

# Origin of the Third Heart Sound

## II. Studies in Human Subjects

YUKIO OZAWA, M.D., DAMON SMITH, B.M.E., AND ERNEST CRAIGE, M.D.

**SUMMARY** We report noninvasive and invasive studies designed to clarify the mechanism of the third heart sound ( $S_3$ ) in humans. The noninvasive observations were made using a miniature accelerometer attached to the skin surface at the cardiac apex. In subjects with no  $S_3$ , the tracings were either flat or showed very low undulations throughout diastole. Those with an  $S_3$ , however, demonstrated a distinct reduction of acceleration, or negative jerk, of the rapid filling movement at the apex at the time of the sound. The invasive studies in the cardiac catheterization laboratory consisted of frame-by-frame measurements of left ventricular dimensions in the transverse and long axes during early diastole in patients with diastolic overload abnormalities to investigate the temporal sequence of filling in these two principal axes. The maximal long-axis filling rate occurred after the short axis, a finding that helps to resolve a discrepancy noted in the time of maximal short-axis filling and  $S_3$  production. These studies support the concept that the  $S_3$  is due to a sudden intrinsic limitation of longitudinal expansion of the left ventricular wall during early diastolic filling, resulting in a negative jerk that is transmitted to the skin surface.

FOR ALMOST a century, the third heart sound ( $S_3$ ) has been known to be an ominous physical sign when found in the presence of a diseased heart.<sup>1</sup> Recently, the clinical value of  $S_3$  has been further established by its use as a signal for catheterization and consideration of surgery in aortic regurgitation<sup>2</sup> and as a marker for patients in heart failure who might benefit from the administration of digitalis.<sup>3</sup>

The pathogenesis of the  $S_3$  is controversial. Our own studies have been divided into two phases: an acute precipitation of  $S_3$  in dogs by means of hypoxia with tracking of the origin of the sound through the several layers of chest wall, pericardium and epicardium,<sup>4</sup> and extension of these findings to patients with a variety of clinical problems characterized by  $S_3$  as well as normal subjects with a physiological  $S_3$ . These studies in patients have been carried out both in the noninvasive cardiac graphics laboratory and in the invasive cardiac catheterization laboratory and constitute the present report.

In the canine experiments,<sup>4</sup> we used a miniature accelerometer that was sequentially attached to the various anatomic layers and demonstrated a sharp negative jerk of the left ventricular wall at the cardiac apex, which we feel is responsible for the  $S_3$ . The noninvasive studies we describe here seek to determine the relationship of this negative jerk to various types of third sounds encountered clinically.

In the invasive studies performed in the cardiac catheterization laboratory, we investigated the temporal sequence of short- and long-axis rapid filling movements in patients who have an  $S_3$  associated with diastolic overload conditions. This study is necessary because of the previous report of Prewitt et al.<sup>5</sup> who,

using digitized measurements of the transverse or short axis obtained by M-mode echocardiography, found no consistent relationship between any aspect of filling movement and the third heart sound.

### Materials and Methods

#### Noninvasive Studies

Patients referred to the cardiac graphics laboratory at North Carolina Memorial Hospital for diagnostic purposes are routinely studied using combinations of phonocardiograms, pulse tracings and M-mode echocardiograms, as deemed appropriate to the suspected clinical problem.<sup>6</sup> Phonocardiograms were recorded using Leatham suction, air-coupled microphones with a medium filter setting. Forty-four patients were studied by our standard methods, to which we added simultaneously a tracing from the cardiac apex through a miniature accelerometer (SAA), details of which were described in part I.<sup>4</sup> Eighteen subjects, ages 22–88 years, had no  $S_3$ . Twenty-six subjects, ages 10–80 years, had an  $S_3$ . Seven of these subjects were normal, six had cardiomyopathy and 13 had volume overload, including two with an incompetent mitral valve prosthesis. For this portion of the examination, patients were supine and breathing normally.

