Researchers develop noninvasive method to detect early-stage liver disease

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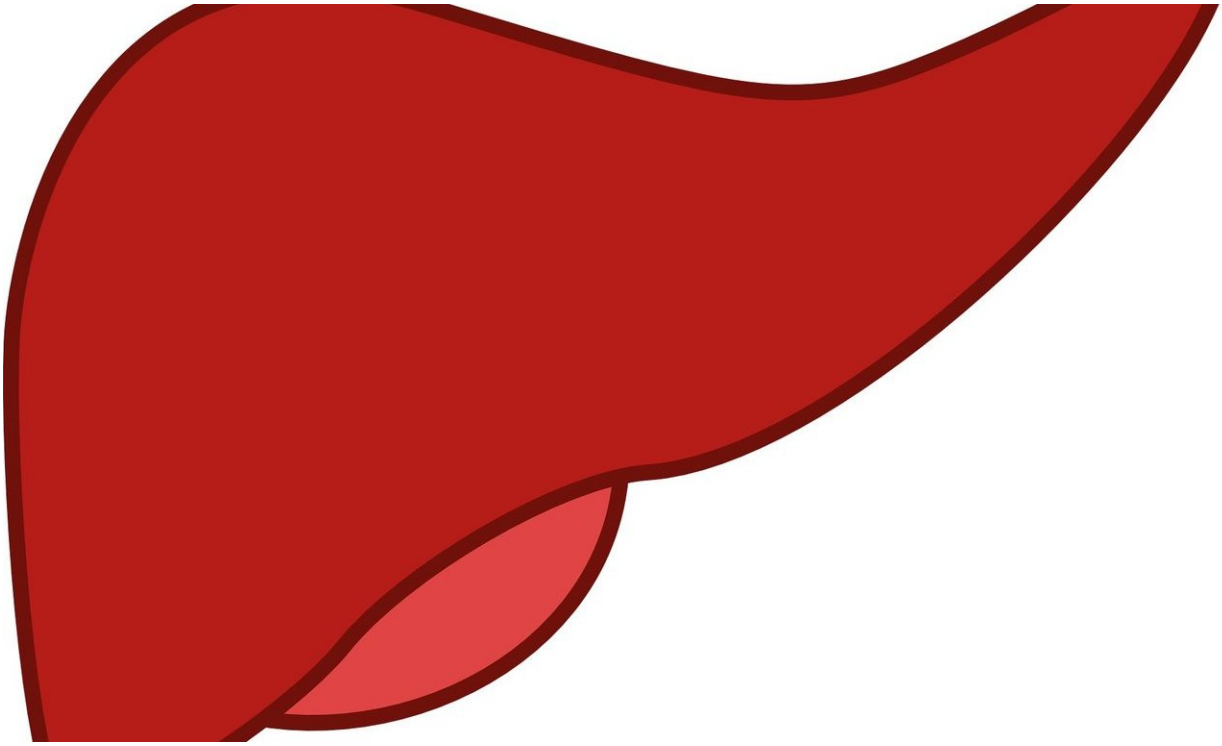

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A safer and more sensitive contrast dye for MRI tests developed by a team led by Georgia State University researchers may provide the first effective, noninvasive method for detecting and diagnosing early-stage liver diseases, including liver fibrosis.

"It's a revolutionary change for the field as the first robust detection of the early stage of liver fibrosis," said Jenny Yang, a Regents' Professor in Chemistry at Georgia State and the associate director of the university's Center for Diagnostics and Therapeutics. "This would help doctors monitor treatment before it is irreversible and help pharmaceutical companies to select the right patients for clinical trials or identify subjects for drug discovery."

The dyes used in MRI tests, referred to as contrast agents, are substances used to enhance the visibility of internal body structures during magnetic resonance imaging. The patented contrast agent ProCA32.collagen1—developed in collaboration with Yang's start-up company, InLighta BioSciences, and biology and chemistry researchers from Georgia State and Emory University—targets over-expression of the biomarker collagen during the disease state and binds tightly with the contrast metal gadolinium.

Tests in animal models show the protein-based ProCA32.collagen1 can detect the early stage of alcohol-induced liver fibrosis and Non-Alcoholic SteatoHepatitis, which is the most severe form of non-alcohol fatty liver disease. Yang's research has also demonstrated the substance is twice as accurate as conventional contrast agents, and can detect tumors as small as 0.1 to 0.2 millimeters—100 times smaller than tumors detected by currently-approved contrast agents. Because it requires a significantly lower dosage than standard contrast agents, it reduces the risk of metal toxicity.

Yang has published the results of her research in *Nature Communications*, in an article titled "Early detection and staging of chronic liver diseases with a protein MRI contrast agent."

From 2010 to 2015, deaths from chronic liver disease increased 31 percent in the U.S. among people ages 45 to 64, due to several factors,

including alcohol abuse and obesity. Liver disease is a slow-moving process, but without an effective, non-invasive means of early diagnosis to prompt treatment, it can progress to more serious stages with severe consequences.

"Most people do not believe they have liver fibrosis and don't want to change their lifestyle and we cannot detect it early," said Yang. "So, what happens is, they continue their lifestyle and at some point develop later-stage fibrosis which can become severe cirrhosis and a large portion become liver cancer."

ProCA32.collagen1's black-and-white contrast imaging can differentiate "invisible" fibrotic regions from healthy background tissue, overcoming the limitations of invasive biopsies that can't analyze the entire liver.

"Our contrast agent can do dual color so you have different contrast-colored features so the sensitivity shows up better and accuracy is a lot better," said Yang.

Yang said the next step is to gain approval from the Food and Drug Administration to conduct clinical trials at Emory University Hospital.

More information: Early detection and staging of chronic liver diseases with a protein MRI contrast agent, *Nature Communications* (2019). DOI: 10.1038/s41467-019-11984-2 , www.nature.com/articles/s41467-019-11984-2

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