Magnetic Nanoparticles for Biomedical Imaging

by **D. L. Huber**

Motivation—Senior Scientific Limited Liability Company (LLC) has been developing a new approach for detecting a variety of diseases using magnetic nanoparticles. The technique requires super-paramagnetic nanoparticles of a very narrow size range to be bound to the diseased tissue of choice. The commercial unavailability of well-defined magnetic nanoparticles of the proper size and with appropriate functionality brought them to the Center for Integrated Nanotechnologies (CINT). The goal was to design and synthesize ideally suited particles for this application.

Accomplishment—This technique uses magnetic sensors to detect and image a variety of diseases by using magnetic nanoparticles with antibodies to specific tissues (e.g., breast cancer and leukemia). The targeted nanoparticles bind to the cells of interest, and their presence is detected magnetically. The magnetic detection is achieved by briefly applying a modest magnetic field (~30 Gauss) and measuring the remanence field as a function of time using a number of extremely sensitive superconducting quantum interference device (SQUID) sensors. The remanence field in magnetic nanoparticles decays through two mechanisms: Brownian motion and Néel relaxation (motion of the internal magnetic moment). Decay by Brownian motion occurs extremely quickly (< 10 msec) for particles that are not bound to cells of interest, while bound nanoparticles decay over the course of hundreds of milliseconds to seconds. The slower Néel relaxation is measured and indicates the presence of the cells of interest. This extremely low background detection method has been shown to have detection limits about three orders of magnitude lower than current diagnostic methods.

Only particles within a narrow range of sizes have an appropriate rate of Néel relaxation; this size has been theoretically calculated to be 25 nm in diameter (for spheres of magnetite). Commercial suppliers exist for magnetite nanoparticles, but the material tends to be polydisperse. The most useful commercial sample found to date has only about 7% of the expected signal due to Néel relaxation. Measurements on commercial samples as part of this project have explained the lack of signal. A transmission electron micrograph of the sample (Fig. 1) shows that the particles are irregularly shaped, polydisperse, and below the optimum size. A synthesis method developed at CINT (Fig. 2) yields magnetite particles with a narrower polydispersity, roughly spherical particles, and an average size of approximately 25 nm. These particles appear to be ideal for this application, and magnetic measurements demonstrate that these particles have a signal of greater than four times the commercial sample. There is still room for improvement in the particle synthesis by optimizing for the precise size that yields the highest signal. The size calculated to yield the maximum signal was based on assumed bulk-like properties of the magnetite and is therefore expected to be imprecise.

Significance—This extremely promising medical imaging technique is completely dependent upon having nanoparticles of precisely the correct size. The materials synthesis expertise available at CINT was quickly able to design a synthesis to meet the exacting needs. Our next goals are to improve the signal, attach functional coatings to enhance the stability, and finally get FDA approval for injection into humans to commercialize this potentially revolutionary imaging technique.

Sponsors for various phases of this work include: DOE Office of Basic Energy Sciences/Center for Integrated Nanotechnology (CINT)

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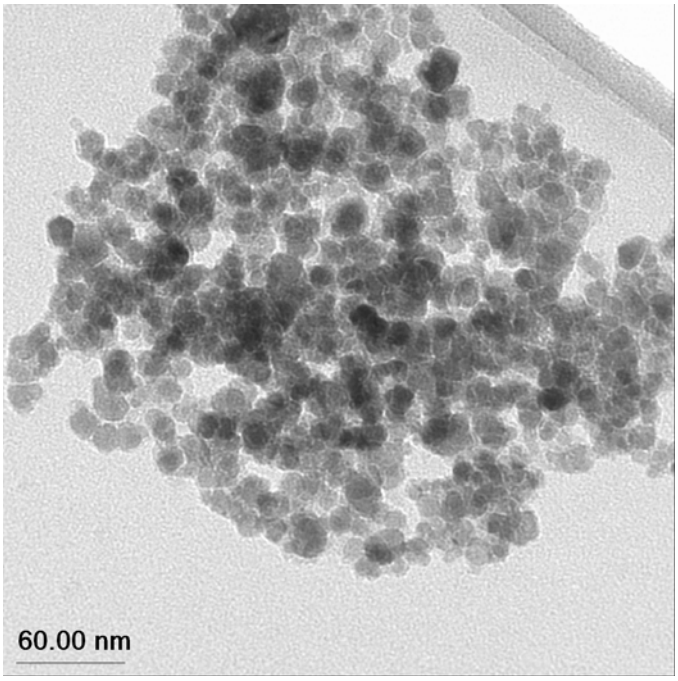

Figure 1. Commercial nanoparticles are agglomerated, polydisperse, oddly shaped, and smaller than the desired 25 nm.

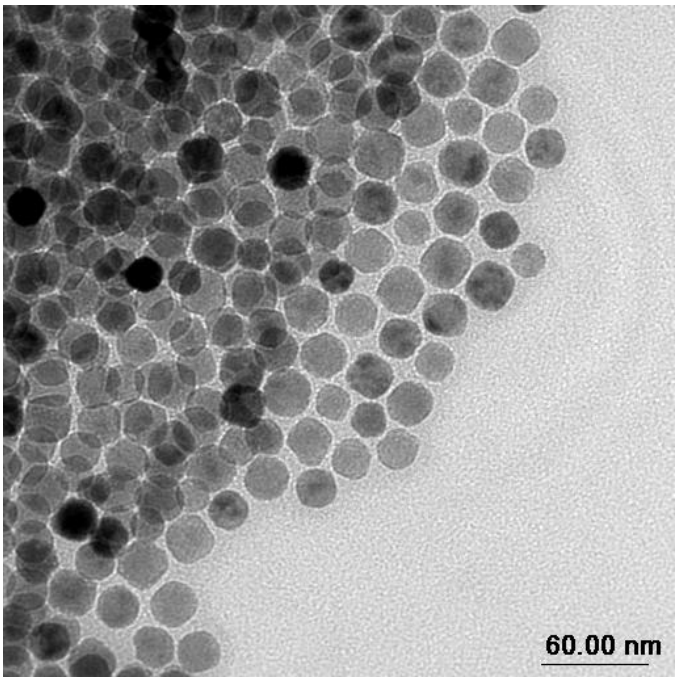

Figure 2. Particles synthesized at CINT are rounder, less polydisperse, and have been synthesized in the desired size range.