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Non-Contrast Enhanced 3D SSFP MRA of the Renal Allograft Vasculature: A Comparison Between Radial Linear Combination and Cartesian Inflow-Weighted Acquisitions

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Abstract

Renal transplant patients often require imaging to ensure appropriate graft placement, to assess integrity of transplant vessel anastomosis and to evaluate for stenosis that can be a cause of graft failure. Because there is risk for nephrogenic systemic fibrosis in the setting of renal insufficiency, the use of non-contrast MRA in these patients is helpful. In this study, the ability of two non-contrast MRA methods – 3D radial linear combination balanced SSFP (VIPR-SSFP) and inflow-weighted Cartesian SSFP (IFIR) – to visualize the transplant renal vessels is compared. Twenty-one renal transplant patients were scanned using the VIPR-SSFP and IFIR sequences. Diagnostic efficacy of the sequences was scored using a four point Likert scale according to the following criteria: overall image quality, fat suppression, and arterial / venous visualization quality. Average scores for each criterion were compared using the Wilcoxon signed-rank test. Besides significantly improved venous visualization, the VIPR-SSFP sequence provided significantly improved fat suppression quality ($p < 0.03$) compared to IFIR. Additionally, VIPR-SSFP identified several pathologies such as renal arterial pseudoaneurysm that were not visible on the IFIR images. However, IFIR afforded superior quality of arterial visualization ($p < 0.005$). These two methods of non-contrast MR imaging each have significant strengths and are complementary to each other in evaluating the vasculature of renal allografts.

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Introduction

Since its development in the late 1980s, contrast-enhanced magnetic resonance angiography (CE-MRA)(1) has served as an important non-invasive means for post-operative assessment of the renal transplant arterial and venous vessels(2). CE-MRA has enabled diagnosis of a variety of transplant-related complications from a single imaging exam, including incomplete vessel anastomosis and pseudoaneurysm formation, donor/recipient renal arterial stenosis (RAS), peri-transplant fluid collections, ureteric obstruction or leak, and renal vein thrombosis(3). Compared with Doppler ultrasound, CE-MRA provides significantly improved sensitivity for detection of RAS by enabling direct visualization of the vessel(4). CE-MRA has also been shown to provide high sensitivity and specificity for detection of renal vein thrombosis in native kidneys(5).

Unfortunately, the implication of gadolinium-based contrast agents in the development of nephrogenic systemic fibrosis (NSF)(6) has resulted in avoidance of CE-MRA exams in renal transplant patients. For this reason, clinical demand for robust non-contrast enhanced (NCE) MR angiographic methods to image the transplant renal vessels, as well as other complications that occur both acutely and chronically in these patients, has increased significantly. Recent work, beginning with the development of Time-SLIP(7), has produced several promising methods that are members of a broader class of inflow-weighted balanced steady state free precession (bSSFP) sequences. These NCE-MRA sequences are designed to generate bright signal only in renal arteries, as suspicion of arterial stenosis is the most common indication for renal MRA exams(8). However, in transplant patients it is essential to visualize both venous and arterial anatomy. This is due to the substantial likelihood of pathologies involving the renal vein, such as anastomotic stricture or thrombus formation. Inflow-weighted bSSFP imaging methods, which are not capable of visualizing these potentially catastrophic complications, are thus inadequate for comprehensive vascular evaluation of the renal allograft.

The purpose of this study was therefore to evaluate the performance of a non-inflow weighted 3D radial balanced steady-state free precession acquisition – VIPR-SSFP(9) – in renal NCE-MRA compared to Inflow IR (IFIR)(10). VIPR-SSFP's radial trajectory permits very short TRs, reducing banding artifacts known to impact SSFP acquisitions in the presence of inhomogeneous magnetic fields(11). Achieving TRs under 3 ms also allows fat suppression to be effected through the linear combination of two acquisitions in which a 180-degree relative change in fat signal phase is generated through the use of different RF phase cycling schedules(12). Meanwhile, IFIR is a commercially-available NCE-MRA method within the family of inflow-sensitive SSFP sequences. IFIR differs from VIPR-SSFP in several significant ways: A) IFIR is based on a Cartesian bSSFP trajectory, B) IFIR uses an inversion slab to null venous signal and produce images with bright arteries, and C) IFIR uses a frequency selective chemical saturation pulse for fat suppression. We hypothesize two significant advantages of VIPR-SSFP over IFIR: 1) improved fat saturation in regions of B_0 inhomogeneity; and 2) arterial visualization quality similar to IFIR with simultaneous visualization of venous structures, enabling evaluation of renal vein pathology. We also present a simple recommendation regarding how current non-contrast enhanced methods could be quickly modified to meet imaging needs in the renal transplant community.