Tracings were made on an Irex 101 or system 2 multichannel recorder at a paper speed of 100 or 200 mm/sec. The plastic base of the accelerometer (Entran Devices) is attached to the chest wall at the apex by double-sided tape. It is practically weightless (mass of approximately 1.1 g); therefore, its presence on the chest wall has a minimal effect on the motion it is designed to perceive. The inertial reference frame utilized by the accelerometer allows it to sense a true measure of motion — acceleration. The overall frequency response curve of the accelerometer and recorder electronics was essentially flat from 1 to 100 Hz. The transducer was oriented such that its sensitive axis was perpendicular to the skin surface. The sensitivity of the accelerometer to the acceleration in a direction at right angles to the sensitive axis was no more than 3%. Since no quantification of the signal is attempted, the baseline or zero level of the SAA signal is

From the Department of Medicine, University of North Carolina School of Medicine, and the C. V. Richardson Laboratory, North Carolina Memorial Hospital, Chapel Hill, North Carolina.

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Address for correspondence: Ernest Craige, M.D., 338 Clinical Sciences Building 229H, University of North Carolina School of Medicine, Chapel Hill, North Carolina 27514.

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not recorded on the tracings. This can be estimated, however, by the level of the signal in late diastole, when the acceleration signal is near zero at moderate heart rates. An upward movement of the SAA signal above the baseline correlates with outward acceleration of the skin. The microphone used to record at the mitral area was placed near the accelerometer. Recordings of the SAA signal were made with and without the microphone to ascertain that the signal was not distorted by the presence of the microphone.

### Invasive Studies

#### Patients

From the computerized files of the cardiac graphics laboratory, we selected 51 patients who had echophonocardiograms of excellent quality and who had been studied in the cardiac catheterization laboratory by left ventricular angiography. Twenty-two patients had an  $S_3$  and 29 had no  $S_3$ . Patients with regional abnormalities of wall motion due to previous infarction and patients with cardiomyopathy were excluded, since in coronary disease the complex filling patterns are not easily expressed as movement in the two principal axes, and in cardiomyopathy, there is a large relative error of measurement resulting from the minimal wall motion. (See table 1 for details of demographic and clinical features of the patient population.) Among the 22 patients with an  $S_3$  were 19 patients with diastolic overload abnormalities, two normal subjects and one patient with aortic stenosis. Among the 29 patients without an  $S_3$  were 11 with valvular disease of minor severity and 18 with chest pain, of whom 14 were free of coronary occlusive disease.

Patients with an  $S_3$  had larger end-diastolic volumes

TABLE 1. *Materials and Clinical Characteristics*

	Third heart sound	No third heart sound	
MR	10	Normal	14
MR, AR	3	MR	2
AR	2	MR, AR	2
VSD	2	AS, AR	1
Right coronary sinus to right atrial fistula	1	Mitral valve prolapse	2
		CAD (mild)	4
MS, MR, AS, AR	1	AR	4
Normal	2		
AS	1		
Total	22	Total	29
Sex (M/F)	11/11		14/15
Heart rate (beats/min)	$87 \pm 18$ ( $p < 0.02$ )		$75 \pm 12$
Cardiac index (l/min/m <sup>2</sup> )	$3.9 \pm 1.8$		$3.4 \pm 0.7$
Ejection fraction	$0.68 \pm 0.12$		$0.62 \pm 0.12$
LVEDP (mm Hg)	$14.2 \pm 7.9$		$13.1 \pm 6.2$
End-diastolic volume (ml)	$150 \pm 48$ ( $p < 0.05$ )		$98 \pm 55$
End-systolic volume (ml)	$58 \pm 30$		$43 \pm 40$

Abbreviations: MR = mitral regurgitation; MS = mitral stenosis; AR = aortic regurgitation; AS = aortic stenosis; VSD = ventricular septal defect; CAD = coronary artery disease; LVEDP = left ventricular end-diastolic pressure.

than those with no  $S_3$  ( $150 \pm 48$  vs  $98 \pm 55$  ml,  $p < 0.05$ ). Heart rates in  $S_3$  group were also somewhat higher than in the group without an  $S_3$  ( $87 \pm 18$  vs  $75 \pm 12$  beats/min.) There was, however, no significant difference between the group with an  $S_3$  and the group with no  $S_3$  in cardiac index or ejection fraction (table 1).

