Ferumoxytol in Pediatric Congenital Heart Disease: Initial Results with 4D Multiphase Steady State Imaging of Contrast (MUSIC) Enhancement

Kim-Lien Nguyen[1,2], Fei Han[2], Daniel Z. Brunengraber[2], Stanislas Rapacchi[2], Ihab Ayad[2,3], Gary Satou[2,4], Peng Hu[2], and J. Paul Finn[2]

[1]Division of Cardiology, Greater Los Angeles VA Healthcare System and David Geffen School of Medicine at UCLA, Los Angeles, CA, United States, [2]Diagnostic Cardiovascular Imaging Laboratory, Department of Radiology, David Geffen School of Medicine at UCLA, Los Angeles, CA, United States, [3]Department of Anesthesiology, David Geffen School of Medicine at UCLA, Los Angeles, CA, Los Angeles, CA, United States, [4]Division of Pediatric Cardiology, David Geffen School of Medicine at UCLA, Los Angeles, CA, United States

Background Purpose: Concerns about NSF in children with immature renal function have prompted the exploration of alternatives to gadolinium enhancement. Ferumoxytol is a USPIO nanoparticle with unique advantages for imaging the blood pool. Approved by the US FDA for treatment of iron deficiency in chronic kidney disease, its use for MRI is still off label. We have recently established the feasibility of a novel technique for high-resolution 4D imaging in the steady state of contrast enhancement, using both cardiac and respiratory gating in children under anesthesia. Our technique allows for definition of detailed cardiac and vascular anatomy as well as dynamic cardiac function. The focus of the current study is the evaluation of 4D MUSIC for assessment of detailed cardiac and vascular anatomy in children with complex congenital heart disease (CHD) and its comparison to breath held first pass and delayed phase MRA. The hypothesis of this study is that all clinically relevant information can be derived from 4D MUSIC without the need for supplemental cine imaging, which is routinely necessary with conventional CEMRA.

Methods: 21 children (age 3 days to 18 years, 11 females) with CHD underwent MRI at 3.0T. Neonates were transported directly from the NICU under sedation and older children underwent general anesthesia. First pass ferumoxytol CE-MRA (4 mg elemental Fe per kg, flow rate 0.3-1.0 mL/s)[1-3] was obtained using traditional ventilator-controlled breath-held (VCBH) acquisition followed by steady-state VCBH 2-3 min later. Subsequently, cardiac-phase-resolved 4D MUSIC (TR/TE= 2.9/0.9 ms; FA=15°; isotropic resolution=0.6-0.9mm, 5-9 cardiac phases, scan time 4-8min, 65-95ms temporal resolution) was acquired, using ventilator gating as previously described.[4] Multiplanar 2D cardiac cine images were also obtained. Image analysis included assessment of the right ventricular outflow tract, pulmonary trunk, coronary arteries, inter-atrial and interventricular septum. Structures were scored as: 1: non-diagnostic; 2: poor definition such that only gross features such as overall patency are evaluable; 3: good definition such that pathology can be confidently visualized or excluded or dimensions can be confidently measured within 3mm of accuracy; 4: excellent definition such that detailed anatomy is clearly visualized with sharp borders or dimensions can be confidently measured with ≤ 2mm of accuracy.

Results: Technically successful MUSIC acquisition was performed in all patients and VCBH. There were no adverse events, major or minor, following ferumoxytol injection. Cardiac and vascular anatomy was significantly better visualized with MUSIC imaging than with VCBH in virtually all structures evaluated and concordance between MUSIC images and reference techniques was excellent. Table 1 demonstrates a statistical significance between the qualitative scores for first-pass ferumoxytol enhanced MRA and 4D MUSIC. Figure 1 is an example in an 18-year old child with Tetralogy of Fallot.

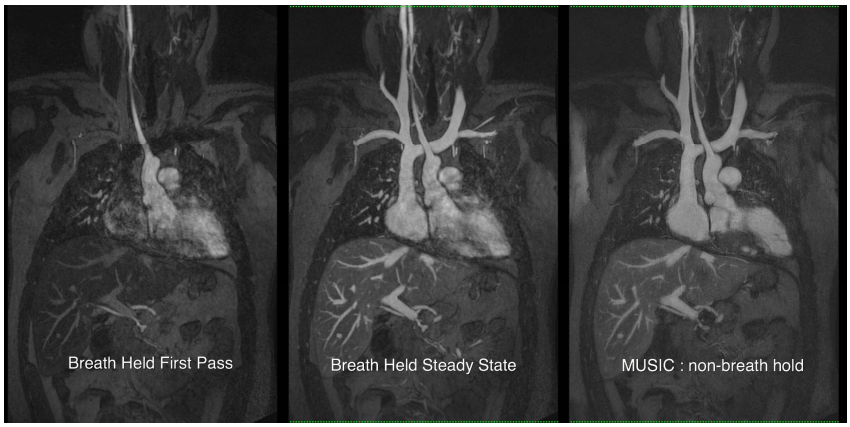

Figure 1: Comparison of Breath Held First Pass vs Steady State vs MUSIC. 18-year old child with Tetralogy of Fallot.

Conclusion: Initial results suggest that 4D MUSIC images with ferumoxytol can yield comprehensive assessment of complex cardiac and vascular anatomy in children with CHD, potentially obviating the need for breath held CEMRA and 2D cine imaging. The implications for safe and rapid streamlining of data acquisition in pediatric CHD are significant.

Table 1: Qualitative Image Scores. *p<0.05. IAS=interatrial septum, IVS=interventricular septum, RCA=right coronary artery, RVOT=right ventricular outflow tract

	RVOT*	Pulmonary Trunk	IAS*	IVS*	Left Main Coronary Artery*	Proximal RCA*
First-pass CE-MRA	2.7±0.4	3.4±0.7	1.2±0.4	2.0±0.6	1.1±0.3	1.0±0.2
4D MUSIC	3.9±0.3	4.0±0.2	3.9±0.3	3.9±0.3	3.3±0.7	2.9±1.1

References:

1. Prince MR, Zhang HL, Chabra SG, Jacobs P and Wang Y. A pilot investigation of new superparamagnetic iron oxide (ferumoxytol) as a contrast agent for cardiovascular MRI. *Journal of X-ray science and technology*. 2003;11:231-40.
2. Sigovan M, Gasper W, Alley HF, Owens CD and Saloner D. USPIO-enhanced MR angiography of arteriovenous fistulas in patients with renal failure. *Radiology*. 2012;265:584-90.
3. Bashir MR, Mody R, Neville A, Javan R, Seaman D, Kim CY, Gupta RT and Jaffe TA. Retrospective assessment of the utility of an iron-based agent for contrast-enhanced magnetic resonance venography in patients with endstage renal diseases. *J Magn Reson Imaging*. 2014;40:113-8.
4. Han F, Rapacchi S, Khan S, Ayad I, Salusky I, Gabriel S, Plotnik A, Finn JP and Hu P. Four-dimensional, multiphase, steady-state imaging with contrast enhancement (MUSIC) in the heart: A feasibility study in children. *Magnetic resonance in medicine : official journal of the Society of Magnetic*. 2014.