ORIGINAL REPORT

In-phase and out-of-phase single-shot magnetization-prepared gradient recalled echo: Description and optimization of technique at 1.5 T

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Adrenal masses;
Motion resistant;
Magnetization-prepared gradient recalled echo imaging

Abstract

\textbf{Purpose:} To implement in-phase and out-of-phase (IP/OP) techniques with Magnetization-prepared gradient recalled echo (MP-GRE) and to evaluate the feasibility and diagnostic image quality among pre and post-optimized MP-GRE sequences, including patients unable to cooperate with breath-hold requirements.

\textbf{Materials and methods:} Institutional review board approval with waiver of informed consent was obtained for this HIPAA-compliant retrospective study. Two groups of patients were included in the study, before and after optimization of MP-GRE parameters, with seventy-three (24 non-cooperative/49 cooperative) and sixty-four (22 noncooperative/42 cooperative) consecutive patients, respectively. The motion-insensitive sequence used in this study was a single-shot 2D MP-GRE. Two radiologists qualitatively evaluated the sequences to identify the presence of phase cancelation artifact in OP images and to determine image quality, extent of artifacts (respiratory ghosting, bounce-point artifact, spatial misregistration and pixel graininess) and lesion conspicuity on the various sequences. The ability to visually detect liver steatosis and fatty adrenal adenomas was evaluated. Qualitative analyses were compared using the Wilcoxon and Mann–Whitney tests.

\textbf{Results:} There were statistically significant differences between all MP-GRE sequences concerning phase cancelation artifact ($p < .0001$) which was present in MP-GRE OP sequences and negligible to absent in the pre (IP\textsubscript{1}) and post-optimized (IP\textsubscript{2}) MP-GRE IP sequences, respectively, in all patients.

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Bounce point artifacts were significantly more pronounced in MP-GRE IP \(_1\) \((p < .0001)\). Spatial misregistration was slightly more prominent in noncooperative patients with MP-GRE IP \(_2\) \((p = .0027)\). MP-GRE OP and MP-GRE IP\(_2\) showed significantly higher overall image quality \((p < .0001)\).

MP-GRE sequences subjectively identified hepatic steatosis \((n = 20)\) and adrenal adenomas \((n = 5)\) based on signal loss from IP to OP sequence.

**Conclusion:** Single shot IP/OP MP-GRE is feasible and allows motion resistant imaging with adequate diagnostic image quality. This technique is able to provide IP and OP information in patients unable to suspend respiration.

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**Secuencia de disparo único eco de gradienfe fase y fase opuesta con preparación de la magnetización: descripción y optimización de la técnica con equipo de 1,5 T**

**Resumen**

**Objetivo:** Implementar técnicas en fase y en fase opuesta (EF/FO) con eco de gradiente con preparación de la magnetización (Magnetization-Prepared Gradient Recalled Echo [MP-GRE]) y evaluar la viabilidad y la calidad de imagen diagnóstica entre las secuencias MP-GRE antes y después de la optimización, incluyendo aquellos pacientes que no pueden colaborar manteniendo la apnea.

**Material y métodos:** Para la realización del presente estudio retrospectivo, llevado a cabo de conformidad con la ley HIPPA de protección de datos médicos de EE.UU., se obtuvo la aprobación del Comité de Ética Institucional con exención de obtención del consentimiento informado. Se incluyeron 2 grupos de pacientes en el estudio, antes y después de la optimización de los parámetros MP-GRE, con 73 \((24 \text{ no colaboradores} / 49 \text{ colaboradores})\) y 64 \((22 \text{ no colaboradores} / 42 \text{ colaboradores})\) pacientes consecutivos, respectivamente. La secuencia no sensible al movimiento usada en este estudio fue 2D MP-GRE con técnica de disparo único. Dos radiólogos evaluaron cualitativamente las secuencias para identificar la presencia de artefactos de cancelación de fase en las imágenes en FO y para determinar la calidad de imagen, la extensión de los artefactos (artefacto de fantasma, artefacto de cancelación de señal, error de registro espacial y granulado de los píxeles) y la visibilidad de las lesiones en las diferentes secuencias. También se evaluó la capacidad para detectar visualmente steatosis hepática y adenomas suprarrenales de contenido graso. Los análisis cualitativos se compararon mediante las pruebas de Wilcoxon y Mann–Whitney.

**Resultados:** Hubo diferencias estadísticamente significativas entre todas las secuencias MP-GRE en lo relativo al artefacto de cancelación de fase \((p < 0.0001)\), presente en las secuencias MP-GRE FO y despreciable o ausente en las secuencias MP-GRE EF, tanto antes \((EF_1)\) como después \((EF_2)\) de la optimización, en todos los pacientes.

Los artefactos de cancelación de señal fueron significativamente más marcados en las secuencias MP-GRE EF\(_1\) \((p < 0.0001)\). El error de registro espacial fue ligeramente más marcado en las secuencias MP-GRE EF\(_2\) \((p = 0.0027)\) en los pacientes no colaboradores. Las secuencias MP-GRE en FO y las secuencias MP-GRE EF\(_2\) mostraron una calidad de imagen significativamente mayor \((p < 0.0001)\).

