of cardioactive agents5,12 has recently been developed. This method involves introducing premature atrial stimuli via a catheter in the right atrium and assessing the sinoatrial responses to these stimuli.5, 6, 13 In addition to its above uses, this method may be utilized to evaluate basic physiological properties of sinoatrial conduction that have hitherto gone unexamined. Using this technique, we examined the relationship between SACT and sinoatrial cycle length during sinus arrhythmia in man. Our results form the basis of this report.

Methods

The changes in SACT that occurred as the sinoatrial cycle length varied were examined in each of ten male and nine female patients with sinus arrhythmia. Ten subjects had asymptomatic, intermittent bradycardia (group 1); three subjects had persistent sinus bradycardia but nonspecific symptoms (group 2); and six subjects had a clinical presentation felt to represent the sick sinus syndrome14,16 (group 3). Seventeen of nineteen patients underwent at least 12 hours of continuous ambulatory ECG monitoring during full activity, including stair climbing, in the hospital. Two patients underwent continuous oscilloscopic monitoring in the Cardiac Intensive Care Unit. None was on cardioactive medications at the time of study. All gave informed, written consent.
Patients were studied in the cardiac catheterization laboratory in the resting, nonsedated, postabsorptive state. Under fluoroscopic monitoring, a #6 F tripolar catheter was passed percutaneously via the right femoral vein to the right atrium to lie across the tricuspid valve, and was used to record the His bundle electrogram; a #6 F quadrupolar catheter was passed via a right antecubital vein into the right atrium with one pair of poles for stimulation and one pair for recording. The stimulating electrodes were positioned along the lateral wall of the mid right atrium while the recording electrodes were positioned at the junction of the superior vena cava and the right atrium. Signals from the atrial and His bundle electrodes and the body surface ECG were displayed simultaneously on an Electronics for Medicine multichannel oscillograph and recorded on FM magnetic tape. Five to ten minute baseline recordings of spontaneous sinus rhythm were obtained prior to the initiation of atrial stimulation. Premature atrial stimuli were introduced via the stimulating electrodes during spontaneous sinus rhythm. The atrial electrogram was used to trigger a programmable Ortec stimulator. In this way, atrial premature stimuli, twice diastolic threshold, 2 msec in duration, were introduced via an isolation transformer after every eighth spontaneous sinus cycle and moved in 20 msec increments. The entire atrial diastolic period was scanned twice. Using the Electronics for Medicine recorder, the data were transferred to photographic paper for analysis at a paper speed of 100 mm/sec. When the spontaneous sinus cycle was interrupted by an atrial premature depolarization (APD), segments of the recording, termed frames, were examined sequentially. In each frame, the following atrial intervals were measured: (1) the interval between the last two spontaneous sinus P waves preceding the APD, i.e., the spontaneous sinoatrial cycle length $(A_1A_1)$; (2) the interval between the last spontaneous sinus P wave and the APD, i.e., the test cycle $(A_1A_2)$; (3) the interval between the APD and the following spontaneous P wave, i.e., the return cycle $(A_2A_3)$; and (4) the spontaneous sinus cycle immediately following the return cycle, i.e., the post-return cycle $(A_3A_4)$. After measuring these intervals, a mean sinoatrial conduction time was calculated from the plot of $A_2A_3$ vs $A_1A_2$ for all frames using previously published principles (fig. 1). The vertical line seen in this display represents an $A_1A_2$ equal to the mean spontaneous atrial cycle length in sinus rhythm as estimated by the mean of all $A_1A_2$ intervals $(A_1A_2)$. The average number of frames per patient and therefore $A_1A_2$s was 97. The horizontal line represents an $A_2A_3$ also equal to the mean spontaneous atrial cycle length. Points falling on the diagonal line represent lack of reset of the sinoatrial node (SAN) pacemaker by the APD $(A_2)$. These late diastolic APDs do not penetrate and reset the SAN before it fires spontaneously and thus are followed by a fully compensatory pause. For these points $A_1A_2$ plus $A_2A_3 = 2 \times (A_1A_2)$. We have designated this portion of the graph as Zone I. APDs elicited earlier in atrial diastole yield $A_2A_3$s that fall below and to the left of the diagonal reference line as SAN pacemaker reset occurs. That is, when the APD penetrates and depolarizes the SAN prior to its next expected spontaneous firing, the SAN pacemaker is reset. The return cycle $(A_3A_4)$ is no longer fully compensatory but is greater than one spontaneous sinus cycle length $(A_1A_1)$. The value of $A_3A_4$ represents the duration of conduction from the induced APD into the SAN, at which point reset occurs, plus the time until the next SAN depolarization occurs (presumed equal to $A_1A_2$), plus the duration of conduction out of the SAN to the atrium when the next atrial depolarization occurs. Thus, $A_2A_3$ equals $A_1A_2$ plus the conduction time into and out of the SAN. Therefore, $A_2A_3$ minus $A_1A_2$ (which is represented by the distance of these points above the horizontal line) equals two times the sinoatrial conduction time. All $A_2A_3$s in this portion of the graph, which we have designated as Zone II, were averaged (the mean $A_2A_3$ is represented by the broken horizontal line) and we calculated the mean SACT (SACT) from the formula:

