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Inversion-recovery-prepared Dixon bSSFP: Initial clinical experience with a novel pulse sequence for renal MRA within a breath-hold

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Abstract

Purpose—To evaluate the capability of a new breath-hold non-contrast-enhanced MRA method (Non-contrast Outer Radial Inner Square k-space Scheme, NORISKS) to visualize renal arteries by comparing the method with a routine clinical but significantly longer non-contrast-enhanced (non-CE) MRA technique.

Materials and Methods—Eighteen subjects referred for abdominal MRI were examined with NORISKS and a routine non-contrast-enhanced MRA technique. Two versions of NORISKS were evaluated: with and without ECG gating. The images were then scored independently and in blinded fashion by two radiologists on 5-point scales for visualization of the proximal and distal renal arteries and quality of fat suppression.

Results—No statistically significant difference was detected between NORISKS and routine clinical non-CE MRA in all categories except for visualization of the distal renal arteries where ungated NORISKS performed poorer than the routine non-CE MRA ($p < 10^{-4}$).

Conclusion—We have demonstrated a promising non-CE MRA method for acquiring renal angiograms within a breath-hold without any compromise in spatial resolution or coverage. ECG-gated NORISKS is able to acquire renal angiograms that are comparable to a routine clinical non-CE MRA method (Inhance IFIR, GE Healthcare), which requires approximately seven times the scan time of NORISKS.

Keywords

Non-contrast-enhanced; MR angiography; Breath-hold; Renal; Balanced SSFP; Dixon

Introduction

Non-contrast-enhanced MR angiography has regained popularity due to a number of factors: advancement in MR hardware and acquisition strategies, discovery of nephrogenic systemic fibrosis (NSF) and its associated risks in patients with severe renal dysfunction, and the high cost of gadolinium-based contrast agents in some countries (1, 2). Apart from these factors, there are other reasons that favor non-contrast-enhanced MRA over contrast-enhanced (CE) MRA (3), which is the gold standard method for MRA. Despite several (semi-) automated strategies of estimating the time delay between the administration of the contrast agent bolus and the start of the acquisition (e.g., SmartPrep, timing bolus), the technique remains relatively user-dependent. When the CE examination fails, the patient has to return on a

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separate appointment to be re-examined, thus decreasing patient throughput. Therefore, several CE developments have shifted focus towards time-resolved methods (e.g., Time Resolved Imaging of Contrast KineticS, TRICKS, and Time-resolved angiography With Stochastic Trajectories, TWIST) to overcome the timing bolus issue. However, in either case, the spatial coverage and resolution of the angiogram is restricted due to a limited acquisition time period between arterial and venous enhancement. Therefore, due to all of the above reasons, there has been a drive towards developing non-contrast-enhanced (non-CE) methods in MRA.

Renal angiography lends itself particularly well to non-CE MRA. First, patients with severe renal dysfunction are most susceptible to NSF and also have a relative contra-indication for CT angiography due to iodinated contrast-induced nephropathy. Therefore, the ability to provide reliable diagnostic renal MRA of these patients is likely to affect treatment and outcomes. Second, CE MRA of the renal arteries is more technically challenging than other vascular regions because the kidney has comparatively low vascular resistance. Therefore, the timing window for arterial-only imaging is narrow (on the order of seconds) before the obscuring renal parenchyma and veins are enhanced by the contrast agent as well.

This work describes a rapid inversion-recovery-prepared, two-point Dixon, balanced steady-state free-precession (bSSFP) technique to acquire renal angiograms within a breath-hold and without the use of an intravenous contrast agent. A number of recent studies comparing 3D, inflow-based bSSFP renal MRA to digital subtraction angiography or CE MRA (4, 5, 6) have found statistically promising results for inflow-based MRA with sensitivities of 75–100% and specificities of 82–99%. Probably largely due to these encouraging findings, several MRI system vendors have added various free-breathing, inflow-based bSSFP MRA implementations to their product lines (Inhance IFIR, GE Healthcare; syngo Native TrueFISP, Siemens Healthcare; TimeSLIP TrueSSFP, Toshiba Medical Systems). However, the method suffers from a relatively long acquisition time of several minutes. Also, irregular respiration patterns and respiratory pattern changes with sleep apnea (7) may cause respiratory-triggered acquisitions to be suspended or fail. We propose the use of a new breath-hold version of inflow-based MRA with much shorter acquisition times, which may permit wider integration of this technique into routine abdominal protocols and increase robustness to variable patient respiratory patterns.

