

Are my muscular dystrophy drugs working?

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In DMD muscles, light-colored fat cells invade the deep-colored cells of healthy muscle, creating a different ultrasound signature that can be converted into easy-to-understand values or signals to be displayed by a gadget to be used for monitoring muscle health. Image courtesy of Wikimedia Commons.

People with muscular dystrophy could one day assess the effectiveness of their medication with the help of a smartphone-linked device, a new study in mice suggests. The study used a new method to process ultrasound imaging information that could lead to hand-held instruments that provide fast, convenient medical information.



In the study presented Oct. 30 at the Acoustical Society of America's annual meeting, researchers determined how well muscles damaged by muscular dystrophy responded to a drug in mice with an animal form of the disease. They did so by processing ultrasound data in a way appropriate for small, low-power and relatively inexpensive instruments. Called point-of-care devices, such instruments allow physicians to bring healthcare to the patient.

Physicist Michael S. Hughes of the Department of Energy's Pacific Northwest National Laboratory performed the work with colleagues John E. McCarthy, Jon N. Marsh, and Samuel A. Wickline while at Washington University in St. Louis, Missouri.

Although a small study involving animals, it builds on work in people that shows noninvasive ultrasound can track <u>muscle</u> health. Duchenne muscular dystrophy—often shortened to DMD—affects one out of 3500 male births. Steroids can help slow muscle degeneration, but too much medication causes other issues such as weight gain and high blood pressure.

"The result implies you can monitor drug therapy with cheap point-ofcare devices," said Hughes. "We'd like to be able to use low-power handheld instruments, such as a microphone-sized ultrasound that can fit on a smartphone."

Healthcare workers and patients want fast, easy-to-use medical instruments and diagnostic tests that they can bring to a patient's bedside, home or to the field. Some treatments for disease require constant monitoring, such as blood glucose in people with diabetes or blood pressure for those with heart disease.

In DMD, muscles fail to repair themselves adequately, causing the muscles to degenerate over a few decades. Young boys and men with the



disease—whom DMD hits the most—usually take steroids to prolong muscle health. Steroids have serious side effects, so patients should only take as much as they need, but it's difficult to monitor effectiveness.

Enter ultrasound. Healthy muscle contains neatly ordered cells, but DMD muscles become fibrous and plum with fat that infiltrates tissue. Because healthy and sick muscles look different in ultrasound images, researchers have been exploring how to use ultrasound to monitor progression of the disease and the muscle's response to drugs.

Previously, researchers, including Hughes, McCarthy and colleagues, have studied mice with genetic mutations that emulate muscular dystrophy. Treating mutant mice with steroids, they found they could process ultrasound information in such a way that they could measure the difference between healthy, damaged and treated muscles—a method that could put out a number on a screen.

But earlier work required more data than small, hand-held ultrasound gadgets, hooked into a smartphone with a USB cable, would be able to collect. Hughes and McCarthy wanted to know if they could also distinguish between healthy, sick and treated muscles if they collected less than 10 percent of the original data. They turned back to the ultrasound data they had collected on five healthy mice, four afflicted with mouse muscular dystrophy left untreated, and four afflicted but treated with steroids for two weeks.

To use less data, they needed to increase the relevant information in the ultrasound data and downplay the irrelevant background "noise". To do so, they used a mathematical trick called a spline, which smooths the data into average values. With a spline added to their processing program, they re-analyzed either one-eighth or one-sixteenth of the data.

The team found that even with only one-sixteenth of the data, they were



able to measure the difference between the treated muscles and the untreated muscles. Of course, people have much larger muscles than mice do, so the researchers would have to adjust the amount of <u>ultrasound</u> data to account for that, but Hughes and McCarthy previously showed that is possible in a different study.

"If we can optimize the processing, we can increase the sensitivity and provide real-time performance," said Hughes. "People with <u>muscular</u> <u>dystrophy</u> have to take the least amount of steroid that will give them the maximum therapeutic effect. This would let them do that."

More information: Reference: ASA 4aSPa1: Michael Hughes; John McCarthy; Jon Marsh; Samuel Wickline. Optimal smoothing splines improve efficiency of entropy imaging for detection of therapeutic benefit in muscular dystrophy, Thursday, Oct. 30, 9:00 a.m., Marriott Indianapolis Downtown Hotel, Indiana G.

Provided by Pacific Northwest National Laboratory

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