Optimizing gated myocardial perfusion imaging processing for phase analysis

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INTRODUCTION

In recent years, analysis of tomographic gated myocardial perfusion imaging (gMPI) has become increasingly sophisticated, and now includes measurement of left ventricle (LV) phase and dyssynchrony. Measurement of dyssynchrony has been suggested to have long-term prognostic value,[1] and as a better way to identify clinically important multivessel coronary artery disease.[2] Characterizing the magnitude of dyssynchrony as well as the area of latest contraction may contribute to the patient's referral to, or exclusion from, high-cost interventions such as cardiac resynchronization therapy (CRT).[3,4]

Careful determination of processing parameters is critically important, to avoid artifacts and ensure consistent and clinically meaningful results. Parameters (apex, base, center, radial extent) which are acceptable for functional analysis, are not necessarily optimal for phase analysis.

Moreover, phase analysis is important in some patient groups not historically referred for gMPI, whose studies can present challenges for processing. In addition to perfusion defects, these patients may have significant heart failure, and have very poor function or large, remodeled volumes.[5,6] In most publications which incorporate phase analysis results, the approach used for verifying processing parameters is not emphasized. A systematic approach to processing for obtaining optimal phase analysis is needed, and is the subject of this article.

gMPI PROCESSING

Analysis of Function

gMPI processing includes the routine calculation of functional measures such as volumes and ejection fraction (EF) of the LV. Parameterization, typically performed automatically by computer software, is first a matter of defining the radial extent (center to outside myocardial boundary) and longitudinal extent (apex to base) of the LV. For analysis of function, this process is reasonably forgiving, in that the small changes in LV length or center minimally affect the calculated EF.

Determination of wall thickening is an extension of functional analysis. Thickening can be inferred from the change in image brightness during the systolic portion of the cardiac cycle. This brightening is an incidental benefit of the partial volume effect, in which objects show variable count density in proportion to their thickness, when that thickness is less than twice the resolution of the imaging device, as measured by full width at half maximum on the imaging system's response curve. End diastolic LV wall thickness falls into the size range of objects subject to this effect.[7-9]

Phase analysis is a further extension of the thickening determination.[10] For every location in the LV, the time during the cardiac cycle at which that location begins to thicken (i.e., begins a cycle of contraction) can be plotted in histogram or polar map form. Since the normal ventricle contracts in a regular, synchronous way, areas of unusually early or late contraction—dyssynchrony—can be seen visually, or described quantitatively.

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LV Longitudinal Extent

Since LV phase analysis depends heavily on counts, locating where the myocardial counts end at the base of the heart is the most important element in determining whether the appropriate set of pixels is subjected to phase analysis. At the base or proximal end of the LV are the aortic and mitral valves, so the last basal slice can be considered the LV valve plane.

In gMPI, no significant structure is imaged proximal to the valve plane. Wall thickening is heterogeneous in the LV, and is less evident approaching the LV base. The same trend is assumed for phase, and, although more-basal slices may include *some* true myocardium, these slices contract minimally, and should be excluded.[11]

Automatic Processing

Automatic gMPI parameterization[10,12,13] is certainly more reproducible than if parameters were always set manually. This step is typically assumed to be correctly done, but this may not be true in all studies. Automatic software may not be optimized for locating the gated valve plane. It is the user's responsibility to make sure processing parameters are appropriate for determination of phase and dyssynchrony.

Parameterization for gated images is theoretically more precise and robust than for ungated images. The ungated study is a summation of the cardiac cycle, and always subject to blur from cardiac motion. While blur is not totally eliminated by gating, it is greatly reduced (Figure 1). Defining the valve plane separately for each gate would seem to lead to more precise analysis than if a single plane, determined from the ungated study, was used.