Materials and Methods

Patient Identification

After obtaining IRB approval for this retrospective study, we identified renal transplant patients who were scanned with both the VIPR-SSFP and IFIR sequences over a 30-month interval ending in November 2010. In total, twenty-one renal transplant patients were identified who received NCE-MRA exams using both sequences during the study period. Of these patients, 13 were male and 8 were female with ages ranging from 20 to 72 years. In each patient, kidney transplantation was performed as a result of chronic renal failure. Nineteen of the allografts were placed in the right iliac fossa, which is standard surgical practice at our institution. Two were placed in the left iliac fossa. The duration of time from kidney transplantation to MR imaging ranged from 2 months to 11 years.

The clinical indication for MR imaging in the study patients was typically to rule out transplant renal artery stenosis as the primary cause of a significant increase in blood pressure or serum creatinine. In one patient, imaging was performed to rule out thromboembolic obstruction of the transplant renal artery secondary to new-onset atrial fibrillation. In 8 of 21 patients, Doppler ultrasound of the transplant renal vessels was performed during the clinical workup for renovascular disease. The presence of any pathological findings on ultrasound was noted in order to assess concordance with findings on NCE-MRA imaging.

To investigate the image quality of the IFIR sequence with the inversion pulse disabled, one healthy volunteer was scanned using this sequence as well as a variant of the IFIR sequence with the inversion pulse disabled. This volunteer was imaged under an institutional IRB protocol that covers non-contrast enhanced research MR sequences.

Data Acquisition

The VIPR-SSFP k-space trajectory acquires two radial half-echoes per TR, which serve as the basis for its bSSFP readout(11). Additionally, by selecting a center frequency halfway between the fat and water resonances and acquiring data from two complete passes of k-space – one without RF phase cycling and one with π -0- π -0 cycling – a linear combination of k-space data can be generated in which the stopband of the SSFP spectral response is centered over the fat resonance. This technique is termed LC-SSFP(12), and allows for robust fat suppression in anatomic regions where B_0 inhomogeneity is a concern.

Both IFIR and VIPR-SSFP scans were prescribed after obtaining scout images in the pelvis to locate the transplanted kidney. For VIPR-SSFP, a 3D spherical FOV was centered over the abdomen. For IFIR, an imaging slab was placed over the transplanted kidney and renal artery; the position of the inversion slab was determined automatically based on the imaging slab's location. Because IFIR utilizes parallel imaging acceleration, a calibration scan(13) was obtained before imaging commenced. The same localized shim volume was placed over the transplanted kidney for both scans.

For both sequences, tracking of the respiratory waveform was provided via respiratory bellows. During VIPR-SSFP scans, respiratory position was recorded for all TRs (radial

projections), and only data from those falling in a certain range of the respiratory waveform – the 50% nearest end-expiration – were used for image reconstruction(14). The IFIR sequence used a respiratory trigger to initiate an inversion pulse during end-expiration of each breath, followed by a chemical saturation pulse(15) and balanced SSFP readout.

All patients were imaged with the IFIR and VIPR-SSFP sequences on a 1.5T scanner (Signa HDxt; GE Healthcare; Waukesha, WI) using an 8-channel phased-array cardiac coil (GE Healthcare). The volunteer was imaged using only the IFIR sequence. Typical scan parameters for the VIPR-SSFP sequence included: 30° flip angle, TR=2.6 ms, TE₁=0.3 ms and TE₂=1.8 ms, FOV=36 cm spherical, and BW= ±125 kHz with a 256³ matrix and 1.4 mm isotropic resolution (total scan time was approximately 5-6 minutes depending on respiratory rate). Typical scan parameters for the IFIR sequence included: 70° flip angle, TR=4 ms, TE=2 ms, TI=1200 ms, FOV=36 × 36 × 24 cm, and BW=±75 kHz with a 256×256 matrix for a true spatial resolution of 1.4 × 1.4 × 2 mm³ resolution interpolated through zero-filling to 0.7 × 0.7 × 1.0mm³ (total scan time was approximately 4 minutes depending on respiratory rate). The inversion time for the IFIR scans was set to 1200 ms per manufacturer recommendation, which effectively nulls signal from venous blood.

