Game-changing nanodiamond discovery for MRI

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A Northwestern University study shows that coupling a magnetic resonance imaging (MRI) contrast agent to a nanodiamond results in dramatically enhanced signal intensity and thus vivid image contrast.

"The results are a leap and not a small one -- it is a game-changing event for sensitivity," said Thomas J. Meade, the Eileen Foell Professor in Cancer Research in the Weinberg College of Arts and Sciences and the Feinberg School of Medicine. "This is an imaging agent on steroids. The complex is far more sensitive than anything else I've seen."

Meade led the study along with Dean Ho, assistant professor of biomedical engineering and mechanical engineering in the McCormick School of Engineering and Applied Science.

Ho already has demonstrated that the nanodiamonds have excellent biocompatibility and can be used for efficient drug delivery. This new work paves the way for the clinical use of nanodiamonds to both deliver therapeutics and remotely track the activity and location of the drugs.

The study, published online by the journal Nano Letters, also is the first published report of nanodiamonds being imaged by MRI technology, to the best of the researchers' knowledge. The ability to image nanodiamonds in vivo would be useful in biological studies where long-term cellular fate mapping is critical, such as tracking beta islet cells or tracking stem cells.

MRI is a noninvasive medical imaging technique that uses an intravenous contrast agent to produce detailed images of internal structures in the body. MRI is capable of deep tissue penetration, achieves an efficient level of soft tissue contrast with high spatial and time-related resolution, and does not require ionizing radiation.

Contrast agents are used in MRI because they alter the relaxivity (contrast efficacy indicator) and improve image resolution. Gadolinium (Gd) is the material most commonly used as an MRI contrast agent, but its contrast efficacy can be improved.

Meade, Ho and their colleagues developed a gadolinium(III)-nanodiamond complex that, in a series of tests, demonstrated a significant increase in relaxivity and, in turn, a significant increase in contrast enhancement. The Gd(III)-nanodiamond complex demonstrated a greater than 10-fold increase in relaxivity -- among the highest per Gd(III) values reported to date. This represents an important advance in the efficiency of MRI contrast agents.

Ho and Meade imaged a variety of nanodiamond samples, including nanodiamonds decorated with various concentrations of Gd(III), undecorated nanodiamonds and water. The intense signal of the Gd(III)-nanodiamond complex was brightest when the Gd(III) level was highest.

"Nanodiamonds have been shown to be effective in attracting water molecules to their surface, which can enhance the relaxivity properties of the Gd(III)-nanodiamond complex," said Ho. "This might explain why these complexes are so bright and such good contrast agents."

"The nanodiamonds are utterly unique among nanoparticles," Meade said. "A nanodiamond is like a cargo ship -- it gives us a nontoxic platform upon which to put different types of drugs and imaging agents."

The biocompatibility of the Gd(III)-nanodiamond complex underscores its clinical relevance. In addition to confirming the improved signal produced by the hybrid, the researchers conducted toxicity studies using fibroblasts and HeLa cells as biological testbeds.

They found little impact of the hybrid complex on cellular viability, affirming the complex's inherent safety and positioning it as a clinically significant nanomaterial. (Other nanodiamond imaging methods, such as fluorescent nanodiamond agents, have limited tissue penetration and are more appropriate for histological applications.)

Nanodiamonds are carbon-based materials approximately four to six nanometers in diameter. Each nanodiamond's surface possesses carboxyl groups that allow a wide spectrum of compounds to be attached to it, not just gadolinium(III).

The researchers are exploring the pre-clinical application of the MRI contrast agent-nanodiamond hybrid in various animal models. With an eye towards optimizing this novel hybrid material, they also are continuing studies of the structure of the Gd(III)-nanodiamond complex to learn how it governs increased relaxivity.

Meade has pioneered the design and synthesis of chemical compounds for applications in cancer detection, cellular signaling and gene regulation. Ho has pioneered the development of nanodiamonds and has demonstrated their efficiency as drug delivery vehicles. Both are members of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

More information: The *Nano Letters* paper is titled "Gd(III)-Nanodiamond Conjugates for MRI Contrast Enhancement."