Microfabricated High-moment Iron Particles for *In Vivo* Cell Tracking

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Audience: Those interested in cell tracking applications.

Purpose. We present an application of microfabricated gold-coated iron particles in an *in vivo* cell tracking experiment. These particles have a pure iron core as opposed to the more commonly used super paramagnetic iron-oxide based particles (SPIO). Due to the higher magnetic moment the size may be reduced and still provide contrast in T_2^* weighted images. The particle volume is approximately $1/10^{th}$ of the 1.6 μm diameter iron-oxide particles (Bangs Laboratories, IN, USA) previously used in cell tracking experiments (1).

Methods. Gold-coated iron particles were microfabricated onto glass wafers in a manner similar to the method of (2). The diameter of each particle was 1 μm at the base with a thickness of ~300 nm. An electron micrograph showing example particles is shown in Figure 1A. The full wafer was sectioned into 5 x 25 mm strips, with a yield of ~ 12 million particles per strip (Figure 1B). The particles may be released by removing the sacrificial copper layer with a copper etchant. To demonstrate in vivo MRI labeling feasibility, the particles are washed and suspended in saline for injection into the lateral ventricle near the subventricular zone (SVZ) niche of the rat brain.The particles were allowed to be taken up by neural progenitor cells (NPCs) that migrate along the rostral migratory stream (RMS) into the olfactory bulb (OB) (1). The particles retain magnetism so rats were not placed in the scanner for at least 24 hours after injection. MRIs for phantom and *in vivo* images were acquired in an 11.7T scanner, and at 14T for the fixed rat brain.

Results. Gradient-echo images (TR/TE = 50/12 ms) of particles dispersed in agarose are shown in fig 2, at an isotropic resolution of (A) 100 μm and (B) 50 μm. At 100 μm the signal drop due to the particles was measured to be 31 +/- 5%, and at 50 μm the signal drop was >80%. (This is compared with Bangs 1.6 μm particles which can vary between 0-80% at 50 μm resolution). *In vivo* MR images were acquired at 24 hours, 2, 4 and 6 weeks post injection. Acquisition parameters were TR/TE = 30/8 ms, with a 75 μm isotropic resolution. Shown in Figure 3A are minimum intensity projections through a 1 mm section of the rat brain covering the RMS and the olfactory bulb. Initially, contrast is seen at the injection site, and then extending into the RMS. Particles may be seen in the olfactory bulb at week 2, and by week 6, contrast from several particles is still apparent in the olfactory bulb. Figure 3B shows a projection of approximately the same section after fixation and immersion in saline, with TR/TE = 30/12 ms at 50 μm isotropic.

Conclusions. We have shown that microfabricated iron particles may be used for *in vivo* cell tracking experiments in the rat brain. We are currently working to determine the extent of any degradation, if any, of the particles after being exposed to the brain environment.

References. 1. Shapiro et al, Neuroimage, 2006 Sep; 32(3): 1150-7. 2. Zabow et al. MagnReson Med. 2011 Mar;65(3):645-55

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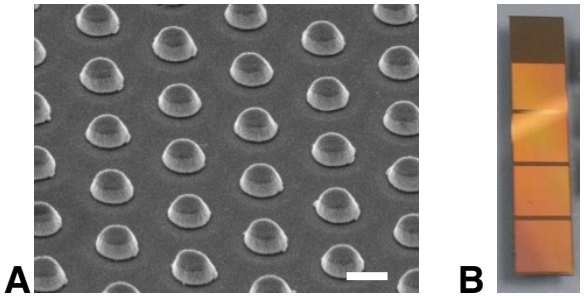


Figure 1A SEM of the microdots as fabricated on to the wafer**.** The white scale bar is 1 μm. **B** Complete chip with 12 million particles.

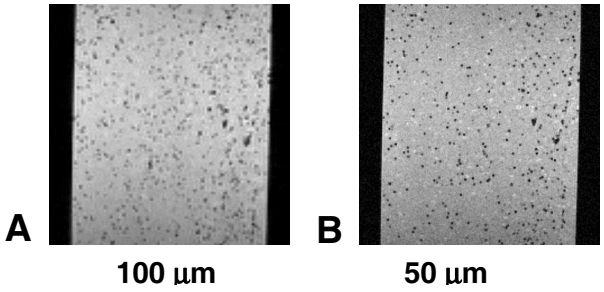
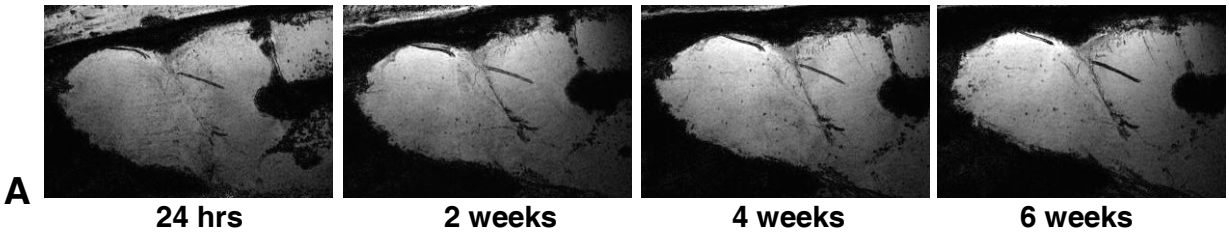


Figure 1 Gradient-echo images of the released particles in agarose at resolution of **A** 100 μm and **B** 50 μm isotropic



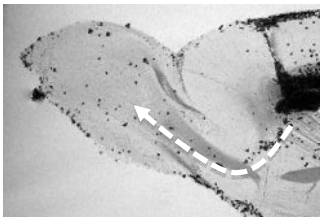


Figure 3A Minimum intensity projections through a 1-mm slab in the olfactory bulb at indicated time points (75 μm isotropic resolution, TE = 8 ms). **B** rat brain after fixation imaged at 50 μm isotropic (projection through approximately the same slab, TE = 12 ms). Arrow shows path of particles to the olfactory bulb through the RMS.