Positive contrast high-resolution 3D-cine imaging of the cardiovascular system in small animals using a UTE sequence and iron nanoparticles at 4.7, 7 and 9.4 T

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Target audience; This work is of great importance for studies involving 4D anatomical visualization of the whole cardio vascular system in small animal.

Purpose: In clinical practice, magnetic resonance angiography (MRA) enhanced by a gadolinium-based contrast agent is the gold standard for many applications. However, the use of this type of contrast agent has two major disadvantages: 1) intra-venous injection entails a risk for the patient to develop nephrogenic systemic fibrosis; 2) these contrast agents are rapidly cleared, which can be an issue for some cardiovascular applications. This is particularly problematic in small animals since its contrast-enhancing effect on blood vessels is too short-lived. The goal of this sudy is to show that, due to a long half-life in blood, Ultra Small Particles of Iron Oxide (USPIO) in combination with a ultra-short echo times (UTEs) sequence can be used as positive blood pool contrast agent[1] to performed 3D time-resolved imaging with a high spatial resolution of the murine cardiovascular system at various high magnetic fields and with different USPIO concentration injected.

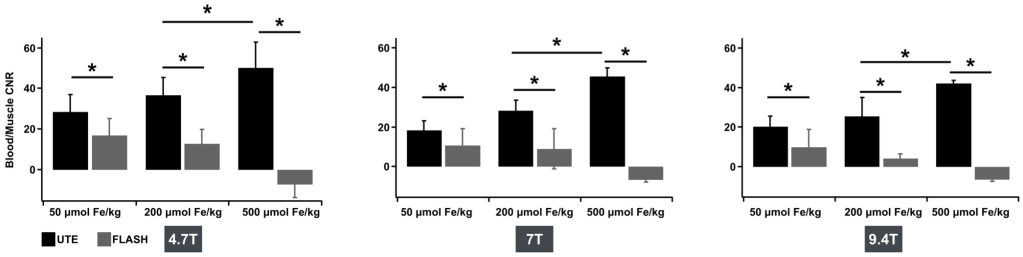

Figure 1. Contrast-to-noise ratio between blood in the aortic arch and muscle at various magnetic fields and UPSIO concentrations with FLASH and UTE sequence

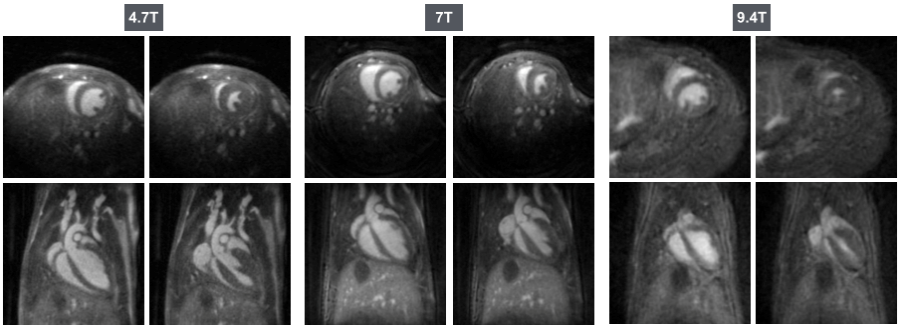

Figure 2. Extracted axial and coronal slices of mouse heart at 4.7, 7 and 9.4T during systolic and diastolic phases (Isotropic spatial resolution: 156 µm)

Methods: Four different concentrations (50, 100, 200 and 500 µmol Fe/kg) of USPIO were injected in mice and static images of the middle part of the animals were acquired at 4.7, 7 and 9.4 T with FLASH (TE/TR = 1.4/4.5 ms) and UTE (TE/TR = 0.05/4.5 ms) sequences. Signal-to-Noise Ratio (SNR) and Contrast-to-Noise Ratio (CNR) of blood and static tissues were evaluated and compared between FLASH and UTE. 3D-cine images (TE/TR = 0.05/3.5ms, scan time < 12 min) at 156 µm isotropic resolution of the mouse cardiopulmonary system were acquired prospectively with the UTE sequence at the three magnetic fields and with an USPIO dose of 200 µmol Fe/kg. SNR, CNR and signal homogeneity of blood were measured. High resolution 3D-cine images at 104 µm isotropic resolution (scan time < 35 min) was also performed at 7T.

Results: UTE imaging generated positive contrast and higher SNR and CNR than conventional FLASH imaging whatever the magnetic field and the USPIO concentration (figure 1). Time-resolved 3D acquisition enables high blood SNR (66.6 ± 4.5 at 7T) and CNR (33.2 ± 4.2 at 7T) without flow or motion artefact (figure 2). Coronary arteries and aortic valve were visible on images acquired at 104 µm resolution (figure 3, arrows). High spatial resolution enables to perform precise volumetry of ventricles[2] (LVSV (µL) = 27.1 ± 3.2; LVEF (%) = 64.1 ± 4.2; RVSV (µL) = 27.4 ± 3.6; RVEF (%) = 61.8 ± 5.2).

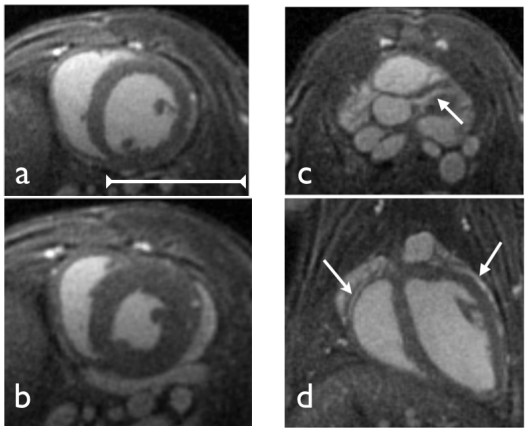

Figure 3. Axial (a,b,c) and coronal (d) extracted slices of mouse heart during diastolic (a) and systolic phases (b) . Arrows show coronary arteries. (Isotropic spatial resolution: 104 µm, scalebar : 7.5 mm)

Conclusion: We demonstrated that by combining the injection of iron nanoparticles with 3D-cine UTE sequences, it was possible to generate a strong positive contrast between blood and surrounding tissues. These properties were exploited to produce images of the cardiovascular system in small animals at high magnetic fields with a high spatial and temporal resolution. An original cine k-space encoding scheme was also developed to generate a posteriori, either high temporal or high spatial resolution images. This approach might be useful to measure the functional cardiac parameters or to assess anatomical modifications of the blood vessels in cardio vascular disease models.

References: 1. Girard et al : Optimization of iron oxide nanoparticle detection using ultrashort echo time pulse sequences: comparison of T1, T2*, and synergistic T1- T2* contrast mechanisms. Magn Reson Med 2011;65:1649-1660. 2. Miraux et al : 4D retrospective black blood trueFISP imaging of mouse heart. Magn Reson Med 2009;62:1099-105.