En las secuencias MP-GRE se identificaron subjetivamente la steatosis hepática \((n = 20)\) y los adenomas suprarrenales \((n = 5)\) basándose en la pérdida de señal desde la secuencia EF a la secuencia en FO.

**Conclusión:** La técnica de disparo único MP-GRE EF/FO es una técnica viable que permite la obtención de imágenes resistentes al movimiento, ofreciendo una calidad de imagen diagnóstica adecuada. Esta técnica puede proporcionar información EF y en FO de pacientes que no son capaces de mantener la apnea.

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**Introduction**

T1-weighted gradient-recalled echo (GRE) in-phase and out-of-phase (IP/OP) imaging is an essential component of comprehensive abdominal MR exams.\(^1\)\(^-\)\(^3\) Out-of-phase images are able to demonstrate the presence of fat, which is necessary to evaluate the liver, and in the characterization of adrenal masses.\(^4\)\(^-\)\(^12\) Despite the importance of IP/OP GRE imaging, to the present time these sequences have been performed as multislice GRE acquisitions that have required that patients suspend respiration, as sequences generally are 10–20s in duration.
As a consequence of the success of MRI to evaluate the full range of abdominal disease, more types of patients are being evaluated by MRI, including those who cannot cooperate with 10–20 s breath holds, such as the elderly, severely debilitated, and young children. Motion resistant T1-weighted imaging is critical for imaging these patient populations. Single-shot MR imaging techniques are considered breathing-independent techniques due to their characteristic robustness to motion.1,13–18 To our knowledge, the T1-weighted magnetization-prepared gradient recalled echo (MP-GRE) is the only single-shot IP/OP technique currently available.

This study was conducted in order to evaluate the feasibility of the technique, determining if MP-GRE sequences provide adequate IP and OP information, using a black ring phase cancelation artifact as a surrogate and to compare image quality between IP/OP MP-GRE sequences in both cooperative and noncooperative patients. In a second phase of the study, following an optimization path, we compared improved IP/OP MP-GRE sequences in both cooperative and noncooperative patients.

**Materials and methods**

**Patients**

Institutional review board approval was obtained for this retrospective HIPAA compliant study with waived informed consent. All abdominal MRI studies performed between September 15, 2009 and November 15, 2009 and between December 1, 2009 and January 1, 2010 were retrospectively evaluated for inclusion in this study. Patients who had MRI examinations in the first study period including precontrast IP/OP MP-GRE were included in the first group (phase 1). Patients who had MRI examinations in the second study period including the optimized sets of IP and OP MP-GRE sequences were included in the second group (phase 2).

The first group of subjects included 24 consecutive noncooperative patients (9 males and 15 females; mean age \( \pm \) standard deviation, 48.9 ± 27.6) and 49 consecutive cooperative patients (24 males and 25 females; mean age \( \pm \) standard deviation, 55.8 ± 15.0). One patient was excluded due to the presence of severe susceptibility artifacts.

The second group of subjects included 22 consecutive noncooperative patients (10 males and 12 females; mean age \( \pm \) standard deviation, 60.3 ± 17.1) and 42 consecutive cooperative patients (24 males and 18 females; mean age \( \pm \) standard deviation, 52.1 ± 18.6) following optimization of the IP/OP MP-GRE sequences.

The difference between cooperative and noncooperative patients is related with the ability to cope with breath-hold requirements. Choice of sequences was at the discretion of the imaging technologist. Before entering the MRI scanner, the technologist explains the exam and evaluates the breath-hold capability of the patients. Also, some patients who originally underwent a cooperative protocol but became noncooperative and unable to hold their breath during scanning were considered noncooperative.

The final study population of the first group included a total of 73 subjects (33 males and 40 females; mean age \( \pm \) standard deviation, 53.6 ± 19.9) and of the second group included a total of 64 subjects (34 males and 30 females; mean age \( \pm \) standard deviation, 54.9 ± 18.2).

Noncooperative patients underwent a free-breathing motion resistant protocol as they were unable to suspend respiration and cooperative patients underwent a standard protocol with the additional MP-GRE sequences. The MP-GRE sequences were added to the MR protocol in patients theoretically cooperative, as motion resistant sequences, to assure the acquisition of adequate T1-weighted information, allowing for the possibility that some of the precontrast breath-hold gradient echo IP and OP sequences might be nondiagnostic due to motion.

The primary indications for imaging are displayed in Table 1.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>138</td>
<td>Examine indications.</td>
</tr>
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<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Evaluation of liver lesions</td>
</tr>
<tr>
<td>44</td>
<td>Cirrhosis surveillance</td>
</tr>
<tr>
<td>23</td>
<td>Evaluation on non-liver malignancy</td>
</tr>
<tr>
<td>9</td>
<td>Evaluation of renal lesions</td>
</tr>
<tr>
<td>7</td>
<td>Post-interventional assessment of the liver</td>
</tr>
<tr>
<td>5</td>
<td>Evaluation of abdominal pain</td>
</tr>
<tr>
<td>9</td>
<td>Post-liver or kidney transplantation</td>
</tr>
<tr>
<td>2</td>
<td>Post-interventional assessment on non-liver malignancies</td>
</tr>
<tr>
<td>3</td>
<td>Evaluation of pancreatic lesions</td>
</tr>
<tr>
<td>9</td>
<td>Evaluation of suspected biliary disease</td>
</tr>
<tr>
<td>9</td>
<td>Evaluation of pancreatitis</td>
</tr>
<tr>
<td>5</td>
<td>Abnormal liver function tests</td>
</tr>
<tr>
<td>1</td>
<td>Screening for arterial hypertension</td>
</tr>
<tr>
<td>4</td>
<td>Evaluation of adrenal incidentalomas</td>
</tr>
</tbody>
</table>