$$SACT = \frac{(A_2A_3) - (A_1A_2)}{2}$$

It should be pointed out, however, that some centers assign the term sinoatrial conduction time to the duration of conduction from the atrium into the SAN plus the duration of conduction out of the SAN to the atrium and hence use the formula:

$$SACT = (A_2A_3) - (A_1A_2)$$.
Each patient's frames were then sorted according to the value of $A_1A_1$, within each frame and divided into multiple subgroups with narrow ranges of $A_1A_1$s such that (1) the mean $A_1A_1$ for each subgroup was different, and (2) there were regions conforming to reset of the SAN pacemaker (Zone II) in the plots which were then generated for each subgroup in the manner described above. Two additional patients, whose data could not be included in this manner, are not included in this report. Using these plots, a mean SACT was calculated for each subgroup. For example, W.K.'s sinoatrial cycle lengths ($A_1A_1$s) ranged from 1041 to 1315 msec. His frames were divided into three subgroups with $A_1A_1$s of 1041–1164 msec (1110 msec), 1168–1210 (1188 msec), and 1216–1315 (1267 msec). Plots were generated for each subgroup (see below and fig. 4) and SACTs of 130 msec, 98 msec, and 76 msec calculated, respectively. Additionally, in eleven patients where Zone II of the original plot (the plot of $A_2A_2$ vs $A_1A_2$ for all frames) was clearly delineated and contained a large number of points (15–55), the data from all frames yielding $A_2A_2$s in this zone were regraphed to display $A_2A_2$ as a function of $A_1A_1$ (fig. 2). The diagonal line in this display represents points where $A_2A_2$s would fall if they were equal to their respective $A_1A_1$s. The upper, more horizontally oriented points represent the actual plot of $A_2A_2$ vs $A_1A_1$. The difference between the line of best fit for these points (by the least squares method) and the diagonal reference line represents twice the SACT for any given value of $A_1A_1$.

Results

Mean SACT

The clinical presentation, mean sinoatrial cycle length, and SACT as calculated by the method described are shown along with atrioventricular conduction intervals for each patient in table 1. The associated ECG abnormalities and results of continuous monitoring are shown for each patient in table 2. Observe that the values for SACT alone do not allow one to distinguish between symptomatic and asymptomatic patients in most cases (table 1; fig. 3). Asymptomatic patient I.C. and symptomatic patient D.G., for example, have very similar SACTs (111 vs 107 msec); note, however, that their basic cycle lengths are different (956 vs 1181 msec). Note also that when asymptomatic and symptomatic patients with similar cycle lengths are compared (I.W. 1193 vs D.G. 1181 msec) their SACTs are quite different (48 vs 107 msec). Therefore, not only must the absolute value of SACT be considered, but SACT must be viewed in light of the associated heart rate. Although SACT does not appear to directly correlate with heart rate from one patient to another, as noted also by Engel et al., it does in any given patient as seen below.

