

FEATURES

Molecular Imaging's Role in Prostate Cancer Imaging

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Multimodality molecular imaging and new developments in imaging agents are beginning to make their mark on diagnosis, staging, detecting recurrence and measuring response to therapy in prostate cancer—PET/CT with choline is the emerging standard.



Molecular imaging connection

Prostate cancer is the second most commonly diagnosed cancer and the fourth most common cause of death from cancer among men in developed countries. "Prostate cancer is clinically and biologically a very heterogeneous disease and one modality may be better than another depending on the phase, although we are moving towards the direction of hybrid imaging" says Hossein Jadvar, MD, PhD, associate professor of radiology and biomedical engineering, director of radiology research at the University of Southern California's (USC) Keck School of Medicine.

Diagnosis of prostate cancer initially comes from prostate-specific antigen (PSA) blood test or from a digital rectal exam and the final confirmation comes via biopsy. Additional studies, such as ultrasound or MRI, are done to determine whether the cancer has spread. "Ultrasound is very easy to use, it is fast and we have endorectal probes that can look at the prostate. It is unfortunately not 100 percent [effective] in detecting cancers, but it can help in guiding biopsies. MRI also can be useful in initial diagnosis and staging," shares Jadvar.

Currently, MRI and CT are used for staging, but lack accuracy. The size of the nodes cannot be used as the criteria. "Nodes less than 1 cm in size are considered to be disease free, but tumors could be present in nodes less than 1 cm and larger nodes [greater than 1 cm] could have no tumors at all harboring cancer," Jadvar adds.

Many patients have their prostates removed for tumors that may not be particularly dangerous, notes Martin G. Pomper, MD, PhD, professor in the department of radiology and radiological science at Johns Hopkins University in Baltimore. "What molecular imaging can particularly do is predict which tumor is aggressive, or in other words going to invade locally, more severely. In future anatomical techniques like MRI, ultrasound can be merged with some of the molecular imaging techniques like choline PET or prostate-specific membrane antigen (PSMA) study."

Imaging can be very helpful to direct treatment based on the localization of the disease—radiotherapy for localized disease and chemotherapy or hormonal therapies for diffuse disease. Jadvar explains, "In patients undergoing androgen ablation, the tumor shrinks, but at some point a number of patients become androgen or hormone-refractory and do not respond to androgen ablation." The survival of patients who become androgen-refractory is 2 to 3 years. "I often use the analogy of HIV infection and AIDS. A lot of people with HIV do well, but when the HIV infection turns into AIDS, it's really different. Now you are dealing with a different ball game where they can develop a lot of infections, cancers and are under close monitoring. Their prognosis drops at that point even after all the advances in AIDS. This is similar when patients develop androgen-refractory prostate cancer and there are not many treatment plans."

Jadvar says that the role of imaging will be to predict whether the androgen-refractory state would occur in a patient. If we can predict the development of androgen-refractory state with non-invasive imaging "then perhaps we can intervene early and push the occurrence back in time and hopefully we can change the course of the disease and increase the survival of the patients."

Emerging imaging agents

Many groups around the world are trying to develop molecular imaging agents for prostate cancer. "Prostate cancer would probably benefit from molecular imaging almost more than other areas because we can't use FDG and we are struggling to find something new," Pomper says. His research focuses on developing new imaging agents for PSMA, a marker for more aggressive hormone-independent prostate cancer.

Patients treated by radical prostatectomy or radiation therapy for prostate cancer can develop PSA relapse, a biochemical failure. "At the moment, we do not have an imaging modality to address PSA relapse. There are some tracers in nuclear medicine like antibody imaging, but their effectiveness and accuracy is very low because of their low target to background ratio of the signal," says Jadvar. His laboratory is working on PET with 18F-deoxy-fluoro-arabino-furanosylthymine (18F-FMAU), a thymidine analog that is phosphorylated by thymidine kinase and incorporated in the DNA and useful for imaging tumor proliferation.

There are a lot of developments with various PET tracers like radiolabeled choline which integrates into phospholipids of cell membrane, radiolabeled acetate which is involved in cytoplasmic lipid synthesis, 18F-fluoropropionic acid (18F-FPA) which mimics acetate in vivo, 18F-fluoro-dihydrotestosterone (18F-FDHT) androgen analog and 18F-labeled bombesin [a neuropeptide with high affinity for gastrin-releasing peptide (GRP) receptors] analogs. "There are a number of tracers trying to address this issue with PET and time will tell how they fit in this kind of scenario and which one would be best at what PSA level or what kind of clinical phases of the disease," Jadvar notes.

PET/CT with choline

PET/CT with choline has demonstrated its merit in improving the detection of prostate cancer in patients with biochemical relapse where conventional imaging methods, such as bone scan, CT, MR or transrectal ultrasound (TRUS) fail.

Paulo Castellucci, MD, of the nuclear medicine unit, hematology/oncology and laboratory medicine department at the University of Bologna in Italy says, the 11C-choline PET/CT detection rate could be improved with PSA kinetics especially when PSA levels are low. Using PSA kinetics as selection criteria, it will be possible to satisfy two needs: reduce the

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