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Abbreviation:

TI = inversion time

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Guarantors of integrity of entire study, G.S.S., S.D.W., T.K.F.F.; study concepts and design, G.S.S., S.D.W., T.K.F.F.; definition of intellectual content, G.S.S., S.D.W., T.K.F.F.; literature research, G.S.S., T.K.F.F.; clinical studies, S.D.W.; experimental studies, G.S.S.; data acquisition, S.D.W.; data analysis, S.N.G.; statistical analysis, G.S.S., S.N.G.; manuscript preparation, G.S.S., T.K.F.F.; manuscript editing and review, all authors.

First-Pass Myocardial Perfusion MR Imaging with Interleaved Notched Saturation: Feasibility Study¹

The authors evaluated a magnetization preparation scheme with a “notched” section profile for T1-weighted first-pass myocardial perfusion magnetic resonance (MR) imaging at 1.5 T. The pulse sequence consisted of a preparation sequence followed by an interleaved gradient-echo echo-planar sequence. Image contrast was evaluated in a feasibility study in 12 adult patients. The notched saturation pulse allowed long magnetization recovery times without sacrificing section coverage. Image contrast between normal and ischemic myocardium was excellent.

Diagnosis of coronary artery disease is a major challenge for noninvasive medical imaging and an active area of research in magnetic resonance (MR) imaging. Although coronary MR angiography can help identify the presence of intracoronary lesions, their hemodynamic or functional significance cannot necessarily be determined (1). Direct visualization or measurement of blood flow to the myocardium would be desirable.

The feasibility of first-pass contrast material-enhanced perfusion MR imaging has been demonstrated by several groups (2–6), but the difficulty in optimizing all aspects of the acquisition sequence has resulted in compromised image quality or reduced anatomic coverage. Successful first-pass perfusion MR imaging requires that several issues be addressed, including the following: (a) coverage of the heart from apex to base (which typically requires at least six short-axis views),

(b) temporal resolution (ie, time between repeated acquisitions at the same section location) that is sufficient to allow adequate sampling of the first pass of the contrast material bolus, (c) a relationship between signal intensity and contrast material dose (ie, input function) that is quantifiable (preferably linear), and (d) contrast- and signal-to-noise ratios that are sufficiently high to allow discrimination between normal and ischemic regions of the myocardium.

To meet these goals, current perfusion techniques make use of fast gradient-echo MR imaging sequences in combination with various magnetization preparation schemes for T1 weighting, including inversion recovery (2–5), saturation recovery (7–10), or partial saturation (11,12). Shortcomings of these approaches include the following: (a) the number of sections acquired is limited owing to long acquisition time or magnetization recovery inversion time (TI), (b) image contrast and signal-to-noise ratio are inadequate owing to use of low preparation flip angles or short TIs, and (c) input functions are not quantifiable owing to sensitivity to arrhythmias.

Regardless of the type of preparation used, the magnetization recovery TI plays a major role in determining contrast, signal-to-noise ratio, and the maximum number of sections that can be acquired. A short recovery time permits the acquisition of more sections per cardiac cycle but sacrifices signal-to-noise ratio and contrast owing to minimal relaxation. A long TI provides higher signal-to-noise ratio and better contrast, but the delay inserted between preparation and acquisition reduces the maximum number of sections that can be acquired.

The purpose of this study was to develop and evaluate a technique for simul-

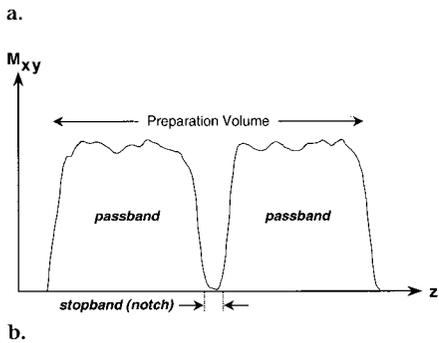
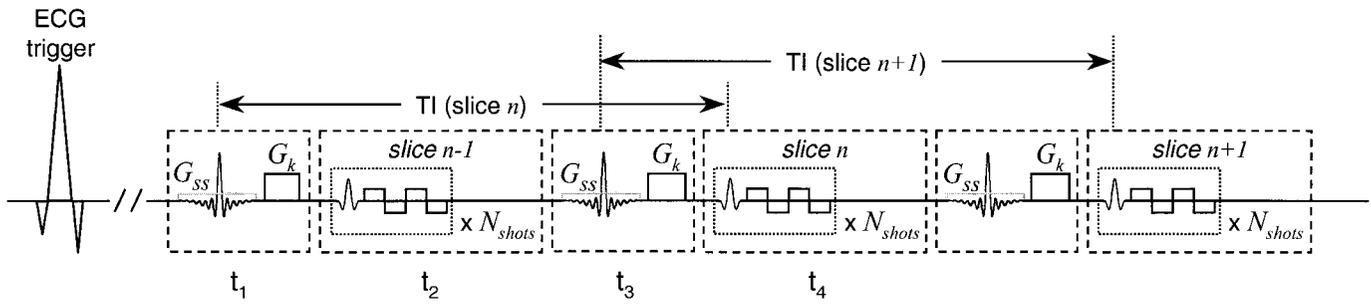


