Comparison of Fixed and Variable Temporal Resolution Methods for Creating Gated Cardiac Blood-Pool Image Sequences

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In each of 50 resting subjects, two gated blood-pool image sequences were created from the same LIST mode data set. One sequence was created using a sorting method that spans each individual cardiac cycle with the same number of images (the "variable temporal" or VT method), while the other (the "fixed temporal" or FT method) spans the average cardiac cycle with images of fixed temporal duration. Left ventricular time-activity curves were extracted from each sequence using identical regions-of-interest and analyzed with identical methods to obtain estimates of ejection fraction, peak ejection rate, peak filling rate, and the times of occurrence of these peak rates. Differences among certain of these parameters in kind and amount support the hypothesis that estimates of resting cardiac function are more accurately portrayed by the FT method. The magnitudes of these differences are small for systolic parameters but large for early diastolic parameters. Thus, although both methods might be used for measuring systolic function, the FT method will yield a more accurate estimate of peak filling rate in resting subjects.

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In gated blood-pool imaging of the heart, scintigraphic image data acquired during many cardiac cycles are additively sorted into an image sequence which portrays cardiac function during a single, average cardiac cycle. Two methods have been proposed for creating such image sequences (1–6). The first and most common of these methods assumes a sequence of consecutive images of equal and fixed duration, the number of which is sufficient to span or exceed the average cardiac cycle length. Scintigraphic image data occurring at the same absolute time after each R-wave in the patient's ECG signal are sorted into the same image in this sequence. If, for example, each image in the sequence is 20 msec in duration, image data occurring between 40 and 60 msec after every R-wave will be sorted additively into

the third image of the sequence. We shall refer to this method as the "fixed temporal" (FT) resolution method since the duration of each image remains fixed during the sorting process (1–2).

A second method, proposed many years ago (3–4), but only recently available commercially, spans each individual cardiac cycle with the same number of images regardless of cycle length. Since cardiac cycle length varies from beat-to-beat, it follows that the duration of the images in one cycle will generally be different from the duration of the images in the next. For example, if 40 images are chosen to span all cardiac cycles, image duration would be set to 20 msec for an 800 msec cycle and to 15 msec for a 600 msec cycle. The final image sequence would be formed by adding together the first image in all cycles, the second image in all cycles, and so on, regardless of the differing duration of images in each individual cycle. We shall call this method of creating a gated blood-pool image sequence the "variable temporal" (VT) resolution method since image duration varies from beat to beat during the sorting process. We note that most commercially available gated blood-pool software utilizes an acquisition protocol in which the user is asked to specify the number of images with which to span the cardiac cycle. Such systems, while perhaps appearing to vary image duration from cycle-to-cycle, do not actually do so. Instead, the number of requested frames is used along with mean cycle length simply to calculate the fixed frame duration required for subsequent application of the FT method. The VT method, in contrast, actually does vary image duration from beat-to-beat.

For a variety of reasons (mostly having to do with the limited memory and computational abilities of early nuclear medicine computer systems) the FT method has been adopted (de-facto) as the standard in nearly all laboratories regardless of whether data is collected in list mode or directly in frame mode. Recently, however, it has become practical to implement the VT sorting method on nuclear medicine computer systems, and in fact this method is now available on at least one commercial system. There are several important prac-

tical differences between the two methods—for example heart rate fluctuations do not cause VT data to "fall off" at the end of the cycle, as often occurs with data from the FT method. In addition, while the two methods appear at first quite similar, they are based on two very different physiologic assumptions. The VT method assumes that variations in cycle length represent a uniform expansion or compression of the LV volume curve in time, depending upon whether the cycle was longer or shorter than usual. A short beat is assumed to be a linearly compressed copy of a long beat. The FT method, however, is based upon the assumption that beat to beat fluctuations in cycle length cause only truncation or elongation of the end of the curve (e.g., during diastasis) when a beat is shorter or longer than usual. The FT method implicitly assumes that the systolic and early diastolic portions of the volume curve remain unaltered in shape from one beat to the next, even though those beats may be of slightly different lengths.

The VT method has some practical advantages over the fixed frame time method which might make it a desirable alternative to the more widely utilized FT method. Before making a decision as to whether to use this newly available VT method, one must know whether the two methods give equivalent results, and if not, which method is the more correct. These are the issues addressed in this paper. In particular, (a) do differences between the methods exist; (b) are these differences clinically significant; and (c) which method most accurately reflects the functional behavior of the resting heart.