Focal liver lesions were detected in 37 patients. Twelve patients had benign liver lesions [cysts (n = 6), regenerative nodules (n = 2), hemangioma (n = 2) and abscesses (n = 2)]. Twenty-five patients had malignant liver lesions [metastatic disease (n = 9), HCC (n = 7), intra-hepatic cholangiocarcinoma (n = 2), post trans-arterial chemo-embolization (n = 1) and post-radiofrequency ablated HCC (n = 6)]. Lesions were diagnosed on the basis of characteristic imaging findings;23 metastatic disease was inferred by the detection of multiple lesions with similar MR findings in the presence of histologically proven primary tumors (n = 6) and HCCs were diagnosed in patients with chronic liver disease by the typical enhancement pattern on gadolinium enhanced dynamic MRI. Intra-hepatic cholangiocarcinoma diagnosis was based on histological findings.

Six patients had adrenal lesions (five patients with adenoma, based on characteristic loss of signal from IP to OP images, and one had an undetermined high T1-weighted signal lesion).

**MRI technique**

MR imaging of the abdomen was performed at 1.5 T (Avanto, Siemens Medical Systems, Malvern, PA) MR systems using a phased-array torso coil in all patients.
In-phase and out-of-phase single-shot magnetization-prepared gradient recalled echo

Table 2  Detailed imaging parameters of MP-GRE and 2D-GRE sequences.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>MP-GRE</th>
<th>2D-GRE*</th>
<th>In-phase/out-of-phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echo time (ms)</td>
<td>2.3</td>
<td>4.09</td>
<td>4.07</td>
</tr>
<tr>
<td>Echo spacing (ms)*</td>
<td>5.9</td>
<td>8.2</td>
<td>8.2</td>
</tr>
<tr>
<td>Repetition time (ms)*</td>
<td>1540</td>
<td>3000</td>
<td>1540</td>
</tr>
<tr>
<td>Inversion time (ms)</td>
<td>900</td>
<td>750</td>
<td>900</td>
</tr>
<tr>
<td>Flip Angle (°)</td>
<td>15</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Bandwidth (Hertz/pixel)</td>
<td>180</td>
<td>150</td>
<td>150</td>
</tr>
<tr>
<td>Thickness (mm)</td>
<td>6</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>No. of signals averaged</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Acquired Matrix</td>
<td>256×156</td>
<td>256×88</td>
<td>256×156</td>
</tr>
<tr>
<td>Parallel Imaging factor*</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Respiratory control</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

* Magnetization-prepared gradient recalled echo (MP-GRE) are acquired as three separate two dimensional acquisitions.
* In-phase and Out-of-phase two dimensional spoiled gradient echo (2D-GRE) is acquired as a dual echo acquisition.
* Echo Spacing is the time between successive readouts.
* In MP-GRE sequences, repetition time is the time between application of the inversion pulse for each individual partition.
* Parallel imaging factor was GRAPPA (Generalized Autocalibrating Partially Parallel Acquisitions).

The motion-insensitive sequence, MP-GRE, used in this study was a 2-D magnetization-prepared turbo-FLASH sequence, which begins with a 180° non-selective inversion pulse to initially prepare the longitudinal magnetization with T1 contrast. This is followed by a rapid train of low flip-angle slice-selective excitation pulses and gradient echo readouts, with the center of k-space being acquired a time T1 (inversion time) after the inversion pulse. All of the phase-encoding lines for a given slice are acquired after a single inversion pulse with total echo-train duration of about 1s, which is sufficient short to avoid respiratory motion artifacts. Due to the fact that the inversion pulse is non-selective the sequence is not strictly a single-shot technique from a magnetization relaxation perspective, although because of the short readout duration it does behave like a single shot sequence in terms of motion artifacts. For the first phase of the study two different MP-GRE sequences provided by the manufacturer were used with slightly different timing parameters and details. We herein named the sequences respectively MP-GRE OP and MP-GRE IP1. As no prior literature detailing these sequences were present, default imaging parameters set by the manufacturer were employed. The details of the parameters of the sequences are shown in Table 2. In the second phase of the study, based on the findings of the first phase, optimization of the IP MP-GRE sequence was performed. We herein named the IP MP-GRE sequence post-optimization MP-GRE IP2 (Table 2). Cooperative patients were instructed to breathe normally during MP-GRE acquisition.

Two-dimensional T1-weighted spoiled gradient echo (2D-GRE) IP and OP sequences were acquired in cooperative patients as a breath-hold dual-echo sequence. The details of the parameters of these sequences are shown in Table 2. Note that the MP-GRE sequences have a lower SNR, which is reflected in the 2 averages (MP-GRE OP and IP1) and no use of parallel imaging acceleration. Early versions of the sequences were sub-optimal and demonstrated bounce-point artifacts as described below. Optimization was done clinically and via computer simulation.

