

**American College of Radiology  
ACR Appropriateness Criteria®**

**Clinical Condition:** Pretreatment Staging Prostate Cancer

**Variant 1:** T1-2 and Gleason score (GS) ≤6 and PSA <10 and <50% biopsy cores positive.

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI pelvis without and with contrast	2		O
CT abdomen and pelvis with contrast	2		☼ ☼ ☼ ☼
ProstaScint scan	2		☼ ☼ ☼ ☼
Tc-99m bone scan whole body	2		☼ ☼ ☼
X-ray area of interest	2		NS
<b>Rating Scale:</b> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			<b>*Relative Radiation Level</b>

**Variant 2:** T1-2 and GS ≤6 and PSA <10 and ≥50% biopsy cores positive.

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI pelvis without and with contrast	5	MRI abdomen may be performed if looking for retroperitoneal adenopathy. Endorectal coil (erMRI) may be considered in patients with high-range PSA or high-volume disease detected by biopsy. Useful for treatment planning. See statement regarding contrast in text under “Anticipated Exceptions.”	O
CT abdomen and pelvis with contrast	2		☼ ☼ ☼ ☼
ProstaScint scan	2		☼ ☼ ☼ ☼
Tc-99m bone scan whole body	2		☼ ☼ ☼
X-ray area of interest	2		NS
<b>Rating Scale:</b> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			<b>*Relative Radiation Level</b>

**Clinical Condition:****Pretreatment Staging Prostate Cancer****Variant 3:****T1-2 and GS ≤6 and PSA 10 to <20 and <50% biopsy cores positive.**

Radiologic Procedure	Rating	Comments	RRL*
MRI pelvis without and with contrast	4	MRI abdomen may be performed if looking for retroperitoneal adenopathy. Endorectal coil (erMRI) may be considered in patients with high-range PSA or high-volume disease detected by biopsy. Useful for treatment planning. See statement regarding contrast in text under “Anticipated Exceptions.”	O
Tc-99m bone scan whole body	3	Bone scan may be indicated in patients with PSA in the high end of this range, especially if it is rising rapidly.	☼☼☼
CT abdomen and pelvis with contrast	2		☼☼☼☼
ProstaScint scan	2		☼☼☼☼
X-ray area of interest	2	If bone scan positive or symptoms dictate.	NS
<b>Rating Scale:</b> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			<b>*Relative Radiation Level</b>

**Variant 4:****T1-2 and GS ≤6 and PSA 10 to <20 and ≥50% biopsy cores positive.**

Radiologic Procedure	Rating	Comments	RRL*
MRI pelvis without and with contrast	6	MRI abdomen may be performed if looking for retroperitoneal adenopathy. Endorectal coil (erMRI) may be considered in patients with high-range PSA or high-volume disease detected by biopsy. Useful for treatment planning. See statement regarding contrast in text under “Anticipated Exceptions.”	O
Tc-99m bone scan whole body	6	Bone scan should be performed in patients with high-volume disease or PSA in the higher end of this range, especially if it is rising rapidly.	☼☼☼
CT abdomen and pelvis with contrast	5	CT should be performed in patients with high-range PSA or high-volume disease detected by biopsy. MRI may be substituted.	☼☼☼☼
X-ray area of interest	5	If bone scan positive or symptoms dictate.	NS
ProstaScint scan	4	Should be reserved for high-volume disease.	☼☼☼☼
<b>Rating Scale:</b> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			<b>*Relative Radiation Level</b>

**Clinical Condition:****Pretreatment Staging Prostate Cancer****Variant 5:****T1-2 and GS = 7 and PSA <20 and <50% biopsy cores positive.**

Radiologic Procedure	Rating	Comments	RRL*
Tc-99m bone scan whole body	7	Decision to perform bone scan depends on PSA, Gleason score (4+3), volume of disease detected by biopsy, and focality of Gleason 7 tumor. Bone scan should be considered in patients with PSA in the higher part of this range, especially if it is rising rapidly.	☼ ☼ ☼
X-ray area of interest	6	If bone scan positive or symptoms dictate.	NS
MRI pelvis without and with contrast	5	MRI abdomen may be performed if looking for retroperitoneal adenopathy. Endorectal coil (erMRI) may be considered in patients with high-range PSA or high-volume disease detected by biopsy. Useful for treatment planning. See statement regarding contrast in text under "Anticipated Exceptions."	O
CT abdomen and pelvis with contrast	5	CT should be performed in patients with high-range PSA or high-volume disease detected by biopsy. MRI may be substituted.	☼ ☼ ☼ ☼
ProstaScint scan	3	If available, reserve for high-PSA, high-volume patients.	☼ ☼ ☼ ☼
<b>Rating Scale:</b> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			<b>*Relative Radiation Level</b>