Changes in SACT with Changes in Heart Rate

When the frames for each patient were sorted by the value of $A_1A_1$, within each frame and divided into multiple subgroups by SCL as described above, the values of $A_2A_2$ vs $A_1A_2$ for each subgroup were displayed in the same manner as was seen in figure 1. In each plot, Zone II was identified, the mean $A_2A_2$ for Zone II calculated, and the SACT obtained. Figure 4 shows the series of subgroup plots for the patient whose full set of frames is shown in figure 1. Panels A, B, and C represent the subgroups whose $A_1A_1$s are 1110 msec, 1188 msec, and 1267 msec. The vertical, horizontal, and diagonal reference lines are generated separately for each plot, i.e., in figure 4A, the vertical
Table 1

Clinical Characteristics, Average SCLs, and Mean Conduction Times

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Etiology</th>
<th>Heart size</th>
<th>Clinical presentation</th>
<th>Mean SCL (in msec)</th>
<th>Mean SACT (in msec)</th>
<th>A-H</th>
<th>H-V</th>
<th>Pacing rate inducing A-H Wenckebach</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 1 — Asymptomatic, intermittent sinus bradycardia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A.G.</td>
<td>61</td>
<td>F</td>
<td>HCVD</td>
<td>N</td>
<td>Asymptomatic</td>
<td>745</td>
<td>119</td>
<td>111</td>
<td>35</td>
<td>*</td>
</tr>
<tr>
<td>R.J.</td>
<td>78</td>
<td>M</td>
<td>HCVD</td>
<td>B</td>
<td>Asymptomatic</td>
<td>815</td>
<td>95</td>
<td>178†</td>
<td>46</td>
<td>120†</td>
</tr>
<tr>
<td>P.H.</td>
<td>64</td>
<td>M</td>
<td>ASCVD/AS</td>
<td>N</td>
<td>Asymptomatic except for syncope 2° to transient complete A-V block</td>
<td>866</td>
<td>91</td>
<td>135</td>
<td>60</td>
<td>150†</td>
</tr>
<tr>
<td>P.S.</td>
<td>20</td>
<td>F</td>
<td>U</td>
<td>N</td>
<td>Asymptomatic</td>
<td>881</td>
<td>32</td>
<td>112</td>
<td>43</td>
<td>*</td>
</tr>
<tr>
<td>B.H.</td>
<td>23</td>
<td>F</td>
<td>RHD</td>
<td>N</td>
<td>Asymptomatic</td>
<td>951</td>
<td>97</td>
<td>133</td>
<td>36</td>
<td>150†</td>
</tr>
<tr>
<td>L.C.</td>
<td>31</td>
<td>M</td>
<td>U</td>
<td>N</td>
<td>Asymptomatic</td>
<td>956</td>
<td>111</td>
<td>113</td>
<td>46</td>
<td>150†</td>
</tr>
<tr>
<td>M.R.</td>
<td>67</td>
<td>F</td>
<td>ASCVD</td>
<td>N</td>
<td>Asymptomatic except for angina</td>
<td>1050</td>
<td>89</td>
<td>105</td>
<td>35</td>
<td>*</td>
</tr>
<tr>
<td>G.R.</td>
<td>77</td>
<td>F</td>
<td>HCVD/AI</td>
<td>N</td>
<td>Asymptomatic</td>
<td>1077</td>
<td>88</td>
<td>126</td>
<td>34</td>
<td>*</td>
</tr>
<tr>
<td>E.M.</td>
<td>49</td>
<td>M</td>
<td>HCVD</td>
<td>N</td>
<td>Asymptomatic</td>
<td>1091</td>
<td>96</td>
<td>113</td>
<td>51</td>
<td>100†</td>
</tr>
<tr>
<td>L.W.</td>
<td>73</td>
<td>M</td>
<td>U</td>
<td>N</td>
<td>Asymptomatic</td>
<td>1193</td>
<td>48</td>
<td>100</td>
<td>38</td>
<td>*</td>
</tr>
<tr>
<td><strong>Group 2 — Persistent sinus bradycardia, equivocal symptoms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.A.</td>
<td>65</td>
<td>M</td>
<td>U</td>
<td>N</td>
<td>Questionable syncope x 1</td>
<td>1110</td>
<td>89</td>
<td>100</td>
<td>48</td>
<td>*</td>
</tr>
<tr>
<td>W.K.</td>
<td>58</td>
<td>M</td>
<td>U</td>
<td>N</td>
<td>Asymptomatic</td>
<td>1187</td>
<td>102</td>
<td>188</td>
<td>79</td>
<td>130</td>
</tr>
<tr>
<td>L.O.</td>
<td>61</td>
<td>F</td>
<td>HCVD</td>
<td>N</td>
<td>Palpitations</td>
<td>1280</td>
<td>98</td>
<td>124</td>
<td>32</td>
<td>*</td>
</tr>
<tr>
<td><strong>Group 3 — Sick sinus syndrome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.F.</td>
<td>78</td>
<td>M</td>
<td>ASCVD</td>
<td>N</td>
<td>Bradycardia-tachycardia syndrome</td>
<td>881</td>
<td>128</td>
<td>141†</td>
<td>63</td>
<td>*</td>
</tr>
<tr>
<td>M.L.</td>
<td>67</td>
<td>F</td>
<td>HCVD</td>
<td>N</td>
<td>Bradycardia-tachycardia syndrome</td>
<td>994</td>
<td>131</td>
<td>188</td>
<td>52</td>
<td>*</td>
</tr>
<tr>
<td>H.B.</td>
<td>77</td>
<td>M</td>
<td>ASCVD</td>
<td>N</td>
<td>Syncope</td>
<td>1095</td>
<td>145</td>
<td>315</td>
<td>97</td>
<td>100†</td>
</tr>
<tr>
<td>D.G.</td>
<td>75</td>
<td>F</td>
<td>ASCVD</td>
<td>N</td>
<td>Bradycardia-tachycardia syndrome</td>
<td>1181</td>
<td>107</td>
<td>133</td>
<td>36</td>
<td>*</td>
</tr>
<tr>
<td>H.H.</td>
<td>19</td>
<td>M</td>
<td>U</td>
<td>N</td>
<td>Bradycardia related fatigue and DOE</td>
<td>1320</td>
<td>70</td>
<td>165</td>
<td>51</td>
<td>70†</td>
</tr>
<tr>
<td>K.K.</td>
<td>55</td>
<td>F</td>
<td>U</td>
<td>N</td>
<td>Palpitations, near syncope</td>
<td>1479</td>
<td>83 with</td>
<td>100</td>
<td>37</td>
<td>120</td>
</tr>
</tbody>
</table>