Data Analysis

Two experienced cardiovascular radiologists scored the IFIR and VIPR-SSFP images for each patient. Due to the obvious differences in appearance between Cartesian and radial acquisitions, it was not possible to blind the readers to the sequence associated with each image set.

The readers were instructed to assess four image quality criteria for each sequence on a four point Likert scale (4 = excellent, 3 = good, 2 = poor, 1 = non-diagnostic). These criteria included overall image quality, quality of arterial visualization and quality of venous visualization (focusing on the ability to identify the vessel anastomoses as well as relevant pathologies, if present), and quality of fat suppression. Readers were instructed to score arterial and venous visualization quality at 2 or below if the vessel anastomosis or suspected vascular pathologies could not be visualized with confidence. Readers were also instructed to score fat suppression quality at 2 or below if unsuppressed fat signal was noted to obscure anatomy of interest due to respiratory ghosting.

In patients who received Doppler ultrasound of the renal vessels in addition to NCE-MR imaging, the clinical impression of the ultrasound scan as documented in each patient's chart was reviewed. Significant findings on ultrasound imaging – in particular, whether any vascular pathology such as RAS was discovered – were compared to the study readers' impression of the MR images to assess for diagnostic concordance between these modalities.

Statistical Analysis

Scores for each of the above image quality criteria were analyzed using the Wilcoxon signed-rank test(16). First, scores for the VIPR-SSFP and IFIR sequences corresponding to the four criteria were averaged between the two readers and across all patients. Next, Wilcoxon signed-rank tests were performed independently for each image quality metric, and p-values for each test were calculated. One of the two imaging methods was determined

to be superior only if the difference in scores achieved statistical significance according to the Wilcoxon test.

Results

Sample images demonstrating the difference in venous contrast between VIPR-SSFP and IFIR can be seen in Figure 1. VIPR-SSFP was determined to be significantly superior to IFIR with regard to quality of venous visualization (Table 1). Neither reviewer scored any of the IFIR images as providing quality sufficient to evaluate the renal vein anastomosis, or to evaluate venous pathology if present. However, the quality of arterial visualization provided by IFIR was statistically superior to that of VIPR-SSFP ($p=0.005$). Because IFIR is designed to enhance signal only from arterial blood, it provides improved arterial visualization versus VIPR-SSFP; nonetheless, the mean score for VIPR-SSFP arterial quality (2.97) remained significantly above the threshold of diagnostic adequacy (2.0).

A comparison of the arterial visualization quality of these two sequences can be seen in Figure 2, which shows IFIR and VIPR-SSFP thin-slab MIPs from a patient with three transplant renal arteries. Although enhancement of arterial signal is superior in the IFIR MIP (Fig. 2A), the presence of venous signal in the VIPR-SSFP image does not significantly impair visualization of the renal arteries (Fig. 2B). While the IFIR sequence attained a slightly higher score in overall image quality, the difference between the two sequences was not statistically significant.

VIPR-SSFP also provided improved fat suppression when compared with IFIR, and this difference was statistically significant ($p = 0.028$). Although excellent (score = 4) fat suppression was not present in all VIPR-SSFP images – likely due to fat spins near areas of abdominal B_0 inhomogeneity falling outside the stopband of the combined VIPR-SSFP spectral response – residual fat signal in these images typically had a less deleterious effect on diagnostic quality than that present in IFIR images. This can be seen in Figure 1, where residual fat signal due to B_0 inhomogeneity has a much more benign, distributed appearance in the VIPR-SSFP image (Figure 1B) relative to the coherent ghosting of fat in the phase-encoding direction with IFIR (Figure 1A).

The two study readers noted that the VIPR-SSFP images depicted several clinically relevant extrarenal findings that were not well visualized in the corresponding IFIR images (Figure 3). This is due to IFIR's use of an inversion pulse before its bSSFP readout, which nulls most signal from background tissue and fluid collections present in the imaging volume. With vendor support, we were able to test the sensitivity of IFIR to image the renal veins after disabling the IFIR inversion pulse. As expected, visualization of venous structures became possible, but segmental renal transplant arterial branches became indistinguishable from their associated renal veins (Figure 4).

Of the eight patients who underwent Doppler ultrasound during their clinical workup, seven received transplant renal ultrasound scans prior to NCE-MR imaging. The clinical findings identified by the readers using VIPR-SSFP images were concordant with the findings on ultrasound in each of these patients, though none had significant renovascular pathology. In

the one patient who received an ultrasound scan after completion of MR imaging, quality of both IFIR and VIPR-SSFP images was limited by the patient's obese body habitus in addition to significant respiratory artifact. Ultrasound imaging was deemed clinically necessary due to findings concerning for RAS in the MRA images. Severe RAS was subsequently confirmed using Doppler ultrasound, and the patient underwent transplant renal artery stenting two weeks later.

