Assessment of the Site of Ventricular Activation by Fourier Analysis of Gated Blood-Pool Studies

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We studied the use of first-harmonic Fourier analysis of gated blood-pool images to assess the site of ventricular activation in a group of 12 patients undergoing electrophysiologic pacing studies. We acquired gated blood-pool studies during pacing at up to four sites at each of two different rates. A total of 50 studies were made. At a pacing rate of 100 beats/min, when the pacing electrode was at the right-ventricular apex, 9/13 times the Fourier activation site agreed; at the right-ventricular outflow tract, 7/8; at the anterolateral left-ventricular wall, 4/4. When the Fourier activation site was at the right-ventricular apex, 9/9 times the pacing electrode was there; at the right-ventricular outflow tract, 7/10; in the left ventricle, 4/4. Fourier analysis of gated blood-pool studies can help identify the site of ventricular activation but is not sufficiently accurate to fully replace endocardial mapping.

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We and others have previously described the use of temporal Fourier analysis (also called phase or first-harmonic analysis) of gated blood-pool studies (*1–3*). Analysis of phase distributions have revealed specific patterns in various disorders of conduction or contraction (*1–3*). Despite these studies, the relationship of phase data to physiologic events, such as electrical depolarization or muscle contraction, remains uncertain (*4*).

In 1982, Swiryn and co-workers described the use of Fourier analysis in a group of six patients with gated blood-pool studies acquired during both normal sinus rhythm and sustained ventricular tachycardia (*5*). They found phase distributions that were consistent with the structure and axis of the QRS complex from electrocardiograms (endocardial mapping was available in only one patient). More recently, investigators have used Fourier analysis to study other conduction abnormalities, as in the Wolff-Parkinson-White syndrome (*6–8*). These results demonstrated the promise of Fourier analysis for the noninvasive identification of ectopic foci within the myocardium. Accordingly, we studied the ability of Fourier analysis to locate noninvasively widely separated sites of electrical activation in a group of 12 patients at risk for sustained ventricular tachycardia.

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METHODS

Patients

Our 12 subjects had histories of sustained ventricular tachycardia and were undergoing a programmed electrophysiologic pacing protocol. All gave written informed consent to undergo radionuclide gated blood-pool studies also during the electrophysiologic examination in the cardiac catheterization laboratory. All 12 patients were male, with an average age of 60 yr. Nine had coronary artery disease, and three had cardiomyopathies. All had left-ventricular (LV) dysfunction, with an average LV ejection fraction of 26% (range 10% to 44%).

Gated blood-pool studies

Data were acquired following blood-pool equilibration of 20–25 mCi Tc-99m on red blood cells labeled in vivo. We used a portable Anger camera with an all-purpose, low-energy parallel-hole collimator, interfaced to a dedicated portable nuclear medicine computer. Each study consisted of 16 frames in 64 × 64 matrix spanning the cardiac cycle. First, studies were acquired during normal sinus rhythm, in the anterior and 40° left anterior

oblique projections for 6 min each. All subsequent studies were acquired for 3 min each in the left anterior oblique projection.

Electrophysiologic pacing

Pacing electrodes were introduced through the femoral vessels and fluoroscopically positioned in the right atrium and right or left ventricle. An additional catheter was introduced into the femoral artery and positioned in the aorta or left ventricle for pressure monitoring during the procedure.

Before the electrophysiologic examination, the patients were paced at a constant rate of both 100 and 120 beats/min for 4 min each. Gated blood-pool studies were acquired during the last 3 min, which allowed the heart 1 min to reach equilibrium during pacing at each site and rate. All 12 patients were paced from the right ventricular (RV) apex (one patient at two sites separated by 2 cm). Eight patients were paced from the RV outflow tract. Three were paced from the anterolateral LV wall (one patient at two sites separated by 2 cm). During ventricular pacing, the right atrium was simultaneously paced to prevent sinus competition and antegrade atrioventricular conduction. Simultaneous atrial and ventricular pacing eliminated the atrial contribution to LV filling ("atrial kick"). A total of 50 studies were acquired: 25 sites at each of two rates.