Other breath-hold non-contrast-enhanced MRA methods have been proposed for renal angiography but these were often achieved at a cost of limited spatial coverage, limited resolution, or using multiple breath-holds (8, 9, 10, 11, 12). In this work, we aim to investigate a 20–30-second breath-hold, non-CE MRA (13) acquisition and compare it to a 3–5 minute respiratory-triggered acquisition without compromising spatial coverage or resolution.

In atherosclerosis, which accounts for 60–90% of renal artery lesions, the stenoses are usually found at the ostium and in the proximal third of the renal artery (14, 15). We aim to demonstrate that the new breath-hold bSSFP method – called Non-contrast Outer Radial Inner Square k-space Scheme (NORISKS) – is able to provide reliable visualization of the proximal renal artery in subjects who have been referred for abdominal MRI.

Materials and Methods

All studies were performed using a 3.0 T MRI body scanner (MR750, GE Healthcare, Waukesha, WI).

Pulse Sequence Design

The pulse sequence used in NORISKS is based on an arterial spin labeling (ASL) technique traditionally used to obtain perfusion information without contrast agent administration. ASL- or inflow-based methods have been shown to be rather effective for 3D non-CE abdominal MR angiography (2) (e.g., as in the hepatic arteries (16) and renal vasculature (17, 8, 4)) and MR venography (18).

The basic acquisition is a dual-echo, balanced steady-state free precession (19) sequence (Fig. 1a). This two-point SSFP has been shown to be effective at providing separated fat and water images (20, 21). We have empirically determined optimal echo times of TE1/TE2 = 1.7/2.7 ms to provide two data sets, which are then reconstructed using the post-processing algorithm of Ma (22) to yield fat and water images. These echo times were achieved using bipolar, fractional echo readouts.

The k-space trajectory is a hybrid of “group-encoded” and radial schemes (Fig. 1b). The k_y - k_z center (10×10 pixels) of k-space was ordered sequentially in y and centrically in z. This k-space center (of 100 views) was acquired after the first IR preparation and only once. The main purpose of the group-encoded center was to provide smooth signal modulation, while maintaining a temporally limited acquisition of the k-space center to maximize the inversion null effect. The k-space center was also “paired” to minimize flow and eddy current effects in bSSFP (23). The rest of k-space was divided into five to six pie segments with each segment consisting of 700–800 views; within each segment, the trajectory was ordered according to increasing k_r (radial distance) while minimizing the step size to reduce eddy current effects. Removal of k-space corners and the addition of auto-calibrated parallel imaging (ARC) (24) reduced the total number of acquired views.

Inversion recovery (IR) preparation was achieved using an adiabatic hyperbolic secant RF pulse. The IR slab was oriented axially, as was the imaging slab, and spanned a superior-inferior region that covered the imaging slab plus a portion inferior to the imaging slab for venous suppression. A key change that occurs when respiratory triggering is removed is that the “effective TR” (Fig. 1a) is now greatly reduced. In fact, it is possible to eliminate all time between the end of a segment and the next IR pulse. From Bloch dynamics, the optimal inversion time (TI) for nulling a particular T1 species at an effective TR (TR_{eff}) is:

$$TI = T1 \ln \frac{2}{1 + \exp(TR_{eff}/T1)} \quad [1]$$

Therefore, reducing the effective TR reduces the inversion time. A reduced TI also means that there is decreased inflow time for arterial imaging. Therefore, in NORISKS, some wait time is inserted to separate the end of an acquisition segment and the following IR pulse to allow the background tissue to recover, which increases the inversion time for effective nulling. In our acquisitions, a wait time of approximately one second is added to reach an effective TR of five to six seconds, which is similar to that of respiratory-triggered schemes.

ECG triggering/gating has been shown to be effective in a few studies (25) but there has not been a direct comparison between ECG-triggered and non-triggered acquisitions (17). Therefore, an optional ECG gating option is added to trigger only the first acquisition of the center segment, which adds only minimal time to the acquisition.

MRI Study

Eighteen patients referred for routine abdominal MRI were enrolled in the study. Informed written consent was obtained from all subjects, and all examinations were performed in a HIPAA-compliant fashion and with IRB approval. The main goal of this initial clinical

study was to test if there was a significant difference between the NORISKS method and a routine, clinical non-CE MRA method in the visualization of the proximal renal artery. As secondary aims, we tested if there was any significant difference in the visualization of the distal renal arteries and overall image quality. Table 1 lists the additional acquisitions that were performed on each subject for the purpose of this study. The total scan time added to the standard protocol was less than five minutes. These scans were typically acquired consecutively just before the administration of intravenous contrast agent, if indicated by the protocol, and in random order.

