Inflow artifact reduction using an adaptive flip-angle navigator restore pulse for late gadolinium enhancement of the left atrium

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Abstract

Purpose: Late gadolinium enhancement (LGE) of the left atrium is susceptible to artifacts arising from the right pulmonary veins, caused by inflowing blood tagged by the navigator restore pulse. The purpose of this study was to evaluate a new method to reduce the inflow artifact using an adaptive flip-angle restore pulse.

Methods: A low-restore angle reduces the inflow artifact but may lead to a poor navigator SNR. The proposed approach aims to determine the patient-specific restore angle, which optimizes the trade-off between inflow artifacts and navigator SNR. Three-dimensional LGE with adaptive navigator restore (3D LGEA) was implemented by incrementing the flip angle of the restore pulse from a starting value of 0°, based on the navigator normalized cross-correlation. Magnetic resonance imaging experiments were performed on a 1.5T scanner. The value of 3D LGEA was compared with 3D LGE with a constant 180° restore pulse (3D LGE180) in 22 patients with heart diseases. The values of 3D LGEA and 3D LGE180 were compared in terms of pulmonary vein blood signal relative to reference blood in the descending aorta (PVrel) and visual scoring to determine level of motion artifacts using a 4-point scale (1 = severe artifacts; 4 = no artifacts).

Results: The value of PVrel was significantly lower for 3D LGEA than for 3D LGE180 (1.16 ± 0.23 vs. 1.59 ± 0.29, \(P < .001\)). Furthermore, visual scoring of the motion artifacts yielded no difference (\(P = .78\)).

Conclusion: Adaptingly adjusting the navigator restore flip angle based on the navigator normalized cross-correlation reduces the 3D LGE inflow artifact without affecting image quality or the scan time.

Keywords
left atrial fibrosis assessment, pulmonary vein inflow artifact, respiratory navigator, 3D late gadolinium enhancement

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Three-dimensional late gadolinium enhancement (3D LGE) can be used to visualize the left atrium and pulmonary veins with high resolution. This is a well-established technique for the assessment of left atrial fibrosis and adverse remodeling of the atrium, which can be an arrhythmogenic substrate in patients with atrial fibrillation. Following an ablation procedure to isolate the pulmonary vein outlets and to terminate arrhythmia, 3D LGE may allow determination of whether the intervention has been effective by showing gadolinium enhancement in tissue affected by the ablation.

Three-dimensional LGE is typically performed using an inversion-recovery acquisition to obtain strong T₁ weighting. A patient-specific inversion delay of a few hundred milliseconds is timed to suppress signal from healthy myocardium. Due to the high resolution and large FOV required to visualize the thin atrial wall, the scan time is typically on the order of 2 to 5 minutes. Consequently, 3D LGE is susceptible to respiratory motion artifacts such as blurring and ghosting. To mitigate these, a respiratory navigator positioned on the right hemi-diaphragm is used, in which data acquisition is gated to a small portion of the respiratory cycle, typically end-expiration, using a gating window of approximately 6 mm. Furthermore, the navigator signal can be used to prospectively update (track) the position of the FOV of the 3D LGE to account for linear respiratory motion within the navigator gating window. A so-called navigator restore pulse, which is a 2D selective inversion pulse overlapping with the respiratory navigator, is often used to re-invert the signal on the diaphragm immediately after the nonselective inversion pulse. The navigator restore pulse ensures a high navigator SNR for the navigator, which is important when estimating respiratory motion with high precision. However, the navigator restore pulse often overlaps with portions of the inferior and/or superior right pulmonary veins (RPVs), which leads to re-inversion of blood that travels back to the left atrium during the inversion delay. Effectively, this inflowing blood can obscure any LGE in the RPVs and left atrium due to the small contrast between inflowing blood with restored signal and atrial wall with high gadolinium accumulation.