Abbreviations: U = none or unknown; N = normal; B = increased; DOE = dyspnea on exertion.
*No A-V Wenckebach at any rate.
†PH interval.
Group 3—Sick sinus syndrome

<table>
<thead>
<tr>
<th>Patient</th>
<th>ECG conduction abnormalities</th>
<th>Min. sinus rate</th>
<th>Max. sinus rate</th>
<th>Holter monitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.F.</td>
<td>IAVB</td>
<td>40's</td>
<td>80's</td>
<td>Sinus arrest vs blocked APDs,* PAT</td>
</tr>
<tr>
<td>M.L.</td>
<td>IAVB</td>
<td>50</td>
<td>110</td>
<td>Rare APD</td>
</tr>
<tr>
<td>H.B.</td>
<td>IAVB, LAFB</td>
<td>26</td>
<td>80</td>
<td>S-A Wenckebach, PAT with 2:1 A-V block APDs with apparent block II A-V block 2:1 S-A exit block with pauses up to 2280 msec, rare JPD and VPD</td>
</tr>
<tr>
<td>D.G.</td>
<td>None</td>
<td>45</td>
<td>90</td>
<td>Freq. APDs</td>
</tr>
<tr>
<td>H.H.</td>
<td>None</td>
<td>40</td>
<td>85</td>
<td>Marked SA, 2:1 S-A exit block S-A Wenckebach, A-V Wenckebach, apparent block II A-V block</td>
</tr>
<tr>
<td>K.K.</td>
<td>None</td>
<td>12</td>
<td>78</td>
<td>VPDs, JPDs, APDs, 3-5 sec asystolic periods, junctional premature depolarization</td>
</tr>
</tbody>
</table>

