

ACR–ACNM–SNMMI PRACTICE PARAMETER FOR THE PERFORMANCE OF FLUORINE-18 FLUCICLOVINE PET/CT FOR RECURRENT PROSTATE CANCER

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PREAMBLE

This document is an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. Practice Parameters and Technical Standards are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care¹. For these reasons and those set forth below, the American College of Radiology and our collaborating medical specialty societies caution against the use of these documents in litigation in which the clinical decisions of a practitioner are called into question. The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the practitioner considering all the circumstances presented. Thus, an approach that differs from the guidance in this document, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in this document when, in the reasonable judgment of the practitioner, such course of action is indicated by variables such as the condition of the patient, limitations of available resources, or advances in knowledge or technology after publication of this document. However, a practitioner who employs an approach substantially different from the guidance in this document may consider documenting in the patient record information sufficient to explain the approach taken.

The practice of medicine involves the science, and the art of dealing with the prevention, diagnosis, alleviation, and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment. Therefore, it should be recognized that adherence to the guidance in this document will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The purpose of this document is to assist practitioners in achieving this objective.

¹ *Iowa Medical Society and Iowa Society of Anesthesiologists v. Iowa Board of Nursing*, 831 N.W.2d 826 (Iowa 2013) Iowa Supreme Court refuses to find that the "ACR Technical Standard for Management of the Use of Radiation in Fluoroscopic Procedures (Revised 2008)" sets a national standard for who may perform fluoroscopic procedures in light of the standard's stated purpose that ACR standards are educational tools and not intended to establish a legal standard of care. See also, *Stanley v. McCarver*, 63 P.3d 1076 (Ariz. App. 2003) where in a concurring opinion the Court stated that "published standards or guidelines of specialty medical organizations are useful in determining the duty owed or the standard of care applicable in a given situation" even though ACR standards themselves do not establish the standard of care.

I. INTRODUCTION

This practice parameter has been developed collaboratively by the ACR, the American College of Nuclear Medicine (ACNM), and the Society of Nuclear Medicine and Molecular Imaging (SNMMI).

Prostate cancer is the most common noncutaneous cancer in American men and the second leading cause of cancer death. One in 8 men will develop prostate cancer during his lifetime, and about 1 in 41 will die from it [1]. Despite initial definitive local therapy, 20%–50% of patients may have recurrence [2-4]. Conventional imaging of prostate cancer has a limitation in the detection and localization of recurrent disease due to indolent disease

biology [5,6]. Thus, different molecular techniques such as targeting amino acid transport have been investigated for the evaluation of recurrent prostate cancer [7].

Amino acids are in demand for cell metabolism and are the building blocks of proteins [8]. The amino acid transporter systems are up-regulated in prostate cancer cells, predominantly large neutral amino acid transporter systems (LAT1, LAT3, and LAT4) and alanine-serine-cysteine transporter systems (ASCT1, ASCT2) [9-15]. The overexpression of ASCT2 and LAT1 is associated with more aggressive disease, whereas the overexpression of ASCT2 and LAT3 is stimulated by androgen signaling in androgen-dependent prostate cancer cells [10,13,14,16,17]. Although prostate cancer imaging can be performed with naturally occurring amino acid (such as C11- methionine), this is not optimal because of increased metabolites and decreased tumor-to-background ratio [18].

Fluciclovine (anti-1-amino-3-F-18-fluorocyclobutane-1-carboxylic acid, FACBC, Axumin™) is an artificial amino acid with many comprehensive clinical studies performed for detection of prostate cancer [19-34]. (The official international nomenclature for the radiotracer is "fluciclovine (F18)," but it will be referred to as "fluciclovine" in this document.) Fluciclovine is predominantly transported via transport systems ASCT2 and LAT1 [16]. Due to influx and efflux of the amino acid via the transporters, there is a declining time activity curve, and peak uptake of the tracer in the tumor will occur quickly and early at 5–20 minutes after injection with a variable rate of washout.

Fluciclovine PET/CT scan was approved by the FDA in May of 2016 for the imaging of patients with suspected prostate cancer recurrence based on the elevation of prostate-specific antigen (PSA) level (biochemical failure) [35].