#### Left Ventricular Angiography

Left ventricular angiograms were obtained at cardiac catheterization in the right anterior oblique projection after injection of 40–60 ml of Renografin 76 into the chamber of the ventricle through a pigtail catheter. Cineangiography provided images of the ventricular silhouette at 50 frames/sec. Outlines of the opacified chamber were made using the single-plane method of Greene et al.<sup>7</sup> or that of Snow et al.<sup>8</sup> Patients who had some arrhythmia during opacification or whose cardiac images were not clear enough for accurate measurement were excluded. The 51 patients who constituted the study group had silhouettes of sufficient clarity that accurate measurements could be made in both the long and short axes from each of the cine frames during the diastolic phase.

The technique of measurement involved projecting the left ventricular image on ruled paper along with that of a standard 4 cm<sup>2</sup> grid for calibration purposes. The long and short dimensions were then marked on the paper for each of the sequential diastolic cine frames. The marked paper was then placed on a digitizer pad which, in turn, was interfaced with an Apple II microcomputer. This pad incorporates a special pen or marking device that allows the computer to accept distance measurements from the paper. The transverse and long axis dimensions from each frame were plotted as shown in figure 1. Changes in dimension in successive frames were then subjected to computerized calculations that provided velocity of motion as well as acceleration in each dimension throughout diastole. This information was plotted in graphic form to show velocity (fig. 2) and acceleration (fig. 3) in the long and short axes and the temporal relation of these events one to the other.

### Results

#### Noninvasive Studies

The 18 subjects with no  $S_3$  had either a flat tracing or very low undulations throughout diastole (fig. 4). In the 26 with an  $S_3$ , the sound was associated with a distinct reduction of acceleration, or negative jerk (defined as the time derivative of acceleration) of the rapid filling movement at the apex (figs. 5–8).

#### Invasive Studies

The dimensional measurements in the long and short axis as shown in figure 1 are differentiated once to yield velocity and twice to derive acceleration (figs. 2 and 3). The patient with no  $S_3$  in figure 2 (velocity) and figure 3 (acceleration) demonstrates inconspicuous and synchronous filling movements in the long and short axes. The  $S_3$  case however, shows exaggerated