Image analyses

Qualitative analyses

Precontrast axial MP-GRE sequences of all patients were independently and retrospectively evaluated on a workstation by two different reviewers (V.H. and M.T. with 4 years and 5 years of experience, respectively) to identify the presence of phase cancelation artifact in OP MP-GRE images and to determine image quality, extent of artifacts and lesion conspicuity on the various sequences. For each data set, both readers scored eight parameters of image quality. Prior to conducting the evaluation the two readers underwent a training data set consisting of 5 patients, and agreed on the interpretations and the scores for each of the evaluated parameters. This training data set was not included in the study. The reviewers were blinded to the parameters of the sequences that they reviewed.

A distinguishing feature of OP imaging is related to the appearance of a black rim at all water/fat interfaces, an artifact that has been called "phase cancelation artifact", "India ink artifact", "boundary artifact," or "chemical shift artifact of the second kind." Since this is a phase-cancelation effect, it is not limited to the frequency-encoding direction such as the classic chemical shift artifact, but may be seen in all pixels along the fat-water interface. The presence of a black rim phase cancelation artifact surrounding abdominal organs in the OP MP-GRE images and its absence in the IP images was considered the surrogate for adequacy of OP and IP image quality, respectively. To recognize an OP sequence, the reviewers considered this artifact only when liver and kidney parenchyma were completely surrounded by a black line to distinguish it from chemical shift artifact of the first kind. Sequences were considered IP if no phase cancelation was present. The reviewers rated OP artifact using a 3-point scale (1, obvious; 2, mild; 3, absent, negligible).

The reviewers graded images from all the MP-GRE sequences for the presence of artifacts (respiratory ghosting, bounce-point artifact, spatial misregistration and
pixel graininess) using a 4-point scale (1, severe; 2, moderate; 3, mild; 4, minimal to absent). Respiratory ghosting was defined as blurring or ghosting of the image in the phase encoding direction. Spatial misregistration was defined as nonconformity of slice position in each sequence and between sequences. Pixel graininess was determined as the presence and extent of graininess and reflected the overall magnitude and inhomogeneity of background noise.

Bounce-point artifact is an artifact that is specific for inversion recovery sequences and manifests as a signal void rim between two contiguous tissues with significantly different T1 values. The source of bounce-point artifacts is signal cancelation within a voxel containing two tissues, which have different T1 values such that one tissue has already passed through the inversion recovery null point while the other tissue has not and the two tissues are therefore out-of-phase.

The overall image quality was assessed for image sharpness, homogeneity of SI, cortico-medullary differentiation and severity of artifacts; and was graded with a 4-point scale (1, poor; 2, fair; 3, good; 4, excellent). The depiction of the intrahepatic vessels was assessed with respect to the main branches of the portal vein and graded with a 4-point scale (1, unacceptable (invisible main portal vein); 2, poor (only main portal vein visible); 3, fair (only main branches of portal vein visible); 4, good (portal portal vein branches visible)). Lesion conspicuity was assessed by using the following considerations: overall evaluation of lesion visibility, margination and extent; and was rated with a 5-point scale (1, poor; 2, fair; 3, good; 4, very good; 5, excellent).

Sequences in which the scores used for the qualitative evaluation were higher than 3 were considered as diagnostic.

Liver steatosis was determined based on characteristic signal features, recognized as regions of liver that demonstrated a decrease in SI on OP images compared to IP images. The difference between IP and OP images was graded on a 4-point scale, ranging from 0 (IP SI equals OP SI), 1 (IP SI mildly greater than OP SI), and SI of the liver converges with the SI of the spleen on OP image), 2 (IP SI moderately greater than OP SI, with liver SI lower than SI of the spleen on OP image) and 3 (IP SI markedly greater than OP SI, with liver SI lower than SI of the spleen on OP image).

Adrenal adenomas were diagnosed on the basis of observed loss of signal from IP to OP images.

When appropriate, subgroups of subjects were established based on subjective identification of fatty infiltration of the liver or in the presence of adrenal lesions. Whenever feasible, subjective visual comparison between these two subgroups with conventional T1-weighted IP/OP 2D-GRE sequences was performed.

Quantitative analyses

When available, adrenal SI index and fat fraction of the liver were calculated with 2D-GRE sequences, and were considered in the comparison to support the presence of fatty adrenal adenomas and liver steatosis. Quantitative measurements of adrenal SI index were calculated as follows: \[ \frac{[\text{SI}_{\text{IP}} - \text{SI}_{\text{OP}}]}{\text{SI}_{\text{IP}}} \times 100\% \]. Lesions were classified as adenoma if the adrenal SI index was greater than 16.5% on in-phase and out-of-phase 2D-GRE images.

Quantitative measurement of the liver fat fraction was calculated as follows:
\[
\frac{[\text{SI}_{\text{IP}} - \text{SI}_{\text{OP}}]}{\text{SI}_{\text{IP}}} \times 100\%/2.
\]

The mean SI of the adrenal lesions and steatotic livers was obtained on IP and OP 2D-GRE sequences using region-of-interest (ROI) measurements. ROIs were placed on each adrenal mass to cover as much of the mass as possible but avoid the lesion edge to avoid chemical-shift artifact on out-of-phase images. The SI measurements for the liver were obtained at homogeneous areas devoid of vessels, lesions, and artifacts, and each SI value was measured twice. The ROIs were placed at anatomically matched locations on paired sequences by using a coregistration tool available on the PACS workstation. The same reviewer performed all measurements.

