Researchers find nanoparticles of a rare earth metal used in MRI contrast agents can infiltrate kidney tissue

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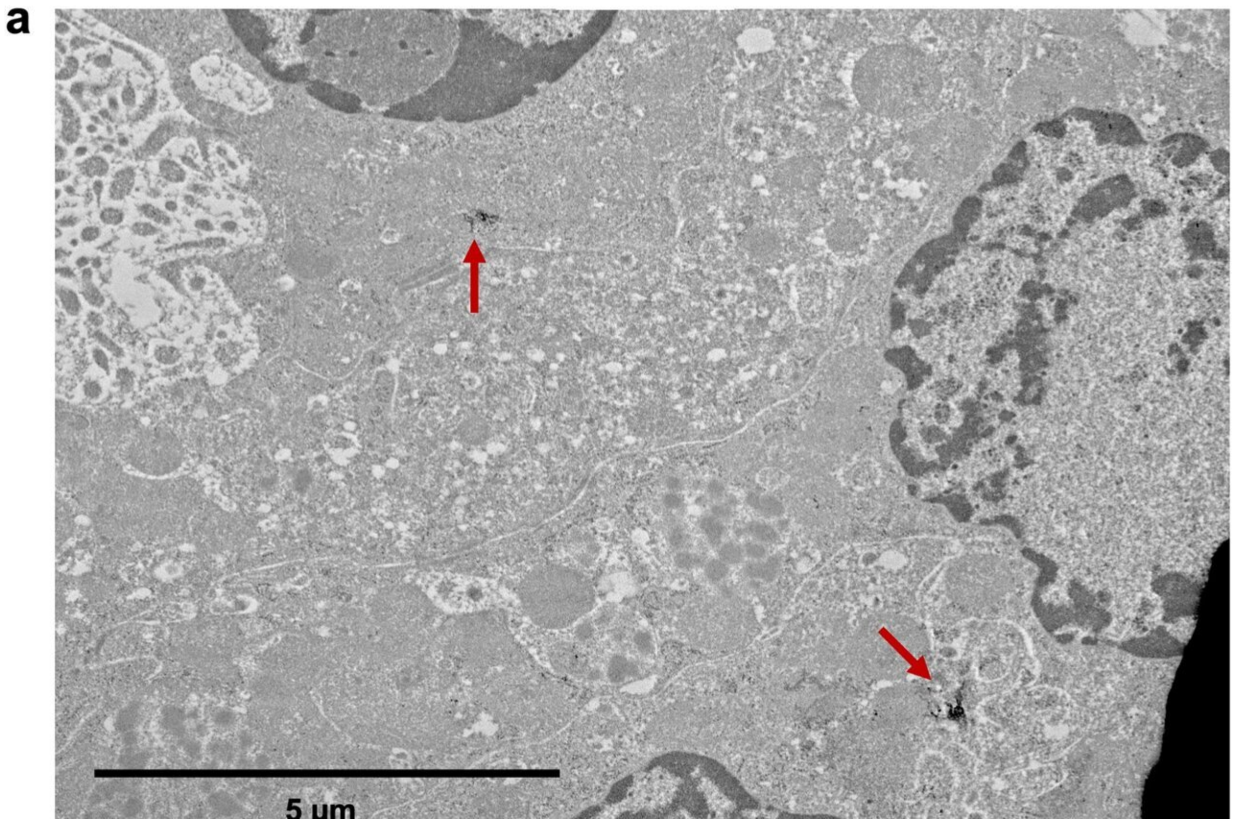

Intracellular gadolinium-rich nanoparticles in human kidneys because of routine diagnostic care. (a) Electron-dense nanoparticles in a kidney from a patient with a history of magnetic resonance imaging contrast agent exposure. This kidney was procured 17 days after magnetic resonance imaging contrast agent (20 mL). TEM, Hitachi HT7700. (b) The electron-dense nanoparticles are gadolinium rich. Embedded kidney from (a) (200 µm sections). XEDS line scanning was performed through an electron-dense nanoparticle. XEDS data revealed gadolinium, oxygen, and phosphorus. JEOL NEOARM 200 kV aberration-corrected scanning transmission electron microscope with dual EDS X-ray analysis system. Credit: *Scientific Reports* (2023). DOI: 10.1038/s41598-023-28666-1

Physicians routinely prescribe an infusion containing gadolinium to enhance MRI scans, but there is evidence that nanoparticles of the toxic rare earth metal infiltrate kidney cells, sometimes triggering severe side effects, University of New Mexico researchers have found.