Figure 2. Schematic of magnetization preparation with interleaved notched saturation. Time points t_n are defined in Figure 1a. The time between the preparation and acquisition of section n (t_4 and t_1 , respectively) is the effective TI. The sections are labeled to reflect the actual temporal order of the interleaved sections (odd sections first, then even sections). *EPI* = echo-planar imaging.

taneously achieving long TIs and multi-section capability (ie, multiple sections per cardiac cycle) for T1-weighted first-pass myocardial perfusion MR imaging. This technique was developed without inserting explicit delays into the sequence or sacrificing section coverage.

Materials and Methods

Pulse Sequence

Pulse sequence timing is shown in Figure 1. The pulse sequence consists of a preparation sequence followed immedi-

Figure 1. (a) Diagram shows pulse sequence for first-pass myocardial perfusion MR imaging with interleaved notched saturation recovery. The preparation sequence (at t_1 and t_3) consists of a radio-frequency pulse with a notched section profile that saturates tissue in the passband of the preparation volume. The resultant transverse magnetization is dephased by means of a gradient crusher pulse G_k , which is immediately followed by a gradient-echo echo-planar sequence (t_2, t_4), during which all the data for one section are acquired. No delay is inserted between the preparation and acquisition sequences. The preparation-acquisition combination is repeated for all prescribed sections across two cardiac cycles, yielding one temporal phase for each section. Thirty phases are acquired during 60 heartbeats. Time points t_n are presented in the text. *ECG* = electrocardiography, G_{ss} = section-select gradient, N_{shots} = total number of acquisitions required for a complete image. (b) Actual section profile of the notched saturation pulse.

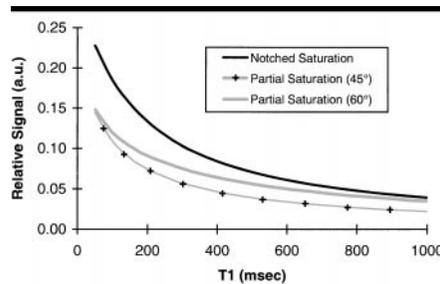


Figure 3. Bloch simulations show signal intensity response versus T1 for magnetization preparation with notched saturation (90° preparation pulse, 185-msec TI, 25° excitation flip angle) and partial saturation (45° or 60° preparation pulse, 10-msec TI, 12° excitation flip angle). Notched saturation produces considerably better contrast between short T1 (enhancing) and long T1 (nonenhancing) tissue. *a.u.* = arbitrary units.

ately by an interleaved gradient-echo echo-planar sequence. The use of echo-planar sequences with short echo trains (ie, data acquisition windows of approximately 10 msec) in the heart (10,13–15) results in good to excellent image quality, while providing immunity to motion and off-resonance effects that can corrupt images obtained with sequences with long echo trains (16).

The basic sequence structure used in this study differs from previously reported perfusion techniques in two ways. First, as depicted in Figure 1, there is no explicit delay for relaxation prescribed between preparation and acquisition. Second, the consecutive preparation and acquisition pulses do not affect the same section. To account for the absence of an

explicit delay, this method makes use of a radio-frequency saturation pulse with a band-stop or “notched” section profile rather than a conventional section-selective or nonselective pulse. As shown in Figure 1b, saturation bands are created on both sides of a notch, which is centered such that spins in the subsequently imaged section are unaffected by the preparation pulse. The presence of the notch essentially decouples the preparation-acquisition combination, causing each preparation pulse to affect the next (as opposed to the immediately following) section. As a result, a longer recovery time is achieved without sacrificing spatial coverage or introducing any delay between preparation and acquisition.

