Measuring Nanoparticle Behavior in the Body Using MRI

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(PhysOrg.com) -- One of the key steps in the development of any drug or imaging agent intended for human use is measurement of the adsorption, metabolism, and excretion of the drug. Quantifying this collection of pharmacological properties, known as ADME, is a challenging and time-consuming process that is even more difficult when the drug or imaging agent includes a nanoparticle as one of its components. But by taking advantage of the magnetic properties of one kind of nanoparticle, a team of investigators at Washington University in St. Louis has demonstrated that they can measure ADME quickly using magnetic resonance imaging (MRI).

Reporting its work in the journal Magnetic Resonance in Medicine, a team of investigators led by Samuel Wickline, M.D., and Gregory Lanza, M.D., members of the Siteman Cancer Center for Nanotechnology Excellence, describe how it used MRI to measure the ADME properties in rabbits of a nanoparticle designed to bind to a molecule known as avb3, which is found on newly growing blood vessels such as those that surround most solid tumors and around atherosclerotic plaques. For comparison purposes, they also measured ADME for an untargeted but otherwise identical nanoparticle. In both cases, the nanoparticles were loaded with up to 90,000 gadolinium molecules, a number that is easily detected by MRI.

Prior to scanning, the animals had been fed a cholesterol-rich diet designed to spur atherosclerosis. After injecting the nanoparticles into the animals, the investigators scanned the animals using a research MRI

instrument every 30 minutes for the next 2.5 hours and then at 8.5, 12.5, and 24 hours. These scans focused on the animals' aortas to determine ADME properties at the site that these nanoparticles were intended to target. The researchers also took blood samples at the time of imaging for calculating ADME using traditional methods.

Using standard modeling methods, the investigators were able to calculate multicompartmental pharmacokinetic parameters for the two different nanoparticles. Although the data showed that the overall blood levels of the two nanoparticles were nearly identical over the course of the experiment, the imaging results showed clearly that the amount of targeted nanoparticle at the aorta was double that of the untargeted nanoparticle, a result that is impossible to determine using standard ADME techniques. The researchers note that measuring local ADME characteristics with MRI, in addition to determining whole-body averaged results using blood samples, should become increasingly important as more targeted nanoparticles move toward human clinical trials.

This study, which was detailed in the paper "Nanoparticle pharmacokinetic profiling in vivo using magnetic resonance imaging," 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. Investigators from Philips Medical Systems and the University of Missouri Research Reactor also participated in this study. An abstract of this paper is available at the journal's Web site. (dx.doi.org/doi:10.1002/mrm.21795)

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