Imaging in Prostate Cancer—Current Standards and Technology in Development

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Imaging is important for both the diagnosis and management of prostate cancer. Standard techniques used in everyday clinical practice depend on the stage of the disease. To initially diagnose a prostate tumor in a patient with an elevated prostate-specific antigen (PSA) level, either ultrasound or magnetic resonance imaging (MRI) is used. The choice to use ultrasound or MRI typically varies from center to center in the United States, with many centers using ultrasound-guided biopsies to diagnose localized disease.

Approximately two-thirds of patients diagnosed with localized prostate cancer are treated either with surgery or radiation therapy. For the prostate cancer patients whose disease escapes local treatment and progresses to a more advanced stage, diagnosis can be difficult. A rising PSA level is detected in most of these patients, but the tumor may be difficult to detect. Several new experimental modalities are currently in development to better identify and diagnose these patients with seemingly progressive disease. Steven M. Larson, MD, professor of radiology and member of the Molecular Imaging and Therapy Service at the Memorial Sloan-Kettering Cancer Center (MSKCC) in New York is involved in the development of these new imaging tools to facilitate prostate cancer diagnosis and treatment.

One imaging tool that has been studied more extensively is positron emission tomography (PET) as a way to noninvasively assess prostate cancer using radiolabeled probes. Choline metabolism is altered in prostate cancer, allowing radiolabeled choline or analogs of choline to be used as an imaging tool. “The chance of a positive PET scan increases steadily with increased PSA detected in the blood,” said Dr. Larson. Because choline is an essential biomolecule for all cells, including phospholipid generation and in specific metabolic pathways, the fluorocholine is taken up by cells that are rapidly growing, including cancer cells. “This is a good test, but it is not terribly sensitive, so small tumors will likely be missed,” explained Larson. This test is accepted as a diagnostic test in Europe, but not yet in the United States. The Mayo Clinic in Rochester, Minnesota received US Food and Drug Administration (FDA) approval in November 2012, to both produce and administer the imaging agent Choline C 11 Injection to be used with a scan to facilitate detection of recurrent prostate cancer sites in patients. This is currently the only institution in North America that is approved to both make and use this imaging agent. Clinicians inject the agent into a patient’s vein, and then use a PET scanner to create a detailed picture of areas where the radiolabeled molecule...
Larson and colleagues at MSKCC are currently studying prostate-specific membrane antigen (PSMA), a marker for prostate cancer and tumor neovasculature. PSMA is a protein expressed on the surface of prostate cancer cells, particularly when the cells are in a growth stage. “We have been using a radiolabeled antibody against PSMA, which is like a guided missile that binds to PSMA,” Larson explained. The radiolabeled 591 antibody is injected into patients, allowed to build up at sites with high PSMA for several days, and then patients are imaged. The long-life isotope used for radiolabel is called zirconium 89 (Zr89).

Larson, along with Michael J. Morris and Howard I. Scher, presented data from a MSKCC and Weill Cornell Medical College phase I study in metastatic castration-resistant prostate cancer patients at the American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GU) in February. The first in human trial, in 10 patients, demonstrated that the radiolabeled antibody was able to localize to tumor lesions and is a promising way to image prostate cancer metastatic tumors. “The preliminary trial was successful in disclosng metastatic tumor sites,” said Larson. The technique could detect even small tumors, on the order of 4 mm in size, which is currently too small to detect with available imaging methods. “We hope to use this antibody technique to find early signs of recurrence in prostate cancer patients,” said Larson. Further testing of this imaging tool, including assessing toxicity to patients, is now underway.

Advanced prostate cancer tumors are particularly difficult to detect, as about 80% of the lesions are found in bone, a difficult tissue to image. MRI or CT are commonly used, as is a bone scan along with technetium-99m, a medically used radioactive isotope and tracer tool. Other imaging modalities are also in development. The technetium-99m bone scan is currently being developed as a marker for disease progression. “It is currently very difficult to do bone imaging to assess the effectiveness of advanced prostate cancer drugs,” Larson explained. Demonstration of any change in bone lesions is particularly challenging.

The method developed for imaging bone lesions as part of advanced prostate cancer clinical trials was part of the Prostate Cancer Working Group criteria, authored by Howard I. Scher, MD, chair in urologic oncology at MSKCC. The recommendations included changing endpoints to the first indication of progression rather than response. Utilization of this imaging methodology was used in the phase III MDV3100 AFFIRM trial. “Technetium-99m MDP bone scanning shows promise as an imaging biomarker to study large populations and determine whether a drug is effective in advanced disease.”

Other tracers that are also being studied in castration-resistant, advanced disease include fluoro-5a-dihydrotestosterone (FDHT), a radioactive form of the active cellular androgen, as well as a synthetic amino acid analog, fluorocyclobutyl-1-carboxylic acid (FACBC), which is still in early stages, but is showing promise in detection of early-stage disease.

Imaging tools to better stage patients and visualize disease spread should lead to more fine-tuned treatment to continue to improve prostate cancer patient outcomes. “The hope is that if treatment is started early enough, the metastatic process will be inhibited, which will prevent prostate cancer death,” said Larson.

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