The effect of the interleaved notched saturation is demonstrated in Figure 2. The radio-frequency preparation pulse for section $n + 1$ (t_3 in Figure 2), which preceded the acquisition of section n (t_4), saturated all tissue in the selected volume except that in section n . Spins in section n were unaffected by this pulse because they fell within the notch. These spins, however, were saturated by the preparation pulse (t_1) that immediately preceded the acquisition of section $n - 1$ (t_2). Therefore, the spins in section n recovered for a time spanning the acquisition of section $n - 1$ and the preparation of section $n + 1$. This time is the effective TI, which equaled 185 msec for the imaging parameters used in this study.

As shown in Figure 3, a saturation recovery preparation with a 90° pulse and a 185-msec TI can provide considerable improvement in signal intensity and

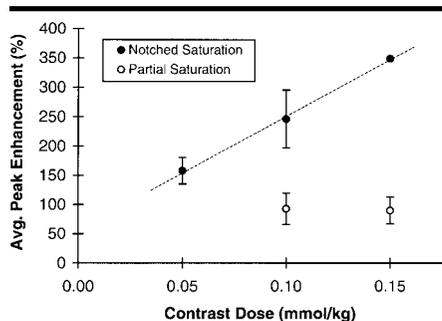


Figure 4. Scatterplot shows mean (Avg.) peak contrast enhancement for notched saturation and partial saturation protocols. Note the linear relationship between peak enhancement and contrast material dose with notched saturation ($r^2 = 0.9989$). Error bars indicate plus or minus 2% for notched saturation with 0.15 mmol/kg.

contrast over a partial saturation preparation with a 45° or 60° pulse and a 10-msec TI. Multisection partial saturation has been reported in two clinical studies (11,12); despite low signal-to-noise ratio, the relatively high contrast material doses (0.14–0.15 mmol per kilogram of body weight) permitted diagnostic accuracies of between 70% and 85% in blinded assessment of the perfusion data. Quantitative analysis of the same data proved difficult, however, owing to the low signal-to-noise ratio.

MR Imaging

MR imaging was performed with a 1.5-T system (Signa CV/i; GE Medical Systems, Milwaukee, Wis) with 40 mT/m peak gradients and 150 T/m/sec maximum slew rate. The acquisition was an interleaved echo-planar sequence (10) with a short echo train, which was also used in the partial saturation protocol. The following parameters were used for all MR imaging studies: electrocardiographic triggering, repetition time msec/echo time msec/TI msec of 6.6/1.4/185, echo train length of four, 20° or 25° excitation flip angle, 36 × 27-cm field of view, 10-mm section thickness with 0–2-mm spacing (adjusted for coverage from apex to base), 250-kHz receiver bandwidth, and 128 × 128 acquisition matrix (96 k_y lines). Seven interleaved short-axis sections were collected after a single electrocardiographic trigger, with data acquisition spanning two cardiac cycles. This yielded a temporal resolution of one image every two R-R intervals. Eight studies were performed with a contrast material (gadopentetate dimeglumine, Magnevist; Berlex Laboratories, Wayne, NJ) dose of

Mean Peak Contrast Enhancement for Notched Saturation and Partial Saturation Protocols

Contrast Material Dose (mmol/kg)	Mean Peak Enhancement		Improvement Factor‡
	Notched Saturation*	Partial Saturation†	
0.05	158% ± 23§	NA	NA
0.10	248% ± 49	93% ± 27	2.7
0.15	349% ± 2	90% ± 23	3.9

Note.—Data are the mean ± SD. NA = not applicable.

* Data from studies acquired with flip angles of 20° and 25°.

† Differences were not statistically significant.

‡ Data are the ratio of peak enhancement for notched saturation to that for partial saturation.

§ Difference compared with dose of 0.10 mmol/kg, $P < .05$.

|| Difference compared with dose of 0.10 mmol/kg, $P < .001$.

