New prostate cancer imaging shows real-time tumor metabolism

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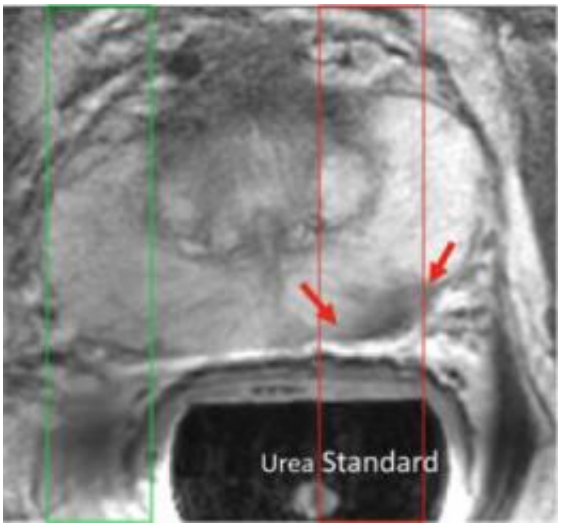

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A UCSF research collaboration with GE Healthcare has produced the first results in humans of a new technology that promises to rapidly assess the presence and aggressiveness of prostate tumors in real time, by imaging the tumor's metabolism.

This is the first time researchers have used this technology to conduct real-time metabolic imaging in a human patient and represents a

revolutionary approach to assessing the precise outlines of a tumor, its response to treatment and how quickly it is growing.

Data on the first four patients will be presented on Dec. 2 at the Radiology Society of North America's weeklong annual conference.

The initial results validate extensive preclinical research that has linked the speed at which tumors metabolize nutrients to the aggressiveness of their growth. The new imaging technique also has been used to show early biochemical changes in animal tumors in real time as they respond to medication therapy, long before a physical change occurs.

So far, the technology has produced the same response in human patients' tumors as it did in laboratory studies, even at the lowest dose, according to Sarah Nelson, PhD, a professor of Radiology and Biomedical Imaging and a member of the California Institute for Quantitative Biosciences (QB3) at UCSF.

"This is a key milestone that could dramatically change clinical treatment for prostate cancer and many other tumors," Nelson said. "We had shown this worked in animal models and tissues samples. Now, in men, we are seeing exactly the type of results we had hoped for."

For an oncologist, that means immediate feedback on whether a patient's therapy is working, either during standard treatment or in a clinical trial.

"If we can see whether a therapy is effective in real time, we may be able to make early changes in that treatment that could have a very real impact on a patient's outcome and quality of life," said Andrea Harzstark, MD, an oncologist with the UCSF Helen Diller Family Comprehensive Cancer Center who is leading the clinical aspects of the current study.

More than 200,000 men are diagnosed with prostate cancer each year and 28,000 die from it, making it one of the most common cancer in men nationwide and also one of the leading causes of cancer death in men, according to the Centers for Disease Control.

Yet the disease ranges widely in its rate of growth and aggressiveness, according to John Kurhanewicz, PhD, a UCSF expert in prostate cancer imaging. As a result, there is great debate over the ideal strategy for treating the disease, he said, leaving patients with a difficult and potentially life-changing decision over how aggressively to respond to the disease.

"This test could give both physicians and patients the information they need to make that decision," said Kurhanewicz, whose work with Dan Vigneron, PhD, and their colleagues from the UCSF Department of Radiology and Biomedical Imaging first linked a prostate tumor's production of lactate to tumor aggressiveness. Other researchers also have linked that lactate production to tumor aggressiveness and response to therapy in other cancers.

The method uses compounds involved in normal tissue function – in this case, pyruvate, which is a naturally occurring by-product of glucose, and lactate, also known as lactic acid – and uses newly developed equipment to increase the visibility of those compounds by a factor of 50,000 in a magnetic resonance imaging (MRI) scanner.

That process requires pyruvate to be prepared in a strong magnetic field at a temperature of minus 272O C, then rapidly warmed to body temperature and transferred to the patient in an MRI scanner before the polarization decays back to its native state.

The result is a highly defined and clear image of the tumor's outline, as well as a graph of the amount of pyruvate in the tumor and the rate at

which the tumor converts the pyruvate into lactate.

The sterile production process requires a dedicated clinical pharmacist with the knowledge of both quality control and of clinical practice. As the birthplace of the field of clinical pharmacy and one of only a handful of schools nationwide with drug production expertise, the UCSF School of Pharmacy and contributions of Marcus Ferrone, PharmD, and his colleagues in the Drug Products Services Laboratory were integral to this process.

The procedure must take place within minutes, which meant integrating a clean room into the scanning facility. QB3 also worked with GE Healthcare in designing Byers Hall, in which the Surbeck Laboratory of Advanced Imaging is housed, to accommodate the extremely strong magnetic field of the MRI scanner and enable time-sensitive experiments.

"All of that insight is why we moved this technology to Northern California," said Jonathan Murray, general manager, Metabolic Imaging at GE Healthcare. "This is a huge accomplishment UCSF and QB3 have achieved. They brought together the best engineering from UC Berkeley and the best bioscience and pharmacy knowledge from UCSF, and are now demonstrating the technology in a world-renowned academic medical center. We are delighted with the speed of progress of this collaboration. The science is very exciting."

The first trial involves men with prostate cancer involved in the "watchful waiting" phase of treatment, Nelson said. Future studies will directly compare these data with the results from surgically removed tumors and will look at how specific therapies change tumor metabolism. UCSF also will be studying the process for use in brain tumor patients.

The project's funding through the National Institute of Biomedical Imaging and Bioengineering, in the National Institutes of Health, was critical in adapting this technology for humans and developing new ways to obtain the MR metabolic imaging data. The project received further support from the American Recovery & Reinvestment Act and the UC Discovery Program.

Initial development of this instrumentation and its demonstration of proof of principle was conducted by Jan Henrik Ardenkjaer-Larsen, Klaes Golman and other colleagues from across GE. UCSF customized that principle and obtained the Investigational New Drug (IND) approval from the Food and Drug Administration to use the hyperpolarized pyruvate in humans.

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