The diagnostic performance of Fluciclovine was found to be superior to In-111-Indium-capromab-pendetide and computed tomography in the diagnosis and localization of prostate cancer recurrence. A single-center study of 115 patients reported overall positive scans (positivity rate) of 82.8% [28]. Biopsy was used as the primary reference standard. Diagnostic performance for prostate/prostate bed recurrence demonstrated 90.2% sensitivity, 40.0% specificity, 73.6% accuracy, 75.3% positive predictive value (PPV), and 66.7% negative predictive value (NPV). Diagnostic performance for extraprostatic recurrence was 55.0%, 96.7%, 72.9%, 95.7%, and 61.7%, respectively. Overall, the localization of extraprostatic lesions was found to be more specific than that of local recurrence with a lower false positive rate. For the evaluation of skeletal lesions, no dedicated analysis was performed to date. According to investigators' overall experience, fluciclovine demonstrates intense focal uptake in lytic prostate cancer lesions, moderate uptake within mixed sclerotic lesions, and may be absent in dense sclerotic lesions [23,27,35-37]. The fluciclovine scan should not replace bone scintigraphy (technetium-99m- MDP, F18-NaF or the more recently approved PSMA specific radiotracers like F18-Piflufolostat, F18-Flotufolostat, or Ga68-Gozetotide) for the evaluation of bone metastatic lesion.

Fluciclovine PET has been used to guide postprostatectomy salvage radiotherapy in prostate cancer patients. In a single-center, phase 2/3 randomized controlled trial, patients with detectable PSA after prostatectomy and negative conventional imaging (no extrapelvic or bone findings) were randomized to radiotherapy directed by conventional imaging alone versus conventional imaging plus F18-fluciclovine-PET/CT. Three-year event-free survival was 63.0% (95% confidence interval [CI] 49.2–74.0) in the conventional imaging group versus 75.5% (95% CI 62.5–84.6) for ¹⁸F-fluciclovine-PET/CT (difference 12.5; 95% CI 4.3–20.8; $p = .0028$). In adjusted analyses, study group (hazard ratio 2.04 [95% CI 1.06–3.93], $p = .0327$) was significantly associated with event-free survival [30]. In the same cohort, there were no significant differences in patient reported toxic effects with long-term follow-up, despite larger clinical target volumes after incorporation of Fluciclovine PET [38].

II. INDICATIONS

Fluciclovine PET/CT imaging is indicated for patients with the suspicion of recurrent prostate cancer based on the elevation of PSA level following prior treatment.

III. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

A. Physician

Physicians' qualifications and responsibilities are detailed in the [ACR–ACNM–SNMMI–SPR Practice Parameter for](#)

[Performing FDG-PET/CT in Oncology](#) [39].

III. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

B. Qualified Medical Physicist

Qualified Medical Physicists' qualifications and responsibilities are detailed in the [ACR–AAPM Technical Standard for Medical Physics Performance Monitoring of PET/CT Imaging Equipment](#) [40].

III. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

C. Radiologic and Nuclear Medicine Technologist

Technologists' qualifications and responsibilities are detailed in the [ACR–ACNM–SNMMI–SPR Practice Parameter for Performing FDG-PET/CT in Oncology](#) [39].

III. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

D. Radiation Safety Officer

The Radiation Safety Officer must meet applicable requirements of the Nuclear Regulatory Commission for training as specified in 10 CFR 35.50, or equivalent state regulations [41].

IV. PET/CT FOR PROSTATE CANCER EXAMINATION SPECIFICATIONS

The written or electronic request for fluciclovine PET/CT for recurrent prostate cancer examination should provide sufficient information to demonstrate the medical necessity of the examination and allow for its proper performance and interpretation.

Documentation that satisfies medical necessity includes (1) signs and symptoms and/or (2) relevant history (including known diagnoses). Additional information regarding the specific reason for the examination or a provisional diagnosis would be helpful and may at times be needed to allow for the proper performance and interpretation of the examination.

The request for the examination must be originated by a physician or other appropriately licensed health care provider. The accompanying clinical information should be provided by a physician or other appropriately licensed health care provider familiar with the patient's clinical problem or question and consistent with the state scope of practice requirements. (ACR Resolution 35, adopted in 2006 – revised in 2016, Resolution 12-b)

IV. PET/CT FOR PROSTATE CANCER EXAMINATION SPECIFICATIONS

A. Patient Preparation

The major goals of preparation are to minimize radiopharmaceutical uptake in normal tissues while maintaining uptake in target tissues (neoplastic disease) [42]. The preparation should include, but not be limited to, the following:

1. Appointment:
 - a. Instruct patients to avoid strenuous activity for 24 hours before fluciclovine
 - b. A minimum fasting for 4 hours before the study, except for small amounts of water to take medication.
 - c. Advise patients to void approximately 30 minutes before administration of fluciclovine injection and then refrain from voiding until after the scan has been completed [43].
2. Prior to fluciclovine injection:
 - a. Obtain a focused history that includes:
 - i. Reason for examination (symptoms, diagnoses, and recent imaging examinations)
 - ii. Treatment (surgical, radiation, and/or chemotherapy)
 - iii. Medications
 - iv. Recent trauma/exercise
 - v. Presence of concurrent infection
 - vi. PSA level

Specific details and dates should be obtained whenever possible

IV. PET/CT FOR PROSTATE CANCER EXAMINATION SPECIFICATIONS

B. Radiopharmaceutical

Fluciclovine average administered activity is 10 mCi. It is given intravenously in a maximum recommended volume of 5 mL, using 0.9% sodium chloride for volume adjustment.

The specific administered activity depends upon the local imaging protocol. The local protocol may require a standard activity, or the activity may vary as a function of various parameters such as patient size, scanning mode (2-D versus 3-D), percentage of scan bed (slice) overlap, clinical indication, or other factors.

The radiation dose to the patient is the combination of the dose from the radiopharmaceutical (~8 mSv) and the dose from the CT portion of the examination. Lower administered activities or changes in CT parameters resulting in decreased radiation dose may be appropriate with advances in PET/CT technology.

When feasible, the radiopharmaceutical should be injected intravenously at a site away from sites of known or suspected disease.

IV. PET/CT FOR PROSTATE CANCER EXAMINATION SPECIFICATIONS

C. CT Imaging Component

Protocol for CT Imaging

The CT performed as part of a PET/CT examination provides attenuation-correction information and diagnostic information that may be relevant to both PET interpretation and overall patient care.

A variety of protocols exist for performing the CT scan in the context of PET/CT scanning, but in general, a higher-quality CT acquisition for anatomic correlation and attenuation correction is recommended with fluciclovine. Although the exact cutoff between high- and low-dose CT may be scanner and site specific, the image quality provided, for example, with a 100 mAs CT is preferred over a 40 mAs CT. Regardless of the CT technique used, a careful review of CT images is necessary for comprehensive interpretation of the PET/CT examination [42].

Gastrointestinal contrast media may be administered to improve visualization unless medically contraindicated. This may be positive contrast media such as diluted barium sulfate or diatrizoic acid or negative-contrast media such as water. Highly concentrated barium collections may result in an attenuation-correction artifact that leads to a significant overestimation of the regional radiopharmaceutical concentration and should be avoided [44]; dilute barium sulfate and oral iodinated contrast media cause fewer artifacts [44-47]. It is recommended that because of the potential for variant bladder activity, the patient should be instructed to withhold from voiding immediately before being placed in the PET/CT scanner [43]. It is best to have the patient void before oral contrast administration approximately 30 minutes before scanning. It is currently believed that a relatively distended bladder may mitigate occasional fluciclovine excretion. Yet, consideration should of course be made for patient comfort while on the PET/CT table.

The patient should be positioned supine with arms above the head. If a patient cannot tolerate this position, a more comfortable position may be used in order to maximize immobility and comfort.

When indicated, the CT scan can be performed with intravenous contrast media using appropriate injection techniques. High intravascular concentrations of intravenous contrast media may cause a localized attenuation-correction artifact on the PET image [45-48], but the impact is usually limited [45-49]. If intravenous contrast use is standard at a site, this should be done after acquisition of the fluciclovine PET so as not to increase radiopharmaceutical bladder excretion due to the diuretic effect of the contrast media.

Breathing patterns during CT acquisition should be optimized so that the positions of the diaphragm on the PET and the CT images match as closely as possible.

If a single-breath-hold technique is used for CT imaging, optimal alignment of the PET and CT images is obtained

with respiration suspended in the shallow end–expiratory (end–tidal volume) phase. If respiration is not suspended during CT imaging, the patient should be coached on shallow/quiet breathing. To optimize breathing pattern, gating of the PET and/or CT could be beneficial.

IV. PET/CT FOR PROSTATE CANCER EXAMINATION SPECIFICATIONS

D. PET Imaging Component

Protocol for PET Imaging

Images should be obtained 3–5 minutes (target 4 minutes) following radiopharmaceutical administration. Because of the relatively rapid kinetics of fluciclovine, tumor to normal tissue activity is highest 4–10 minutes after injection. If the scan is started too early, biodistribution will be altered with increased blood pool. If too late, there may be increased muscle activity. This potential for altered biodistribution should be taken into account during interpretation.