The index of relative SI loss of the liver on OP images was considered to be a reasonable measurement of liver fat on the basis of the known effect of fat on SI values, but was not considered to be a direct measurement of liver fat content.

Statistical analyses

A Kolmogorov–Smirnoff test was performed to verify the non-parametric distribution of the data. The Wilcoxon signed rank test for paired samples was used to compare IP and OP MP-GRE qualitative scores. Mann–Whitney was used to qualitatively compare MP-GRE qualitative scores between cooperative and noncooperative patients in both groups (independent samples). To assess interobserver variability in image interpretation, weighted kappa statistics were used to measure the degree of agreement between the two interpreters.

The qualitative analysis between cooperative and noncooperative patients and interobserver variability were performed by using MedCalc for Windows, version 11.3.0.0 (MedCalc Software, Mariakerke, Belgium). In all cases, a value of \( p < .05 \) was considered to be a statistically significant difference.

Results

Kappa values for agreement between the two reviewers for the independent qualitative data analyses ranged from 0.44 to 0.83. The kappa value was 1.0 for bounce-point artifact in MP-GRE OP and MP-GRE IP, and for identification of phase cancelation artifact in all sequences. There were no significant differences in rating between readers. Averaged data are shown to simplify and improve clarity at display.

Phase 1

The results of the qualitative analysis for overall image quality, artifacts and for conspicuity of liver lesions for the first group of patients are displayed in Table 3.

All patients (73/73) demonstrated obvious phase cancelation artifact in MP-GRE OP sequences and it was rated absent
in all patients in MP-GRE IP, by both reviewers (Fig. 1). Both sequences were rated mild to absent concerning artifacts, with the exception of bounce-point artifacts, which had a significantly higher occurrence with MP-GRE IP, (p < .0001).

Respiratory ghosting, spatial misregistration and pixel graininess had mean ratings greater than 3.6 (minimal to absent) in both MP-GRE sequences, without significant differences.

Bounce-point artifact was significantly worse in MP-GRE IP, (p < .0001), and was rated severe in 15% (11/73) of the subjects by at least one reviewer (Fig. 1). For MP-GRE OP, both reviewers rated this artifact minimal to absent in 100% of patients (73/73).

The depiction of intrahepatic vessels had significantly higher ratings on MP-GRE IP, (p = .0021). The mean score for MP-GRE OP and MP-GRE IP, was 3.66 and 3.84, respectively (fair to good depiction of the intrahepatic vessels for both sequences).

Concerning the conspicuity of liver lesions, both MR-GRE sequences were considered diagnostic, without significant difference, with mean rates between 4.61 (MP-GRE OP) and 4.66 (MP-GRE IP,).

MP-GRE OP showed significantly higher overall image quality compared to MP-GRE IP, (p < .0001). Overall image quality was considered excellent for at least one reviewer in 50.6% (37/73) of the subjects for the MP-GRE OP sequence but only in 23.2% (17/73) of the subjects for the MP-GRE IP, sequences.

There were no significant differences in qualitative evaluation of the MP-GRE sequences between cooperative and noncooperative patients for all the evaluated parameters (Table 4).

Hepatic steatosis was detected in 12.3% (9/73) of the patients using a comparison of MP-GRE IP, to MP-GRE OP. Hepatic steatosis was detected in both cooperative (n = 7) and noncooperative (n = 2) patients (Fig. 2). The scores of subjective fatty infiltration appearance and the calculated fat fraction (2D-GRE) are displayed in Table 7.

Six patients were identified as having adrenal nodular lesions (ranging from 10 mm to 40 mm in size). Five of these lesions demonstrated homogeneous loss of signal intensity on MP-GRE OP consistent with fatty adrenal

<table>
<thead>
<tr>
<th>Qualitative parameters</th>
<th>MP-GRE sequences</th>
<th>p value&lt;sup&gt;c&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>OP</td>
<td>IP&lt;sub&gt;1&lt;/sub&gt;</td>
<td></td>
</tr>
<tr>
<td>Respiratory ghosting</td>
<td>3.91±.34 (3.83–3.98)</td>
<td>3.95±.34 (3.87–4.02)</td>
</tr>
<tr>
<td>Phase cancelation artifact</td>
<td>1.0±0 (1.00–1.00)</td>
<td>3.0±0 (3.00–3.00)</td>
</tr>
<tr>
<td>Depiction of intrahepatic vessels</td>
<td>3.6±.62 (3.51–3.80)</td>
<td>3.8±.44 (3.73–3.94)</td>
</tr>
<tr>
<td>Bounce-point artifacts</td>
<td>4.0±0 (4.00–4.00)</td>
<td>2.97±.97 (2.74–3.19)</td>
</tr>
<tr>
<td>Misregistration</td>
<td>3.8±.37 (3.76–3.93)</td>
<td>3.9±.21 (3.87–3.96)</td>
</tr>
<tr>
<td>Pixel graininess</td>
<td>3.6±.66 (3.48–3.79)</td>
<td>3.7±.61 (3.55–3.84)</td>
</tr>
<tr>
<td>Overall image quality</td>
<td>3.3±.72 (3.36–3.69)</td>
<td>2.84±.80 (2.65–3.02)</td>
</tr>
<tr>
<td>Lesion conspicuity</td>
<td>4.61±.49 (4.49–4.72)</td>
<td>4.66±.57 (4.52–4.79)</td>
</tr>
</tbody>
</table>

Values are mean ± SD. Numbers in parentheses are 95% CI. Wilcoxon signed rank test was used for statistical analysis.