Working against the advantage of gating are two main challenges. First, the individual gate images are each a fraction of the count density of ungated images, which is problematic for base selection due to noise.[2] Second, the parameters for each gate must be considered both individually and in the context of other gates from diastole through systole, to ensure they make physiologic sense. Consistent parameterization is important in comparing studies, particularly as analysis software is evolving to characterize the phase of individual segments of the 17-segment model. Studies are likely to be compared in many contexts. In the normal and infarct instances, more synchrony is expected at stress than rest, while for severe ischemia, more dyssynchrony is expected at stress.[14] After an intervention such as CRT placement, synchrony at rest may be better, the same, or poorer than baseline. Optimal image processing increases the clinician's confidence in the clinical significance of the phase results.

In our experience, automatic determination of gated center, radial extent and apex is robust and repeatable. Defining the valve plane too far proximally (toward the aorta) is probably the main error in both automatic and manual parameterization.

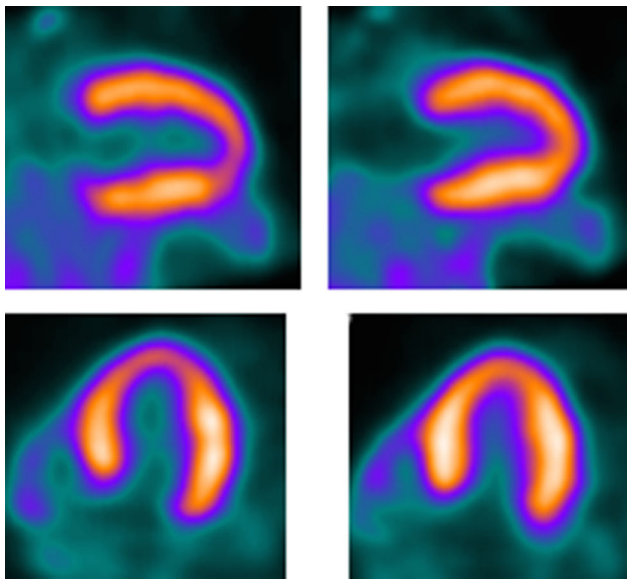

Figure 1. Images from a single patient showing matched pairs of *vertical* and *horizontal long axis* slices. Gated end diastolic images (*left column*), have reduced blurring and better luminal contrast compared to ungated slices (*right column*).

An Approach for Consistent Parameterization

Our recommended algorithm for optimizing gated parameters begins by using the ungated images as a guide. Automatic software typically uses ungated parameters as a starting point for an iterative process of defining gated parameters.[9] The user verifies that all ungated parameters are appropriate. In the typical case, the last ''true'' base slice presents as a characteristic ''backwards C'' shape, which may be rotated, depending on the orientation of the heart.

Next, the user should ensure that the gated base at end systole is not further out than the ungated base. The rationale is that the ungated images incorporate motion blurring, and base selection is more dependent on the systolic phase, since these slices are brighter, (have more counts), owing to the partial volume effect. In a few cases, visual review may suggest the end systolic base should be moved one slice further in; however, this may also be a sign that the ungated base selection should be revisited.

The base slice (the valve plane) is then allowed to move outward in frames approaching diastole. The base may change during the cardiac cycle by one slice in studies with low to moderate EF, and by up to two slices in studies with moderate to high EF. The apex may also change by up to one slice at systole, due to thickening, but this has less impact than the base on phase analysis.

The goal of this algorithm is to exclude from phase analysis those regions which are non-contracting and therefore irrelevant for phase. The phase polar map and histogram artifacts created by including inappropriate pixels can be reduced by following a logical, repeatable process for parameterization. The algorithm makes assignment of the critical gated valve plane location more objective, because it depends on a systematic relation to the ungated parameters, and is less dependent on user's judgment of the visual appearance of individual gated images.

