High Resolution Non-Gadolinium CEMRA in Renal Failure: Initial Results in Pediatric Patients at 3.0T

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Target Audience: Clinicians and researchers working with Contrast Enhanced MRA (CE-MRA)

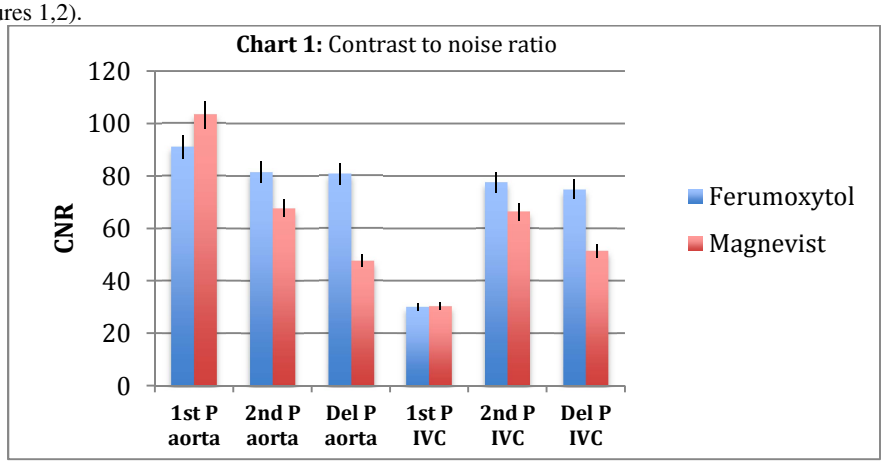
Purpose: Although the incidence of nephrogenic systemic fibrosis (NSF) has fallen dramatically in recent years, fear persists within the clinical community about using gadolinium in renal impairment. As a result, numerous patients who previously would have been candidates for MRI have undergone more invasive tests or tests involving radiation. Recently, Bashir et al (1) and Sigovan et al (2) reported the successful use of the parenteral iron supplement ferumoxytol to image renal transplants and arteriovenous fistulae respectively. Whereas these reports have highlighted the potential of ferumoxytol as a viable substrate for CEMRA, little has been reported on its more general use or on its use in children or at higher field strength.

Methods: We evaluated 9 patients aged 6 days to 14 years with first pass and steady state CEMRA following ferumoxytol (Feraheme, AMAG) infusion at a dose of 0.05-0.07 mmol/kg. All patients were studied on a Siemens Magnetom TIM Trio system. Coil configurations included combinations of head-neck, body array and spine array, depending on patient size. Two patients had complex congenital heart disease and 8 were being considered for organ transplantation. The patients with CHD had supplemental cardiac gated high-resolution 3D CEMRA. The imaging FOV for all sequences routinely included head, neck, thorax, abdomen and pelvis with sub-mm voxels. Multiple CEMRA phases were acquired up to 30 minutes following ferumoxytol injection and measurements of SNR and CNR in the thoracic aorta and inferior vena cava (IVC) were recorded at each phase. These were compared to similar measurements in a group of weight-matched controls examined with gadopentetate dimeglumine (Magnevist, Bayer-Schering) at 0.2 mmol /kg. Phantom measurements of T1 and T2* were made at 3.0T over a range of ferumoxytol dilution factors to include the estimated blood concentration during first pass and steady state distribution phases.

Results: Phantom results of relaxation times at 3.0T vs dilution factor for ferumoxytol are summarized in table 1. The T1 relaxivity of ferumoxytol in saline solution was approximately 9.0 $mM^{-1}s^{-1}$ and the T2 relaxivity was approximately 90 $mM^{-1}s^{-1}$. The estimated blood Fe concentration during first-pass was approximately 256X dilution of the stock ferumoxytol formulation and the steady state intravascular concentration was approximately 1000X dilution. The CNR measurements in the patient studies are summarized in Chart 1 for first pass, second phase and delayed phase. Two patients studied early in the series had signal loss in the aorta on first pass, felt to be due to too rapid injection resulting in T2* signal decay and this decreased the average value. Whereas in the magnevist group, aortic SNR decreased significantly over time, SNR in the ferumoxytol group remained stable to the last measurements, up to 35 minutes post injection. The stability of the vascular signal was felt to be advantageous for the gated CEMRA acquisitions and for venous imaging (figures 1,2).