Imaging guidelines recommend 5 minutes per bed position acquisition in the pelvis and 3–5 minutes per bed position in the remainder of the body, but these suggestions are entirely scanner dependent. An example of a successful scanning protocol on a modern time-of-flight instrument is provided below. Scanning should start from mid to upper thigh and proceed to base of the skull, with a total scan time of approximately 20–30 minutes. Starting acquisition caudally for the indication of suspected recurrent prostate cancer is especially critical with fluciclovine due to its specific kinetics [50].

Imaging protocols should be optimized for imaging equipment-specific recommendations. Consultation with a medical physicist may be helpful to optimize image quality on any specific scanner.

Estimation of radiopharmaceutical accumulation using the standardized uptake value (SUV) is based on local radioactivity concentration measured on images corrected for attenuation and normalized for the injected activity and body weight, lean body mass, or body surface area. The accuracy of SUV measurements depends on the accuracy of the calibration of the PET device, among other factors. Because the SUV is becoming a more common value for determining tumor response over time, measures should be taken to minimize the factors that may affect it. These include using the same scanner configuration on subsequent examinations (including reconstruction algorithms, attenuation maps, etc), maintaining the same interval between injection and scanning, avoiding infiltration of injected activity, and using the same measurement techniques [51].

Recording changes in the intensity of radiopharmaceutical uptake with SUV measurements, expressed in absolute values and percent changes, may be appropriate in some clinical scenarios. However, the technical protocol and analysis of images needs to be consistent in the 2 data sets.

IV. PET/CT FOR PROSTATE CANCER EXAMINATION SPECIFICATIONS

E. PET/CT Fluciclovine Sample Protocol:

Optimally the study would be performed by 2 technologists or other qualified personnel.

1. Position patient supine on scanner table with arms above head. Ensure maximal comfort for the patient. If a patient cannot tolerate this position for the duration of the study, a different arm position may be chosen.
2. Obtain topogram to define the region to be scanned by CT and PET.
3. Bring the patient out of scanner (being careful not to move patient or shift position) and have patient place arms by the side/arms down position. Have a stopwatch ready.
4. Inject fluciclovine as intravenous bolus and flush with no less than 10 mL of 9% sodium chloride solution. At the time of injection, start stopwatch.
5. After completing the injection and starting stopwatch, ask the patient to raise the arms above the head in the same position for CT and CT will be performed from mid to upper thighs below ischium to skull base (be sure to set the thigh level first and then adjust the number of beds to cover or get through the skull base).
6. Start CT scan with scanning in the craniocaudal direction. To diminish breathing artifacts, the patient

is instructed to perform quiet tidal breathing while scanning through the diaphragm.

7. At 4 minutes on stopwatch, start PET emission scan, with scanning in the caudocranial direction (from below ischium to skull base).
8. After completion of the scan, the patient should be removed from the scanner and encouraged to void before leaving the PET facility. The patient should be encouraged to drink plenty of fluids and void frequently throughout the day.

Note that in case of specific workflow and equipment challenges with a single technologist present, it would also be possible to acquire the CT first and then inject fluciclovine and proceed to emission acquisition, but this would have greater risk of misregistration between CT and PET as the arm would have to be moved after CT for injection of fluciclovine.

IV. PET/CT FOR PROSTATE CANCER EXAMINATION SPECIFICATIONS

F. Interpretation

With integrated PET/CT systems, the software packages typically provide a comprehensive platform for image review, including registered and aligned CT images, fluciclovine PET images with and without attenuation correction, and PET/CT fusion images in the axial, coronal, and sagittal planes. In addition, maximum-intensity-projection (MIP) images of the PET examination should be generated for review.

No absolute PSA threshold is recommended for fluciclovine imaging; however, positive fluciclovine uptake is more likely with PSA >1 ng/mL with rapidly rising PSA kinetics before it reached 1 ng/mL. The detection rate for patients with a PSA level = 0.5 ng/mL was 31% (n = 81) in the LOCATE trial [33]. The detection rate was 33% (6/18) for patients with a PSA = 0.2 ng/mL in the FALCON trial [31]. Marcus et al demonstrated a positivity rate of 57.8% (n=64) in patients with a PSA = 0.3 ng/mL [52-54].

Fluciclovine PET/CT scan may be especially useful before salvage therapy for accurate treatment planning. Fluciclovine PET/CT should be interpreted with knowledge of typical locations for prostate cancer recurrence (eg, prostatectomy bed and deep pelvic lymph nodes like obturator, proximal external iliac, internal iliac/presacral, common iliac, mesorectal followed by retroperitoneal, versus distal external iliac or inguinal nodes).