Fourier analysis

The gated blood-pool data were transferred to a second computer for analysis and display. Each study was first displayed cinematically to assess technical adequacy. They were then smoothed with a three-dimensional spatial and temporal filter to reduce random variation due to the Poisson nature of radioactive decay (*9*). No normalization of the frames for count losses due to varying cardiac cycle lengths during acquisition was necessary, since pacing throughout acquisition ensured a constant heart rate. The temporal Fourier transform at the fundamental frequency (the heart rate) was obtained on a pixel-by-pixel basis, as previously described (*2*). In essence, each pixel's time-activity curve was fitted with a single cosine whose period equalled the R-R interval. Given a single-cycle cosine fit for every pixel, differences could be fully characterized by two parameters: amplitude, representing the maximum value of a given pixel's cosine, and phase, which represented the shift in time of a given pixel's cosine. Phase data were expressed in degrees between 0° and 360°, with 0° arbitrarily defined to be that of a cosine whose maximum occurred at the peak of the QRS complex. The phase data were displayed along with the end-diastolic image, which served as an anatomic guide, and a color-coded phase histogram, which was helpful in establishing phase/temporal sequence relationships (Fig. 1). The phase data were then displayed cinematically as a "wave of emptying," in which pixels within a static image of the heart blacked out a given time, based on their phase value (Fig. 2).

The pacing studies were transferred to the analysis and display computer in an order that was random as to patient, site, and rate. The studies were interpreted by two of us as to location of the earliest phase site within the ventricles, which we took to represent the initial site of electrical activation. The interpretation was based on the use of both the color-coded phase image and the "wave of emptying." The phase image was first examined to identify the site of earliest phase. The "wave of emptying" was then viewed both cinematically and frame-by-frame for improved perception of the overall sequence of emptying.

The studies acquired during normal sinus rhythm were analyzed separately to serve as a "control." We felt it was important to use each subject for his own control, because of the presence of wall-motion abnormalities in these patients, which could affect the phase data independently of electrical activation.

RESULTS

Fourier analyses of the data acquired during normal sinus rhythm were clearly abnormal in all 12 patients, with areas of reduced amplitude and relatively broad spreads of phase values within the heart. The earliest phase site occurred simultaneously on both sides of the interventricular septum in three patients, on the RV side of the septum alone in three patients, and on the LV side

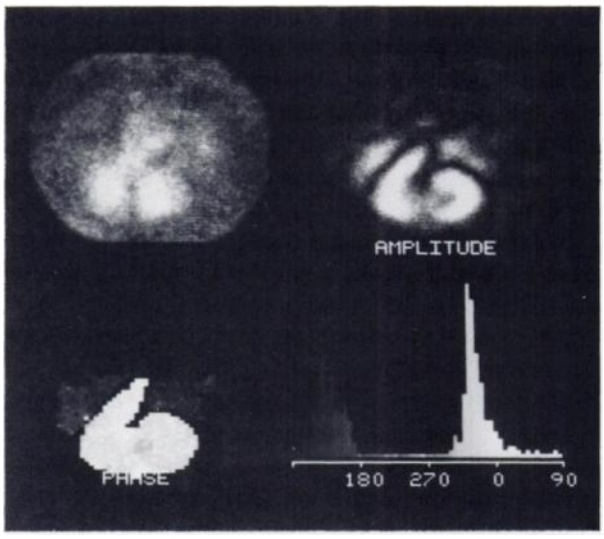

FIGURE 1
Quadrant display of Fourier data. Upper left: End-diastolic frame from gated blood-pool study, which serves as anatomic guide. Upper right: Fourier amplitude image. Lower left: Fourier phase image. Lower right: Phase histogram, color (or gray-scale) coded so that bar of given color (or shade of gray) represents those pixels of same color (or shade of gray) in phase image

