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Why Outpatient Centers May Be Your Best Bet for Advanced Imaging of Prostate Cancer

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Weighing the potential advantages of 2 of today's advanced imaging modalities

Prostate cancer continues to devastate too many lives in the US. It is the second most common cause of both cancer and cancer-related deaths among men. One out of every 8 men will receive a prostate cancer diagnosis at some point in their lives. The disease occurs most commonly in African American men and in men who are older than 65 years of age.[1]

Survival rates vary based on how well-contained the spread of prostate cancer is. According to the Surveillance Epidemiology and End Result (SEER) database, 5-year survival rates are as follows:[2]

- Nearly 100% for localized and regional spread
- 85% for unknown stage
- 30% for distant metastasis

In addition, 50% of patients treated with salvage therapy will develop biochemical recurrence.

Given these statistics, it is clear that staging of prostate cancer malignancy with imaging is more critical than ever for triaging and managing the disease. And yet, particularly because of the COVID-19 pandemic, accessibility to hospital-based outpatient imaging is quite limited. Fortunately, both conventional and advanced imaging are available at many outpatient imaging centers and offer a practical alternative to hospital settings.

United Medical Imaging Healthcare (UMIH) of California has extensive experience with both conventional and advanced imaging staging modalities—including prostate-specific membrane antigen (PSMA) based positron emission tomography (PET) tracers. Conventional imaging staging for prostate cancer includes computed tomography (CT) scan, bone scan, and magnetic resonance imaging (MRI). Prostate MRI has emerged as a staging modality that is superior to CT for the detection of lymph node metastasis and comparable to bone scan for bone metastasis detection.[3] Unfortunately, it is not uncommon with these conventional imaging modalities to have occult, indeterminate, or equivocal imaging findings with biochemical evidence of active prostate malignancy.

In such situations—and in cases of high-risk initial disease or elevated prostate-specific antigen (PSA) levels following salvage therapy or biochemical recurrence—advanced imaging staging with PSMA-based PET tracers can better delineate recurrence or metastasis.[4] PSMA is a glycoprotein peptidase enzyme partially similar to the transferring receptor and is highly expressed in membranes of malignant prostate cells. This is why various iterations of PET and single-photon emission computerized tomography (SPECT) based PSMA ligands have been investigated in efforts to improve staging.[4,5]

The US Food and Drug Administration (FDA) recently approved two important PSMA-targeted PET radiotracers:

- Gallium-68 PSMA-11 in December 2020
- F-18 piflufolastat (18F-DCFpyl, Pylarify®) in May 2021

In 2016, the FDA approved another PET radiotracer (not PSMA-targeted) for biochemical recurrence: F-18 fluciclovine (FACBC, Axumin®). This radiotracer is a synthetic analogue of the amino acid leucine, which binds to amino acid transporters that tend to be heavily expressed in prostate cancer cells.[6]

Before evaluating some of the differences between the PSMA-targeted radiotracers and F-18 fluciclovine, it is important to consider how these advanced imaging modalities perform relative to conventional alternatives. All of the PET radiotracers have outperformed both CT and bone scan for detection of nodal and organ metastasis.[7] But PET, along with CT, remains largely less sensitive and specific than prostate MRI for detection of regional extraprostatic invasion of disease.[8]

The following table provides a comparison of key differences between the PSMA-targeted PET radiotracer F-18 piflufolastat and the PET radiotracer F-18 fluciclovine, based in part on experience with both agents at UMIH. While F-18 fluciclovine is more widely ubiquitous compared to the PSMA-targeted PET radiotracers, greater accessibility to all of these advanced PET radiotracers in the outpatient setting remains especially important due to the aforementioned limitations on hospital outpatient services.

	PSMA tracers	Fluciclovine
Mechanism	PSMA ligand	Synthetic leucine analog
FDA approval	Suspected metastasis for candidates eligible for initial therapy Suspected recurrence based on elevated PSA levels	Suspected recurrence based on elevated PSA levels
Physiologic uptake	Prostate, duodenum, small intestine, kidneys, urinary tract, salivary and lacrimal glands, liver, gallbladder, breast	Pancreas, liver, salivary glands, pituitary gland, skeletal muscle, marrow, very low renal and urinary tract activity (facilitates detection of periprostatic disease)
PSA level with best sensitivity	0.2 ng/L and above	1.05 ng/L and above
Current availability in outpatient setting	Less widely available	More widely available
Cost	$4000-5000 per dose	$4000-5000 per dose
Scan time	Greater than 60 min (due to 60 min uptake time)	Within 15 min (uptake time within 5 min)
Fasting	Not required	Required (4 hours)
Side effects	< 1% (headache, dysgeusia, fatigue)	< 1% (injection site pain and erythema, dysgeusia, allergy extremely rare)

When considering the use of these FDA-approved PET radiotracers for staging for prostate malignancy, it is important to evaluate their inherent advantages and limitations. F-18 piflufolastat (one of the two PSMA-targeting radiotracers), however, largely prevails over F18-fluviciclovine, primarily because it can detect active disease during early biochemical recurrence (it is more sensitive than F18-fluciclovine in patients with PSA levels between 0.2 and 0.5 ng/mL, the typical range for early biochemical recurrence).[9,10] All of these radiotracers are available in outpatient imaging centers, which provide practical alternatives to hospital imaging centers where capacity continues to be limited, in part due to the COVID-19 pandemic.

At most institutions today, these radiotracers are largely reserved as second-line imaging modalities when conventional imaging findings are indeterminate or equivocal, because of the excessively high cost of the radiotracers. There is adequate literature to support the replacement of conventional CT and bone scan (but not MRI) with prostate PET, a foreseeable future once these radiotracers become less cost prohibitive.

Learn more at UMIH

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