Common acquisition parameters for both routine non-CE MRA and NORISKS were: axial, FOV = 32–38×26–30 cm²; matrix resolution = 256×180×44–56; slice thickness = 2.8 mm interpolated to 1.4 mm (so a total of 88–112 slices were obtained); flip angle = 60°; inversion time (TI) = 1400 ms. For the non-CE MRA method (Inhance IFIR, GE Healthcare), other parameters were: TR = 4.6–5.1 ms; TE = TR/2; views per segment = number of k_y lines; receive bandwidth = 977 Hz/pixel; respiratory triggering; spectrally selective fat inversion; ASSET parallel imaging 2×. For NORISKS, other parameters were: TE1/TE2 = 1.7/2.7 ms; TR = 4.6–4.9 ms; views per segment = 800; receive bandwidth = 1116 Hz/pixel; ARC net acceleration factor 2×.

The images were analyzed independently by two radiologists. The images were anonymized and scored in three categories: visualization of the (A) proximal and (B) distal renal arteries and (C) fat suppression quality. For vessel visualization in each subject, a score was given for each observable vessel segment; i.e., one score for the proximal right, another for the proximal left, a third for the distal right, and a fourth for the distal left. The proximal renal artery was defined as the first 3-cm segment of the renal artery from the ostium. The distal renal artery was defined as the remaining part, including the segmental vessels. The categories for vessel visualization and quality of fat suppression are listed in Table 2.

Statistical analyses were performed on the results. The scores from the right and left vessel segments were averaged so that there were eighteen independent samples for each category to be evaluated, preventing statistical errors from correlated data. Spearman rank correlation of the scores was calculated to evaluate reader agreement. As the results were from categorical scores and are not Gaussian distributed, nonparametric statistics were used throughout. Differences were investigated using Friedman tests (since matched subjects were used in this study). For groups that showed a significant difference with the Friedman test, further post hoc (or a posteriori) pairwise differences among the methods were investigated using a Wilcoxon matched-pairs signed-rank test. A *p* value of less than 0.05 was considered statistically significant; no correction was done to the *p* values to prevent Type 2 statistical errors (26).

Results

Eighteen subjects (22% female, age range 19–78 years and mean±s.d. 57±19 years) were evaluated. A total of 34 renal arteries were available for scoring of visualization; one subject had a missing right kidney while another subject had a missing left kidney. The average acquisition time was 201±21 seconds for the routine non-CE MRA method, and 29±2 seconds for NORISKS.

The agreement of both readers was moderate (Spearman correlation $r_s=0.75$). A distribution of the scores and reader agreement are plotted in Fig. 2. Results from the Friedman tests showed that there were no significant differences among all three acquisitions for the visualization of the proximal renal artery ($\chi^2=3.86$, $p=0.15$) and quality of fat suppression

($\chi^2=5.25$, $p=0.072$). However, the Friedman test showed a statistically significant difference among the methods for the visualization of the distal renal artery ($\chi^2=12.6$, $p=0.0019$).

Post hoc Wilcoxon pairwise investigation for the visualization of the distal renal artery showed that there were no significant differences between ECG-gated NORISKS and routine non-CE MRA ($N=15$, $Z=27.5$, $p=0.064$) and between ECG-gated and ungated NORISKS ($N=17$, $Z=36.5$, $p=0.057$); however, the routine clinical MRA method was statistically better than ungated NORISKS ($N=14$, $Z=4.5$, $p=8.5 \times 10^{-5}$).

Figure 3 shows maximum intensity projections (MIPs) of images from two subjects that are representative of the group examined. One can observe the excellent level of venous and background tissue signal suppression in all images. The second subject shown, subject B, has only one kidney (on the right side). Also in subject B, the distal renal vessels are less well visualized with the NORISKS methods compared to the routine, respiratory-triggered non-CE MRA method. A severe stenosis was observed on the right renal proximal renal artery with all three methods. Further follow-up on the case revealed that the subject had hypertension, which could be due to presumed renal artery stenosis or from the subject's inherent renal failure.

Figure 4 shows paired images (routine non-CE MRA on the left and NORISKS on the right) from six subjects to illustrate the fat suppression efficacy. Generally, both fat suppression methods (fat-selective IR and Dixon water-fat separation) performed well (Fig. 2). The Dixon method appeared to perform better at the peripheral region (fat failures in Fig. 4 are denoted by the red arrows) but this difference was not statistically significant.