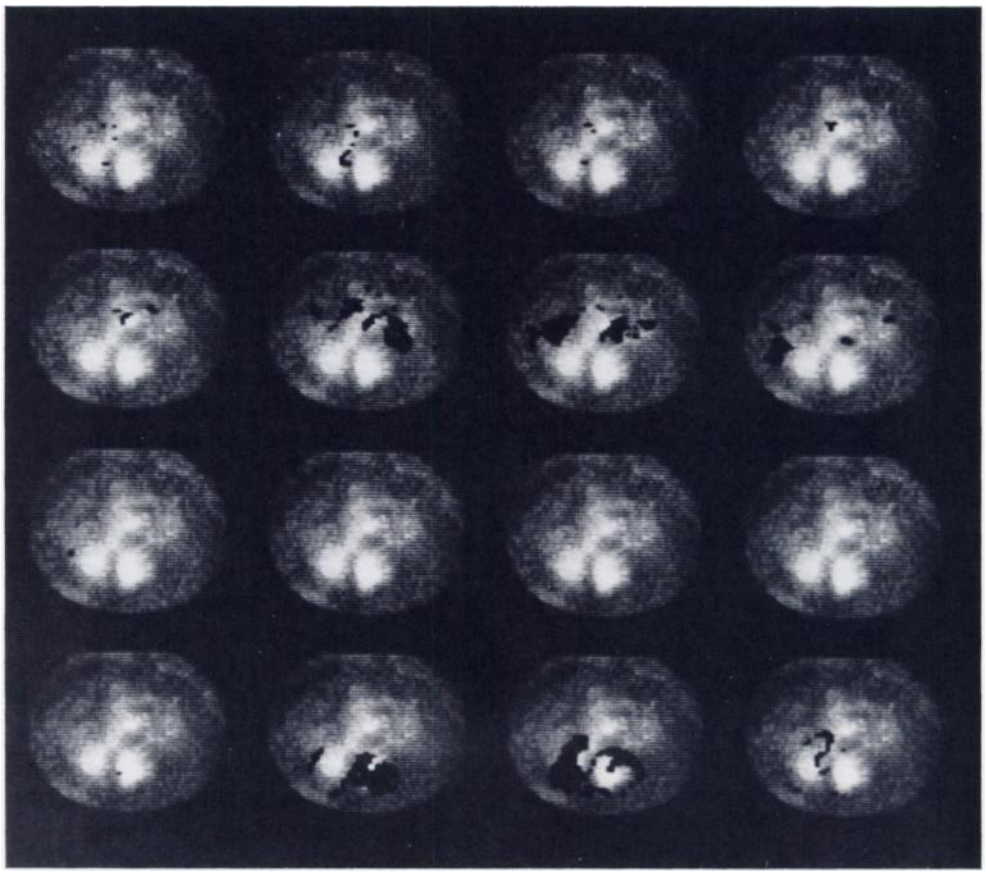

FIGURE 2
"Wave of emptying" display, consisting of 16 frames that are displayed cinematically as continuous-loop movie. Each pixel is blacked out in one of 16 frames, as determined by its phase value (*2*)

of the septum alone in two patients. In two patients the earliest site was simultaneously along the RV free wall and the LV base. In one patient the earliest site was along the LV free wall, and in one patient in the middle of the RV wall. Of these studies, two were indistinguishable from studies (in other patients) acquired during pacing: one of the RV septum sites was so high as to mimic RV outflow-tract pacing, and the LV site mimicked LV pacing. For comparison, in normal people the earliest phase site is either simultaneously on both sides of the interventricular septum (*2,3*) or on one of its sides (*3*).

The phase data from the different pacing sites in one patient are shown in Fig. 3. In this patient, the initial four frames of the "wave of emptying" are clearly different for each of the four pacing sites shown. All four sites were correctly located.

The results from the 25 studies at a pacing rate of 100 beats/min are shown in Table 1. There was a single, unambiguous earliest phase site in all studies. When the pacing electrode was at the RV apex, 9/13 times the Fourier activation site agreed; at the RV outflow tract, 7/8; in the anterolateral LV wall, 4/4. When the Fourier activation site was at the RV apex, 9/9 times the pacing electrode was there; at the RV outflow tract, 7/10; in the left ventricle, 4/4. The results were unchanged at a pacing rate of 120 beats/min.

DISCUSSION

The findings indicate that Fourier analysis is accurate in determining the site of electrical activation in 80% of the pacing sequences studied. These results are in good agreement with the work of others who utilized pacing to validate Fourier analysis (*6,10–12*). They also agree well with studies of bundle branch blocks (*13–15*) and of other conduction sequence abnormalities, such as Wolff-Parkinson-White syndrome (*6–8*).

