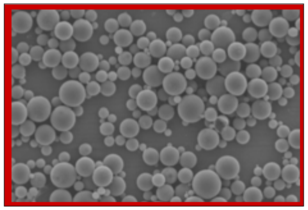
Functionalized Nanoparticle Development for Impacting a Wide Range of Biomedical Applications

C. J. Mertz, M. R. Finck, Y. Xie, and M. D. Kaminski, Chemical Engineering Division, Argonne National Laboratory

Introduction

Tiny engineered particles (smaller than red blood cells) are the key to revolutionary technology that could:

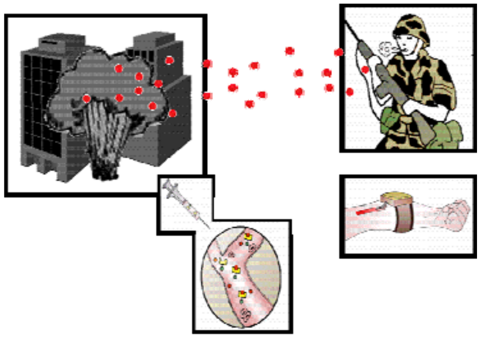
- Help detoxify humans following exposure to biological, chemical or radiological weapons
- Provide better-targeted drug delivery (for example, help stroke victims by decreasing the side effects of invasive treatment and increasing the time window for successful treatment)
- Provide earlier diagnosis
- Selectively remove natural toxins that result from trauma or auto-immune disease (for example, cardiac arrest and lupus, respectively)



PLA-PEG Magnetite Encapsulated

Detoxifying Humans from Blood-Borne Radiological, Biological and Chemical Biohazards

People exposed to radiological, biological or chemical toxins would be injected with magnetic nanoparticles containing an appropriate anti-toxin (chelators, antibodies, or receptor mimetics) that would attach to the nanoparticle surface and capture the toxin.



The nanoparticles/toxin would then be drawn out through a magnetic filtration system strapped to an artery or vein, and magnetically separated from the blood in tiny channels that pass through a strong magnetic field gradient.

The system was originally designed for use by soldiers in the battlefield, who would self-administer nanoparticles by injection and then strap on the magnetic filtration unit. The concentrated toxin within the filtration unit can then be assayed for diagnosis, extent of detoxification, or bioforensics.

Many Disciplines, Many Institutions

The team conducting this revolutionary research is made up of materials scientists, protein biologists, neurosurgeons, polymer chemists, chemists, chemical engineers, hydrodynamic modelers, and physicists from Argonne, seven universities, and two hospitals.

Traditional Stroke Treatment Can Be Risky

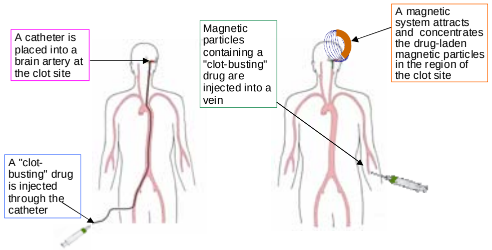
The most frequently used treatment is injection of clot-busting drug into a vein, from where it circulates throughout the body and finds its way to the clot site. The window for such treatment is about 3 hours, after which the medical side effects from the drug are too great. Some specialized centers inject clot-busting drugs directly to the clot site through a catheter, extending the window to 6 hours. This requires less of the drug, since it is more direct.

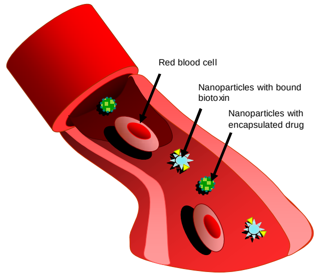
BUT--catheter-based treatments are high-risk and require specialized centers and staff around the clock, making them unavailable to most stroke patients.

Magnetic-Particle Drug Delivery Could Provide Advantages of Traditional Treatments with Less Risk

Injection of clot-busting drugs embedded in magnetic nanoparticles into a vein would present the same risk as the current treatment. But because the clot-busting drug would be guided directly to the clot site by magnetic force, less of the drug would be needed, as with delivery by catheter.

This delivery concept could offer decreased side effects and a longer window for successful treatment.





Multi-functional nanoparticles shown in cross-section of artery: nanoparticles sequestering biotoxin, and nanoparticles with encapsulated drug. The nanoparticles are smaller than red blood cells and magnetic component allows for removal of biotoxins or targeted drug delivery.

Speeding Commercialization

Engineering and manufacturing companies are being integrated into the development team for magnetic nanoparticle technology. Their participation will keep research focused in a practical direction and speed commercialization.

Early Diagnosis and Better Drug Delivery

The work also will have application in the early diagnosis of certain medical conditions. Blood tests rely on a minimum detectable quantity of disease marker to show positive. By concentrating the marker from the entire blood stream into a tiny collection of nanoparticles, detectable limits can be greatly reduced, giving an early sign of disease.

Drugs can be concentrated at specific sites in the body via magnetic nanoparticles. For example, cancer patients undergoing chemotherapy have formidable drugs throughout their entire systems that threaten harmful side effects. But if the drugs had magnetic markers attached, doctors could use magnets to concentrate the drug only at the relevant therapy site.

Potential Collaborative Research

These are just some of the potential research areas identified with collaborators at The University of Chicago and other institutions:

- Monitoring the brain' microglia activity (important in diagnosing neurodegenerative diseases)
- Transport of drugs through the blood/brain barrier
- Sustained release of drugs (radioprotectants and radiomitigators)
- Targeted arterial clot lysis ("clot busting")
- Post-myocardial infarction therapy (removal of TNF-α, an inflammatory trigger)
- Enhanced intracellular targeting of drugs
- Precise intravascular magnet targeting
- Triggered in-vivo drug release
- Enhanced NMR imaging
- Magnetic-based sensors
- Computational modeling (pharmacokinetics, system performance)

Funding for this work provided by U.S. Department of Defense, Defense Advance Research Projects Agency; BioMagnetiCs; and the Cancer Research Foundation and Brain Research Foundation of The University of Chicago

Argonne National Laboratory is operated by The University of Chicago for the U.S. Department of Energy Office of Science