Although the pattern of fluciclovine uptake and associated CT findings as well as correlation with history, physical examination, and other imaging modalities are usually the most helpful in differentiating benign from malignant lesions, SUV measurement may also be used in sites typical for prostate cancer with comparison to nontarget tissue backgrounds (eg, lumbar spine bone marrow and blood pool).

Abnormal positive uptake in soft tissue will be defined as uptake visually clearly above that of the bone marrow (preferred L3 vertebrae) for lesions >1 cm. Soft-tissue lesions <1 cm are subject to partial volume effect and in a suspicious location, may still be considered suspicious if uptake is visually equal to or approaches marrow and significantly greater than blood pool [50].

1. Diagnostic criteria of prostate cancer recurrence in sites typical for recurrent or metastatic prostate cancer:
 - a. Prostatectomy bed and seminal vesicles
 - Focal uptake greater than bone marrow should be considered suspicious for cancer.
 - If anatomical correlate for a focus of fluciclovine uptake is small (<1 cm) and if the uptake approaches marrow and is significantly greater than blood pool, it may also be considered suspicious for cancer.
 - b. Prostate
 - Focal asymmetric uptake equal to or greater than bone marrow should be considered suspicious for cancer recurrence, as above. If anatomical correlate for a focus of asymmetric fluciclovine uptake is small (<1 cm) and if the uptake approaches marrow and is significantly greater than blood pool, it can also be considered suspicious for cancer.
 - If the uptake is diffuse and homogenous, apply a threshold significantly greater than marrow

(visually apparent).

- Note that anecdotally, median lobe uptake (central base invaginating into bladder) has a higher false positivity.

c. Lymph nodes

- Uptake in lymph nodes >1 cm with a distribution typical for recurrent prostate cancer, greater than bone marrow as above, should be considered suspicious for cancer.
- If a lymph node is small (<1 cm), is located in a distribution typical for recurrence, and has uptake that approaches marrow and is significantly greater than blood pool, it is also suspicious for cancer.
- If uptake is seen in lymph nodes with an atypical location for recurrence (eg, inguinal, distal external iliac, hilar, and axillary nodes) it may be considered suspicious for recurrence if seen in the context of other clearly malignant disease. Otherwise, mild symmetric uptake in atypical lymph nodes may be considered physiologic.
- Apart from location and uptake, other factors to consider include shape (rounded nodes are suspicious), grouping (multiple nodes are more suspicious than solitary nodes which may occasionally be metastatic too) and absence or presence of necrosis.

d. Bones

- Focal uptake clearly visualized on MIP or PET images is considered suspicious for cancer. Fluciclovine uptake in lytic metastatic lesions is typically intense and has moderate intensity in mixed sclerotic lesions.
- A bone abnormality visualized on CT only (eg, dense sclerosis without uptake) is considered nonspecific and does not exclude the presence of metastasis; CT findings without fluciclovine uptake may be further evaluated with alternative imaging modalities for further characterization (eg, MRI, F18-NaF or PSMA specific PET/CT, technetium-99m MDP single-photon emission computed tomography imaging [SPECT]-CT).
- Degenerative disk and facet uptake may be seen but is less common and intense than F18-FDG uptake. Focal uptake in what initially appears to be a Schmorl node with irregular borders and which on follow-up manifests as a prostate metastasis have been described.

e. Liver

- Metastatic lesions in the liver are typically photopenic in relation to the liver background. However, the intensity of uptake could be greater than the bone marrow.

Tissues other than neoplastic disease may show substantial physiologic fluciclovine uptake (eg, liver and pancreas). Alternatively, other conditions may lead to poor fluciclovine uptake in neoplastic tissue. The following list includes situations in which fluciclovine uptake is caused by processes other than prostate cancer and in which fluciclovine uptake does not occur despite the presence of recurrent prostate cancer:

1. Typical tissue with physiologic uptake:

- Pituitary gland has moderate uptake
- Salivary glands and lymphoid tissue of Waldeyer's ring have moderate symmetric uptake
- Thyroid gland may have mild diffuse uptake
- Breast parenchyma has mild diffuse uptake that may be absent or less than blood pool with increasing fatty changes
- Esophagus and stomach have mild to moderate uptake, more frequently involving the distal esophagus and gastroesophageal junction
- Liver and pancreas have diffuse intense physiologic uptake
- Renal parenchyma has mild to moderate uptake
- Physiologic mild to moderate periurethral activity is common. Sagittal images can help differentiate physiologic uptake in the urethra from disease in the prostatectomy bed.
- Urinary bladder wall has mild diffuse uptake
- Adrenal glands have mild diffuse unilateral or bilateral uptake. A subset of patients may have intense unilateral or bilateral uptake, which does not imply pathology
- Small and large bowels have mild to moderate uptake
- Bone marrow and muscle (cardiac and skeletal) may have heterogeneous activity. In particular, bone

marrow activity is more heterogeneous than is typically seen with F18-FDG PET.