In the worst cases, gadolinium, an element that has no biologic function, can trigger nephrogenic systemic fibrosis, a painful disease that affects the skin and organs and is often fatal.

In a new study published in *Scientific Reports*, a team led by Brent Wagner, MD, MS, associate professor in the UNM Department of Internal Medicine, describes the use of electron microscopy to detect tiny deposits of gadolinium in the kidneys of people who had been injected with contrast agents prior to their MRIs.

"These are nanoparticles," Wagner said. "They're actually forming nano material inside these cells."

Gadolinium-based contrast agents were first introduced in the 1990s as MRI studies became more routine, he said. Gadolinium aligns with an MRI scanner's powerful magnetic field, making for sharper images, but because of its toxicity, the metal must be tightly bound to chelating molecules so that it can be filtered through the kidneys and eliminated.

But the researchers have found that some gadolinium atoms can leach out of the contrast agents into the kidneys and other tissues, Wagner said. The effect was found in both rodent and human specimens, he said.

"We got five tissues from patients with histories of MRI contrast exposure, and another five from control patients who were contrast-naive, and I was astounded, because all five of those exposed to the contrast agent had gadolinium in them."

Contrast agents containing gadolinium are used in about 50% of MRI scans, Wagner said. A major question is why some people develop the disease, but most people who are exposed never exhibit negative symptoms.

"Patients have gotten the full-blown disease after just a single dose," he said. "Some have gotten disease eight years after exposure." There are even reports of people who received heart or kidney transplants developing symptoms.

The odds of developing disease appear to increase with greater exposure to the contrast agent and as gadolinium deposits build up in tissues, Wagner said. "There are people who get five doses, and then you can start detecting the gadolinium inside the brain when you do an MRI without any contrast."

It's unclear how some of the gadolinium detaches from the chelating molecules, he said.

"The big question is how does this contrast agent liberate the gadolinium and modulate its deposition in the cell," said Wagner, who also serves as director of the Kidney Institute of New Mexico and Renal section chief for the New Mexico Veterans Affairs Health Care System.

The study brought together collaborators from the UNM Department of Earth and Planetary Sciences, the UNM Department of Mathematics and Statistics, the Chan Zuckerberg Initiative, the New Mexico VA Health System and the Center for Integrated Nanotechnologies at Los Alamos National Laboratory and Sandia National Laboratories.

Wagner voiced concerns about the widespread use of gadolinium-based contrast agents, suggesting that many physicians might not be aware of the risks. "Quite often, contrast is given where it's not needed—or maybe you don't even need an MRI."

An additional concern is that gadolinium seems to be finding its way into the environment. Because the MRI contrast agent is expelled through urine, it released into sewer systems, but wastewater treatment plants aren't equipped to remove it, he said.

Gadolinium levels have grown twenty-fold in the San Francisco Bay, and in Germany gadolinium can be detected in soft drinks made from tap water. The same phenomenon is evident in New Mexico, he said.

"We all went out to various sources of surface water, grabbed samples and had them measured at UNM," Wagner said. "The Rio Grande at Alameda had massive levels."

Gadolinium appears to trigger the release of white blood cells called fibrocytes. "When they get into the skin they start participating in wound healing," he said. But in cases of systemic fibrosis, "it's like aberrant wound healing."

But Wagner thinks there might be a way to harness this process to help diabetes patients on dialysis. "They tend to have very poor wound healing," he says. "I like to see potential positives in addition to finding out what the mechanism of disease is."

More information: Joshua DeAguero et al, The onset of rare earth metallosis begins with renal gadolinium-rich nanoparticles from magnetic resonance imaging contrast agent exposure, *Scientific Reports* (2023). DOI: 10.1038/s41598-023-28666-1

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