<sup>a</sup> Magnetization-prepared gradient recalled echo.
<sup>b</sup> Data are mean ± standard deviation.
<sup>c</sup> Results were considered statistically significant when p < .05.
Table 4 Results of quality analysis between cooperative (n = 49) and noncooperative (n = 24) patients before sequence optimization.

<table>
<thead>
<tr>
<th>Qualitative parameters</th>
<th>OP</th>
<th>p value</th>
<th>IP</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Cooperative</td>
<td>Noncooperative</td>
<td>Cooperative</td>
<td>Noncooperative</td>
</tr>
<tr>
<td>Respiratory ghosting</td>
<td>3.95 ± .19</td>
<td>3.82 ± .52</td>
<td>.489</td>
<td>3.98 ± .14</td>
</tr>
<tr>
<td></td>
<td>(3.89–4.00)</td>
<td>(3.60–4.03)</td>
<td></td>
<td>(3.93–4.02)</td>
</tr>
<tr>
<td>Depiction of intrahepatic vessels</td>
<td>3.68 ± .55</td>
<td>3.60 ± .77</td>
<td>.966</td>
<td>3.82 ± .41</td>
</tr>
<tr>
<td></td>
<td>(3.52–3.83)</td>
<td>(3.27–3.92)</td>
<td></td>
<td>(3.70–3.93)</td>
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<tr>
<td>Bounce-point artifacts</td>
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<td>4.0 ± 0</td>
<td>1</td>
<td>2.85 ± 1.05</td>
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<tr>
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<td>(4.00–4.00)</td>
<td>(4.00–4.00)</td>
<td></td>
<td>(2.54–3.15)</td>
</tr>
<tr>
<td>Misregistration</td>
<td>3.80 ± .42</td>
<td>3.95 ± .20</td>
<td>.184</td>
<td>3.93 ± .25</td>
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<td></td>
<td>(3.67–3.92)</td>
<td>(3.86–4.03)</td>
<td></td>
<td>(3.85–4.00)</td>
</tr>
<tr>
<td>Pixel graininess</td>
<td>3.64 ± .63</td>
<td>3.62 ± .71</td>
<td>.974</td>
<td>3.79 ± .50</td>
</tr>
<tr>
<td></td>
<td>(3.45–3.82)</td>
<td>(3.32–3.91)</td>
<td></td>
<td>(3.64–3.93)</td>
</tr>
<tr>
<td>Overall image quality</td>
<td>3.31 ± .72</td>
<td>3.45 ± .73</td>
<td>.319</td>
<td>2.80 ± .81</td>
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<tr>
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<td>(3.10–3.51)</td>
<td>(3.14–3.75)</td>
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<td>(2.56–3.03)</td>
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<tr>
<td>Lesion Conspicuity</td>
<td>4.68 ± .47</td>
<td>4.50 ± .70</td>
<td>.548</td>
<td>4.73 ± .55</td>
</tr>
<tr>
<td></td>
<td>(4.54–4.81)</td>
<td>(4.20–4.79)</td>
<td></td>
<td>(4.57–4.88)</td>
</tr>
</tbody>
</table>

Values are mean ± SD. Numbers in parentheses are 95% CI. Mann–Whitney test was used for statistical analysis.

Table 5 Comparison of qualitative results between MP-GRE OP and MP-GRE IP2 in all patients (n = 64)—post IP sequence optimization.

<table>
<thead>
<tr>
<th>Qualitative parameters</th>
<th>MP-GRE sequences</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OP</td>
<td>IP2</td>
</tr>
<tr>
<td>Respiratory ghosting</td>
<td>3.80 ± .43 (3.69–3.88)</td>
<td>3.82 ± .40 (3.72–3.91)</td>
</tr>
<tr>
<td>Phase cancelation artifact</td>
<td>1.0 ± 0 (1.00–1.00)</td>
<td>3.0 ± 0 (3.00–3.00)</td>
</tr>
<tr>
<td>Depiction of intrahepatic vessels</td>
<td>3.76 ± .47 (3.64–3.87)</td>
<td>3.84 ± .35 (3.75–3.92)</td>
</tr>
<tr>
<td>Bounce-point artifacts</td>
<td>4.0 ± 0 (4.00–4.00)</td>
<td>4.0 ± 0 (4.00–4.00)</td>
</tr>
<tr>
<td>Misregistration</td>
<td>3.69 ± .46 (3.57–3.80)</td>
<td>3.65 ± .52 (3.52–3.77)</td>
</tr>
<tr>
<td>Pixel graininess</td>
<td>3.47 ± .54 (3.33–3.60)</td>
<td>3.49 ± .53 (3.35–3.62)</td>
</tr>
<tr>
<td>Overall image quality</td>
<td>3.51 ± .58 (3.36–3.65)</td>
<td>3.42 ± .58 (3.27–3.56)</td>
</tr>
<tr>
<td>Lesion conspicuity</td>
<td>4.43 ± 1.05 (4.16–4.69)</td>
<td>4.55 ± .78 (4.35–4.74)</td>
</tr>
</tbody>
</table>

Values are mean ± SD. Numbers in parentheses are 95% CI. Wilcoxon signed rank test was used for statistical analysis.