Discussion

We have demonstrated a promising inflow-based bSSFP MRA technique that is able to acquire good-quality angiograms of the renal artery within breath-holding times. NORISKS is fast (approximately 7 $\times$ reduction in acquisition time compared to respiratory-triggered, routine clinical non-CE MRA) and reliable – renal angiograms were successfully collected with all acquisitions in all subjects examined. Our initial clinical experience shows that ECG-gated NORISKS is not significantly different to the routine, respiratory-triggered renal non-CE MRA method (Fig. 2) for the visualization of the proximal renal artery and quality of fat suppression. However, we did find a statistically significant difference between ungated NORISKS and routine non-CE MRA for the visualization of the distal renal artery.

Central to the ability to perform breath-hold, non-CE MRA is the use of a Dixon-type approach for fat suppression. Two-point Dixon removes the timing limitation of using a fat inversion recovery (IR) pulse. The main issue with fat IR is that the nulling or effectiveness is limited in time due to the relatively short T1 of fat; therefore, each bSSFP segment needs to be fairly short (around half a second) to avoid edge enhancement of fat that could confound arterial delineation. The use of Dixon removes that timing limitation and allows for much longer segments (up to 800 views per segment, or four seconds, in our study) and flexible k-space ordering schemes such as NORISKS and radial fan-beam (27), etc. No statistical difference was found between routine non-CE MRA and NORISKS for quality of fat suppression. At 3.0 T, the optimal echo times for two-point Dixon are relatively short and does not cause any significant increase in TR, which is important as banding artifacts can occur in bSSFP with a long TR. Another benefit of Dixon is its immunity to B1 variations, which can be a problem at 3.0 T systems or when imaging large subjects. However, this B1 sensitivity problem can also be solved for fat IR by using adiabatic

¹N refers to the number of pairs that had a non-zero difference. There are 18 comparison pairs for the Wilcoxon tests.

inversion pulses. Dixon methods are also less sensitive to B0 inhomogeneity compared to spectral RF suppression methods.

Compared to previous breath-hold non-CE methods, NORISKS has several improvements. First, a single breath-hold is used to cover a volume of interest that previously required several breath-holds (12). 3D axial volumes (see Fig. 3) with superior-inferior coverage of 12–16 cm, much higher than those obtained previously (12, 10, 8), were routinely acquired. Second, the use of a slice-selective inversion recovery slab provides excellent suppression of venous and tissue signal, while allowing for a reasonable inflow time. Coenegrachts et al. showed bSSFP angiograms acquired within several breath-holds but mentioned poor image quality due to hyperintense background tissue in MIPs (12). Both Coenegrachts et al. (12) and Maki et al. (8) used saturation bands to suppress venous signal at a cost of reduced inflow time and limited distal vessel visualization. Herborn et al. showed bSSFP angiograms that were acquired within a breath-hold but the source of vessel contrast in those angiograms was from T2 weighting and hence suffered from venous overlay issues (10). Although our breath-holding time is considered relatively long (about 25 seconds), the subjects tolerated the scans well. Also, immunity to breath-hold loss could be attributed to the NORISKS k-space segmentation scheme that captures the bulk image contrast early during the acquisition.

In this work, the effect of ECG triggering or gating is investigated for the first time for inflow-based bSSFP MRA methods. Although many groups have applied ECG-gating for inflow MRA (17), no previous work, to the best of our knowledge, has specifically investigated the use of ECG-gating for inflow-based bSSFP MRA. The use of ECG-gating has not been obvious in previous work owing to the favorable flow characteristics of bSSFP (due to the balanced gradients). However, our results show that ECG-gating improves the visualization of the distal renal vessels. The reason for this could be due to cardiac-related motion of the renal artery rather than flow pulsatility. Kaandorp et al. described that the renal artery does move significantly during a cardiac period and this phenomenon could affect the distal arteries more than the proximal renal arteries (28).

Although not systematically investigated in this work, we found the NORISKS acquisition to be more robust when the breath-hold was executed during end expiration than during end inspiration. This finding could be related to that of Holland et al., where they found that the motion of the diaphragm during suspended breathing was more complex at end inspiration than at end expiration (29). Also, Vasbinder et al. showed significant motion of the distal renal artery when imaging during an end inspiration breath-hold (30).