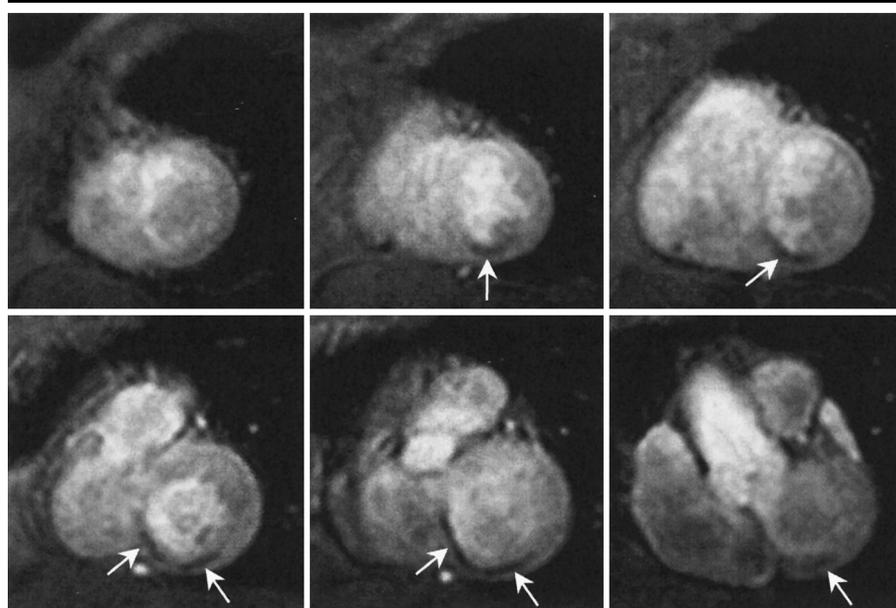


Figure 5. Stress perfusion MR images depict six sections at one time point in a patient with 80% stenosis of the right coronary artery, as determined at conventional angiography. The region of perfusion deficit in the posterior septal wall (arrows) conforms to the vascular territory of the right coronary artery and does not appear in the rest images (not shown), indicating reversible ischemia.

0.10 mmol/kg, and two studies each were performed with doses of 0.05 and 0.15 mmol/kg.

The preparation sequence was a 15-msec radio-frequency pulse with a notched frequency response and 2,600-kHz bandwidth that was used in the presence of a section-select gradient. Because seven sections were acquired in an interleaved manner (ie, sections 1, 3, 5, 7, 2, 4, 6), the passband needed to be at least as wide as the largest spacing between any two consecutive sections. In this case, section 2 was saturated when the notch was at section 7. Therefore, the width of each saturation band was designed to be five times the width of the notch; the overall width of the preparation volume was 165

mm. To allow some motion of the section during the TI, the notch width was 50% greater than the section thickness. The total duration of the preparation sequence was 18 msec, including time for the gradient dephasers. The shape of the radio-frequency pulse is shown in Figure 1a, and an actual section profile is shown in Figure 1b.

Patient Study

A feasibility study to evaluate image contrast was conducted with 12 outpatients (eight men and four women; age range, 54–76 years; mean age, 66.6 years ± 6.2 [SD]) with known or suspected coronary disease. All patients had undergone

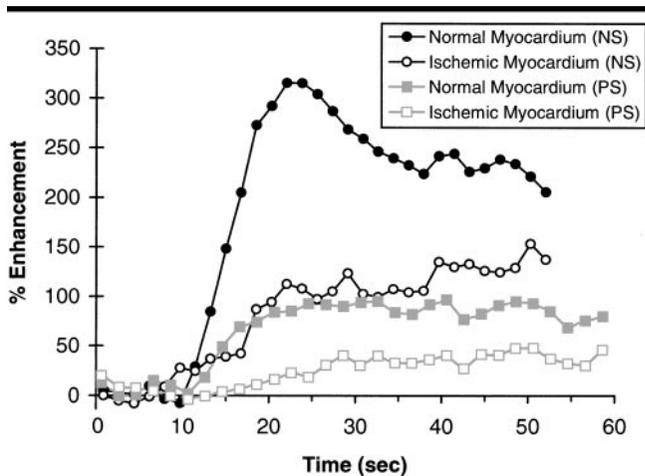


Figure 6. Line graph presents the percentage contrast enhancement versus time for regions of normal and ischemic myocardium from perfusion MR imaging studies with notched saturation (NS) and partial saturation (PS). In addition to greater contrast enhancement with notched saturation, the actual baseline signal intensity is desirably lower than that with partial saturation, even with the use of a higher excitation flip angle (25° vs 12°). The notched saturation data are from section 4 in Figure 5. Each time point corresponds to two cardiac cycles.