Phase 2

The results of the qualitative analysis of phase 2 are displayed in Tables 5 and 6. All patients (64/64) demonstrated obvious phase cancelation artifact on MP-GRE OP sequences and it was considered absent in all patients on the optimized MP-GRE IP2, by both reviewers (p < .0001).

MP-GRE OP and MP-GRE IP2 showed no bounce-point artifacts with any other significant differences between the remaining evaluated artifacts (Fig. 3) (Table 5). Both MP-GRE sequences had high mean ratings concerning overall image quality, 3.51 for MP-GRE OP and 3.42 for MP-GRE IP2 (good to excellent) (p = .098).

The MP-GRE IP2 sequence had significantly higher misregistration in noncooperative patients (mean score of 3.45) compared to cooperative patients (mean score of 3.74).
In-phase and out-of-phase single-shot magnetization-prepared gradient recalled echo

<table>
<thead>
<tr>
<th>Qualitative parameters</th>
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<th>p value</th>
</tr>
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<tr>
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<td>OP</td>
<td></td>
</tr>
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<td>Cooperative</td>
<td>Noncooperative</td>
</tr>
<tr>
<td>OP</td>
<td>p value†</td>
<td></td>
</tr>
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Concerning the conspicuity of liver lesions, all ratings were above 4 (diagnostic), either in cooperative or noncooperative patients (Tables 5 and 6).

Hepatic steatosis was visually detected in 17.2% (11/64) of the patients in the second study group (post-optimization), using a comparison of MP-GRE IP2 to MP-GRE OP (Figs. 3 and 4), in both cooperative (n = 9) and noncooperative (n = 2) patients (Table 7).

Within both patient groups there were no differences in the number of patients identified as having steatotic livers by the visual assessment of 2D-GRE and MP-GRE images in cooperative patients.

Discussion

MP-GRE sequences are a standard component of most abdominal MRI strategies for T1-weighted imaging in patients who cannot suspend respiration.1,12–18 Respiratory-triggering and navigation are routinely used for T2-weighted imaging and coronary imaging.13,16,23,24 However, there has been less attention to their use in mitigating motion artifacts in T1-weighted imaging of the abdomen, and to our knowledge never described to IP/OP imaging. Furthermore these techniques require additional steps in the clinical workflow and can fail in cases of irregular and superficial respiration.23,29

Our preliminary results show that IP/OP imaging can be implemented with MP-GRE, which may represent an important advance in abdominal imaging.

The pre-optimized MP-GRE IP1 and the post-optimized MP-GRE IP2 sequences demonstrated IP properties, with negligible to absent phase-cancelation artifact. Clear phase-cancelation artifact was observed in all patients with the MP-GRE OP sequence, features that in our study were considered as surrogate for defining IP/OP characteristics.

Bounce-point artifacts were principally noticed on the interface between hepatic vessels and hepatic parenchyma. In this case, for the MP-GRE IP1 sequence the combination of the 3000 ms TR (repetition time) and the 750 ms T1 allows relatively short T1 tissues like hepatic parenchyma to have passed through the inversion recovery null point while long T1 tissues like the hepatic vessels had not. In contrast, the combination of the relatively longer T1 (900 ms) and shorter TR (1540 ms) on the MP-GRE OP and later the optimized MP-GRE IP2 ensures that all abdominal tissues have crossed the inversion recovery null point, thereby eliminating the bounce-point artifact. We did not perceive any diagnostic advantages with the combination of a T1 of 750 ms and a TR of 3000 ms, but it did have the disadvantage of bounce point artifacts that were problematic in 9/73 cases.

The misregistration found between some MP-GRE sequences, although well within the diagnostic range, reflect the single-shot nature of the technique.

Our data demonstrate that the depiction of intra-hepatic vessels is superior with IP MP-GRE sequences. This is explained by the presence of fatty infiltration in some patients where the vessels might be obscured due to the decreased SI of the liver in OP images. This feature explains why lesion conspicuity was also slightly higher in IP MP-GRE sequences, which is consistent with the literature.30,31

(p = .027). However, these scores represent mild to minimal misregistration in both MP-GRE sequences.

