Biochemical profile may help diagnose, determine aggressiveness of prostate cancer

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Magnetic resonance (MR) spectroscopy -- which analyzes the biochemistry rather than the structure of tissues -- may someday be able both to pinpoint the precise location of prostate cancer and to determine the tumor's aggressiveness, information that could help guide treatment planning. In the January 27 online issue of *Science Translational Medicine*, Massachusetts General Hospital (MGH) researchers report how spectroscopic analysis of the biochemical makeup of prostate glands accurately identified the location of tissue confirmed to be malignant by conventional pathology.

"Collectively analyzing all the metabolites measurable with a 7-Tesla MR scanner maps out prostate cancer in a way that cannot be achieved by any other current radiological test or by analyzing changes in a single metabolite," says Leo L. Cheng, PhD, of the MGH Imaging and Pathology departments, the study's senior author. "It detects tumors that cannot be found with other imaging approaches and may give us information that can help determine the best course of treatment."

Prostate-specific antigen screening indicates the potential presence of a tumor, but since benign prostate conditions also affect PSA levels, a surgical biopsy is necessary to detect cancer. Since a tumor may be confined to only a small portion of the prostate, without a way to identify the most suspicious regions, a biopsy sample can miss the malignant area. In 2005, Cheng and his colleagues found that information provided by MR spectroscopy could distinguish prostate cancer from benign tissue and was superior to traditional pathological

studies in determining a tumor's prognosis. That investigation analyzed tiny tissue samples with an advanced technique utilizing a powerful research magnet. The current study, building on the 2005 study, used a clinical MR scanner to analyze whole prostate glands, an approach that could be applied to patient care.

Spectroscopic readings were taken across sections of five cancerous prostate glands that had been removed from patients. The scans measured proportions of metabolites - biochemicals produced by various metabolic processes - that had been associated with the presence of cancer using data from the 2005 study. After scanning was complete, the prostate glands were examined by standard histological techniques, which determine the presence of tumor based on the tissue's appearance. The histological analysis was done in a way that preserved the tumor's location within the prostate.

When the two analyses were compared, five out of seven prostate regions where histologically identified tumor was located also scored high on a spectroscopy-based "malignancy index." The two other tumor regions were near the outer edge of the prostates, where exposure to the air compromised the accuracy of MR spectroscopy results. For those tumors that did match, higher malignancy index scores also corresponded with larger tumors. And while the malignancy index was most accurate in identifying stage II tumors - those confined to the prostate and large enough to be felt in a physical exam - its overall accuracy was more than 90 percent.

Cheng explains that a prostate tumor's complete metabolomic profile has the potential to give essential information on its biological status. "As we analyze more and more tumors with spectroscopy, we should be able to define profiles that reflect specific clinical and pathological states, achieving a true needle-free, MR biopsy," he explains. "And once these spectra are measured, they can be recombined to provide profiles

reflecting parameters from the tumor's location to, ultimately, its aggressiveness."

Since the current study was conducted using a whole-body clinical MR scanner, it should be adaptable to scanning patients. Because it used the powerful 7-tesla magnetic resonance equipment at the MGH's Martinos Center for Biomedical Imaging, Cheng plans to further test the approach using 3-tesla equipment, which is available at centers across the country. He and his colleagues are also working on more powerful software to process the amount of data in a full metabolomic screen in real time. After further studies verify their current results, they hope to move into clinical trials within a year or two.

"As long as we can define appropriate metabolomic profiles, this concept could someday be used for any kind of tumor or medical condition," adds Cheng, an assistant professor of Radiology (Pathology) at Harvard Medical School. "Furthermore, this concept can be extend from mapping tissue metabolites to include other disease-sensitive parameters. Eventually we hope to move the field of radiology from analyzing images that show the effects of disease to producing images that reveal the disease process itself."

Provided by Massachusetts General Hospital

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