There are several reasons why Fourier analysis is not perfectly accurate. In general, a gated blood-pool study registers the radioactivity (presumed proportional to volume) within the heart chambers throughout the cardiac cycle. In a normal person, its changes are the result of mechanical contraction, which closely follows electrical depolarization. Thus, in normal people the phase data represent the sequence of electrical depolarization. However, studies have shown that contraction abnormalities, such as those that result from ischemia

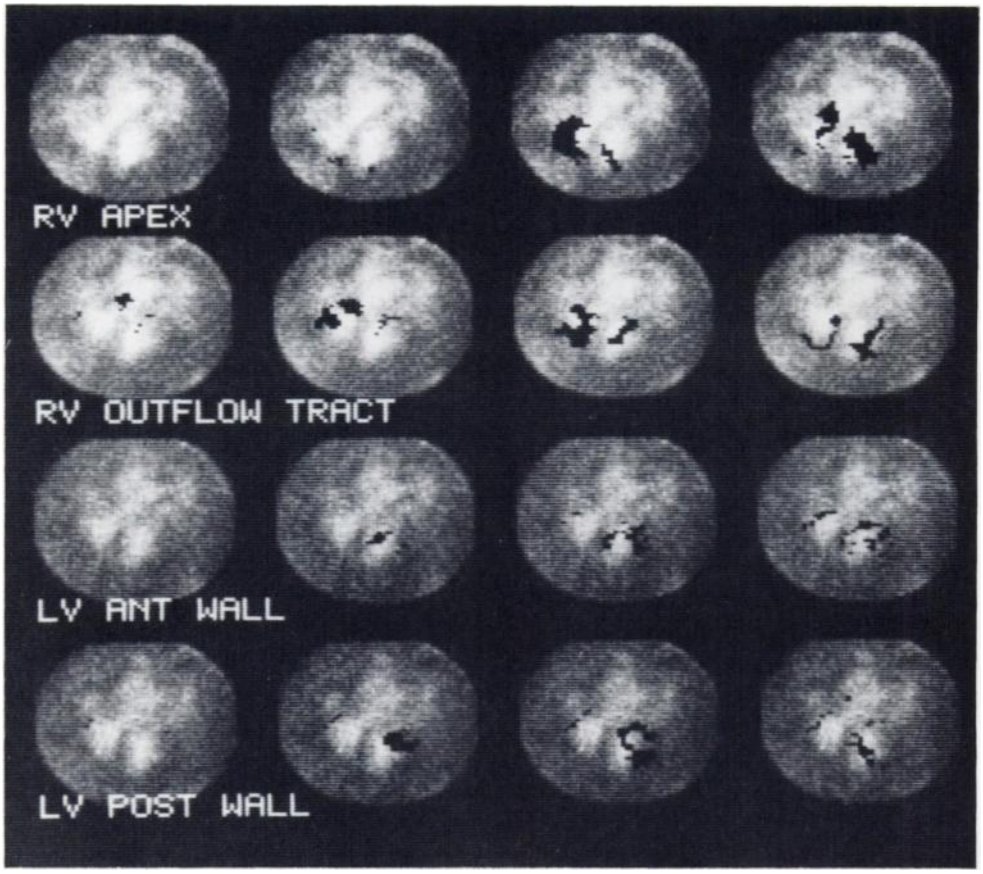

FIGURE 3
First four frames of wave-of-emptying display, from four studies at different pacing sites, in one patient. Two sites are in right ventricle, as labeled; other two are in anterolateral part of LV; one more anterior (LV ANT WALL), other more lateral (LV POST WALL)

or myocardial infarction, can result in a "delayed" phase value, representing delayed contraction despite the presence of a normal depolarization sequence (*3*). In the presence of heart disease, therefore, the phase sequence cannot be strictly interpreted as representing the depolarization sequence. For example, if an ectopic focus lies in an area of abnormal contraction, such as an aneurysm, the earliest phase site may be adjacent to the true ectopic focus, reflecting the closest area that has enough functioning myocardium to contract upon depolarization (*16*).

TABLE 1
Initial Site of Activation

		Location of pacing catheter		
		RVA*	RVOT†	LVAL‡
Fourier activation site	RNA	9	0	0
	RVOT	3	7	0
	LVAL	0	0	4
	Other	1	1	0

* RVA = right-ventricular apex.
† RVOT = right-ventricular outflow tract.
‡ LVAL = left-ventricular anterolateral wall.

In addition, a change in activity in a pixel is not necessarily the result of emptying of the heart in that area. For example, we frequently observe significant amplitude in the area of the great vessels, where lateral motion and rotation of the heart shift the vessels in and out of some pixels' "fields of view." Generally, these pixels have phase values close to those of the atria. Fortunately, the areas around the valves (such as the RV outflow tract) have such limited mobility that the amplitude in these regions is very low. Lateral heart motion was not a problem in this study.

