# Nanoparticle Detection of Vascular Inflammation in Mouse Carotid Artery at 7T

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**Introduction:** Inflammation plays a critical role in the progression of atherosclerosis. Novel iron-based nanoparticle platforms may allow noninvasive high-field MRI detection of vascular macrophages in mouse arteries.

**Purpose:** To evaluate two novel nanoparticle platforms – magnetite incorporated human ferritin protein cages (HFn-Fe) and graphite/FeCo core-shell nanocrystals (G-FeCo) – for MRI of mouse carotid atherosclerosis at 7T.

**Methods:** *1) Mice* - A total of 11 FVB mice were studied. One group of normal mice (N=5), 3 undergoing left carotid artery ligation and 2 controls. A second group of diabetic mice (N=6), induced by high fat diet for 4 weeks then 5 daily intraperitoneal injections of streptozotocin, followed 2 weeks later by left carotid ligation. *2) HFn-Fe nanoparticles* – Composed of recombinant human heavy chain ferritin protein cages with chemically synthesized magnetite ($Fe_3O_4$) in their interior cavity. HFn-Fe nanoparticles have been shown to have high uniformity (size-12nm), allow high internal concentration of iron, and can provide good cellular imaging in vitro [1]. Dosage used - 25 µgFe/kg. *3) G-FeCo nanocrystals* – Composed of an iron-cobalt (FeCo) core encapsulated by a biocompatible graphite shell (size – 7nm) with Cy5.5 also attached for fluorescence imaging. G-FeCo nanocrystals have superior MRI properties with both cellular imaging and heating attributes [2]. Dosage used - 32 µgFe/mouse, 8nmol Cy5.5/mouse. *4) MRI* - 2 weeks post-ligation, mice were imaged on a 7T MRI scanner (Varian, Inc., Walnut Creek, CA) using a gradient echo sequence (TR/TE=50/3.6-4.2ms, slice thickness=0.5-1.0mm, FOV=3cm, matrix=256x256, FA=50). In diabetic mice, one of the two different nanoparticles, HFn-Fe or G-FeCo, was injected via mice via tail vein (N=3 for each nanoparticle) with post-contrast MRI performed at 24 and 48hrs. Detection of nanoparticle accumulation was assessed by measuring the extent of T2*-induced reduction in carotid lumen size (% reduction of carotid lumen area). *5) Histology* - Perl's iron staining and immunohistochemistry was also performed to confirm co-localization of nanoparticles and macrophages.

**Results:** Normal mouse carotid arteries were well visualized at 7T (Figure 1). In mice after carotid ligation and prior to any nanoparticle contrast administration, the visualized left carotid artery (solid arrow) was smaller than the right (dashed arrow) (Figure 2, upper left panel). Post-contrast, serial MRI images showed further reduction in left carotid lumen area due to signal loss from nanoparticle accumulation, a reduction that was not seen in the non-ligated right carotid arteries or in sham-operated mice (Figure 2). The measured % reduction of carotid lumen area was statistically significant for both HFn-Fe and G-FeCo nanoparticles (Figure 3), with a trend toward greater effect from HFn-Fe. Perl's iron staining for iron and immunofluorescence for Cy5.5 showed colocalization of HFn-Fe and G-FeCo nanoparticles, respectively, with vascular macrophages (Figure 4).

**Conclusions:** MRI at 7T can detect vascular macrophages with magnetite protein cage nanoparticles and graphite/FeCo core-shell nanocrystals in mouse atherosclerotic lesions. High-field MRI using novel nanoparticle platforms is a promising approach for noninvasive assessment of vascular inflammation.

**Reference:**

1. Uchida M, et al. Magn Reson Med 2008; 60: 1073-1081
2. Seo WS, et al. Nature Materials 2006;5:971-976.

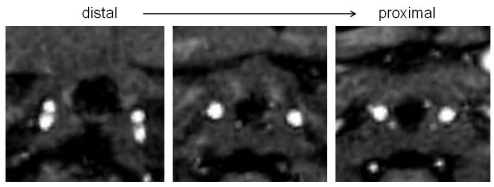


**Fig 1. Normal mouse carotid arteries at 7T**

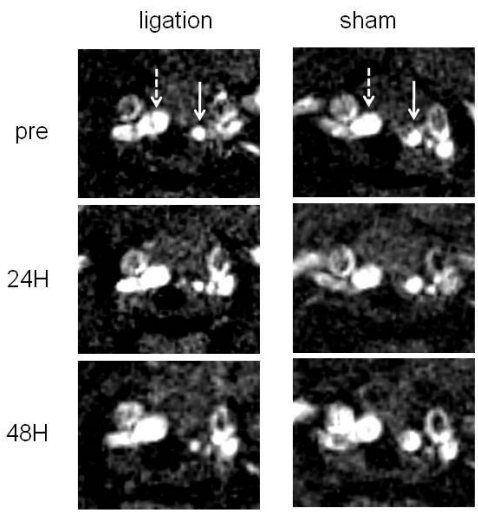


**Fig 2. In vivo MRI of mice injected with HFn-Fe**

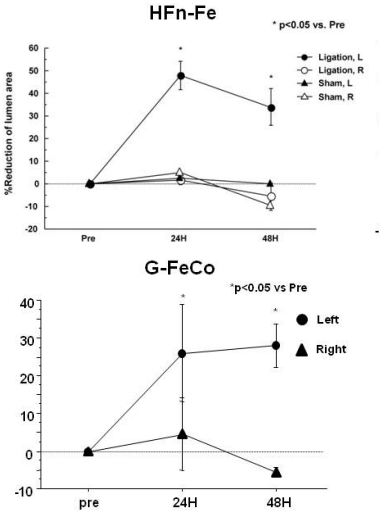


**Fig 3. Quantitative analysis**

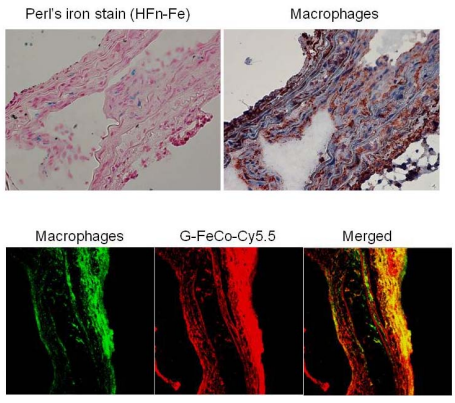


**Fig 4. Histology**