This systematic approach is intended to better satisfy the assumption of phase analysis that there is consistent count density in all gated time intervals, so that the interval-to-interval change is meaningful. The approach is also consistent with an earlier published recommendation by Trimble et al to use manual base selection to reduce low frequency image noise, thus making phase analysis more repeatable.[6]

It is important to note that visual cues which usually guide manual parameter adjustment can be variable, and are therefore not the ideal guide for locating the valve plane. Very low EF means little change in image brightness or LV size during the cardiac cycle, making it harder to identity systole. The ''backwards C'' shape may not be present because of LV shape or perfusion defect (see Figure 2). End diastole may occur not at the first gated interval as expected, but at the last one. If the last gated slice has an obviously larger volume than the first gated slice, and is not count deficient, its base may be set one slice further out. Of course, as for perfusion and function, all parameters are important, not just the base slice selection. Figure 3 shows an example of center placement affecting phase results.

This algorithm can be applied to both normal and abnormal studies. The task is always to define longitudinal LV extent, as shown in Figure 4. For any type of study, incorrect processing parameters can affect quantitative phase results. In the normal study, incorrect processing can introduce false areas of apparent dyssynchrony in the phase map, most often at the base, as shown in Figure 5. For the abnormal study, suboptimal processing is unlikely to prevent significant dyssynchrony from being detected, but it can make additional

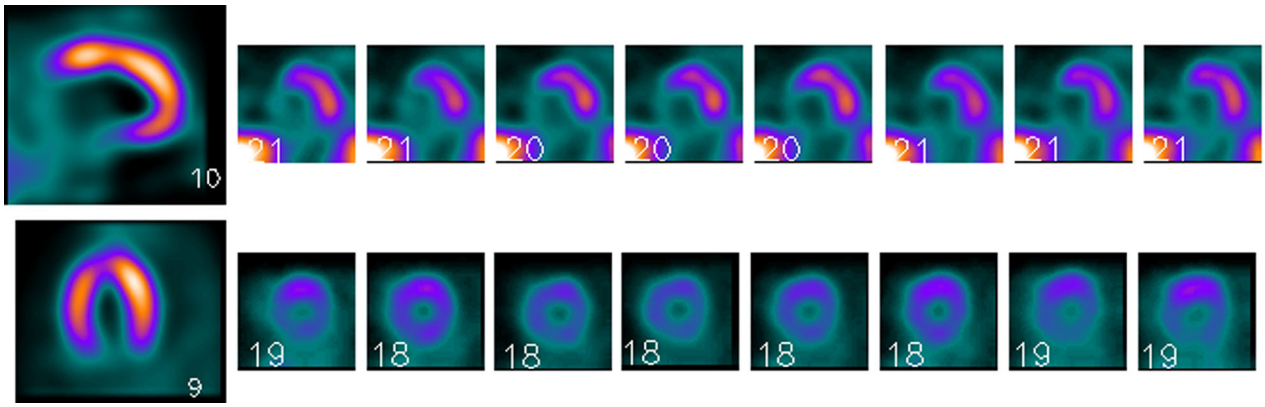

Figure 2. Two different patient studies in which the optimal gated base does not reflect the backwards ''C'' pattern: severe inferior wall perfusion defect (**A**), and atypically long septal wall (**B**).

myocardial segments appear abnormal, and change the location and severity of existing dyssynchrony. Figure 6 is an example of this.

Minimizing Errors in Phase Analysis

The following elements of functional analysis can be used to help minimize the occurrence of phase artifacts and ensure appropriate analysis of dyssynchrony.

- *The ECG/heart rate histogram* Especially in patients with known arrhythmias, verify if possible that the HR from the ECG trigger matches the true HR of the patient. Significant arrhythmia can impair functional analysis, wall thickening,[15] and phase analysis.[16] If the acquisition is list-mode, it may be possible to exclude the arrhythmic or heart-rate-variable portion of the study.
- *The gated cine display* Verify LV boundaries, to make sure these track wall motion throughout the cardiac cycle. If the boundaries ''wander''[1] at the base,[2] on the septal side where myocardium is thinner, or[3] in one or more gates, then parameters may need to be adjusted. If anomalous boundaries cannot be corrected, both EF and phase results should be viewed with caution.
- *The phase polar map* Note the presence of white partial ring, or white spots surrounded by black pixels, at the base (Figure 7), suggesting that the valve plane is incorrect, probably too far out in one or more gates. This is more common on the septal side due to myocardial thinning, and may not be entirely fixable. When adjusting any parameter to fix a phase map artifact, make the minimum number of changes necessary to eliminate the artifact. In general, late