- It is common to see retention of radiotracer in the axillary, subclavian vein, or other venous structures on side of injection, and can be differentiated from nodal disease by correlation on PET/CT.

2. Causes of potential false-positive fluciclovine PET/CT interpretation:

a. Prostate

- Benign prostatic hypertrophy
- Acute and chronic inflammation, including after radiation
- Infection
- Higher false positive rates are seen in patients with an intact prostate

b. Lymph nodes

- Infection and inflammation, especially if symmetric and in atypical locations for prostate cancer spread
- Nodal disease from extraprostatic malignancies. Fluciclovine can be taken up by other cancer cells with upregulated amino acid transport (eg, breast cancer, colon cancer, lymphoma).
- Mild physiologic uptake can be seen in the celiac ganglia which should not be mistaken for metastatic nodal disease.

c. Musculoskeletal system

- Benign and malignant bone lesions (eg, osteoid osteoma and multiple myeloma) have variable uptake
- Mild uptake may be seen in degenerative disk and facet disease, but this finding is less common and less intense than usually seen with FDG
- Cutaneous and musculoskeletal inflammation has variable uptake
- Intense though benign activity within a joint or at a muscular insertion has been observed

d. Extraprostatic tumors or neoplasms

- Primary brain tumors (eg, glioma, meningioma) and brain metastases have variable uptake that is usually greater than brain parenchyma. Physiologic brain parenchyma has uptake less than blood pool. Fluciclovine may be helpful in distinguishing active intracranial metastasis from radiation necrosis in patients treated with stereotactic radiosurgery [55].
- Pituitary and adrenal adenomas can have focal uptake greater than surrounding tissue
- Breast, lung, colon, and other carcinomas
- Lymphoma
- Any focal uptake in renal masses should be considered suspicious for malignancy. Papillary renal cell carcinoma has been shown to have increased uptake, whereas clear cell carcinoma has uptake equal to renal parenchyma.

3. Causes of potential false-negative fluciclovine PET/CT interpretation:

a. Low PSA levels

- Fluciclovine PET performance is affected by PSA levels and doubling time. Fluciclovine PET is less likely to be positive in patients with a PSA <1 ng/mL unless doubling time is rapid.

b. Bone

- Densely sclerotic metastatic lesions may have no fluciclovine uptake

c. Early bladder activity in a small percentage of patients can interfere with evaluation of the prostatectomy bed, prostate, and seminal vesicles

Recent approval of PSMA radiotracers: Although Fluciclovine served as the most common radiotracer for the diagnosis of recurrent prostate cancer, it has been replaced by PSMA radiotracers in many practices. The currently approved PSMA radiotracers include F18 Piflufolastat (PYLARIFY) and Ga68 Gozetotide, which is available as kits, one from Telix (ILLUCCIX) and the other from Novartis (LOCAMETZ). These are approved in prostate cancer patients with suspected metastasis who are candidates for initial definitive therapy and with suspected recurrence based on elevated PSA level. In addition, Ga68 Gozetotide is also approved for selection of patients with metastatic prostate cancer, for whom Lutetium Lu 177 vipivotide tetraxetan PSMA-directed therapy is indicated.

Future utility of Fluciclovine in the context of PSMA PET tracers [50]:

- a. Due to low bladder excretion, Fluciclovine may be superior to the currently approved PSMA radiotracers in the detection of local recurrence adjacent to bladder.
- b. Approximately 5-10% of prostate cancers may be equivocal or negative on PSMA PET and there is a potential benefit of Fluciclovine in such cases.
- c. Flare phenomenon is reported on PSMA PET scans due to upregulation of PSMA with androgen deprivation therapy. In these patients, Fluciclovine PET may potentially be used to evaluate response to hormonal therapy.
- d. PSMA PET may be limited in some patients with suspected tumor heterogeneity during the course of Lutetium 177-PSMA therapy. Fluciclovine may potentially have a role in such cases, however, this observation needs to be validated in prospective studies.