Discussion

In this work, we have demonstrated VIPR-SSFP to be an excellent NCE-MRA method for visualization of the transplant renal vein and artery. The VIPR-SSFP acquisition provided diagnostic-quality images of the renal vein over 80% of the time, while IFIR did not allow for assessment of this structure in any cases. However, IFIR provides improved visualization of the renal artery, likely due to its suppression of venous signal. Importantly, the average arterial quality score for VIPR-SSFP images was above the threshold for diagnostic adequacy – in fact, nearly 70% of the VIPR-SSFP exams were scored as providing high- or good-quality visualization of the renal artery. Diagnosis of both RAS and venous stenosis was therefore possible in a majority of patients using VIPR-SSFP images alone.

VIPR-SSFP's linear combination method of fat suppression provided improved reduction of fat signal compared to the chemical saturation pulse used by IFIR. This is due to the flat phase profile over the fat resonance that alternates by 180 degrees between the two VIPR-SSFP acquisitions(12). A wide stopband can thus be generated over the fat resonance with appropriate selection of imaging parameters, making VIPR-SSFP relatively less susceptible to off-resonance fat spins than IFIR. Moreover, unsuppressed fat present in VIPR-SSFP images was typically less deleterious to overall image quality due to incoherent aliasing of its signal across the numerous effective phase encode dimensions of the radial sequence. Although VIPR-SSFP's method of fat saturation could potentially be used with IFIR, Cartesian SSFP trajectories typically do not satisfy the short-TR constraint necessary to produce the spectral response required for fat suppression, and would therefore be incompatible.

The two readers noted that the effect of residual subcutaneous fat signal on VIPR-SSFP image quality tended to be benign, while on IFIR images the presence of unsuppressed fat signal would frequently impair vessel visualization quality. This is because residual fat signal combined with uncompensated respiratory motion will generate ghost artifacts in the phase-encoding dimensions of Cartesian acquisitions such as IFIR. Radial acquisitions such as VIPR-SSFP, which lack a phase-encode dimension, are significantly less susceptible to motion-induced fat ghosting(17). VIPR-SSFP's fat saturation method may thus be superior to the chemical saturation pulse used by IFIR when imaging individuals with significant subcutaneous adiposity.

VIPR-SSFP is clearly superior to IFIR in its ability to detect non-arterial and extrarenal vascular pathology due to the fact that it does not utilize an inversion pulse. Because VIPR-SSFP generates contrast in stationary tissue and fluid, it is useful for detection of transplant- and biopsy-related complications such as perinephric fluid collections, abscesses

and pseudoaneurysms (Figure 3). When IFIR's inversion pulse is disabled, it also becomes capable of visualizing venous vessels and static fluid collections (Figure 4B, renal cyst). However, this comes at the expense of its arterial visualization quality – as seen in Fig. 4B, the segmental branches of the renal artery clearly visible in Fig. 4A are difficult to distinguish from the renal veins and surrounding renal parenchyma. It seems that while IFIR is capable of visualizing venous vessels and fluid collections when the inversion pulse is disabled, its arterial visualization quality – the sole metric where it was superior to VIPR-SSFP – must be sacrificed for it to do so. An interim solution would include having MR manufacturers provide the capability to perform non-contrast enhanced imaging with and without preparatory inversion or saturation pulses. Though patients would need to be scanned twice to properly image the arterial and venous vasculature, this modest change could be effected quickly and inexpensively, and make available a feasible solution for this limited patient population.

A major limitation of this study is that none of the patients' VIPR-SSFP images depicted significant renal vein pathology. Although the readers were able to score the images based on their ability to visualize the transplant renal vein, in no case was a thrombus or stenosis noted. However, an incidental finding of external iliac vein thrombosis was made in one patient's VIPR-SSFP images (not shown), demonstrating the ability of this sequence to detect venous pathology. A second study limitation is that no patients were imaged within seven days following the transplant operation. It was therefore not possible to detect pathologies such as anastomotic pseudoaneurysm that tend to occur shortly after graft placement. Of note, it does not appear this study was limited by sample size as statistically significant differences were detected in three of four image quality metrics evaluated.