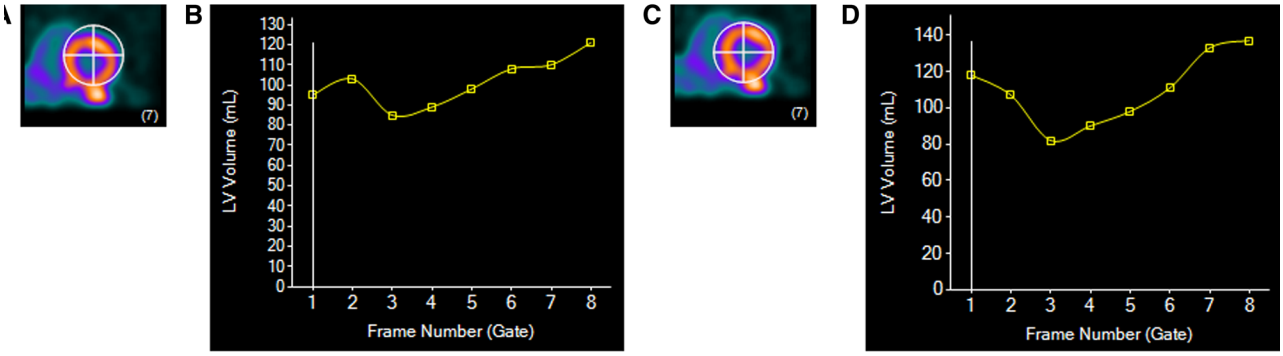

Figure 3. In this study, the LV center was manually adjusted to avoid bowel tracer activity (**A**) resulting in truncation of the inferior LV and an unusually shaped volume curve (**B**). Adjusting the center (**C**) results in a more plausible volume curve (**D**). After correction, LV ejection fraction changed from 30% to 40%, phase histogram bandwidth changed from 94 to 69, and histogram standard deviation changed from 35 to 26.

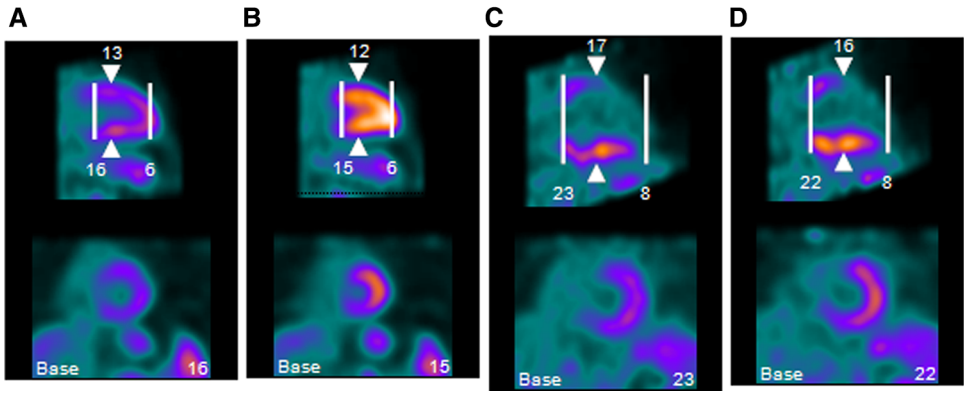

Figure 4. Base slice selection shown on vertical long axis (*top row*) and short axis. (**A**, **B**) Show end diastole and end systole, respectively, in a normal study. (**C**, **D**) Show end diastole and end systole in an abnormal study with poor function. Note that the abnormal study shows much less brightening at systole.

