Multigated Blood-Pool Imaging Using Heart Sounds

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A method to trigger multigated blood-pool (MGBP) acquisition using both the first and second heart sound has been developed. The heart sound gating (HSG) circuitry identifies, individually, both the first (S1) and second (S2) heart sounds from their timing relationship alone, and provides two trigger points during the cardiac cycle. First heart sound gating may be performed to assess the systolic ejection portion of the cardiac cycle, with S2 gating utilized for reproduction of the diastolic filling portion of the cycle. Heart sound gating has been applied to twenty patients who underwent analysis of left ventricular function, and compared to conventional ECG-gated MGBP. Left ventricular ejection fractions calculated from MGBP studies using a first and a second heart sound trigger correlated well with conventional ECG gated acquisitions in patients adequately gated by HSG and ECG. Heart sound gating may be utilized in patients with rapidly changing heart rates, as S1 and S2 precisely define end-diastole and end-systole, respectively, and in situations when the ECG is inadequate for gating purposes.

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In nuclear medicine, ventricular function both of the right and left heart is routinely assessed using multigated blood-pool imaging (MGBP) techniques. As extensively reported, the R-wave of the electrocardiogram (ECG) provides the trigger point within the cardiac cycle to synchronize computer acquisition (*1–6*). In certain clinical situations, the ECG may not be adequate for gating purposes, such as in patients undergoing chemotherapy, patients with pacemakers, etc. Further, due to "time jitter" in MGBP acquisition using the R to R interval as the triggering cycle, the diastolic filling portion of the ventricular volume curve may not be reproduced accurately, even when backward and forward-backward gating modes are utilized (*7–10*). With increasing interest in the diastolic filling phase, accurate reproduction of this end phase of the cardiac cycle is important (*9–15*). Heart sounds can provide an alternative method to ECG gating, providing two reference points within the cardiac cycle, to uniquely define ventricular systolic ejection (S1 to S2) and diastolic filling (S2 to S1).

Berman et al. used the R-wave to trigger a single frame acquisition of the diastolic ventricle on film, and identified the second heart sound to aid in establishing a delay control from the R-wave for the definition of the systolic image window (*16*). Heart sounds alone (without ECG reference) have not been heretofore used as single or multiple sources of cardiac triggers, due to practical problems in distinguishing the first (S1) and second (S2) heart sounds components. We investigated the use of heart sounds (first and second) triggering for evaluation of both the systolic and diastolic portion of the cardiac cycle and have developed a microprocessor controlled heart sounds gate (HSG), which automatically identifies the first and second heart sound from the phonocardiogram alone, using their timing relationship (*17*). We report an alternative, hearts sounds method for triggering MGBP imaging and our experience in patients gated with both conventional ECG triggering and the HSG.

MATERIALS AND METHODS

The patient phonocardiogram is obtained from a small transducer (piezo-electric) microphone, coupled with gel to the patient's chest, at the location of the loudest second heart sound, determined by a stethoscope, and so as not to interfere with visualization of the left and right ventricular blood pool. Typically, the S2 heart sound is softer than the S1 sound, and finding the location of the maximal second heart sounds provides the best location for obtaining equal amplitudes of S1 and S2.

The S1 and S2 heart sound triggers are generated as illustrated in Figure 1 (analog portion of the HSG). The heart sounds are first amplified and bandpass filtered. An absolute value amplifier is then used to fold the negative portions of the waveform onto the positive voltage axis and the S1 and S2 signals are enveloped. The peak signal amplitude is conditioned to drive an automatic gain circuit, and a squaring circuit is used to minimize noise. Finally, the gating point for each heart sound is set by a variable threshold, using a comparator circuit to generate a trigger pulse when the threshold level is exceeded.