To avoid this inflow artifact, the restore pulse can be removed and the navigator pulse instead positioned after the 3D LGE readout in time. However, this may still lead to a relatively low navigator SNR, is incompatible with prospective slice tracking, and leads to a relatively long time between acquisition of center of k-space and navigator, which compromises the temporal correlation between the motion detection and image acquisition. An external respiratory sensor such as an abdominal bellows signal can also be used to gate the 3D LGE to end-expiration, which obviates the need for a navigator restore pulse. Moghari et al proposed a navigator technique without a restore pulse, in which a 1-dimensional projection of the diaphragm in the anterior–posterior direction was acquired and shifted in time relative to the 3D LGE readout. However, this technique is still susceptible to low navigator SNR, depending on the T₁ of the diaphragm, and has a lower temporal correlation with the 3D LGE compared to a navigator without a time delay. Keegan et al proposed a time-shifted restore pulse, in which the restore pulse is closer in time to the 3D LGE. This mitigates the inflow artifact, in part due to the shorter time between restore pulse and imaging, but also because of the reduced signal of the partially inverted blood signal. However, optimal timing of the restore pulse may be difficult to pinpoint and depends on a number of factors that may change during the scan, such as heart rate and contrast material washout.

The purpose of this study was to evaluate a new method to reduce the inflow artifact using an adaptive flip-angle restore pulse, while ensuring a high navigator SNR. This approach only partially restores the signal on the right hemi-diaphragm (and blood in any overlapping RPVs) following an inversion pulse by the smallest possible amount, which is patient-specific and optimized to provide sufficient navigator signal.

2 | METHODS

2.1 | Adaptive navigator restore pulse sequence

The proposed inversion-recovery pulse sequence consisted of an adaptively adjusted navigator restore pulse. This involved increasing the restore flip angle from a starting value of 0° by increments of 15° to a maximum of 180°. The navigator restore pulse was adjusted in this way, while the normalized cross-correlation (nCC) of the navigator signal was used as a metric to determine whether sufficient navigator signal was available for reliable motion detection. The nCC is a measure of the similarity between two signals, such as two navigator readouts, and is proportional to the navigator SNR. Previous studies have shown that the navigator motion-compensation performance is highly dependent on the navigator SNR. For this implementation, we used the maximum nCC calculated by the navigator for motion detection. The nCC is obtained through a 1-dimensional template matching operation, in which a kernel from the reference navigator is convolved with each new navigator acquisition, and the position of the maximum nCC is used to estimate respiratory displacement. By considering the maximum nCC for the adaptive restore flip-angle algorithm, the influence of respiratory motion on the nCC is mitigated. The use of normalized cross-correlation, rather than just cross-correlation, ensures that this metric is robust to beat-to-beat changes in global signal intensity, which may occur during arrhythmia.
The adaptive restore flip angle was first determined before the start of the 3D LGE scan, preceding the navigator preparation phase, to find the end-expiratory gating window. During the restore flip-angle determination, if the average nCC across three navigator acquisitions was below a certain threshold, it was considered insufficient for precise motion detection and the process was automatically started over with a higher restore pulse, including the re-acquisition of the navigator reference. As contrast material can wash out during the scan, which may affect the navigator signal, a running average of three consecutive navigator nCCs was calculated during the scan, and if it fell below the threshold the navigator restore was increased by 15°. A schematic of the adaptive navigator restore approach is illustrated in Figure 1.

2.2 Simulations

Simulations were performed to investigate the tradeoff between navigator restore flip angle, navigator signal, and contrast between scar and inflowing blood. The inflowing blood signal in the simulations considered blood that experienced both the inversion and adaptive re-inversion pulses. The longitudinal magnetization ($M_z$) was simulated for an inversion-recovery sequence with imaging parameters identical to those used for the in vivo experiments described subsequently, including the RF pulses for the image acquisition. A range of different heart rates were simulated, and the effective inversion time for each heart rate was defined as the inversion delay that nulled $M_z$ for healthy myocardium, which was assumed to be 450 ms.26 The navigator $M_z$ was simulated (liver $T_1 = 400$ ms), along with the contrast ($M_z$ difference) between scar ($T_1 = 200$ ms) and inflowing blood ($T_1 = 300$ ms), experiencing both the 180° inversion and adaptive restore pulses.27,28 The simulations were performed for navigator restore flip angles ranging from 0 to 180°.

2.3 Magnetic resonance imaging experiments

All MRI experiments were performed on a 1.5T Philips scanner (Philips Healthcare, Best, The Netherlands) using a 24-channel cardiac coil.

