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Gram scale synthesis of magnetite nanoparticles optimized for single-core MPI tracers

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Introduction

Magnetite nanoparticles with diameters of about 25-30 nm are promising candidates for MPI tracers [1]. When preparing single-core tracers, controlling nanoparticle size and size distribution are critical. Thermal decomposition approaches can produce monodisperse nanoparticles over a range of sizes, but the reactions are kinetically driven and sensitive to fluctuations that yield batch-to-batch variation in size and quality. Furthermore, if not carefully controlled, the reaction chemistry can produce variations in iron oxide phase and phase purity. Published protocols typically provide examples performed at small-scale and procedures that may not be scalable and frequently omit magnetic characterization that is critical for establishing suitability for MPI. Here we present a scalable procedure for producing high quality, single-core magnetite nanoparticles that are confirmed to be suitable for MPI after rigorous characterization.

Methods

Magnetite nanoparticles were prepared by thermal decomposition of iron (III) oleate with excess oleic acid in octadecene at 318°C, at the scale of 40 mmol Fe (2.23 grams) per reaction. Particles were oxidized *in situ* with subsequent annealing at 318°C for up to 30 hrs. Particle size was measured using bright field transmission electron microscopy (TEM), powder x-ray diffraction, and by fitting magnetization data to a Langevin function. Magnetic particle spectrometry and phantom MPI imaging were used to evaluate tracer performance.

Results

Grams of magnetite particles with median diameter of 24-27 nm and geometric standard deviation of 1.06 were reproducibly synthesized. Diffraction confirmed the particles were phase-pure magnetite (Fe₃O₄). Critically, oxidation and annealing were necessary steps for achieving desired magnetic properties, including highly non-linear magnetization response under standard MPI excitation conditions. Typical saturation magnetization measured by vibrating sample magnetometer was 350 kA/m. MPS performance of nanoparticles

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transferred to aqueous phase using PEG-based amphiphilic copolymers, measured by the peak intensity of dm/dH, was 5x greater than *Resovist* (Bayer-Schering Pharma).

Conclusion

This work demonstrates that thermal decomposition synthesis of MPI tracers can be scaled without compromising quality to enable pre-clinical animal safety and efficacy studies [1].

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REFERENCES

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Figure 1.

A) bright field TEM image of 25 ($\pm$ 1.5) nm diameter particles. B) powder x-ray diffraction pattern with magnetite reference. C) Magnetization curve with magnetic size determined from Langevin fit. D) Harmonic spectrum off example tracer, with *Resovist*® reference and E) dm/dH of tracer sample, with *Resovist* reference measured by magnetic particle spectrometer at 20 mT/ μ_0 amplitude, 25 kHz.