V. EQUIPMENT SPECIFICATIONS

See the [ACR–AAPM Technical Standard for Medical Physics Performance Monitoring of PET/CT Imaging Equipment](#) the [ACR–ASNR–SPR Practice Parameter for the Performance of Computed Tomography \(CT\) of the Extracranial Head and Neck](#) the [ACR–SABI–SPR–STR Practice Parameter for the Performance of Thoracic Computed Tomography \(CT\)](#) and the [ACR–SABI–SAR–SPR Practice Parameter for the Performance of Computed Tomography \(CT\) of the Abdomen and Computed Tomography \(CT\) of the Pelvis](#) [40,56-58]. The equipment specifications for the performance of fluorine-18 fluciclovine PET/CT are the same as for FDG-PET/CT.

A. Performance Guidelines

For patient imaging, the PET/CT scanner should meet or exceed the following specifications:

1. For the PET scanner
 - a. In-plane spatial resolution: <6.5 mm
 - b. Axial resolution: <6.5 mm
 - c. Sensitivity (3-D): >4.0 cps/kBq
 - d. Sensitivity (2-D): >1.0 cps/kBq
 - e. Uniformity: <5%
2. For the CT scanner
 - a. Spiral scan time: <5 seconds (<2 seconds is preferable)
 - b. Slice thickness and collimation: <5 mm (<2 mm is preferable)
 - c. Limiting spatial resolution: >8 lp/cm for >32-cm display field of view (DFOV) and >10 lp/cm for <24-cm DFOV
3. For the combined PET/CT scanner
 - a. Maximum coscan range (CT and PET): >160 cm
 - b. Maximum patient weight: >350 lb
 - c. Patient port diameter: >59 cm

B. Appropriate emergency equipment and medications must be immediately available to treat adverse reactions associated with administered medications, to include iodinated contrast. The equipment and medications should be monitored for inventory and drug expiration dates on a regular basis. The equipment, medications, and other emergency support must also be appropriate for the range of ages and sizes in the patient population.

- C. A fusion workstation with the capability to display PET, CT, and fused images with different percentages of PET and CT blending should also be available. The workstation should also have the capability to measure SUVs with volumetric regions of interest (ROIs).
- D. PET/CT scanning done specifically for radiation therapy planning should be performed with a flat table top, immobilization devices as needed, and the use of appropriate positioning systems in order to best match patient positioning during radiation

VI. DOCUMENTATION

Reporting should be in accordance with the [ACR Practice Parameter for Communication of Diagnostic Imaging Findings](#) [59].

The report should include the radiopharmaceutical, administered activity and route of administration, as well as any other pharmaceuticals administered, also with dosage and route of administration.

The technique section of the report should include the radiopharmaceutical (eg, ¹⁸F-Fluciclovine), the administered activity, route, and site of administration. The patient weight, time from injection to scanning, and technique for calculating SUVs (ie, body weight, lean body weight, or body surface area) should also be reported.

Details of oral or intravenous contrast agents, if used for the CT attenuation-correction portion of the examination, should also be reported to include the volume and route of administration. Other information relevant to contrast administration, such as steroid preparation, prehydration, or dialysis history, should be included. The report should also include documentation of contrast reactions and subsequent treatment, if observed during the examination.

The history section should include the clinical indications for the examination (eg, biochemical recurrence of disease) as well as available information regarding prior treatments (eg, prostatectomy, brachytherapy, radiotherapy), level and date of concerning PSA, and any details of suspicious abnormalities identified on prior imaging studies (eg, new adenopathy on CT abdomen/pelvis or MRI pelvis, indeterminate lesions on bone scan).

The findings section should include a description of the location, extent, and intensity of abnormal radiopharmaceutical avidity in relation to normal comparable tissues (bone marrow and blood pool) and should describe the relevant morphologic findings on the CT images. Ideally, anatomic abnormalities related to areas of abnormal radiopharmaceutical avidity should be compared to prior cross-sectional examinations when available and the image with series numbers should also be included. Optionally, lesion/background ratio may be reported but a recommended absolute cutoff ratio has not been established. Often injection-site infiltrates, such as in arms, or attenuation-correction errors can significantly alter radiopharmaceutical uptake in lesions, leading to false conclusions and therefore should be used as an adjunct to the qualitative assessment of lesion avidity.