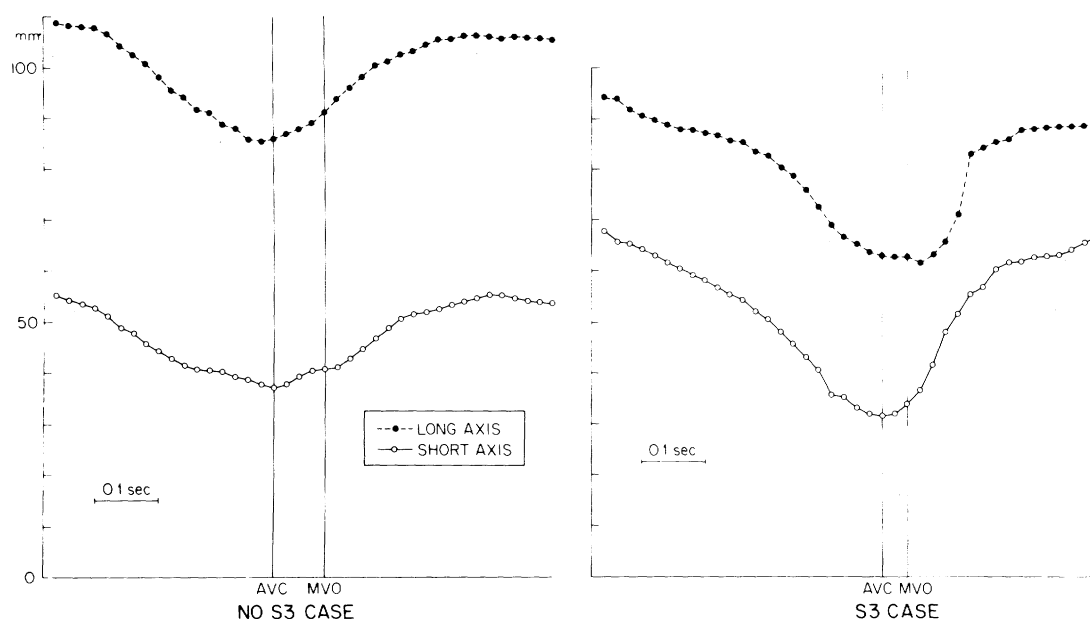


FIGURE 1. Dimensional measurements of the long and short axes for each cineangiographic frame in a case with no third heart sound ( $S_3$ ) (left) and an  $S_3$  (right). AVC = aortic valve closure; MVO = mitral valve opening.

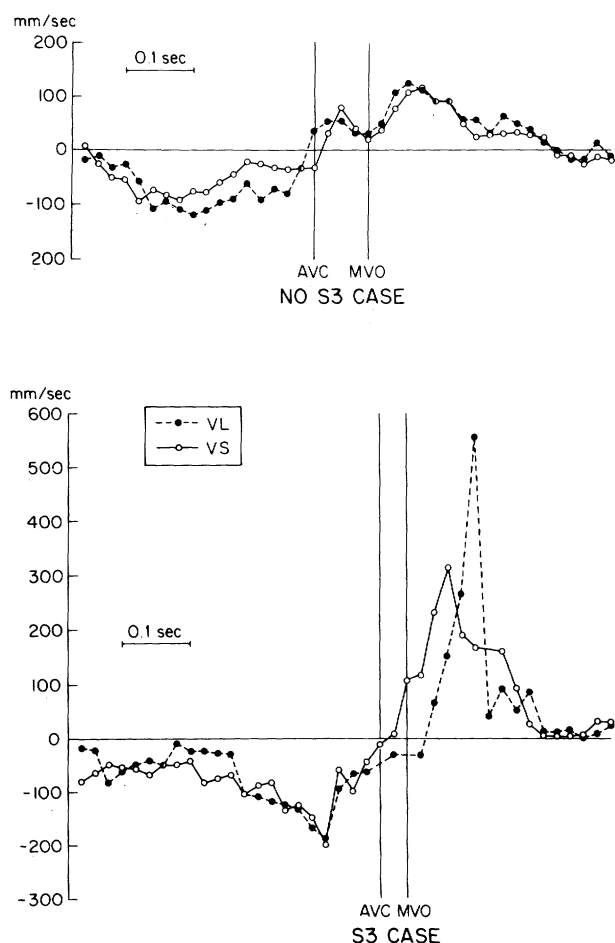


FIGURE 2. Velocity measurements in the long (VL) and short (VS) axes obtained by differentiation of the positional measurements from the two patients shown in figure 1. Abbreviations are as in figure 1.

filling movements, especially in the long axis with asynchrony of filling in the two major axes.

### Discussion

The auscultatory characteristics of gallop sounds and the accompanying movements of the chest wall were originally investigated by Potain.<sup>1</sup> He attributed the  $S_3$  to sudden cessation of distention of the ventricle at the end of the rapid filling phase of the cardiac cycle in early diastole: "If the cardiac muscle has lost its tone, the ventricle, in dilating, quickly arrives at a point where the fibrous resistance of its wall limits its distention and then, abruptly stopped, produces a tension — a shock, and the gallop sound."

Subsequent investigators, using hemodynamic data from the left ventricle and atrium, attributed the  $S_3$  gallop to a momentary closure of the mitral valve in response to rapidly fluctuating pressure differentials in the left-sided chambers.<sup>9</sup> These observations appeared to support a valvular mechanism for the origin of the  $S_3$  as proposed by Dock *et al.*<sup>10</sup> With improved methods, however, Kuo<sup>11</sup> showed that at the time of production of the  $S_3$ , left atrial pressure exceeded left ventricular pressure. In patients whose mitral valves have been replaced by a prosthesis, the  $S_3$  generally disappears, and this observation was thought to favor a valvular origin of  $S_3$ .<sup>12,13</sup> More recently, however, an  $S_3$  has been found in patients with an incompetent mitral prosthesis when there is no remnant of the valve.<sup>14,15</sup> This led Coulshed and Epstein<sup>15</sup> to support the concept of Potain, with normal mitral valve structures not being thought necessary for the production of a third heart sound.