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Our opinion is that this study benefited from the displayed data prior to and following optimization. In phase 1 we evaluated sequences using parameters provided by the manufacturer. As we had observed, with novel techniques there may be no a priori knowledge of optimized parameters, and perhaps only after performing such a trial phase can one evaluate how parameters should be optimized. In phase 2 we evaluated IP/OP MP-GRE following our optimization. Without the pre-optimization phase of the study, it may not have been apparent what was the effect of certain sequence properties, and hence what modifications were necessary. We believe this was only possible by running this study in clinical settings. As no prior study of this type has been performed, we had no guidance on selection of sequence parameters. On the basis of our findings, we have now reduced TR to 1540 ms and increased the TI time to at least 900 ms duration in the new IP MP-GRE, as bounce-point artifacts may be problematic, as we did not observe clinical advantages to the shorter TI. The bandwidths are different between IP/OP MP-GRE sequences due to a limitation in the user interface (UI). Specifically, there is no direct mechanism to select TE, but it is indirectly set via bandwidth. For the optimized MP-GRE IP2 sequence, it was chosen via computer simulation. Furthermore we incorporate 2 averages and increased the matrix size from 256 × 88 to 256 × 156, as we noted no higher pixel graininess with the MP-GRE OP sequence.

Following IP MP-GRE sequence parameters modifications on the basis of the preliminary investigation in phase 1, the MP-GRE IP2 sequence revealed a higher image quality, similar to MP-GRE OP.

This present study can therefore act as a foundation for future research into MP-GRE sequence optimization for IP/OP abdominal imaging.

Evaluations of fat in liver and in adrenal masses are two important indications for IP/OP imaging. Hepatic steatosis was visually detected in 14.6% (20/137) of the patients. Subjective loss of signal intensity in the liver together with clear phase cancelation artifact was demonstrated with MP-GRE OP, allowing confident diagnosis of fatty deposition. Both fatty liver and adrenal mass subgroups were subjectively compared with T1-weighted IP/OP 2D-GRE images when available (16/20 for hepatic steatosis and 3/5 for adrenal adenomas) which served as a reference. Differences between 2D-GRE and MP-GRE in the qualitative grading of the extent of fatty infiltration were observed in three patients, suggesting greater visualization of fat content in 2D-GRE sequences. The scoring system used a visual signal comparison between the liver and the spleen. The nature of inversion recovery sequences, combined with the slightly different longitudinal relaxation times of the spleen and liver may have caused this difference suggesting that comparison to spleen may be less reliable in MP-GRE sequences. Quantitative data from fat fraction calculation support the findings observed on IP/OP MP-GRE, showing significant loss of liver SI on 2D-GRE OP images in sixteen patients with steatosis. Concerning adrenal lesions, the finding of loss of signal intensity from IP to OP allowed characterization of adrenal adenomas in five patients (5/6) using the MP-GRE sequence. Quantitative data from adrenal SI index calculation on the 2D-GRE were available in three patients supported these findings. Following our optimization and using analogous sequence parameters, IP/OP MP-GRE sequences have recently shown promising results for imaging liver steatosis and for the characterization of adrenal nodules.

This study has some limitations: The first is the retrospective design of the study. The use of two different MP-GRE sequences with differing parameters in the first phase of the study contributed to the dissimilar quality ratings of the sequences. For example, the fact that 2 averages were used for the OP and 1 average for the IP MP-GRE sequence may have resulted in bias regarding image quality, since respiratory motion artifacts are decreased when multiple averages are used. We did however employ the default parameters of the equipment manufacturers as no prior studies had evaluated these types of sequences. The retrospective design

<table>
<thead>
<tr>
<th>Table 7</th>
<th>Scores of subjective fatty infiltration of the liver and calculated fat fractions in 20 patients.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
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<tr>
<td></td>
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<tr>
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<tr>
<td>10</td>
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</tr>
<tr>
<td>11</td>
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</table>

N/A, not applicable.

a In-phase and out-of-phase two dimensional spoiled gradient echo 2D-GRE) is acquired as a dual echo acquisition.

b Fat fraction was calculated in 2D-GRE sequences.
of the study implied that the pre- and post-optimized MP-GRE IP sequences were not performed in every patient. Another limitation is the small number of noncooperative patients included. However, we acquired the MP-GRE data in cooperative patients using a free-breathing approach, which is considered to be a suitable model for noncooperative patients. There were no significant differences regarding qualitative assessment when comparing these two patient populations in both patients groups. An additional limitation was that the noncooperative protocols did not include pre-contrast IP/OP 2D-GRE for the obvious reason that it requires the patient to breath-hold in order to achieve good image quality. Based on our findings we routinely employ IP/OP MP-GRE in noncooperative patients.

In conclusion, we have described the implementation and optimization of an IP/OP technique on a motion resistant single-shot MP-GRE sequence. This initial clinical experience shows considerable promise, with good image quality and consistent presence and absence of phase cancelation artifact on OP and IP MP-GRE sequences, respectively.

**Ethical responsibilities**

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this investigation.

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

**Right to privacy and informed consent.** The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

**Authors**

1. Responsible for the study’s integrity: RCS.
2. Conception: MR, VH, ROPC, MDT, BMD and RCS.
3. Design: MR, VH, ROPC, BMD and RCS.
Conflicts of interest

One author (BMD), an employee of Siemens Medical Solutions (Cary, NC), assisted in designing the imaging protocol. The other authors had full control of inclusion of any data and information that might present a conflict of interest.

References

30. Rosfny MA, Weinreb JC, Ambrosino MM, Safir J, Krinsky G. Comparison between in-phase and opposed-phase T1-weighted