A phantom experiment was performed to investigate the relationship between navigator nCC and motion-detection precision. This experiment was performed in a static phantom with $T_1 = 400$ ms, approximately that of the diaphragm 20 minutes after contrast injection. An inversion-recovery sequence was used with imaging parameters identical to those used for the in vivo experiments described later. The navigator restore flip angle was adjusted to achieve navigator signals with different nCC, from 0.96 to 0.99 with increments of 0.01. Motion-detection precision was qualitatively evaluated as the variability in the motion estimation of the stationary phantom.

Twenty-two patients referred to our hospital for a clinical cardiovascular MR scan, including LGE assessment, were recruited. All participants provided written informed consent before participation, and the study was approved by the regional ethics committee. Patient demographics and
clinical indications are provided in Supporting Information Table S1. The LGE scans were performed 20-30 minutes after contrast agent administration (0.2 mmol/kg gadobutrol). The 3D LGE acquisition was performed using a dual-echo spoiled gradient-echo readout with the following parameters: TR = 7.1 ms, TE1/TE2 = 2.3/4.9 ms, flip angle = 20°, FOV = 340 × 340 × 130 mm², spatial resolution = 1.2 × 1.2 × 4 mm³, and bandwidth = 431 Hz. Compressed sensing was applied with an acceleration factor of 5, using a vendor-provided wavelet-based algorithm. Images were electrocardiogram-triggered to atrial diastole, as visually determined from a 2D cine scan, with an acquisition window of approximately 100 ms depending on the patient-specific rest period. Water-fat separation was performed using the Dixon technique to eliminate fat signal from the LGE images. For patients in sinus rhythm, the inversion pulse was performed each cardiac cycle, while for patients with persistent arrhythmia or atrial fibrillation the inversion pulse was performed every two cardiac cycles. With these imaging parameters, the nominal scan time was approximately 2 minutes and 30 seconds, assuming a heart rate of 60 bpm.

A respiratory navigator was used for respiratory motion compensation with a gating window of 6 mm and a tracking factor of 0.45. The navigator used a 2D-selective RF pulse of 90° with a thickness of 25 mm, whereas the 2D-selective restore pulse had a thickness of 50 mm. Two 3D LGE scans were performed consecutively, using either the proposed adaptive navigator restore approach (3D LGEA) or the conventional fixed-angle restore pulse of 180° (3D LGE180). An nCC threshold of 0.98 was used for the 3D LGE using navigator 3D LGEA based on the phantom experiments. The order of the 3D LGEA and 3D LGE180 scans was randomized to minimize bias. A Look-Locker sequence was performed before the first 3D LGE scan to determine the optimal inversion delay. The same inversion delay was used for both 3D LGE scans to ensure similar inflow conditions.

### 2.4 Image analysis and statistics

Pulmonary inflow enhancement was quantified by calculating the ratio between the signal intensity in the pulmonary veins and the descending aorta in the same slice (“pulmonary blood intensity ratio”). Because the amount of inflow enhancement may vary between the inferior and superior vein depending on patient-specific overlap with the navigator restore pulse, for each patient we only chose the vein with the highest inflow enhancement, representing the worst-case scenario in that particular patient. However, for each patient the same vein (inferior or superior) was analyzed with both techniques. The amount of respiratory motion artifacts in the left atrium was visually determined using a 4-point Likert scale with the following criteria: 1 = severe, 2 = moderate, 3 = mild, and 4 = no motion artifacts. The visual scores were performed in a randomized order by an experienced observer with 20 years of cardiovascular MR experience blinded to the acquisition technique used.

All statistical analyses were performed using MATLAB (MathWorks, Natick, MA). Continuous variables were compared for statistical significance using a paired student’s t-test with a significance threshold of P < .05. For the nonparametric variable (image artifact score), a paired Wilcoxon signed-rank test was used, also with a significance threshold of P < .05.

### 3 RESULTS

#### 3.1 Simulations

The simulation results, performed to investigate the relationships between the navigator restore flip angle and the navigator M0 as well as the restore angle and M0 difference between inflowing blood and scar, are visualized in Figure 2. A navigator restore pulse of 180° yields the highest navigator M0, although this results in a blood signal higher than that of scar (negative contrast), which could be interpreted as an inflow artifact. Conversely, a navigator restore pulse of 0° results in an approximately 8-fold reduction in navigator M0. However, in this case the signal of the inflowing blood is the same as in the rest of the blood pool, yielding the maximum scar-to-blood contrast. The figure also shows that a small increase in the restore flip angle of 45° results in almost doubling navigator M0, while only reducing scar-to-blood contrast moderately (approximately 25%). Although navigator M0 increased slightly with the RR-interval for navigator restore of 90° and higher, there was only a marginal change in the contrast at different heart rates.