METHODS

Fifty consecutive resting subjects in sinus rhythm underwent gated blood-pool scintigraphy using 15–20 mCi of technetium-99m (^{99m}Tc) [in vivo labeled red blood cells and a 15° modified left anterior oblique (LAO) view]. In all subjects image data were collected in LIST mode for at least 10M events (8–10 min) with timing marks inserted into the LIST mode data stream at a rate of 1000/sec. Full field (16 cm diameter) count rates under these conditions averaged ~20k events/sec.

In one of these subjects (a normal volunteer), a much larger (~25M) number of counts was accumulated. Just before this study, it was observed that although in normal sinus rhythm, this subject exhibited a very wide range of cardiac cycle lengths (a finding typical of young athletes with low heart rates). The opportunity thus presented itself to construct multiple image sequences from this subject's image data, accepting for each sequence a successively greater range of cardiac cycle length variations about the mean cycle length. A greater number of events was collected to maintain, in part, the statistical precision of measurement when these data were fractionated into image sequences utilizing a narrower than normal range of cycle lengths.

Before processing of the LIST mode image data acquired in each subject, all cycles with lengths outside ±16% (on

average) of the mean cycle length were rejected, eliminating image data that occurred during "bad" beats, e.g., premature ventricular contractions, ectopic beats, mis-triggers, etc. Each LIST mode data set was then sorted into two complete image sequences. One of these sequences was created using the FT method while the other used the VT method. With the VT method, each individual cardiac cycle was divided exactly into 40 images, the average duration of which was computed for each study. The FT sequence for this same subject was then created using this same (fixed) frame duration so that the FT and VT sequences in the same subject would have almost exactly the same temporal resolution. The possibility of introducing artifactual differences between the sequences due to differences in gross temporal resolution was thus minimized. Temporal resolution averaged over all studies was 22 msec/frame.

Following these maneuvers, a single fixed left ventricular region of interest (ROI) and a background ROI were defined (manually) for each subject (7). This pair of regions was then applied to the FT and VT image sequences created for that subject to obtain an FT and a VT left ventricular time-activity curve. These paired curves were then analyzed with identical methods (8) to obtain: left ventricular ejection fraction (EF), peak ejection rate (PER), peak (early) filling rate (PFR), and the times of occurrence of these peak rates relative to the R-wave (TPER and TPFR, respectively). Rates of change were measured in end diastolic volumes per second (EDVs/sec) and times in milliseconds. EF was expressed as a dimensionless quantity. PFR and PER (and their associated times) were calculated from a polynomial fit to a small region of the LV curve, exactly as described in Reference 8. No prior filtering was performed on the data, and in any case the analysis was identical for the VT and FT curves.

In the individual subject with large sinus rhythm cycle length fluctuations, three additional paired VT and FT image sequences were created. Each pair was processed so as to include an increasing range of cycle lengths about the mean cycle length (from ~±50 msec to slightly more than ±200 msec). Left ventricular time-activity curves were extracted from all six of these sequences using the same left ventricular and background ROIs. These curves were analyzed with the same method (8) to obtain paired estimates of peak filling rate as a function of cycle length fluctuations.

Since the ROIs and analytic methods applied to the VT and FT sequences in each subject were identical and the temporal resolution of these paired sequences essentially the same, differences between parameters computed from these sequences should be due only to inherent differences between the VT and FT sorting methods or, equivalently, to the different assumptions that underlie these methods.

RESULTS

Population averages of EF, PER, PFR, TPER, and TPFR determined from the FT and VT image sequences in all 50 subjects are listed in Table 1. The difference between these means and the significance of these differences (by paired t-test) are also shown.

The dependence of VT and FT estimates of peak filling rate on cycle length fluctuations is shown in Figure 1 for the individual subject in whom these

TABLE 1
Fixed Versus Variable Temporal Resolution Estimates of Left Ventricular Function*

	Fixed temporal (FT)	Variable temporal (VT)	(Difference) (FT-VT)	Significance level Paired t-test
EF	0.550	0.546	0.004	<0.001
PER	-2.800	-2.720	0.080	<0.001
PFR	2.645	2.356	0.289	<0.001
TPER	193	193	0	N.S.†
TPFR	522	532	-10	<0.001

† Not significant.