Another potential source of error arises from the use of first-harmonic Fourier analysis, which represents each pixel's time-activity curve as a single cosine, obtained by least squares fit. While previous cineangiographic studies at high frame rate have shown that about 75% of the temporal information in a LV volume curve is at the fundamental frequency (i.e., the first harmonic, the heart rate) (*17–18*), the fit is not perfect and errors can be introduced. Recently, investigators have described the use of more than one harmonic to fit each pixel's observed time-activity curve (*19–20*). Such multiharmonic Fourier filtering, followed by first-derivative analysis of the filtered time-activity curves, may provide a more

accurate approach for fully characterizing the magnitude and time course of regional ventricular volume changes through the cardiac cycle. At present, however, such analyses require additional computer hardware or significant processing time.

The temporal resolution required for acquisition, analysis, and subsequent data display must also be considered. Because each pixel's time-activity curve is fitted by a single cosine, 16 frames spanning the cardiac cycle appear adequate for acquisition (*2*). The phase data themselves range from 0° to 360°, and thus represent a temporal resolution of $1/360$ of a cardiac cycle. The phase data are then scaled to the 256 colors of our display. The "wave of emptying" could consist of any number of frames up to 360, as it is generated from the phase data and is independent of the number of frames used for acquisition. In practice we have found that 16 frames give adequate temporal resolution (i.e., $1/16$ of a cardiac cycle) (*2*). This is probably due to the much slower contraction/emptying sequence compared with the electrical depolarization sequence.

While first-harmonic Fourier analysis can be considered as the most severe low-pass temporal filter possible, random noise on a pixel-by-pixel basis may still be on the same order as the true changes in activity through the cardiac cycle, especially in patients with global hypofunction. We attempted to reduce random noise by processing the data with a weighted spatial and temporal filter before Fourier analysis. In addition, the use of only 16 frames for the "wave of emptying" meant that larger groups of contiguous pixels "blacked out" in the same frame, which made them distinguishable from "noise" (individual pixels that were randomly "blacked out" in a given frame). However, since the studies were acquired for only 3 min and all of our patients had abnormal ejection fractions at rest, random noise could still have been a problem. This was examined by assessing the spatial coherence of the "wave of emptying" as it "washed over" the ventricles. Of the six studies felt to be technically poor in this sense, three gave the correct pacing site and three did not.

A final source of error was introduced by the use of only one projection to determine the site of activation. Since each pixel's time-activity curve represents three-dimensional changes in activity compressed into two dimensions, the use of more projections might have increased our accuracy (*10,12*), but this was not clinically feasible during our study.

We have previously observed (unpublished data), that, at heart rates high enough to induce ischemia, the phase distribution becomes so broad as to "wrap around," and thus have no clear beginning, middle, or end to the emptying sequence. In such cases it is difficult or impossible to determine an earliest phase site. We attempted to examine this potential problem by pacing at two rates that mimic "slow" ventricular tachycardia. While we found no change in results with a 20% increase in heart rate (from 100 to 120 beats/min), there may still be a problem during faster tachycardias, especially if ischemia is present. Indeed, Swiryn and co-workers noted this effect, which they also termed "wraparound," during sustained ventricular tachycardia (*5*).

We believe that Fourier analysis of gated blood-pool studies is useful in several ways in the management of patients with ventricular tachycardia. We have shown that it can be used to distinguish reliably between right- and left-ventricular activation sites. The treatment of patients with arrhythmogenic RV dysplasia, in which tachycardias originate in the right ventricle, can be quite different from that of patients with ischemia-induced LV tachycardias. Fourier analysis can also help distinguish unifocal from multifocal tachycardias. While the majority of patients with ventricular tachycardia have a single LV focus, pleomorphic tachycardia is common. These different tachycardias in the same patient may be due to a single ectopic focus with different "exits," or multiple ectopic foci. Fourier analysis can help distinguish between the two. In the case of monomorphic ventricular tachycardia, a gated blood-pool study before the electrophysiologic examination can serve as a guide for better-localized endocardial mapping. This can result in shorter catheter residence time, reducing the risk of complications. In some cases, moreover, endocardial mapping guided by Fourier analysis may be precise enough to permit catheter ablation of the ectopic focus during the catheterization procedure, using an electrical current passed through the tip of a special catheter (*21*).

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