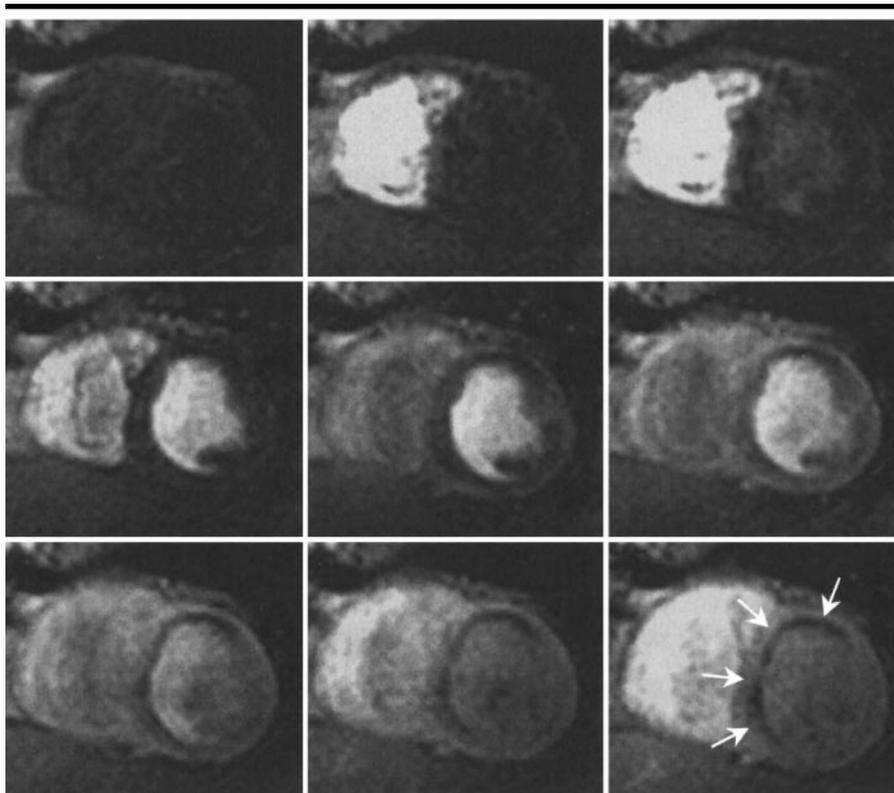


Figure 7. Stress perfusion MR images depict the time course of the first pass of the contrast agent through a midventricular section in a patient with severe three-vessel disease, as determined at conventional angiography (not shown). An extensive region of perfusion deficit can be seen in the septal and anterior walls of the myocardium (arrows). Images are shown at every second time point (1.9 second per time point).

cardiac catheterization as part of their clinical evaluation. The only exclusion

criteria were contraindications to adenosine or contrast-enhanced MR imaging.

All studies were performed after signed informed consent was received from each patient, in accordance with a protocol approved by our institutional review board.

Patients underwent first-pass perfusion MR studies both at rest and with pharmacologic stress. A cardiologist was present in the MR imaging room during all studies. For imaging with stress, adenosine (Adenoscan; Fujisawa Healthcare, Deerfield, Ill) was administered intravenously into an antecubital vein at $140 \mu\text{g}/\text{kg}/\text{min}$, starting 2 minutes before the start of MR imaging. After 2 minutes of adenosine infusion, gadopentetate dimeglumine was administered intravenously into the contralateral arm at $5 \text{ mL}/\text{sec}$ with use of a power injector (Spectris; Medrad, Pittsburgh, Pa), simultaneous with the start of MR imaging. Patients were instructed to hold their breath and to continue the breath hold as long as possible during imaging. Thirty images (phases) were acquired at each section location during 60 heartbeats. The adenosine infusion was discontinued at the completion of MR imaging. After 15 minutes, the rest study was performed with a second dose of contrast material and identical imaging parameters.

Regions of interest were drawn by one of the authors (S.N.G.) in the posterior or anterior septal wall of a midventricular section for each of the 30 phases. Regions of interest were approximately 150 mm^2 . In each case, signal intensity as a function of time was measured and averaged for each contrast material dose. Peak enhancement was calculated as the difference between peak and baseline signal intensity in the regions of interest divided by the baseline signal intensity. These results were compared with those of the partial saturation study (45° preparation pulse, 10-msec TI, 12° excitation flip angle, contrast material doses of 0.10 and 0.15 mmol/kg) (11). Ten cases with each contrast material dose in the partial saturation study were selected retrospectively with use of the criterion that no lesions were detected in the left anterior descending coronary artery with conventional coronary angiography. Results were evaluated with a two-sample *t* test. Differences with a *P* value less than .05 were considered statistically significant.