* Ejection fraction (dimensionless); PER: peak ejection rate (end diastolic volumes/second); PFR: peak (early) diastolic filling rate (end diastolic volumes/second); TPER: time (from R-wave) to peak ejection rate (msec); TPFR: time (from R-wave) to peak filling rate (msec).

fluctuations were large. Peak filling rate determined from the VT sequences declines steadily as the range of cycle lengths included in the study increases. In contrast, peak filling rate determined from the FT sequences does not change significantly over the (large) range of cycle length fluctuations available in this subject. The 1 s.d. error bars bounding each of the three paired data points in this figure represent the uncertainty in each estimate of PFR due to counting (or statistical) fluctuations in the associated left ventricular time-activity curves. Mean cycle length in this subject
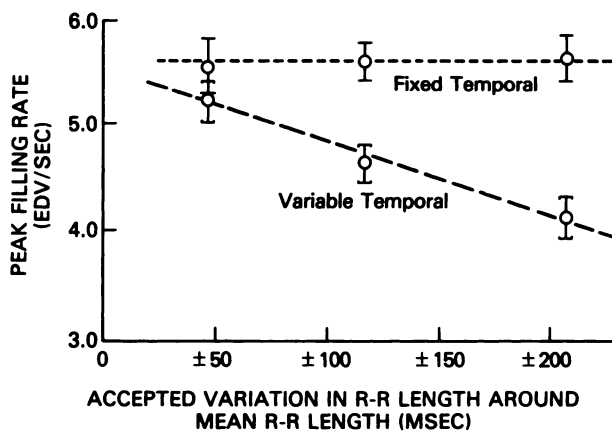
FIGURE 1
Dependence of resting peak filling rate on the range of cycle lengths (around the mean) included in VT and FT image sequences in the same (normal) subject. This subject exhibited an unusually large sinus rhythm variation in cycle length. Peak filling rate by the FT method does not appear to depend on these variations whereas peak filling rate by the VT method declines progressively as a greater and greater range of cycle lengths are included in the VT image sequence. Dashed lines are included only to suggest trends in peak filling rate and are not the result of fitting. Error bars indicate the ±1 s.d. uncertainty in peak filling rate due to counting fluctuations in the left ventricular time-activity curves. Peak filling rate is expressed in end diastolic volumes per second (EDV/sec).

was 860 msec. For this one subject EF and PER did not change significantly as a function of cycle lengths included for either the FT or VT method.

DISCUSSION

As noted in the introduction, the present study was undertaken for three interrelated purposes. We first sought to determine whether the VT and FT sorting methods would yield different estimates of cardiac function if applied to the same LIST mode data set. Inspection of Table 1 indicates that, in general, the answer to this question is yes: statistically significant differences exist in four of the five parameters selected for comparison. Note particularly the pattern of these differences: the magnitudes of PER, PFR, and EF obtained by the FT method are greater than with the VT method; the percentage difference in PER (a systolic parameter) is smaller than the percentage difference in PFR (a diastolic parameter). Of the two timing measures compared, only one, TPFR, differed significantly between methods.

In the event that significant differences between the VT and FT methods were found, the second purpose of the study was to determine whether these differences might be of practical, i.e., clinical, importance. Inspection of Table 1 suggests that the answer to this question for the subject population is, for the most part, no. With the exception of PFR, the observed differences between methods are small. EF, PER, and the timing parameters differ by a few percent or less. Such differences are usually less than the statistical error in these measurements when determined in individual subjects. This is not the case, however, for PFR. The difference between VT and FT estimates of this parameter is >10%, a difference at least comparable to the error in PFR due to counting fluctuations present in individual left ventricular time-activity curves. Thus, while both methods yield similar values of EF, PER and the timing parameters, the magnitude of PFR appears to depend importantly on the data sorting method used to create the blood-pool image sequence. It follows, therefore, that when PFR is to be determined, a choice between the VT and FT methods must be made.

The results obtained in the present study combined with the argument outlined below permit this choice to be made and the third goal of the study to be realized: selection of the sorting method yielding values of resting cardiac function that are closest to the "true" values of these parameters in the patient. We note at the outset that these data and this argument do not permit the absolute accuracy of either method to be determined. We may establish only the relative accuracy of the methods and the comparative validity of the assumptions upon which the methods are based.