#### 3.2 Phantom experiments

A time-series of navigators with different nCC, from 0.96 to 0.99, obtained in a static phantom is shown in Figure 3. The spatial resolution in the foot–head direction of the navigator was 1 mm, and as shown in Figure 3, higher navigator nCC yielded lower variability in motion measurements. An nCC above 0.97 resulted in motion-estimation variability smaller than the pixel size.

#### 3.3 In vivo experiments

All 3D LGE scans were successfully completed using both navigator restore techniques. The mean scan time ± SD for 3D LGEA was 4:45 ± 0:43 (minutes:seconds) and
4:31 ± 0:38 for 3D LGE_{180} (P = .25). The navigator gating efficiency was 48% ± 12% for 3D LGE_{A}, and 49% ± 10% for 3D LGE_{180} (P = .51). The distribution of actual restore flip angles (determined during the navigator preparation phase) for the 3D LGE_{A} approach is shown in Supporting Information Figure S1. In 8 patients (36%), the navigator restore was maintained at 0°, as this produced a navigator nCC of more than 0.98. In the remaining cases, navigator nCC over 0.98 was obtained for restore angles between 15° and 105°. Navigator restore updates occurred during the LGE 3DA scan in 5 patients (23%). In 4 of these patients, the navigator restore flip angle only incremented once, whereas in 1 patient the flip angle incremented twice.

The mean quantitative pulmonary blood intensity ratio for was 1.59 ± 0.29 3D LGE_{180} and 1.16 ± 0.23 for 3D LGE_{A} (P < .001). Representative images from 3 patients are shown in Figure 4, with significant inflow artifacts in the right pulmonary vein using 3D LGE_{180}, while the artifacts are minimized using 3D LGE_{A}. Images from a patient with atrial fibrillation acquired using 3D LGE_{A} and 3D LGE_{180} are shown in Figure 5. The inflow artifact arising from the right pulmonary vein obscures
the scar in the left atrial septum in the 3D LGE180 scan. However, the artifact is reduced using 3D LGE_A, which allows clear visualization of the scar. The visual scoring of motion artifacts in the left atrium yielded the same median, 25th, and 75th percentile score of 3, 3 and 4, respectively, for both 3D LGE_A and 3D LGE_180 ($P = .78$).

4 | DISCUSSION

In this proof-of-concept study, we have implemented a method to reduce the inflow artifact in the right pulmonary vein in navigator-gated inversion-recovery LGE of the left atrium and evaluated it in 22 patients with various heart diseases. The proposed approach adaptively attempts to find the optimum navigator restore flip angle that balances the tradeoff between high navigator signal and re-inversion of inflowing blood in the right pulmonary vein. Compared with the conventional approach of using a fixed 180° restore pulse, the proposed adaptive restore pulse reduces the inflow artifacts as measured by the pulmonary inflow ratio, without introducing motion artifacts.

Previous techniques to reduce the inflow artifacts, notably by Moghari et al.\textsuperscript{24} and Keegan et al.,\textsuperscript{25} have modified the delay between navigator restore or navigator acquisition. However, in both implementations the time delay was fixed, and if it was adjusted it was determined before the scan. In contrast, the proposed approach adaptively determines optimal settings for the restore pulse during the scan based on the navigator-normalized cross-correlation, which is indirectly related to the patient-specific T1 of the liver. Although the restore angles—rather than any time delays—were adapted in the proposed feedback loop, a similar strategy could be applied to adaptively adjust the restore delay to minimize inflow artifacts while ensuring high navigator signal.

In the proposed approach, the navigator nCC was used as a proxy for the SNR. On our software platform, the navigator relies on the nCC for motion estimation, and therefore is a readily available metric without requiring any additional computation. The SNR may be calculated directly from the navigator signal, although automatically defining areas of tissue and background for the SNR calculations is nontrivial. Other metrics of motion-estimation precision could also be considered, such as the edge sharpness of the lung–liver interface.