Results

Figure 4 shows the mean peak contrast enhancement at the three contrast material doses in the notched saturation protocol. The mean peak enhancement for

each of the two contrast material doses in the partial saturation protocol is also shown in Figure 4. Results from both protocols are summarized in the Table. Statistically significant differences between contrast material doses were noted for the notched saturation data, but no significant difference was noted for the partial saturation data. Furthermore, compared with the partial saturation protocol, the notched saturation protocol resulted in a 3.9-fold improvement in the mean peak enhancement with a contrast material dose of 0.15 mmol/kg and a 2.7-fold improvement with a dose of 0.10 mmol/kg. Even with a much lower dose of 0.05 mmol/kg, peak contrast enhancement was still 1.8 times greater than that with partial saturation at 0.15 mmol/kg. As a result, lower contrast material doses can be used with notched saturation, while still providing at least twice the peak enhancement of partial saturation. The notched saturation results in Figure 4 also exhibit a linear relationship between peak enhancement and contrast material dose, which is not seen in the partial saturation results. This is due to the longer magnetization recovery TI and higher preparation flip angle. These results suggest that the current protocol could be amenable to quantitative evaluation.

Figure 5 shows six sections (of the seven sections acquired) at one phase in a perfusion MR imaging study performed in a patient under pharmacologic stress. Figure 6 depicts a plot of the percentage enhancement versus time for regions of normal and ischemic myocardium from the fourth section in Figure 5. Also shown in Figure 6 are enhancement curves for normal and ischemic myocardium from a typical partial saturation perfusion MR imaging study. As reflected in Figures 5 and 6, notched saturation provided greater enhancement and better contrast between enhancing and nonenhancing myocardium. Figure 7 shows the time course of the contrast agent through a midventricular section from another stress perfusion MR imaging study.

Discussion

This study evaluated a magnetization preparation method for multisection first-pass contrast-enhanced myocardial perfusion MR imaging. Use of a radio-frequency saturation pulse with a notched frequency profile enabled interleaving of the preparation and acquisition sequences to produce a long magnetization recovery time.

Unlike with other methods, insertion of a physical dead time into the sequence to allow relaxation between the preparation and acquisition of each section was not necessary. Section coverage was thereby maximized for the heart rate and imaging parameters. A 90° flip angle was used in the radio-frequency preparation pulse to provide stronger T1 weighting and insensitivity to arrhythmias.

The long recovery time and high preparation flip angle also provided better image contrast than did short TI saturation recovery or partial saturation and greater anatomic coverage than did conventional long TI recovery. Furthermore, because blood is saturated on both sides of the imaged section immediately prior to data acquisition, the presence of the notch provides a potential mechanism for blood pool suppression. If saturated blood moves into the imaging plane, it may help discriminate the myocardial wall from the ventricular space and reduce the intensity of flow-related artifacts. The degree of expected in-plane blood suppression is determined by the width of the notch.

Because a given section was prepared before acquisition of the preceding section, the first section represented a special case. The first phase of the first section (ie, the very first image to be acquired) had no preparation. Subsequent phases of the first section, however, were prepared with the saturation pulse that preceded the last section of the previous phase. For example, phase two of the first section was saturated by the preparation pulse preceding phase one of the last section. Consequently, the time between the preparation and acquisition of the first section (ie, the TI) spanned an R wave. The TI for the first section was therefore longer than that for the other sections and was also variable, depending on the R-R interval of the particular heartbeat. Although this effect was not detrimental to image quality or clinical diagnosis, it is possible to apply a custom preparation scheme for the first section.

Imaging was performed through the R wave of the second cardiac cycle for two reasons. First, it maintained the preparation-acquisition timing for all sections except the first, as discussed previously. If half the sections were acquired in each of two cardiac cycles, the middle section would also have a heart-rate-dependent TI. Second, imaging through the R wave obviated two trigger windows. This afforded more time for data collection, often allowing the acquisition of an additional section. It should be noted that registration of the sections acquired dur-

ing the second R-R interval was not appreciably affected by modest changes in heart rate.

In light of the results of this study, we are continuing to optimize the sequence to further improve image quality, by characterizing the blood pool suppression and minimizing any image artifacts due to non-steady-state effects that can result from imaging with higher flip angles. Bloch simulations of a variable flip angle excitation (17,18) indicate that point-spread-function side lobes can be substantially reduced without loss of overall signal intensity. We confirmed these results in preliminary studies in animal models (unpublished data).

This study evaluated an alternative way of performing magnetization preparation with saturation recovery. The interleaved preparation and acquisition sequences and the overlapping recovery times allowed the most time-efficient implementation of long TI saturation recovery for multisection myocardial perfusion MR imaging. This implementation resulted in substantially better image contrast than can be achieved with short TI saturation recovery or partial saturation and greater section coverage than can be achieved with conventional long TI saturation recovery or inversion recovery.

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