Using the heart sound trigger pulses, the timing relationships between the S1 to S2 pulses and the S2 to S1 pulses are determined using digital logic circuitry. The circuit logic is capable of distin-

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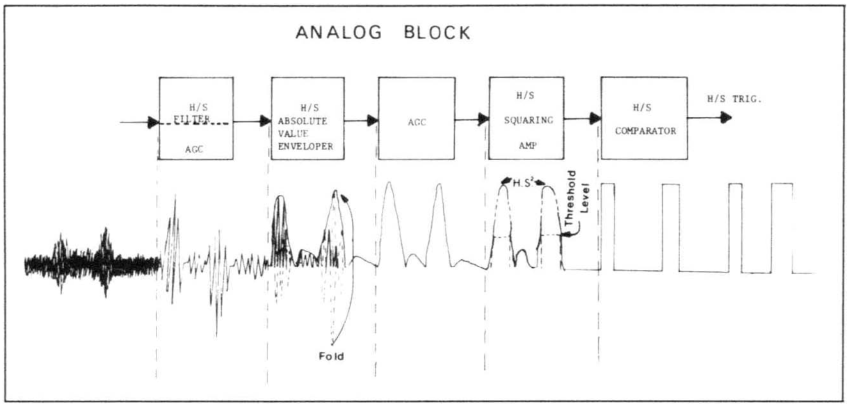

FIGURE 1. Analog portion of the heart sounds (H/S) gate, where trigger pulses are generated from each significant sound in the phonocardiogram. The circuitry uses bandpass filtering, automatic gain control (AGC), absolute value enveloping and pulse squaring to provide a positive voltage waveform, above noise, for the generation of heart sound triggers. A comparator circuit generates trigger pulses when a threshold voltage value is exceeded. See text for further description.

guishing the S1 and S2 pulses from the heart sounds themselves using their timing relationships and the assumption that initially the S1 to S2 interval will be shorter than the S2 to S1 interval. The logic is illustrated in Figure 2. After each heart sound trigger, a lock-out pulse is generated which inhibits any further triggers for its duration. The lock-out additionally serves to eliminate false triggers due to murmurs, or the third heart sound (S3), (following the S2 sound). Concurrently with the lock-out window, a timing, or "listening" window is opened for a duration only long enough for the S2 sound to occur, if the instigating pulse was an S1 pulse. A second trigger pulse is only allowed if it occurs within the timing window and after the lock-out interval. The timing window and lock-out window are continuously variable and are controlled by the logic circuitry monitoring the time intervals. In general, the timing window varies between 200 and 400 msec and is initially set to be one-half the longest sound-to-sound interval heard.

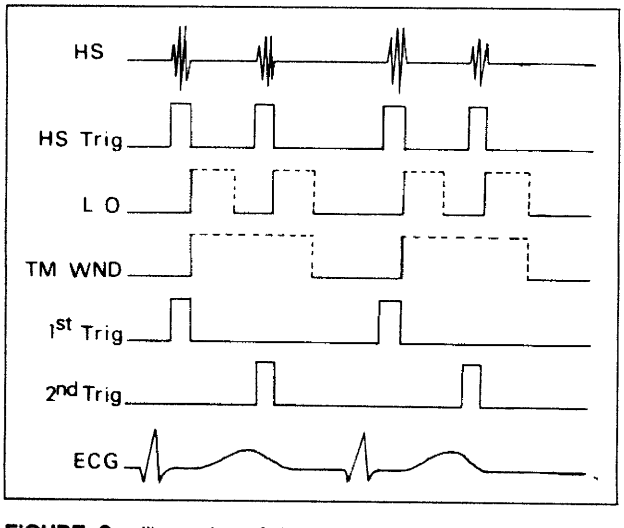

FIGURE 2. Illustration of the logic utilized to identify the first (S1) and second (S2) heart sounds from the phonocardiogram. Heart sounds (HS) triggers (Trig) are identified as either first (1st Trig), second (2nd Trig) or extraneous (no trigger) by use of lock-out (LO) and listening, or timing, windows (TM WND). The LO window serves to remove murmurs and/or multiple triggers. The TM WND is set to the estimated S1 to S2 interval by a microprocessor look-up table. The timing window logic identifies the specific S1 and S2 sounds, as described in the text.