**Variant 6:****(T1-2 and GS ≤6 and PSA >20) or T1-2 and GS = 8-10 and PSA <20 and <50% biopsy cores positive.**

Radiologic Procedure	Rating	Comments	RRL*
Tc-99m bone scan whole body	8		☼ ☼ ☼
CT abdomen and pelvis with contrast	7	CT should be performed in patients with high-range PSA or high-volume disease detected by biopsy. MRI may be substituted.	☼ ☼ ☼ ☼
MRI pelvis without and with contrast	6	MRI abdomen may be performed if looking for retroperitoneal adenopathy. Endorectal coil (erMRI) may be considered in patients with high-range PSA or high-volume disease detected by biopsy. Useful for treatment planning. See statement regarding contrast in text under "Anticipated Exceptions."	O
X-ray area of interest	6	If bone scan positive or symptoms dictate.	NS
ProstaScint scan	5	If available, reserve for high-PSA, high-volume patients.	☼ ☼ ☼ ☼
<b>Rating Scale:</b> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			<b>*Relative Radiation Level</b>

**Clinical Condition:****Pretreatment Staging Prostate Cancer****Variant 7:****T1-2 and GS >7 and PSA ≥20 or ≥50% biopsy cores positive.**

<b>Radiologic Procedure</b>	<b>Rating</b>	<b>Comments</b>	<b><u>RRL*</u></b>
Tc-99m bone scan whole body	9		☼ ☼ ☼
MRI pelvis without and with contrast	7	MRI abdomen may be performed if looking for retroperitoneal adenopathy. Endorectal coil (erMRI) may be considered in patients with high-range PSA or high-volume disease detected by biopsy. Useful for treatment planning. See statement regarding contrast in text under “Anticipated Exceptions.”	O
CT abdomen and pelvis with contrast	7	MRI may be substituted.	☼ ☼ ☼ ☼
X-ray area of interest	6	If bone scan positive or symptoms dictate.	NS
ProstaScint scan	5	If available, reserve for high-PSA, high-volume patients.	☼ ☼ ☼ ☼
<b>Rating Scale:</b> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			<b>*Relative Radiation Level</b>

**Variant 8:****Clinical T3, seminal vesicle or bladder neck invasion.**

<b>Radiologic Procedure</b>	<b>Rating</b>	<b>Comments</b>	<b><u>RRL*</u></b>
Tc-99m bone scan whole body	9		☼ ☼ ☼
MRI pelvis without and with contrast	7	MRI abdomen may be performed if looking for retroperitoneal adenopathy. Endorectal coil (erMRI) may be considered in patients with high-range PSA or high-volume disease detected by biopsy. Useful for treatment planning. See statement regarding contrast in text under “Anticipated Exceptions.”	O
CT abdomen and pelvis with contrast	7	MRI may be substituted.	☼ ☼ ☼ ☼
X-ray area of interest	6	If bone scan positive or symptoms dictate.	NS
ProstaScint scan	5	If available, reserve for high-PSA, high-volume patients.	☼ ☼ ☼ ☼
<b>Rating Scale:</b> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			<b>*Relative Radiation Level</b>

## PRETREATMENT STAGING PROSTATE CANCER

Expert Panels on Urologic Imaging and Radiation Oncology–Prostate: Gary M. Israel, MD<sup>1</sup>; Isaac R. Francis, MD<sup>2</sup>; Mack Roach III, MD<sup>3</sup>; May Abdel-Wahab, MD, PhD<sup>4</sup>; David D. Casalino, MD<sup>5</sup>; Jay P. Ciezki, MD<sup>6</sup>; Pat Fulgham, MD<sup>7</sup>; John R. Leyendecker, MD<sup>8</sup>; Gregory Merrick, MD<sup>9</sup>; James Lloyd Mohler, MD<sup>10</sup>; Sheila Sheth, MD.<sup>11</sup>

### **Summary of Literature Review**

Prostate cancer is the most common noncutaneous malignancy of men in the United States and is the second-leading cause of cancer death in American men. The American Cancer Society recommends that men over the age of 50 have an annual digital rectal examination (DRE) and a serum prostate-specific antigen (PSA) test, and that men with a family history of prostate cancer or who are of African-American descent begin annual screening at age 45 [1].

If either the DRE or PSA test suggests neoplasm, a transrectal ultrasound-guided needle biopsy of the prostate gland is usually performed. Alternatively, prostate cancer may be found in the tissue obtained during a transurethral resection of the prostate (TURP), although this procedure is becoming less common. Pretreatment staging is important, because clinically localized disease (stage T1 or T2) is generally amenable to local therapy, while more advanced disease may require multimodal therapy (eg, androgen deprivation therapy and radiation therapy). The staging system developed by the American Joint Committee on Cancer (AJCC) encompasses the status of the primary tumor (T), the lymph nodes (N), and any metastasis (M) ([Appendix 1](#)).