Prewitt *et al.*<sup>5</sup> studied the relationship of the  $S_3$  to the maximum velocity of filling in the transverse axis from digitized sequential chamber diameters obtained by M-

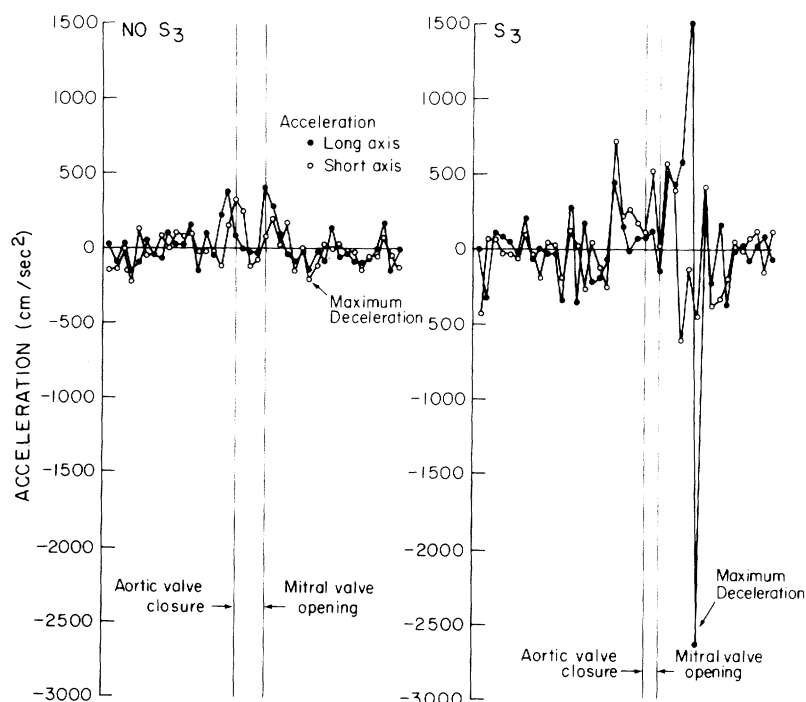


FIGURE 3. Acceleration measurements in the long and short axes for each cineangiographic frame obtained by differentiation of the velocity measurements from the two patients shown in figure 1.

mode echocardiography. They found that the  $S_3$  occurred some  $51 \pm 40$  msec on the average after the peak rate of filling in the transverse axis. They concluded that the  $S_3$  bore no consistent relation to any aspect of left ventricular wall movement, and that the rapid filling wave of the apexcardiogram, which is the subaudible counterpart of the  $S_3$  vibration, does not reflect the time of peak rapid ventricular filling.

Dimensional changes in the short axis are of major importance in volume filling.<sup>16, 17</sup> Short-axis velocities, in turn, are of primary importance in the determi-

nation of volume inflow rate. It does not necessarily follow, however, that the short axis is directly responsible for the production of the  $S_3$ , because in an elliptical chamber, one might anticipate completion of filling in the short axis before the long axis. It is also reasonable to expect that, if there is an asynchrony in the time of distention of the two principal dimensions of the left ventricular chamber during the rapid filling phase, the second of the two distentions would be the more sig-

