Tissue stiffness is a "mosh pit" where cancer cells thrive

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Imagine being at a packed concert hall with a mosh pit full of dancers creating a wall against outsiders. When targeted drugs try to make their way toward a pancreas tumor, they encounter a similar obstacle in stiff

tissue that surrounds and protects the cancer.

A new University of Rochester study demonstrates how imaging technology can be used to accurately measure tissue stiffness—thereby predicting the likelihood that drugs will be able get through to the tumor and guide drug penetration.

"Being able to 'see' stiff tissue in the tumor microenvironment is a detection strategy that could help oncologists plan treatments for their patients and monitor progress," said senior author Marvin Doyley, Ph.D.

In recently published data in the journal *Clinical Cancer Research*, Doyley's team showed for the first time in a mouse model a clear correlation between tissue stiffness and high tissue pressure, the characteristic that stops drugs from targeting the tumor. They also showed that a type of imaging called elastography, which is similar to ultrasound technology, can display tissue stiffness on an ultrasound screen.

In fact, their technique is as easy to read as a weather map. The imaging technology uses sound waves to hunt down stiff and high-pressure tissue, and then projects the tumor and stiff tissue in colorful hues, with blues and greens depicting softer tissue, and hotter colors such as red and reddish-brown representing stiff tissue.

Tissue stiffness is an important factor in cervical and breast cancer as well as pancreatic cancer, but Doyley said he was struck by the dismal five-year survival rate of less than 7 percent in pancreas cancer and chose to initially focus on ways to boost outcomes for that disease.

A medical physicist and associate professor of Electrical and Computer Engineering and Biomedical Engineering, Doyley is collaborating with David Linehan, M.D., director of clinical operations at UR Medicine's

Wilmot Cancer Institute, and a surgeon/scientist who also has a special interest in pancreatic cancer. For years Linehan has been investigating the critical role the microenvironment plays in promoting pancreas tumors, and he has designed clinical trials for drugs that stimulate the immune system to attack pancreas tumors.

Their collaboration recognizes that chemotherapy followed by surgery is currently the best treatment, and therefore reducing tissue stiffness is critical for that goal.

Doyley and Linehan are seeking funding to continue the investigation in humans. They would like to confirm that ultrasound technology can be used effectively to guide drug delivery; their team is also working with Wilmot scientist Edward Brown, Ph.D., an associate professor of Biomedical Engineering, who studies the collagen-rich fibers near tumors that contribute to tissue stiffness and cancer metastasis.

More information: Hexuan Wang et al. Elastography can map the local inverse relationship between shear modulus and drug delivery within the pancreatic ductal adenocarcinoma microenvironment, *Clinical Cancer Research* (2018). DOI: 10.1158/1078-0432.CCR-18-2684

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