New Technique Could Allow MRI to Do Ultra-Sensitive Molecular Imaging Studies

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In the race to make MRI technology suitable for molecular imaging studies, one lab gets a step closer thanks to a technique involving the reconstruction of MR images using captured xenon gas.

Alex Pines, Xin Zhou and Dominic Graziani, (from left) developed a technique that could allow MRI scanners to do molecular imaging studies

Research published online in the Proceedings of the National Academy of Sciences suggests the technique, called Hyper-SAGE, could amplify signals from tiny molecular detectors enough so MRI could pick up the faint biomarkers that indicate cancer or other clinically interesting targets.

Hyper-SAGE, which stands for hyperpolarized xenon signal amplification by gas extraction works, in essence, by vastly increasing faint signals from minuscule molecular readers called xenon biosensors.

Xenon biosensors are tiny cage-shaped sensors that can bind to xenon gas and different biomarkers or other proteins that might be investigated in a study. While these biosensors can indicate the presence of cancer or other targets, there's a catch: the signal given off by the sensor is too weak to get picked up by most MRI scans. And this is where Hyper-SAGE comes in.

How Hyper-SAGE boosts the signal

Hyper-SAGE depends on a complicated technique called remote detection, developed in MRI-pioneer Alexander Pines' lab in Lawrence Berkeley National Laboratory and the University of California, Berkeley, where these studies took place.

"With remote detection, you perform an MRI experiment on your sample as usual, however instead of reading out the results of the experiment immediately, you store the information so it can be detected at a later time," Dominic Graziani, co-writer and graduate student in the Pines lab, tells DOTmed News. Xin Zhou, a fellow researcher in the lab, co-wrote the study.

That's right, remote detection means fully re-creating an MR image by taking a sample and re-assembling its spatial arrangement using tags left by magnetic fields.

Sounds complicated? It is, and it works like this: Xenon biosensors would be injected into the patient. Then, the patient would be made to inhale a lungful of xenon gas, which would harmlessly pass through the lungs, dissolve in the bloodstream and spread throughout the body. When this happens, magnetic fields are then overlaid on the xenon gas. These fields tag each gas particle with a unique coordinate by slightly altering its magnetic direction or spin that can be used later to reassemble the particle picture.

Next, the patient would exhale and the tagged gas particles, bound to the biomarker-bearing biosensors, would leave the body and be gathered in a bag or some other container. They would then be processed and because the magnetic coordinates for each particle are unique they could be used to reconstruct the exact location of the particles in the body and reassemble a spatially accurate image from the scan -- but with sensitivity to the biomarkers orders of magnitude greater than before.

"The advantage of this method is [that] the concentration of the exhaled xenon is much higher than the concentration of the xenon dissolved in the body, and therefore provides a much larger signal," Graziani explains. "Furthermore, since the sample is in the gas phase, the concentration of xenon can be increased dramatically by either compressing the gas or liquefying it, further increasing the strength of the signal."

Clinical use

Clinical applications are some years away, according to Graziani. For their experiments, the Berkeley team didn't use living subjects, but rather a mechanical set-up meant to mimic human respiration, with membranes to act as lungs and flowing water to act as circulating blood delivering the xenon to different parts of the body.

Graziani says after these proof-of-concept studies, the real challenge is signal enhancement. "We are currently testing a second-generation design in which we compress the extracted gas before detection to see how far we can push the sensitivity gains," he says.

As for its true value in the field, it all depends on the xenon biosensor. Right now, Pines' lab is in the planning stages on animal studies to see how effective they are in real-world situations. If those go well, they could move to Hyper-SAGE animal models in a few years. But actual "point-of-care diagnostics is a much longer-term goal," Graziani cautions. "It would require the miniaturization of many of the components involved in the experiment."