Table 1: T1/T2 relaxation times of various ferumoxytol dilutions at 3 Tesla

Dilution	T2*(ms)	T1(ms)	T2(ms)
32X	0.5	N/A	N/A
64X	0.8	12.6	1.6
128X	2.5	24.8	2.7
256X	4.0	51.1	5.8
512X	6.1	103.3	10.8
768X	16.0	163.5	18.7
1024X	15.0	199.4	20.9
2048X	18.2	434.1	48.0
Saline	93.0	2152.0	N/A



Conclusion and Discussion: Initial experience suggests that high resolution CEMRA with ferumoxytol can be successfully performed at 3.0T in pediatric patients with renal failure, eliminating concerns for NSF. Initial results are highly encouraging and compare favorably with Magnevist in controls, but further experience is warranted before definitive conclusions can be drawn about the ultimate role of ferumoxytol in these patients.

References: 1. Bashir MR, et al. Transplantation. 2013 Jul 15;96(1):91-6.

2. Sigovan M, et al. Radiology. 2012 Nov;265(2):584-90. doi: 10.1148/radiol.12112694.

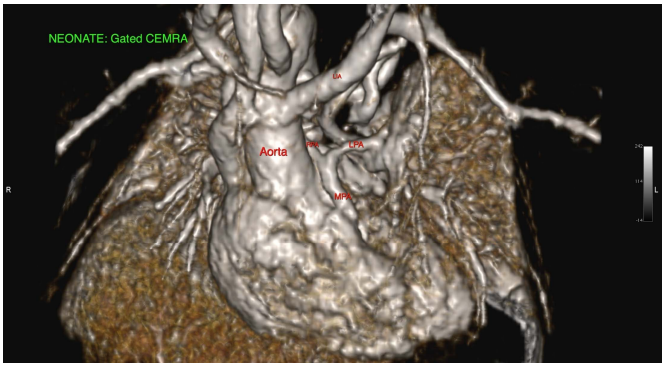


Figure 1: Volume rendered display in a 6 day old female with pre-test diagnosis of pulmonary atresia. Gated ferumoxytol CEMRA confirms the presence of native main and branch pulmonary arteries, presumed not present before the MRI, as well as multiple collaterals. The diameter of the left pulmonary artery (LPA) is 1 mm.

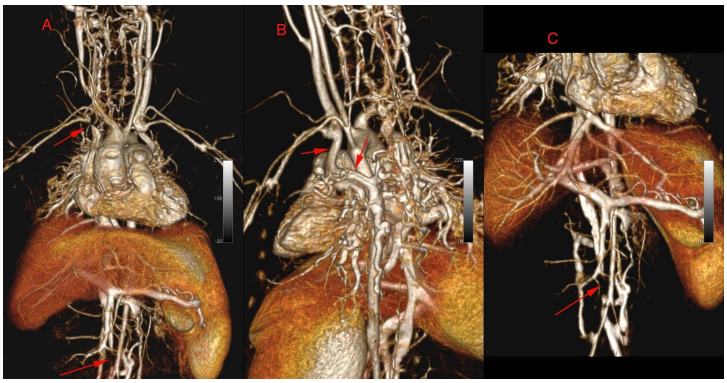


Figure 2: Volume rendered display of gated ferumoxytol CEMRA in an 8 year old male with treated Tetralogy of Fallot undergoing workup for renal transplantation. Extensive venous disease is present (arrows in a and c) and a left sided SVC drains to the azygous system (arrows in b), in aggregate precluding candidacy for transplantation.