When the HSG is first applied, if the instigating pulse is S1, the S2 sound will occur after the lock-out and within the listening timing window. If the instigating pulse happens to be S2, since the S2 to S1 interval is longer, the listening window will have expired before the next pulse is seen and will not be accepted as a valid trigger. The next pulse will be an S1, which will reinstigate the listening window, catching the following S2. Thus, within two beats, the circuit will identify and lock on to the proper heart sounds in sequence. The digital logic circuitry will vary the lock-out and listening windows to track increasing or decreasing heart rates. A 16-bit ROM controls the window lengths for the lock-out and timing windows.

The S1 to S2 listening window can be estimated using the equation:

$$\text{S1-S2 Interval (msec)} = (455 - 1.878 \times \text{HR}) + (0.0026 \times \text{HR}^2),$$

where HR is the patient's heart rate (*18*).

The first, second, or both S1 and S2 heart sound triggers can be selected as the trigger input to initiate multigating in the computer. An ECG R-wave trigger is available for reference.

Patient Studies

Twenty patients, who underwent normally prescribed multigated blood pool imaging at rest, were evaluated concurrently, with both ECG and HSG MGBP imaging. The patients were imaged with a small field of view mobile gamma camera (LEM gamma camera, Siemens Medical Systems, Hoffman Estates, IL) equipped with a low-energy all-purpose collimator, and minicomputer (MicroDELTA and Scintiview, Siemens) dividing the cardiac cycle into 16 frames, using an internally designed and built ECG R-wave trigger circuit and the heart sounds gate. The ECG gate was set to trigger at a voltage 75% of the peak amplitude, on the downslope of the R-wave, typically triggering less than 5 msec from the peak of the R-wave. For this comparative study, the patients were gated with computer data acquisition initiating on: (a) the R-wave of the ECG, (b) the first heart sound, S1, and (c) the second heart sound, S2. Left ventricular ejection fraction (LVEF) was computed for each of the three gating modes using standard methods, with regions of interest (ROIs) drawn around the end-diastolic (ED) and end-systolic (ES) ventricles. The ventricular time-activity curves (TACs) were generated by weighted interpolation of the TACs from both the ED and ES ROIs (*19*). Ventricular volume curves were compared subjectively, for each of the three gating modes. The time from peak R-wave to peak S1 was noted for each patient from the displayed ECG and phonocardiogram tracings, as measured on a calibrated dual-storage oscilloscope (Tektronic Model #464).

RESULTS

Of the 20 patients studied, 15 patients could be adequately gated by both methods. Five patients were excluded from the study due to inadequate ECG (one patient), indistinguishable S1, S2 (two patients), or both (two patients). In the patients studied, there was a delay of 5–40 msec between the peak R-wave and S1, with a mean delay of 25 msec. This corresponds to known differences in electrical stimulation and the onset of mechanical contraction of the heart (*20*).

Adequate phonocardiograms were obtained in these patients in less than 2 min by survey of the mid-sternal area with a stethoscope to locate the area of loudest S2. We found that in general the loudest second heart sound occurred in the aortic area over the mid-sternum (as expected), as the rush of blood in the aorta back towards the aortic valve after its closure is thought to be the predominant mechanism generating the S2 sound. It is fortuitous that this general area was optimum for microphone placement as this location was ideal to prevent the shadow of the microphone from interfering with the analysis of ventricular wall motion. We found the algorithm used to identify S1 and S2 from the phonocardiogram performed well at heart rates of up to 185 bpm using a simulated phonocardiogram.

LVEF was computed from each of the three gating modes for the 15 patients, listed in Table 1, who could be adequately gated by both methods. The LVEFs determined by conventional ECG gating correlated well with both the LVEFs obtained from the S1 and S2 triggered studies, as illustrated in Figure 3. An excellent correlation, r = 0.93, $p < 0.05$, was obtained between the ECG-gated LVEF and the LVEF obtained from the patient study gated by the second heart sound. An even better correlation in LVEF, r = 0.96, $p < 0.05$ was obtained between the ECG-gated and first heart sound gated studies. The fit of the LVEF correlation (Fig. 3) yielded a slope of 0.98 and 0.89 between the ECG-gated LVEFs and the S1 and S2 gated LVEFs, respectively, with an intercept near zero for both comparisons (−0.01, +0.04).