If the CT scan was requested and performed as a diagnostic examination, the CT component of the examination should be reported separately to satisfy regulatory, administrative, or reimbursement requirements. In that case, the PET/CT report should refer to the diagnostic CT scan report for findings not related to the PET/CT combined findings [60-62]. Even if the CT scan was not requested as a diagnostic examination, clinically important nononcologic findings (eg, pneumothorax, aortic aneurysm, bowel obstruction, pneumoperitoneum, fracture) on the CT scan should be reported.

VII. EQUIPMENT CONTROL

PET performance monitoring should be in accordance with the [ACR–AAPM Technical Standard for Nuclear Medical Physics Performance Monitoring of Gamma Cameras](#) and the [ACR–AAPM Technical Standard for Medical Physics Performance Monitoring of PET/CT Imaging Equipment](#) [40,63].

CT monitoring should be in accordance with the [ACR–AAPM Technical Standard for Diagnostic Medical Physics Performance Monitoring of Computed Tomography \(CT\) Equipment](#) [64].

The quality control (QC) procedures for 18F-Fluciclovine PET/CT should include both the PET procedures and the CT procedures according to the ACR Technical Standards. The equipment QC for 18F-Fluciclovine PET/CT are the same as for fluorine-18 FDG-PET/CT. The QC procedures for PET should include a calibration measurement of activity in a phantom containing a known radiopharmaceutical concentration, generally as a function of axial position within the scanner field of view. The QC procedures for the CT should include air and water calibrations in Hounsfield units for a range of kV. A daily check on the stability of the individual detectors should also be performed to identify detector failures and drifts.

In addition, for PET/CT, the alignment between the PET and CT scanners should be checked periodically. Such a check should determine an offset between the PET and CT scanners that is incorporated into the fused image display to ensure accurate image alignment.

VIII. RADIATION SAFETY IN IMAGING

Radiologists, medical physicists, non-physician radiology providers, radiologic technologists, and all supervising physicians have a responsibility for safety in the workplace by keeping radiation exposure to staff, and to society as a whole, "as low as reasonably achievable" (ALARA) and to assure that radiation doses to individual patients are appropriate, taking into account the possible risk from radiation exposure and the diagnostic image quality necessary to achieve the clinical objective. All personnel who work with ionizing radiation must understand the key principles of occupational and public radiation protection (justification, optimization of protection, application of dose constraints and limits) and the principles of proper management of radiation dose to patients (justification, optimization including the use of dose reference levels). https://www-pub.iaea.org/MTCD/Publications/PDF/PUB1775_web.pdf

Nationally developed guidelines, such as the [ACR's Appropriateness Criteria](#)[®], should be used to help choose the most appropriate imaging procedures to prevent unnecessary radiation exposure.

Facilities should have and adhere to policies and procedures that require ionizing radiation examination protocols (radiography, fluoroscopy, interventional radiology, CT) to vary according to diagnostic requirements and patient body habitus to optimize the relationship between appropriate radiation dose and adequate image quality. Automated dose reduction technologies available on imaging equipment should be used, except when inappropriate for a specific exam. If such technology is not available, appropriate manual techniques should be used.

Additional information regarding patient radiation safety in imaging is available from the following websites – Image Gently[®] for children (www.imagegently.org) and Image Wisely[®] for adults (www.imagewisely.org). These advocacy and awareness campaigns provide free educational materials for all stakeholders involved in imaging (patients, technologists, referring providers, medical physicists, and radiologists).

Radiation exposures or other dose indices should be periodically measured by a Qualified Medical Physicist in accordance with the applicable ACR Technical Standards. Monitoring or regular review of dose indices from patient imaging should be performed by comparing the facility's dose information with national benchmarks, such as the ACR Dose Index Registry and relevant publications relying on its data, applicable ACR Practice Parameters, NCRP Report No. 172, Reference Levels and Achievable Doses in Medical and Dental Imaging: Recommendations for the United States or the Conference of Radiation Control Program Director's National Evaluation of X-ray Trends; 2006, 2009, amended 2013, revised 2023 (Res. 2d).

IX. QUALITY CONTROL AND IMPROVEMENT, SAFETY, INFECTION CONTROL, AND PATIENT EDUCATION

This practice parameter was developed according to the process described under the heading *The Process for Developing ACR Practice Parameters and Technical Standards* on the ACR website (<https://www.acr.org/Clinical-Resources/Practice-Parameters-and-Technical-Standards>) by the Committee on Practice Parameters and Technical Standards – Nuclear Medicine and Molecular Imaging of the ACR Commissions on Nuclear Medicine and Molecular Imaging in collaboration with the ACNM and the SNMMI.

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