As shown in Table 1, the FT method gives slightly higher values for EF, PER, etc., than does the VT

method. It is not known a priori which of the two methods is the more "correct". An examination of the assumptions upon which each of the two methods is based leads us to conclude that the fixed frame time method is the appropriate one for studies performed at rest. If it were instead true that the VT method was the more correct one to use at rest, then the basic premise of the VT method—that shorter beats are compressed uniformly compared to longer beats—would have to be true. The FT method under this premise would "blur" data temporally by not accounting for this compression and expansion of the LV volume curve from one beat to the next. This blurring would result in decreased FT values of EF and of slope dependent parameters relative to the VT method. Such a decrease was not observed. To the contrary, the results showed that the FT method produced values for EF and ejection/filling rates that were systematically higher than those computed using the VT method—exactly what one would expect if the assumptions of the FT method were correct, and those of the VT method were incorrect. This view is further supported by the results portrayed in Figure 1 for the normal volunteer. When cycle length fluctuations are negligible, the two methods should give identical results. This is indeed what was observed (Fig. 1) when beat length fluctuations were minimized by selecting only a narrow range of beat lengths for study. Furthermore, as the range of permitted beat lengths increased, Figure 1 shows that PFR decreased when measured by the VT method, but remained constant by the FT method. These findings are entirely consistent with the conclusion that the assumptions underlying the VT method are violated, while those underlying the FT method are satisfied. In addition, this conclusion would predict that blurring by the VT method because of cycle length fluctuations would be greatest toward the end of the cycle where the VT method must "stretch" or "compress" the curve the most. For this reason, one expects diastolic parameters (such as PFR), to be most affected compared to systolic parameters. This again is exactly what was observed in Table 1—there is a much larger fractional reduction in PFR than PER by the VT method.

Without knowledge of the results obtained here one might have been tempted to conclude that the VT method was based on more sound physiologic ground than the fixed FT method. Other authors have shown that a relationship exists between *mean* resting heart rate and systolic and diastolic timing parameters (9) (e.g., time to end systole is shorter for subjects with high resting mean heart rates than subjects with low resting mean heart rates). Such data might seem to imply that in a particular subject, shorter than average beats might produce ventricular volume curves "compressed" in time, compared to volume curves from longer than average cycles. If this were the case, the VT method

would be the proper method to employ. The FT method, by ignoring this compression, would result in a temporally blurred volume curve and concommitant reduction in EF and slope parameters such as PER and PFR. In fact the opposite is observed in the present study. The reason for this apparent discrepancy is that although there is a relationship between systolic timing and *mean* heart rate from one subject to the next, there is no such relationship between systolic timing and the resting heart rate variations caused by the random, beat to beat fluctuations in RR length, of a single subject in stable sinus rhythm. In such a single subject in normal sinus rhythm, a shorter than average beat occurs due to a slightly earlier than usual arrival of the next beat (10, 11). The current beat is simply truncated. The current beat has no advance "knowledge" that the next beat will occur either early or late. It cannot, therefore, be uniformly "stretched" or "compressed", but simply truncated.

It should be pointed out that the subjects studied had an average heart rate of 72 bpm. The present results, therefore, are not germane to the higher heart rates found during exercise. Possibly at exercise the assumptions of the VT method are more valid, but this remains untested. It should be noted that at stable exercise, the RR interval width is usually much narrower than at rest. Since the two methods are identical when there are no beat length variations, one might expect either method to give similar results during exercise. Finally, it must be remembered that although the FT method gives only slightly "better" results on average than the VT method, the results presented here have been extracted from population averages, so larger differences between the methods that might occur in individual subjects are not evident. Results obtained in the individual subject (Fig. 1), however, indicate that in some instances these differences can be both large and strongly dependent on the amount of cycle length fluctuation. In this subject, and to a lesser degree in all subjects, a gated blood-pool study performed with the VT method would yield not only reduced estimates of PER and PFR but a preferentially reduced estimate of PFR in relation to PER. Moreover, the magnitude of this reduction would depend strongly on the cycle length rejection criterion applied to the study. Most of these difficulties could be avoided by simply using the FT method for all resting studies.

CONCLUSION

A population of subjects in normal sinus rhythm was investigated with two different gating methods—the fixed FT method and the variable time (VT) method. In general, small but statistically significant differences in various indices of resting ventricular function were found between the two methods. Because the FT method gave consistently higher values for these param-

eters, and because this method was less sensitive to beat length fluctuations, it was concluded that the assumptions underlying this method were, on average, the more valid of the two. Since the differences between the resting parameters measured with the two methods were small (with the exception of PFR), however, it is likely that either method is suitable to evaluate systolic function in subjects in normal sinus rhythm. In these restricted circumstances the VT method offers the practical advantage of not having any drop off of counts at the end of the cycle. For studies of resting diastolic function, however, the VT method may significantly underestimate diastolic parameters such as peak filling rate. Also, in certain individual subjects (especially those with large heart rate fluctuations) parameters measured with the VT method may be even more severely underestimated than the population mean values shown in Table 1. Most of these difficulties can be avoided by using the conventional FT method to assess cardiac function in resting subjects.

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