As shown in Figure 4, in a substantial proportion of cases the navigator nCC was sufficiently high even without a restore pulse (flip angle = 0°). However, this depends primarily on the liver T1 and how similar it is to the myocardial T1, which is nulled. This justifies a patient-specific adaptive approach in which the restore is gradually increased to ensure high navigator signal for precise motion estimation. Nevertheless, most patients (63%) had a sufficiently high
navigator nCC for restore flip angles of 45°. As our simulations show (Figure 2), contrast between scar and inflowing blood is preserved primarily with such minor perturbation of the inflowing blood signal. However, the simulations show that increasing the restore angle beyond 45° leads to a rapidly diminishing contrast.

An alternative navigator acquisition technique in which the respiratory motion is measured directly on the heart using self-navigation or image-based navigators would circumvent the need for a navigator restore flip angle. However, the potential drawback of such techniques is the sensitivity of the navigator to changes in heart rate or arrhythmia, which could affect the motion-estimation performance. In contrast, by positioning the navigator on the diaphragm and using restore pulses, the navigator signal becomes inoculated against beat-to-beat signal intensity variations that may occur on the heart. A further advantage of the diaphragmatic navigator is the ability to use obliquely positioned imaging FOV, while self-gating and image-based navigation typically require image readout in the foot–head direction.

The short scan time using compressed sensing with acceleration factor 5 resulted in few updates during the scan, as it provided little time for contrast washout and hence changes in T₁ of the liver. A scan protocol with conventional image acceleration using parallel imaging, or with higher spatial resolution, would increase the scan time and likely result in more navigator-restore updates during the scan. High undersampling factors may increase the risk of aliasing artifacts and reduce the image SNR. Further studies are required to optimize the tradeoff between compressed-sensing acceleration and image quality for 3D LGE. Nevertheless, the short scan time afforded by the compressed-sensing acceleration resulted in a close temporal proximity between the two 3D LGE scans, minimizing contrast material washout and yielding similar image contrast, which was an important experimental consideration for the study to ensure similar conditions. Apart from a high acceleration factor, we also increased the navigator gating window from 5 mm to 6 mm, to obtain a slightly higher scan efficiency. Previous work on respiratory navigation for 3D coronary MRA has demonstrated that the gating window can be increased from 5 mm to 7 mm, without increasing motion artifacts, if prospective slice tracking is used. Furthermore, the use of slice tracking will exacerbate any reduction in motion-compensation performance due to noise in the navigator signal, as demonstrated in previous studies investigating the relationship between navigator SNR and image quality.

A limitation of this study is that we did not scan any patients who had undergone pulmonary vein isolation ablation, where this technique would be particularly valuable. Further studies are planned to evaluate the clinical utility of the proposed approach in this cohort. Nevertheless, we demonstrated the value of the adaptive restore approach in a patient with atrial fibrillation, in whom the amount of atrial scar has been correlated with the likelihood of recurring arrhythmia following ablation. In this patient, atrial scar could be visualized with 3D LGE but not 3D LGE. Further studies in patients with atrial fibrillation before the ablation procedure are also scheduled. The simulations are limited due to the assumptions made on T₁ of liver, blood, healthy myocardium, and scar post-contrast, which are subject to variability due to contrast agent type and dose used, time from injection, and field strength. Another limitation of the study is that we did not investigate alternative approaches to mitigate the inflow artifact, such as angulating the navigator beam away from the pulmonary veins rather than perpendicular to the lung–liver interface, or reducing the restore pulse diameter. However, modifying the scan planning will introduce additional operator dependence, and there appears to be no widely adopted navigator planning strategy to mitigate inflow artifacts.

5 CONCLUSIONS

Adaptively adjusting the navigator restore flip angle based on the navigator normalized cross-correlation reduces the 3D LGE inflow artifact originating from the right pulmonary vein without affecting the image quality in terms of motion artifacts or the scan time.

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SUPPORTING INFORMATION
Additional Supporting Information may be found online in the Supporting Information section.

FIGURE S1 Histogram of effective navigator restore angles for all 22 patients

TABLE S1 Patient characteristics and clinical indications

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