Abbreviations: SB = sinus bradycardia; SA = sinus arrhythmia; RAD = right axis deviation; IAB = intra-atrial block; IAVB = incomplete A-V block (prolonged PR interval); LAFB = left anterior fascicular block; LBBB = left bundle branch block; CHB = complete heart block; PAT = paroxysmal atrial tachycardia; RBBB = right bundle branch block; APD = atrial premature depolarization; JPD = junctional premature depolarization; VPD = ventricular premature depolarization.

*ICU monitor = not Holter monitor.
Interestingly, this figure suggests that two patients have SACTs which approach zero at their longest cycle lengths. The plots for one such patient, K.K., whose curve is labelled C in figure 5 are shown in figure 6. Note that figure 6A, representing the subgroup with an $A_1A_1$ of 1368 msec, appears similar to the plots shown in figure 4. However, when $A_1A_2$s occur earlier in the cycle than the plateau of Zone II, the $A_2A_3$s shorten, and may be even less than $A_1A_1$ (labelled Zone III). Figure 6B shows the results using the subgroup of K.K.'s longest sinoatrial cycle lengths ($A_1A_1 = 1732$ msec). All $A_2A_3$s appear to be less than or similar to the $A_1A_1$ of this subgroup, as were the $A_1A_2$s (not shown). In this particular instance, it is difficult to be sure whether the plateau phase of the $A_2A_3$ response represents reset of the SAN pacemaker without a change in sinus cycle length, i.e., Zone II behavior (in which case the calculated SACT would approach zero), or whether other factors, including a possible inadequacy of the method in patients with marked sinus arrhythmia, are present. This uncertainty is indicated by the broken segment of curve C in figure 5. Figure 6C, the plot for K.K.'s subgroup with the shortest cycles ($A_1A_1 = 1188$ msec), reveals no $A_2A_3$ less than $A_1A_1$ and no Zone III behavior. The mechanism for the variation in the $A_2A_3$ response noted with different $A_1A_1$ subgroups in this patient will be discussed subsequently. Figure 6C also demonstrates the interesting finding of 2:1 sinoatrial exit block. The upper horizontal line represents an $A_2A_3 = 2(A_1A_1)$. The point falling nearest the upper diagonal line indicates an APD which failed to reset the SAN pacemaker but caused sinoatrial exit block of the next beat. The two points falling below and to the left of this line represent two responses where the APD reset the SAN pacemaker and caused exit block of the subsequent sinus depolarization. These two $A_2A_3$s are located a distance equal to one $A_1A_1$ above...
the lower points in Zone II. The point above the upper diagonal line may represent an even greater degree of sinoatrial exit block.

Beat to Beat Variation in SACT

In 11/19 patients, Zone II of their original plot, i.e.,

![Figure 6](image)

**Figure 6**
The return cycles $(A_2 A_3)$ plotted as a function of the test cycles $(A_1 A_2)$ during atrial premature stimulation for patient K.K. using only a subgroup of frames defined by a select range of $A_1 A_2$. Panel A: the subgroup of $A_1 A_2$s between 1275 msec and 1448 msec; Panel B: the subgroup of $A_1 A_2$s between 1459 msec and 2340 msec; Panel C: the subgroup of $A_1 A_2$s between 1090 msec and 1275 msec. See text for discussion of the low values of $A_2 A_3$ seen in Zone III of panel A and in all areas of Panel B. Panel C demonstrates the unusual finding of 2:1 sinoatrial exit block. To calculate the over-all SACT for this panel, one must use the formula:

$$ SACT = \frac{(SACT_1) \cdot (n) + (SACT_2) \cdot (m)}{n + m} $$

where SACT$_1$ is computed by the formula SACT$_1 = \frac{1}{2} \frac{[\bar{A}_2 A_3] - (\bar{A}_1 A_2)}{n}$, $n =$ the number of return cycles without 2:1 sinoatrial exit block measured in Zone II and used to obtain the $\bar{A}_2 A_3$, $\bar{A}_1 A_2 =$ the mean of all return cycles in Zone II not exhibiting 2:1 sinoatrial exit block. SACT$_2$ is computed by the formula SACT$_2 = \frac{1}{2} \frac{[\bar{A}_2 A_3] - 2 (\bar{A}_1 A_2)}{m}$, $m =$ the number of return cycles in Zone II with 2:1 sinoatrial exit block, $\bar{A}_2 A_3 =$ the mean of all return cycles in Zone II exhibiting 2:1 sinoatrial exit block.

Since these cycles $(A_2 A_3)$ include conduction time from atrium to sinus plus conduction time from sinus to atrium plus two sinus cycle lengths rather than just one, $2A_1 A_2$s are subtracted from $A_2 A_3$s in the calculation.

In figure 6C: SACT$_1 = \frac{1}{2} [1547-1188] = 177$ msec; SACT$_2 = \frac{1}{2} [2847-2(1188)] = 236$ msec; $n = 6; m = 3$; $SACT = \frac{(177)(6) + (236)(3)}{9} = 197$ msec.
line are more similar. Figure 7C is the plot of $A_2A_3$ vs $A_1A_1$ obtained in patient K.K. who had episodes of 2:1 sinoatrial exit block. As predicted, the episodes of exit block occur only at her shortest sinoatrial cycle lengths.

**Discussion**

The evaluation of sinoatrial conduction time (SACT) has recently become possible in man through modern intracardiac recording and stimulating techniques. Through premature atrial stimulation in a programmed sequence, the principles used by Langendorf et al. to estimate the SACT in a case with atrial parasystole can be applied to any given patient. Investigation of human sinoatrial conduction has thus far focused mainly on measuring SACTs in patients with sinus node dysfunction and on changes in SACT induced by a limited number of cardioactive medications. In the present study, we evaluated the changes in SACT that occurred as a function of spontaneous changes in sinoatrial cycle length in nineteen patients with sinus arrhythmia and a history of sinus bradycardia. Eight of nineteen had normal heart rates on the day of study. The results clearly show that sinoatrial conduction time in man varies inversely and linearly with sinoatrial cycle length — that is, SACT prolongs as sinoatrial cycle length decreases. This resembles the increase in PR interval that accompanies decreases in atrial cycle length during atrial pacing but contrasts sharply with the unchanged or

![Figure 7](http://circ.ahajournals.org/)

**Figure 7**

The return cycles ($A_2A_3$) from Zone II of the patients' original plots (the plot of $A_2A_3$ vs $A_1A_3$ using all frames) plotted as a function of the last spontaneous atrial cycle ($A_1A_1$) (as in fig. 2). Panel A, the plot for patient W.K. (whose curve in fig. 5 is labelled A and whose subgroups are plotted in fig. 4) is typical of most patients and clearly shows the variation in SACT that occurs with variations in SCL. Panel B shows the plot for patient H.B. (the patient whose curve in fig. 5 is labelled B). She demonstrates less of a change in SACT per unit change in SCL than the patient in panel A as noted by the greater similarity between the slope of the line of best fit and the slope of the diagonal reference line. Panel C is the plot for patient K.K. (whose curve is labelled C in fig. 5 and whose subgroups are plotted in fig. 6). Note that the $A_2A_3$ demonstrating 2:1 sinoatrial exit block only occur at the shorter atrial cycle lengths.
decreased PR interval that accompanies spontaneous decreases in atrial cycle length. Possible mechanisms for this phenomenon may be gleaned from *in vitro* studies of (1) conduction within the sinus node and (2) conduction in the sinus node perinodal fibers.