A ventricular volume curve was generated using each of the three trigger modes. The volume curve obtained using ECG and S1 gating appear similar in form, with the familiar sequence of display: end-diastole – end-systole – end-diastole. The multigated study initiated with an S2 trigger yielded an unconventional, but expected pattern, displayed: end-systole – end-diastole – end-systole. Ventricular volume curves from the ECG-gated and S2-gated studies for three representative patients are illustrated in Figure 4. Ventricular volume curves obtained by the three gating modes illustrated qualitatively, for the three cases presented, superior definition of the diastolic filling phase for the second heart sound gated study (refer to Fig. 4), compared to the ECG-gated study. The passive and active phases of diastolic filling as well as the atrial "kick" are visualized with superior fidelity using S2 as the initiating trigger point, particularly in Patients B and C.

TABLE 1
Comparison of Left Ventricular Ejection Fractions Obtained By First Heart Sound, Second Heart Sound, and ECG-Triggered Studies

	LVEF (%)		
Patient	ECG R-Wave	First heart sound	Second heart sound
A	52	56	48
B	46	44	48
C	55	52	56
D	38	51	45
E	70	62	62
F	13	13	16
G	46	46	49
H	54	50	53
I	26	20	30
J	58	55	53
K	75	71	66
L	31	25	25
M	38	31	36
N	79	77	71
O	46	42	40
mean	48.5	46.3	46.5

DISCUSSION

MGBP imaging provides a host of data to assess cardiac function, such as ejection and filling rates, time to peak filling, etc. Accurate reproduction of the time course of ventricular contraction and relaxation is essential to the evaluation of these ejection and, particularly, filling indices. Errors in the reproduction of, principally, the late diastolic filling phase of the ventricular volume curve by

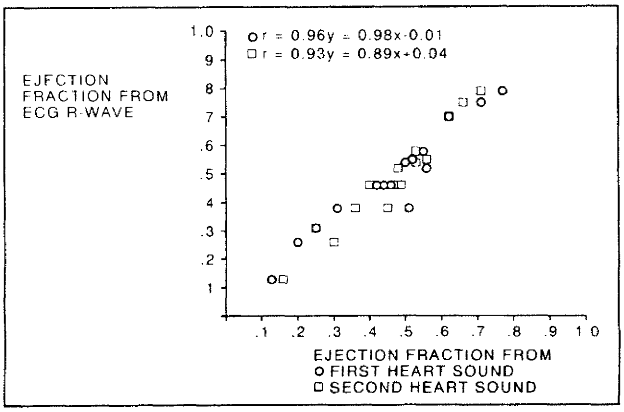

FIGURE 3. Comparison of LVEFs determined from multigated blood-pool studies triggered on the ECG R-wave, and by the first (CIRCLE) and second (SQUARE) heart sound. An excellent correlation coefficient is obtained, with the fit of the correlations indicating a good correspondence in LVEF, for the n=15 patients, gated adequately by both ECG and S1 and S2 heart sounds.