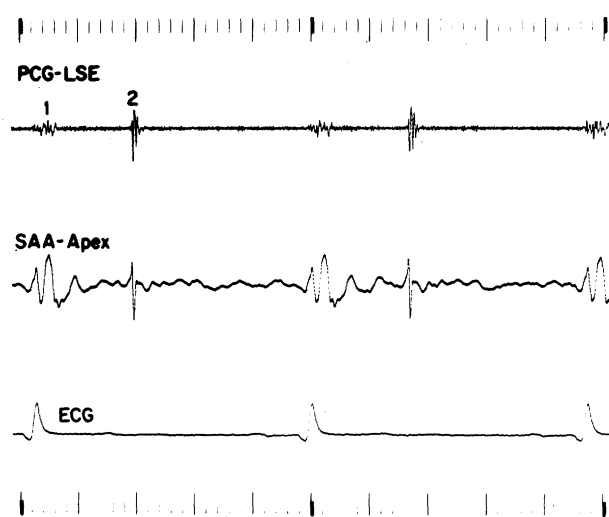


FIGURE 4. Tracing from a subject with no third heart sound ( $S_3$ ) showing inconspicuous diastolic movements in the acceleration signal at the apex (SAA-Apex). PCG-LSE = phonocardiogram at left sternal edge.

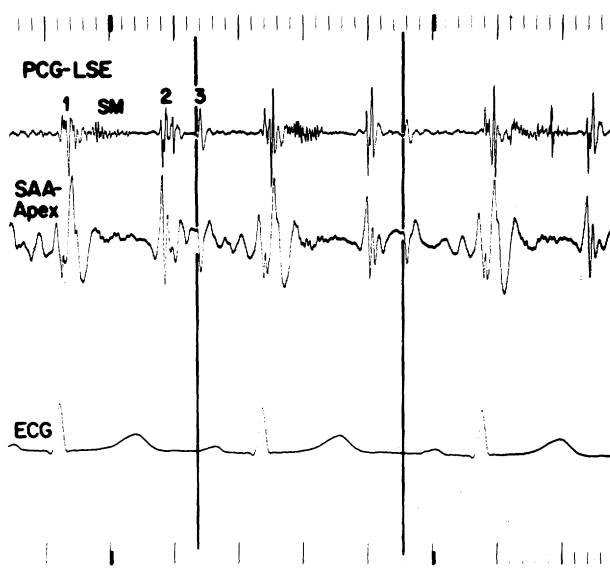


FIGURE 5. A normal youth with a physiologic third heart sound. The third heart sound in the phonocardiogram at the left sternal edge (PCG-LSE) is synchronous with a distinct negative jerk of the acceleration signal at the apex (SAA-apex).

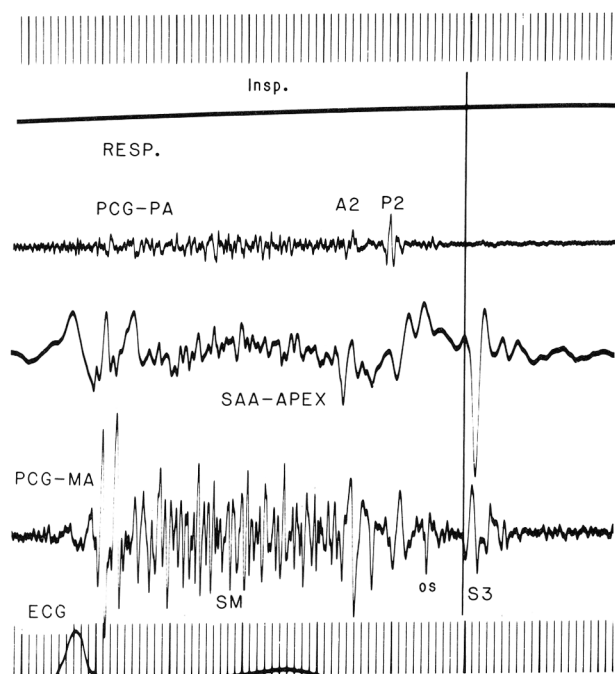


FIGURE 6. Recording from a patient with mitral regurgitation. The third heart sound ( $S_3$ ) is synchronous with a distinct negative jerk on the acceleration signal tracing at the cardiac apex (SAA-APEX). PCG-MA = phonocardiogram at the mitral area; PA = pulmonary area; SM = systolic murmur; OS = opening snap;  $A_2$  and  $P_2$  = components of second heart sound.

