Detection and Treatment Possibilities of Disease with Magnetic Nanoparticles

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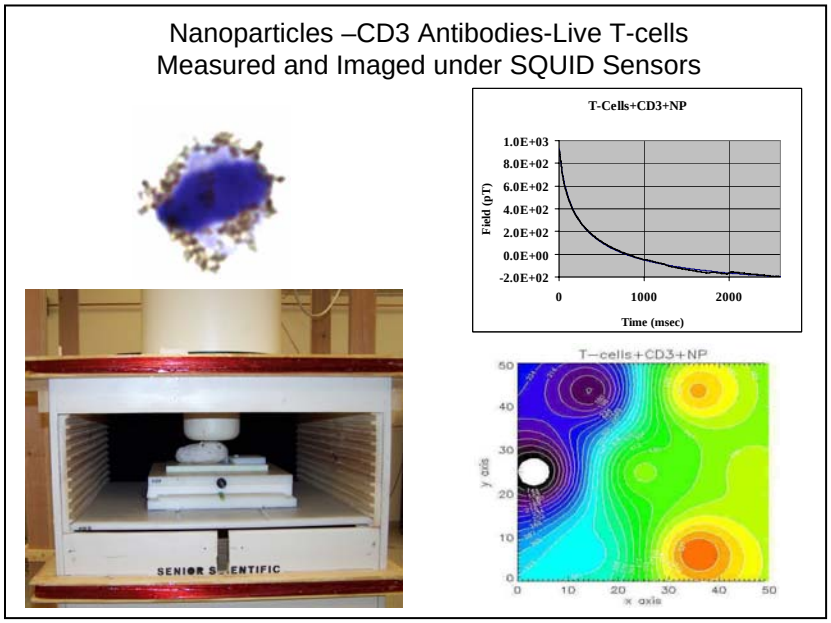
Superparamagnetic nanoparticles have numerous properties for unique detection of diseases in humans. The particles' iron oxide cores are well tolerated by the body and are commonly used as contrast agents in MRI studies and generally accepted by regulatory agencies. Their magnetic characteristics do not lead to agglomeration, hence they remain as independent particles when introduced into the body. They are available with biocompatible coatings that permit attachment of specialized ligands or other agents for targeting specific cell types or structures such as angiogenesis sites. They are easily polarized magnetically, exhibiting large magnetic moments, making them useful for imaging, magnetic enhancement of drug delivery, or collection methods. Magnetic depolarization after a magnetizing field is switched off depends strongly on particle size and whether the particles are bound to cells or microvascular structures. This feature provides large signal-to-background ratios of bound to circulating particles.



We have used these single-domain nanoparticles to investigate the detection, imaging and collection of a variety of disease cells in humans, including breast and ovarian cancer, leukemia, and detection of organ transplant rejection. Our studies currently involve the use of realistic phantoms and specific targeting antibodies and live cells obtained from human subjects or immortal cell lines.

We will discuss the procedures for coating the nanoparticles with antibodies, e.g., CD2, CD3, CA125, and attaching them to the cells, e.g., T-cells and ovarian cancer cells. We will describe detection and imaging methods, using full-sized phantoms injected with labeled cells, by an array of SQUID sensors. We can detect 10^3 - 10^4 cells with spatial resolutions of 3-5 mm. The accompanying figure illustrates our work with: (1) a leukocyte T-cell shown with ~10^5 nanoparticles bound with CD3 antibodies, (2) a magnetic remanence signal from these cells following a brief magnetizing pulse as measured by the SQUID system, (3) a kidney phantom containing two nanoparticle sources under the SQUID sensor with magnetizing coils above and below, and (4) a magnetic contour plot showing the measured positions of the two injected sources.

We will also discuss methods for using a "smart" biopsy needle to increase the efficiency of extracting cancer cells during bone marrow biopsies. The magnetic needle will extract cancer cells that have been targeted by ligands attached to nanoparticles without removing contiguous non-cancerous marrow. For this purpose, we have made laser scattering measurements of collection times to study effects of viscosity on cell and particle mobilities.