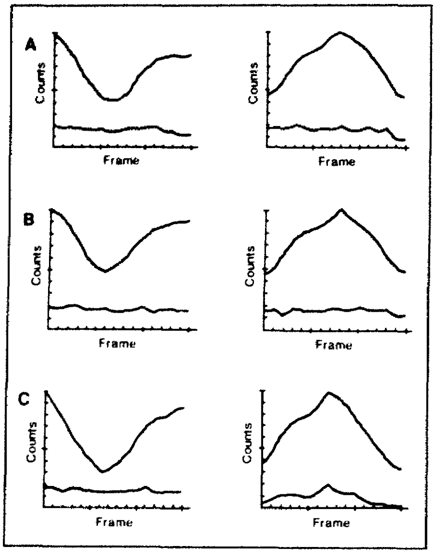

FIGURE 4. Ventricular volume curve and background curve (below) obtained from three patients comparing the ECG R-wave triggered volume curve (left) to the curve obtained using the second heart sound (S2) as the instigating trigger pulse (right). The S2 gated ventricular volume curves display a pattern shifted from the conventional volume curve display. S2 triggered curves begin at end-systole with diastolic filling observed first, followed by systolic ejection. Note the definition of both the active and passive phases of diastolic filing, and the atrial "kick" in S2 gated studies. (A) Fifty year-old female with recurrent chest pain and previous subendocardial myocardial infarction. (B) Thirty-nine-year-old female with hypertension. (C) Thirty-year-old male with lung cancer and liver metastases on Adriamycin therapy.

MGBP, compared to biplane angiography, have been demonstrated (*21*). The need to estimate the R-to-R interval to set computer timing windows causes time jitter, distorting the ventricular volume curve near the end of the gating cycle, when the R-to-R interval varies from the initial estimate. The advent of forward/backward gating has not been shown to "cure" the effects of time jitter (*7–10*). With HSG, two reference points in the cardiac cycle are available to potentially reduce the effects of time jitter. It is reasonable to expect that S2 initiation of the multigated acquisition sequence would result in superior reproduction of the filling phases of the cardiac cycle, since the time jitter associated with the end of the ventricular volume curve occurs during systolic ejection. Concomitantly, S1 gating should reproduce the systolic ejection phase at least as well as ECG R-wave gating.

Limitations of heart sound gating include patients with faint heart sounds, murmurs, clicks; the presence of third (S3) and fourth (S4) heart sounds, excessive room noise, and other bodily noises such as bowel gas. However, the digital logic employed with this new generation heart sounds processor, effectively reduced problems due to S3 and S4 as well as murmurs and clicks, by use of listening and lock-out windows and expectation logic for the heart sounds timing intervals. Obtaining adequate coupling of the transducer microphone to the patient occasionally posed a problem.

Heart sound gating may perform better than ECG gating in rapidly changing heart rates, as seen in MGBP stress tests, because S1 and S2 can define the beginning and end of systole without need for setting an acceptance window for the R-to-R interval (which may change substantially during a 2-3 min exercise level). Further, HSG may be useful in patients with atrial fibrillation, since S1, S2 define precisely the opening and closure of the aortic and mitral valves, and HSG may be more immune than ECG gating to changing cardiac cycle. It has been demonstrated that the systolic ejection period does not substantially vary, as does the R-to-R interval, in patients with atrial fibrillation (*22, 23*). Thus, the S1-S2 interval would readily define the limits of systole for LVEF and, perhaps, HSG may permit somewhat better assessment of ventricular filling parameters in atrial fibrillation, by separating the diastolic (S2-S1) interval specifically from the R-to-R-interval. Heart sound gating, with S1 and S2 triggers to denote end-diastole and end-systole specifically for each beat, should eliminate problems in obtaining adequate MGBP studies in patients with rapidly changing heart rates in general. These potential advantages of HSG need to be verified clinically.

CONCLUSIONS

We have developed a heart sound gating device that identifies both the first and second heart sounds from their temporal relationship, providing two trigger points corresponding to mechanical events in the cardiac cycle. MGBP imaging can be performed using a diastolic trigger point (S1), a systolic trigger point (S2), or a diastolic trigger with a "mid-course correction" second heart sound trigger. Heart sound gated studies have been shown to yield LVEFs which correlate well with ECG-triggered studies. Qualitatively, S2 gating provided superior definition of the diastolic filling phase of the ventricular volume curve in the cases presented. Heart sound gating may be utilized in patients with rapidly changing heart rates and in situations when the ECG is inadequate for gating purposes. With increased interest in diastolic filling indices, S1-gated (or ECG-gated) imaging may be used to assess the systolic ejection portion of the cardiac cycle, with S2 gating utilized concurrently for reproduction of the diastolic filling portion of the ventricular volume curve without increasing study time.

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