New MRI signaling method could picture disease metabolism in action

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Duke University chemists are using modified magnetic resonance imaging to see molecular changes inside people's bodies that could signal health problems such as cancer.

Their new method, reported in the March 27 issue of the research journal *Science*, makes more of the body's chemistry visible by MRI, said Warren Warren, James B. Duke Professor of chemistry at Duke.

Standard MRI and the functional MRI used for brain imaging enlist the hydrogen atoms in water to create a graphic display in response to magnetic pulses and radio waves. But a huge array of water molecules are needed to pull that off.

"Only one out of every 100,000 water molecules in the body will actually contribute any useful signal to build that image," Warren said. "The water signal is not much different between tumors and normal tissue, but the other internal chemistry is different. So detecting other molecules, and how they change, would aid diagnosis."

The Duke team has been able to see these other molecules with MRI by "hyperpolarizing" some atoms in a sample, adjusting the spins of their nuclei to drastically increase their signal. This creates large imbalances among the populations of those spin states, making the molecules into more powerful magnets.

Unlike normal MRI, hyperpolarization and a technique called "dynamic

nuclear polarization" (DNP) which was used for this research, can produce strong MRI signals from a variety of other kinds of atoms besides water. Without hyperpolarization, detecting signals from atoms besides water is exceedingly difficult because the signal size is so small. But "these signals are strong enough to see, even though the molecules are much more complex than water," Warren said.

Warren's group uses what he calls the "first DNP hyperpolarizer in the South," which is installed in his laboratory. It also uses Duke's Small Molecule Synthesis Facility to create custom molecular architectures.

"You thus have a signal that, at least transiently, can be thousands or ten thousands times stronger than regular hydrogen in an MRI," Warren said. "It lets you turn molecules you are interested in into MRI lightbulbs."

Duke's hyperpolarizer includes a superconducting magnet, a cryogenic cooling system that initially plunges temperatures to a scant 1.4 Kelvin degrees while microwave radiation transfers spin polarization from electrons to nuclei, and a heating system to rapidly warm the molecules back up.

Hyperpolarized spin states don't last for long inside the body, but ways have been found to lengthen them. Several years ago, another group discovered a method to make DNP work at room temperature in some biological molecules by substituting carbon-13 atoms for some of those molecules' normal carbon-12s. Unlike carbon-12, carbon-13 emits an NMR signal like hydrogen atoms do.

Using this room-temperature DNP, the biological molecule pyruvate can retain its MRI signal for as long as 40 seconds -- long enough to observe it undergoing rapid chemical change. "So you can watch pyruvate metabolize to produce lactate, acetic acid and bicarbonate -- all

breakdown products that might correlate with cancer," Warren said. But most biological processes are much slower, and thus can't be seen with this method.

In its Science report, the Duke team describes a new method that can further extend the signals of molecules carrying swapped carbon-13s. It works by temporarily bottling-up the hyperpolarization in the longest-lived spin states -- called "singlet eigenstates" -- within specially designed molecular architectures. "You can actually use their own chemistries to get the molecules in and out of those protected states," Warren said.

For example, hyperpolarized populations locked within a specially prepared form of diacetyl -- a bacterially-made chemical that imparts buttery flavoring to foods -- can be stored using this method, according to the report. Once triggered, the MRI signal can be extended over many minutes before the spin states decay.

Thus bottled-up, the signals could be kept in temporary isolation. By dehydrating and shielding them from water within microscopic capsules, for example, these "signaling" molecules could be transported through the bloodstream to a potential disease site, Warren said.

Once at that site, a focused burst of ultrasound or heat could restore the molecules' missing water. That would cause a telltale signal to be released just as a rapidly progressing metabolic event was unfolding.

The Duke group is evaluating the potentials for a number of other possible signaling molecules, such as those involved in Parkinson's disease, osteoporosis and bladder control, said Warren, who has filed for a provisional patent.

Source: Duke University (news : web)