Our study has several limitations. First, we compared the NORISKS method to a commercially available, routine non-CE MRA technique. Although this type of inflow-based method has been demonstrated to compare well with CE MRA and X-ray catheter DSA in a few recent studies (4, 5, 6), a better comparison might have been to compare our method to CE MRA or X-ray catheter DSA to increase the impact of this study. Second, we have only examined a limited number of patients who were referred for abdominal MRI. In our study, there was a trend towards inferior performance of ECG-gated NORISKS compared to the routine non-CE technique, but this did not reach statistical significance. Our study simply showed that a possible difference between ECG-gated NORISKS and routine non-CE MRA was not detected. A larger study is needed to confirm this finding. Third, a majority of these subjects did not suffer from renal disease. Although two renal stenoses were detected with both routine non-CE MRA and NORISKS, this result is not conclusive and future studies should include the evaluation of the sensitivity and specificity of NORISKS.

The NORISKS method may have several clinically relevant roles. First, the method may find greatest use on patients who cannot breathe regularly and often lead to suboptimal or failed free-breathing acquisitions. Also, NORISKS may find particular use in multi-station examination of the entire abdominal vasculature, such as for transplant planning, where the speed gains of the breath-hold technique are essential.

Conclusion

We have demonstrated a promising non-CE MRA method for acquiring renal angiograms within a breath-hold without any compromise in spatial resolution or coverage. NORISKS is able to acquire renal angiograms that are comparable to a commercially available, routine clinical non-contrast-enhanced MRA method, which takes about 7× longer scan time. The new method provides excellent visualization of the proximal renal artery, which is an important vessel segment as the majority of atherosclerotic renal artery stenoses are found there. We anticipate that the development of methods such as NORISKS will improve robustness and encourage wider integration of non-CE MRA techniques into routine abdominal protocols.

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Figure 1.

(a) Pulse sequence diagram and (b) k-space trajectory used to obtain non-contrast-enhanced renal angiograms within a breath-hold. (a) A dual-echo bSSFP sequence is used to provide high SNR images of blood with favorable T2/T1 contrast and flow properties, and separated water and fat images. (b) A center group-encoded scheme is combined with a radial/center-out pie segmentation scheme to reduce the total number of segments required to acquire the data while preserving the IR nulling effect. Within each wedge, all Cartesian points are ordered in increasing k_r and sampled.

Figure 2.

(a) Distribution of scores from radiologist rankings of visualization of vessel segments and quality of fat suppression. The red line represents the median, the box represents the inter-quartile range, the whiskers represent data within $1.5 \times$ inter-quartile range, and the red crosses represent individual data points outside the range of the whiskers. There were no significant differences found among the methods for visualization of the proximal renal artery ($p=0.15$) and quality of fat suppression ($p=0.072$). However, the Friedman test showed a significant difference among the three methods for visualization of the distal renal artery ($p=0.0019$). Further post hoc pairwise analysis showed that ungated NORISKS performed significantly worse than the routine non-CE MRA method. (b) Reader agreement ($r_s = 0.75$) illustrated using a histogram.

Figure 3. Maximum intensity projections of axial slices and coronal reformats from two subjects. The solid arrows in subject A point to the left proximal renal artery, which was scored 5, 4, 5 in the order shown. Although not significant in the overall results, better fat suppression at the subcutaneous fat layer was observed in this particular subject using the Dixon method in NORISKS (dashed arrows). Subject B had a missing left kidney; a stenosis was also observed in this subject who suffered from hypertension.

Figure 4.

Pairs of images (routine non-CE MRA on the left and NORISKS on the right) from six subjects illustrating the different fat suppression levels and features between fat-selective IR (routine non-CE MRA) and Dixon water-fat separation (NORISKS). The red arrows point to regions of fat suppression failure. No statistically significant difference ($p=0.072$) was found for the quality of fat suppression between the methods. All images were automatically windowed and leveled to the full dynamic display range.

Table 1

MRI acquisitions added to the standard abdominal protocol for purpose of this study.

Scan	Motion compensation	ECG gating	Acquisition time
Routine non-CE MRA	Respiratory-triggered	Ungated	3–5 minutes
NORISKS	Breath-hold	Ungated	20–30 seconds
NORISKS	Breath-hold	ECG-gated	20–30 seconds

Table 2

Categories used to evaluate vessel visualization and quality of fat suppression.

Score	Visualization of proximal and distal vessels	Quality of fat suppression
1	Non-diagnostic – Unable to assess vessel	Unsatisfactory – Total failure
2	Limited – Limited confidence in assessment	Poor – Fat was brighter than vessels
3	Diagnostic – Greater than 50% confidence in assessment of vessel for stenosis	Average – Failure in some parts but vessels were still brighter
4	Good – Greater than 90% confidence in assessment for stenosis, with minimal motion artifact and uniform signal in vessel	Good – Effective fat suppression in region over kidneys
5	Outstanding – Good, with sharp delineation of vessel along entire segment	Excellent – Uniform fat suppression over entire image