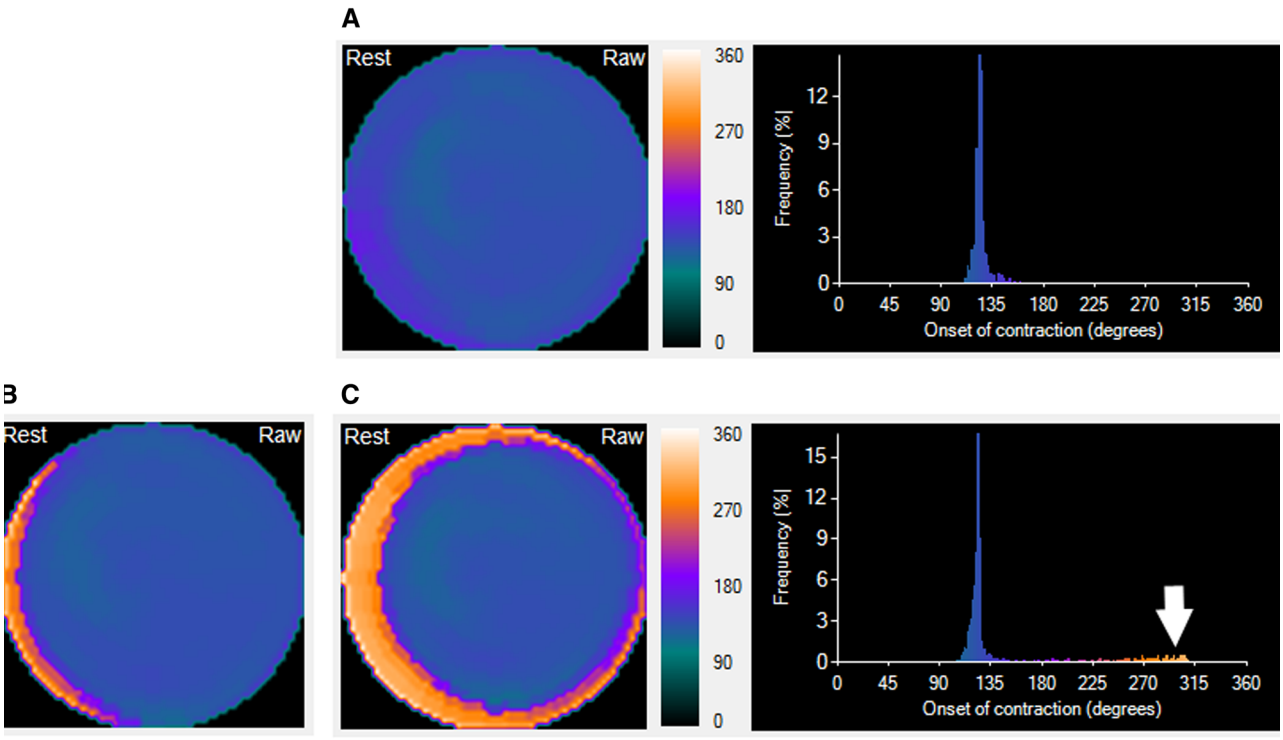

Figure 5. A study with normal, synchronous phase. (**A**) Shows the phase polar map and histogram with optimal processing parameters. When one or more gated bases are chosen too far toward the valve plane by one slice (**B**), a basal artifact begins to appear, which is more pronounced as the base moves further out (**C**). Valve plane artifact represents phases that are 180° different from the LV peak phase, as shown by the *arrow*. These can be removed with adjustment of the gated base.