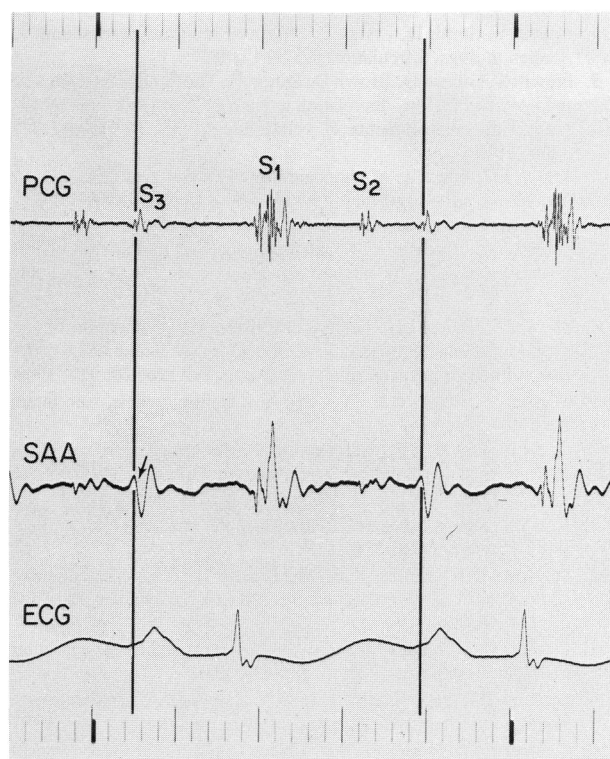


FIGURE 7. A patient with cardiomyopathy. The third heart sound ( $S_3$ ) in the phonocardiogram (PCG) is associated with a distinct negative jerk on acceleration signal (SAA) tracing.

nificant hemodynamic event, because at this time the blood suddenly encounters a relatively unyielding barrier.

The results of our studies on patients with volume overload show that long-axis filling reaches maximum deceleration an average of  $48 \pm 21$  msec after maximum velocity in the transverse axis. We believe that this asynchrony resolves the apparent lack of temporal correlation reported by Prewitt *et al.*<sup>5</sup> and that our study reaffirms that there is indeed a significant feature of left ventricular wall movement at the approximate

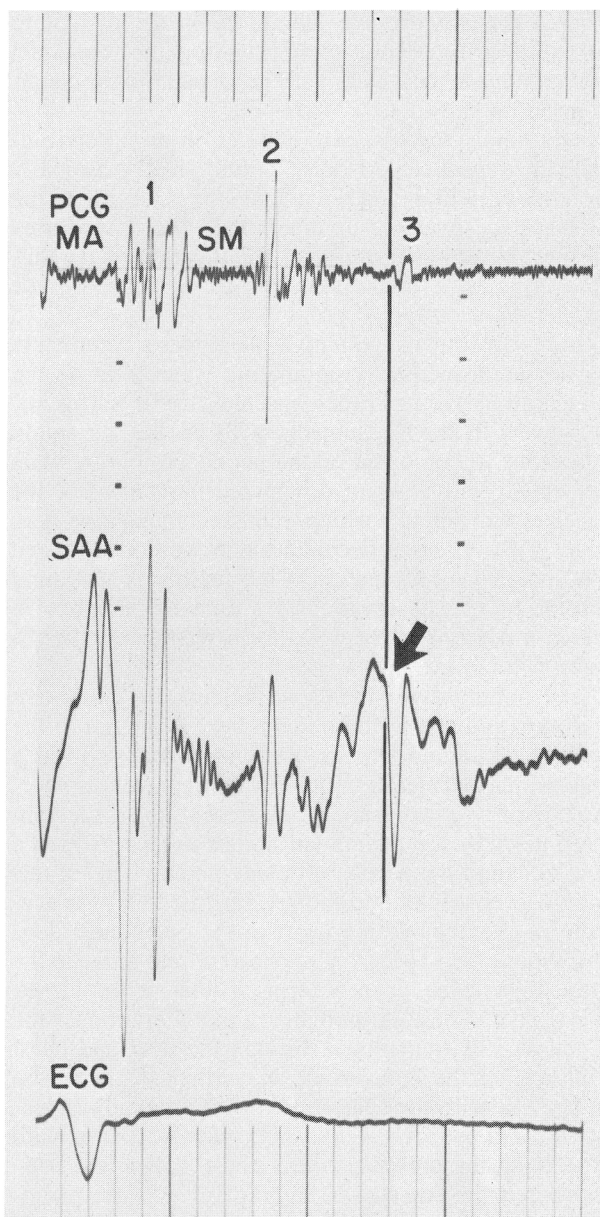


FIGURE 8. Tracing in a patient with an incompetent mitral valve prosthesis. The third heart sound is associated with a negative jerk on the acceleration signal (SAA) tracing (heavy arrow). SM = systolic murmur; PCG MA = phonocardiogram at the mitral area.