Conduction Within the Sinus Node

James, Bonke, and others have pointed out that the sinoatrial node (SAN) is composed of clusters of specific S-A nodal or P cells separated by relatively large areas of connective tissue and transitional cells. Several groups of these cells may discharge spontaneously and successfully propagates its impulse to the atrium is considered the dominant pacemaker of the heart. According to Bonke and Bouman et al., this dominant group often lies in the center of the node where impulse conduction is quite slow when compared to the more rapid conduction in more peripheral areas of the node. When conditions in the SAN are altered as by vagal stimulation or catecholamine administration (in contrast to sympathetic stimulation), pacemaker function may shift to another cluster of fibers. This shift in pacemaker site within the SAN may be associated with a shift in the pathways of conduction to the atrium and thus may change the time required for the SAN impulse to reach the atrium. If vagotonia were to preferentially shift pacemaker function to more peripheral areas of the node, then a decrease in sinoatrial conduction time might occur; this would be in keeping with Bouman's findings. Such a decrease in sinoatrial conduction time during increased vagal activity could accrue from (1) the more rapid impulse conduction in the peripheral rim of the node, (2) the decreased distance over which the impulse must propagate in order to reach the atrium, or (3) a favorable change in the pathway of conduction to the atrium. Our finding that SACT shortens as the cycle lengths of sinus arrhythmia increase (apparently as a result of enhanced vagotonia since sinus arrhythmia is abolished by atropine) is in keeping with such a hypothesis. Direct evidence for continuous, graded shifts in pacemaker locus under the influence of dynamic changes in autonomic balance in awake mammals is, however, not currently available. Several observations which suggest that retrograde intra-sinus node conduction slows as the paced atrial cycle length of an isolated rabbit right atrium shortens, are also consistent with our findings.

Conduction Within the Sinus Node Perinodal Fibers

The conduction properties of the perinodal fibers may also contribute to the findings of increasing SACT with decreasing sinoatrial cycle length. In contrast to the atrial muscle fiber, recovery of peak values of phase 0 amplitude and V max are markedly time dependent in the perinodal fiber, with recovery of V max occurring well after full repolarization, according to Strauss and Bigger. Moreover, these workers showed that shortening of atrial cycle length by an APD increased conduction time between the atrium and the sinus node. This is to be expected since phase 0 amplitude and V max are major determinants of conduction velocity. Shortening the cycle length during atrial pacing has a similar effect on the perinodal fiber and thus progressive lengthening of sinoatrial conduction time will accompany decreases in driven atrial cycle length. How these properties may be altered in awake, intact animals and how they may be altered by factors which alter sinus rate is also undetermined. However, it is known that high concentrations of acetylcholine have much less effect on the time-voltage course of the perinodal fiber action potential than on the action potentials of the atrial muscle cells which are remarkably abbreviated.