### **Clinical Staging Methods**

#### *Digital Rectal Examination*

The DRE is considered insensitive for detecting extracapsular tumor extension [2-4]. At least 40% of patients with cancers judged to be clinically confined (T1 or T2) by DRE are found to have extraprostatic extension at surgery [4]. Thus, DRE alone has proven unsatisfactory for determining stage.

#### *Prostate-Specific Antigen*

Serum PSA is used as a biomarker, not only in identifying men with prostatic cancer but also in predicting pathologic stage, especially when combined with a patient's Gleason score, and for monitoring treatment response [5]. In general, the higher the PSA, the more advanced the disease; moreover, the likelihood of having organ-confined disease is inversely proportional to the level of the PSA. Despite its utility, it is clear that as many as 15% of men with a normal PSA will have prostate cancer on one or more biopsy specimens [2]. Recent data also suggest that the correlation with extent of disease is poor for men with relatively low PSA levels (eg, <9 ng/ml) [6].

The initial PSA value correlates with the likelihood of being free of biochemical evidence of persistent disease and surviving prostate cancer [7-9]. PSA measurements are evaluated alone or by comparison with a prior measurement (PSA velocity and PSA doubling time [PSADT]), or in the context of the patient's gland volume (PSA density) [10,11]. There are also age-specific PSA levels available. The density and age specificity help to separate the elevations in PSA due to benign prostatic hyperplasia (BPH) from those due to cancer; however, these methods provide guidance only on the likelihood of cancer versus benign disease [12]. The capability of PSA level alone to accurately predict final pathologic stage in an individual has a prohibitively high false-positive rate [13]. The bound and free components of PSA have been measured; the proportion of free PSA (ie, not bound to plasma proteins) was found to be lower in patients with cancer than in those with BPH [14]. For instance, free PSA values <15% were associated with more aggressive tumors, whereas free PSA values >25% generally had low-risk tumors.

#### *Prostate Acid Phosphatase*

With the introduction of PSA in the 1980s, prostate acid phosphatase (PAP) fell into disfavor because PSA performed significantly better in terms of screening and monitoring response to treatment. However, recent radical prostatectomy, external-beam radiation therapy, and brachytherapy series have demonstrated that PAP is a statistically significant predictor for biochemical progression-free survival and/or cause-specific survival in patients with intermediate- and high-risk prostate cancer [15-18]. PAP appears to be particularly valuable in predicting distant failure in higher-risk patients for whom high levels of local control are achieved with aggressive local treatment. If PAP is to be introduced as a standard component of the initial diagnostic workup of prostate cancer, additional clinical studies are necessary to corroborate the currently published data.

#### *Gleason Score*

The Gleason scoring system has been shown to correlate well with the extent of disease and prognosis. It is the single best predictor of the biological activity, and therefore the stage, of the tumor. The scoring ranges from

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two (well differentiated, minimally aggressive) to 10 (anaplastic, highly aggressive) [19]. The probability of seminal vesicle and lymph node involvement (LN+) increases with the Gleason score, and some investigators have found a combination of the Gleason score and the serum PSA level to give the greatest prognostic information [5,20].

#### *Nomograms and Risk Group Stratification*

The work by Partin and others has led to the development of nomograms that predict the probability of extracapsular extension (ECE), seminal vesicle involvement (SV+), and LN+ [5,20,21]. This work was subsequently validated by others and led to attempts to correlate nomograms with prognosis [22-28]. Most nomograms use combinations of clinically available prognostic factors such as PSA level, grade, and clinical T stage to estimate the risk [29]. Estimates of the probability of LN positivity derived from such nomograms have subsequently been shown to be of use in determining the utility of staging studies and in guiding therapy [30,31].

Clinicians have widely adopted a simplified approach to predicting outcome based on the same pretreatment parameters used in the nomograms. Using such an approach, patients with similar risk of biochemical recurrence can be divided into risk groups that, with additional follow-up, have been correlated with mortality [32]:

- Low risk: AJCC clinical stage T1c or T2a and PSA  $\leq 10$  ng/ml and biopsy Gleason score  $\leq 6-8$ , 10-year PSA failure-free survival rate.
- Intermediate risk: AJCC clinical stage T2b or PSA  $> 10$  and  $\leq 20$  ng/ml or biopsy Gleason score 7-8, 10-year PSA failure-free survival rate.
- High risk: AJCC clinical stage T2c disease or PSA  $> 20$  ng/ml or a biopsy Gleason score  $\geq 9-10$ , 10-year PSA failure-free survival rate.