time of the  $S_3$  vibration in patients with diastolic volume overload conditions.

Conventional phonocardiographic studies, while providing a graphic analog of the audible vibration, do not afford an analysis of chest wall dynamics because the vibrations of the phonocardiogram do not represent a true parameter of motion. We used miniature accelerometers in our studies, and on open-chest dogs found that the  $S_3$  vibration was associated with a definite negative jerk in the rapid filling movement as it was tracked from chest wall to pericardium and to the epicardial surface. Our present studies extend these findings to the noninvasive laboratory in an attempt to determine if the conclusions drawn from the dog model are applicable to a wide variety of pathologic conditions in humans.

The noninvasive studies depend on an accelerometer, a transducer of very small size, practically weightless, which can be attached by adhesive to the skin surface over the cardiac apex. The device uses an inertial reference frame. Amplification of the signal provides a continuous record of skin surface acceleration.

In the 18 subjects with no  $S_3$  there was a completely flat or inconspicuously undulating wave form on the acceleration tracing at the expected time of  $S_3$  (fig. 4). However, in the 26 subjects with an  $S_3$ , the sound vibrations as perceived on the phonocardiogram were associated with a sharp downward movement of the acceleration signal, which represents negative jerk (figs. 5–8). A large deceleration wave corresponded with an intense  $S_3$  (fig. 5). This finding is strikingly similar to the observations by cineangiography, in which a deep negative wave form was seen in the  $S_3$  cases (fig. 3).

The noninvasive studies in patients are consistent with our findings in the dog studies. Although in the open-chest canine studies the SAA signal showed a plus-minus (acceleration-deceleration) wave form during rapid filling when an  $S_3$  was present, the SAA from the skin surface in the human studies usually showed a dominance of the deceleration movement. This difference is probably due to the greater freedom of movement of the apex of the heart in the open-chest dog. One would not expect that the heart would move in the same way in the open chest as it does in the closed chest. Also, there is probably some alteration of the signal as it is transmitted through the lung and chest wall to reach the skin surface. Nevertheless, the  $S_3$  was coincident with the sharp downward inflection (negative jerk) of the SAA signal. This was always true with or without the presence of the chest wall or the pericardium in the dog studies and regardless of the pathologic condition in the human studies. We believe that this sharp negative jerk and deceleration of the chest wall in humans is inconsistent with the concept of the sound resulting from an impact of the underlying heart against the inner chest. If such an impact theory were correct, the dominant feature of the SAA signal at the beginning of  $S_3$  would necessarily be an outward or

positive jerk of the skin surface as the chest wall is struck from beneath by the underlying heart. Our studies show that this is clearly not the case. This negative jerk might more realistically be brought about by a tensing of the intracardiac supporting structures — papillary muscles and chordae tendineae — or by an inherent limitation in the distensibility of the wall itself. The presence of an  $S_3$  and its associated negative jerk in two of our patients with an incompetent mitral valve prosthesis (fig. 8) in whom the original valve and supporting structures had been removed favors the mechanism of an inherent tensing and negative jerk emanating from the ventricular wall, as suggested by Potain.<sup>1</sup>

Our studies in both canine and human subjects have concentrated on the characterization and localization of the dynamic event giving rise to the audible vibration called the third heart sound. We have not studied the hemodynamic conditions and ventricular wall characteristics predisposing to this phenomenon. This will be the subject of future investigations.

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## Origin of the third heart sound. II. Studies in human subjects.

Y Ozawa, D Smith and E Craigie

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