Exceptionally Brief SACTs at Very Long Sinoatrial Cycle Lengths

Note should be made here of the very short values of SACT that were associated with relatively long sinoatrial cycle lengths in some patients (see fig. 6). Neither changes in intra-sinus conduction nor changes in perinodal fiber conductivity could account for a calculated SACT of zero. Three additional factors, however, may account for this result. First, the effects of sinus arrhythmia must be considered. During Zone II the A2A3 interval should be equal to conduction into and out of the SAN plus the time from reset of the SAN pacemaker to the next spontaneous sinus depolarization, A3A1. However, in patients with a significant degree of sinus arrhythmia, the interval from one beat to the next constantly varies and only occasionally equals the average interval A3A1. The return cycles therefore may be greater or less than (A3A1 + 2) SACT. The longest intervals encountered during spontaneous sinus rhythm are likely to be followed by one or more shorter intervals. Should an APD interrupt what would have been a series of shorter cycles, the return cycle will be less than would have otherwise been expected (i.e., less than A3A1 + 2 SACT). Since the formula for SACT assumes the absence of sinus arrhythmia, i.e., assumes A3A1 to always be the interbeat interval, the effect of this apparently foreshortened A2A3 is to falsely lower the calculated value of SACT. For similar reasons, when the A1A3 is the shortest of all cycle lengths seen, the effect will be the opposite, i.e., the calculated SACT will be falsely high. The effect of this calculation error should tend to overestimate the degree of variation.
SACT with sinoatrial cycle length only at the extremes of the sinoatrial cycle. The variation of SACT with sinoatrial cycle length observed over the wide middle range of cycle lengths is affected little if at all by this statistical effect. When we are able to predict what any given interval would be if it were unperturbed by a preceding APD, we will be able to eliminate the error induced in calculations of SACT at the extremes of cycle lengths in sinus arrhythmia. Fortunately the effects on SACT are opposite at each extreme of sinus cycle length and negate each other when a mean SACT is calculated from the A2A3 vs A1A2 plot for all frames.

Second, Klein et al.22 showed that at least in isolated rabbit atria, early APDs may induce a shortening of the subsequent sinus node cycle, which, depending on conduction phenomena, may or may not manifest itself as a shortened atrial return cycle. Thus, A2A3 may be less than A1A1 + 2 SACT or even less than A1A1. If this occurs in the intact human heart, and if the extent of atrial diastole over which this phenomenon occurs varies with sinoatrial cycle length, it could conceivably shorten all return cycles at long sinoatrial cycle lengths and alter none at short sinoatrial cycle lengths. This would not only falsely lower the calculated SACTs at long cycle lengths as in figure 6B, but might explain why only some A2A3s were less than A1A1 + 2 SACT in figure 6A (the middle range of K.K.’s sinoatrial cycle lengths) and why none at all were shortened at even shorter sinoatrial cycle lengths (fig. 6C).

Third, and probably of least significance in the calculation of short SACTs at long sinoatrial cycle lengths, is a decrease in the return cycle duration due to electronic shortening of the sinus nodal cell action potential.28 This phenomenon has been shown only for the brief portion of the atrial cycle where Zone I and Zone II intersect and only while the SAN pacemaker is still not reset by the APD. The effect is to pull the A2A3 points below and left of the line of non-reset in the plot of A2A3 vs A1A2 and therefore to mimic a region of reset. As this shift is gradual, many of these points fall below those truly in the plateau of Zone II; but if they are included as Zone II points (since they may not be easily recognizable on the graph), they could falsely lower the calculated value for A2A3 and thus lower the calculated SACT.

Conclusion

Whatever the underlying electrophysiological mechanism, the observations on the changes in SACT which occur with alterations in sinoatrial cycle length are important in themselves and, in light of the current interest in SACT, are of considerable clinical relevance. For example, in order to make the best use of the value obtained for SACT as a diagnostic parameter for sinus node dysfunction, the range and behavior of SACT in normals should be fully determined first. In order to interpret the effect of a medication on the SACT, one must know the direction and degree of change in SACT to be expected simply from a change in sinoatrial cycle length induced by the drug. Conclusions based on the values of SACT alone such as currently exist in the literature must be evaluated with caution. Although these statements seem almost obvious, to our knowledge, they have not been previously considered. While our observations were made only in patients who had a history of sinus bradycardia, the relationship between SACT and SCL was remarkably similar in 18 of 19 patients, despite varied clinical presentations and varied heart rates (from bradycardia to normal) on the day of study. Although the present study is not conclusive on this point, our findings suggest that a similar relationship may exist in patients without a history of sinus bradycardia as well. Only with a complete understanding of the basic physiological properties of sinoatrial conduction such as the one reported herein can the measurement of SACT reach its full potential of clinical usefulness.

References

The Relationship Between Sinoatrial Conduction Time and Sinus Cycle Length During Spontaneous Sinus Arrhythmia in Adults

JAMES A. REIFFEL, J. THOMAS BIGGER, JR. and MARVIN A. KONSTAM

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