Nanodiamonds Produce 'Game Changing Event' for MRI Imaging Sensitivity

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A Northwestern University study shows that coupling a widely used 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 Meade, who led the Northwestern research team and is a member of the Nanomaterials for Cancer Diagnostics and Therapeutics Center for Cancer Nanotechnology Excellence. "This is an imaging agent on steroids. The complex is far more sensitive than anything else I've seen."

Dean Ho, Meade's colleague at Northwestern, had demonstrated previously that 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 in the journal Nano Letters, 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 circulating tumor cells, beta islet cells, or 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 - an indicator of how strong the MRI signal will be - 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 Gd-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-nanodiamond complex demonstrated a greater than 10-fold increase in relaxivity -- among the highest value per atom of Gd 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, undecorated nanodiamonds, and water. The intense signal of the Gd-nanodiamond complex was brightest when the Gd 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-nanodiamond complex," said Ho. "This might explain why these complexes are so bright and such good contrast agents."

The biocompatibility of the Gd-nanodiamond complex underscores its clinical relevance. In addition to confirming the improved signal produced by the hybrid, the researchers conducted toxicity studies using cultured cells. The investigators 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.)

Meade, Ho and their colleagues are now conducting preclinical studies with 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.

This work, which is detailed in a paper titled, " Gd(III)-Nanodiamond Conjugates for MRI Contrast Enhancement," was supported by the NCI Alliance for Nanotechnology in Cancer, a comprehensive initiative designed to accelerate the application of nanotechnology to the prevention, diagnosis, and treatment of cancer. An abstract of this paper is available at the journal's Web site.

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