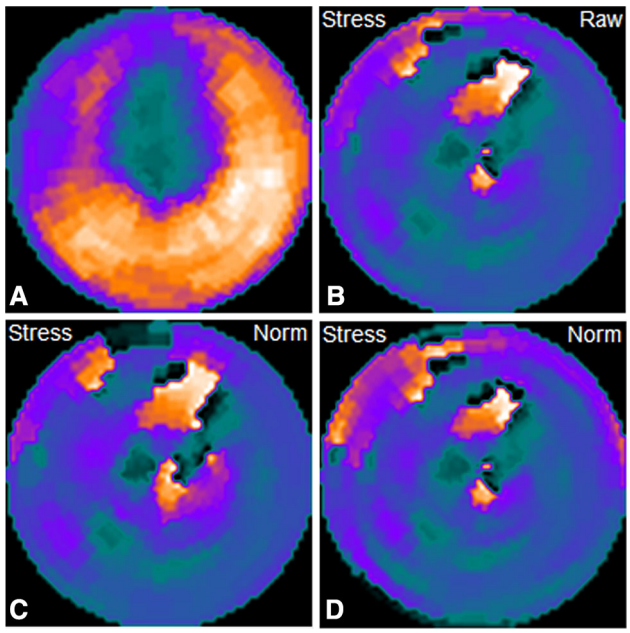

Figure 6. A study with an abnormality in the perfusion polar map (**A**), and dyssynchrony in the same region (**B**). When gated base slices are chosen too far in, away from the valve plane, the anterior wall dyssynchronous area appears larger (**C**) because it is represented by fewer slices or rings. When gated bases are too far out, anterior dyssynchrony is smaller, and basal dyssynchrony is larger (**D**).

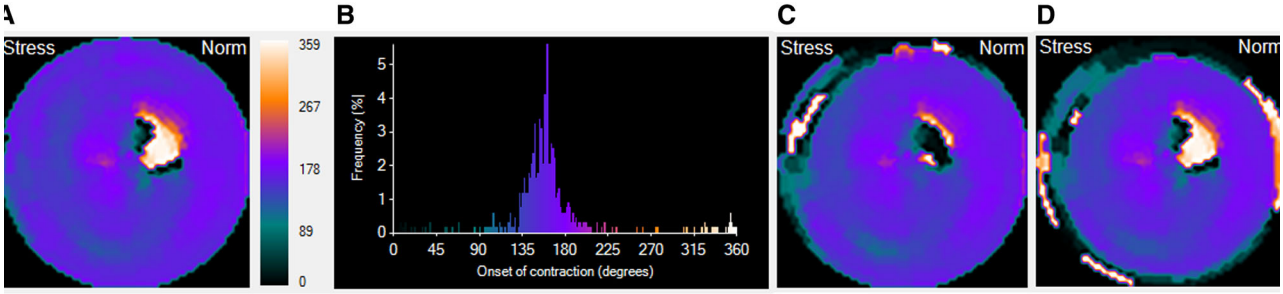

Figure 7. A study with true dyssynchrony on phase polar map and histogram (**A**). As the base is moved further out, characteristic artifact appears on the polar map (**B**, **C**), but the true abnormality is still apparent.

phases that are 180 degrees from the histogram peak are more likely to be artifact.

- *The LV volume curve* This curve can be an indicator of gating error, but also of incorrect parameters. The curve, calculated EF, and phase are related, and any of these can be affected by suboptimal parameterization. EF as shown by the volume curve should be compatible with the visual impression from gated slice cine playback.

CONCLUSIONS

The availability of phase analysis, and its proposed use to derive important prognostic information, places an increased emphasis on optimal processing. While automatic parameterization algorithms have proven robust and reproducible for analysis of function, definition of the valve plane is a critical parameter for phase analysis, and may not be automatically optimized in some patient studies.

To minimize error in phase results we can use the relation between gated and ungated images to help define the valve plane. In this approach, the end systolic base can be set to the ungated base slice number (valve plane), and the base for diastolic gates can be allowed to move outward by one or at most two slices, reflecting myocardial excursion during LV contraction. A physiologically plausible shape of the volume curve and absent or minimal artifact on the phase polar map, especially at the base, help confirm appropriate parameterization.

Disclosure

The authors receive royalties from the sale of Emory Cardiac Toolbox (ECTb) software, and have an equity position with Syntermed, Inc., which markets ECTb. The terms of these arrangements have been reviewed and approved by Emory University in accordance with its conflict of interest policies.

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