A third limitation of this study is that no gold standard imaging exams, such as contrast-enhanced MR or CT angiography, were available for comparison to the VIPR-SSFP and IFIR data. However, Doppler ultrasound scans were acquired for seven patients prior to MR imaging during the patients' clinical workup for renovascular pathology. Findings on Doppler ultrasound agreed with the findings on non-contrast MRA imaging in each of these patients. In the sole patient whose Doppler ultrasound imaging was ordered after non-contrast MRA, the finding of transplant renal artery stenosis was concordant between the two modalities.

Although comparison of VIPR-SSFP to established technologies such as contrast-enhanced CTA or MRA would be ideal, the study population consisted of renal transplant patients who were being scanned due to derangements in renal function. The use of CT or MR contrast agents was therefore contraindicated due to the risks of contrast nephropathy and NSF. Additionally, bSSFP inflow-based sequences such as IFIR are now available from all major MR vendors and have become well-established in the clinical workflow at many institutions(18). Inflow-weighted bSSFP has thus become a standard in its own right with regard to non-contrast angiographic imaging of the abdomen/pelvis, and represents a reasonable benchmark to which other NCE-MRA sequences may be compared.

From a clinical standpoint, VIPR-SSFP appears to play a complementary role to existing NCE-MRA methods, due to its ability to generate contrast in both arterial and venous

vessels as well as surrounding tissue. Inflow-based sequences such as Time-SLIP and IFIR will remain useful because in many cases, identification of RAS is the only indication for renal MRA, particularly in native kidneys. Although radiologists may prefer to use methods such as IFIR to generate high-quality MIP images of the renal artery, the diagnosis of RAS is always made from thin multiplanar reformatted (MPR) images where arterial-venous separation is less important. Grading of vascular stenosis should never be made from MIP images alone, as these are known to exaggerate the degree of stenosis significantly(19).

In conclusion, this preliminary study has demonstrated feasibility of using the VIPR-SSFP sequence to visualize the renal transplant arterial and venous anastomoses and their patency. Given the benefits in venous visualization and fat suppression that the VIPR-SSFP pulse sequence provides over inflow-weighted Cartesian SSFP sequences, we expect this method to be of considerable utility in our future NCE-MRA evaluations of renal transplant patients. Moreover, we have shown that relatively modest changes to commercially available inflow-weighted pulse sequences would provide renal vein visualization for transplant patients, though an additional scan would be needed. Future prospective comparison studies must be performed to confirm these findings.

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Figure 1. Representative (A) VIPR-SSFP and (B) IFIR images demonstrating the quality of renal vein visualization (arrow) and fat suppression provided by the VIPR-SSFP sequence. Note that respiratory ghosts of unsuppressed fat signal overlie but do not obscure the renal allograft in the IFIR image.

Figure 2.

Thin-slab MIP images generated using (A) VIPR-SSFP and (B) IFIR image volumes from a patient with three transplant renal arteries. Although the background and venous suppression in (B) improves arterial conspicuity, the presence of venous signal does not interfere with identification of the renal arteries in (A). Also note the improved resolution in the VIPR-SSFP image (A, 1.4 mm^3) versus the IFIR image (B, $1.4 \times 1.4 \times 2 \text{ mm}$) along the SI direction.

Figure 3. VIPR-SSFP image (A) depicting a biopsy-related perinephric fluid collection (arrow) and left iliac artery pseudoaneurysm (arrowhead). The pseudoaneurysm is not visualized on the corresponding IFIR image (B), while the fluid collection is poorly visualized.

Figure 4.

Thin-slab IFIR MIPs acquired (A) with and (B) without an inversion pulse that depict the renal vessels of a healthy volunteer. The renal arteries are clearly visible in (A), along with several segmental vessels of the right renal artery. In (B), the IVC as well as the renal veins (arrows) are visible, but the renal arteries have become more difficult to distinguish from surrounding renal veins and parenchyma. A renal cyst (arrowhead) is seen in (B), which appears as an area of signal void in (A).

Table 1

Scores for the four image quality criteria averaged across all patient images and between the two reviewers. VIPR-SSFP demonstrates statistically superior fat suppression and venous visualization, while IFIR provides superior arterial visualization. Note that no IFIR images were scored as being in the diagnostic range (3) with regard to venous visualization quality.

Mean Score by Criterion	IFIR	VIPR	p-value
Overall Image Quality	3.52	3.43	0.431
Quality of Fat Suppression	3.40	3.69	0.028*
Quality of Arterial Visualization	3.71	2.97	0.005*
Quality of Venous Visualization	1.00	3.13	0.00007*