Alternative risk stratification schemes have also been described, and despite their differences they support the notion that Gleason score, clinical T stage, and PSA can be used to predict survival and direct therapy [8,33]. More recently the number of positive biopsies (eg,  $> 5$ ) and the percentage of each core that is positive at biopsy (eg,  $> 50\%$ ) have been associated with increased risk of recurrent disease [34].

#### **Summary of Nonimaging Methods of Staging**

While DRE, PSA, or Gleason score individually predict stage, they are less accurate than when they are combined into nomograms that provide estimates of risk. Patients can be stratified by their risk for extraprostatic, nodal, and disseminated disease.

Imaging potentially improves these general estimates of risk by specifically identifying lesions with anatomic abnormalities. However, interpretation of imaging findings should be made in the context of the nonimaging findings. Due in part to the limitations of clinical staging,

efforts have been made to use imaging modalities to better predict the extent of disease and outcome [35].

#### **Imaging Methods**

##### *Ultrasound*

Gray-scale ultrasound (US) has not proven satisfactory for local staging of prostate cancer. The ability of transrectal US to predict ECE varies widely from 37%-83% in different settings and populations; however, it is generally acknowledged that US is of limited value due to limitations of its spatial resolution [36-39]. The addition of color Doppler and power Doppler has been reported to improve the detection of prostate cancer by identifying increased vascularity but has not yet been shown to improve staging accuracy [40-42]. Failure to identify a neurovascular bundle near the site of a tumor is suggestive of ECE, but there is not yet consensus that its use is mandatory for staging. Contrast-enhanced US has the potential to substantially improve the staging of prostate cancer but has not yet been tested in a multi-institutional trial. Similarly 3D US is under investigation to improve the delineation of the cancer and prostate capsule.

##### *Magnetic Resonance Imaging*

Endorectal coil magnetic resonance imaging (erMRI) provides the highest spatial resolution among the imaging modalities currently available. Three major techniques have been used to stage prostate cancer with erMRI: T2-weighted MRI, MR spectroscopic imaging (MRSI), and dynamic contrast-enhanced MRI (DCE-MRI). It is generally accepted that an endorectal coil is required to achieve sufficient signal-to-noise ratios to allow small-field-of-view (12-16 cm) imaging which, in turn, allows images to be acquired with high resolution ( $\sim 0.5$  mm) [43-46]. Additionally, 3-Tesla (3T) erMRI may be beneficial by providing higher signal, thus further improving spatial (or temporal, in the case of DCE-MRI) resolution. Futterer et al [47] have shown that 3T erMRI imaging is accurate for staging of prostate cancer, that there is moderate to substantial interobserver agreement, and that minimal capsular invasion could be detected. However, there are insufficient data in the literature to support the routine use of 3T erMRI [48].

##### *T2-Weighted Magnetic Resonance Imaging*

Over 15 years of clinical experience exists with T2-weighted erMRI. Improvements in coil design (dual endorectal coil and torso coil arrays), pulse sequences, and image intensity correction have led to improvements in the performance of T2-weighted imaging, but some inherent limitations remain. Low-signal lesions on T2-weighted imaging can be due to cancer or can be caused by benign processes such as prostatitis. Endorectal coil MRI remains limited in its ability to identify microscopic or early macroscopic capsular penetration due to restrictions on spatial resolution and motion artifacts [49]. Moreover, individual radiologist expertise is an important determinant of staging accuracy. In one study, one reader achieved an accuracy of 91%, while the other had an accuracy of only 56% [50].

Early studies from the 1990s reported accuracies of 51%-82% in distinguishing T2 and T3 disease [45,46]. More recently, erMRI has been shown to improve the prediction of neurovascular bundle invasion prior to radical prostatectomy [51]. Seltzer et al [52] demonstrated that the differences between “expert” readers and less experienced readers could be reduced by incorporating other clinical data (eg, PSA value, tumor grade) and using strict imaging criteria. Futterer et al [53] have shown that using dynamic contrast-enhanced MRI rather than T2-weighted images can improve staging performance by less experienced readers, when compared to more experienced readers. Endorectal MRI has also been shown to be accurate in demonstrating seminal vesicle invasion [54]. The combination of a tumor at the base of the prostate that extends beyond the capsule combined with low signal in the seminal vesicles that have lost normal architecture is highly predictive of seminal vesicle invasion.

More recently, similar strategies to include erMRI in a neural network have resulted in overall accuracies of 88%-91% depending on the exact implementation. These results are superior to conventional results with Partin’s tables [55]. In this study Gleason score was the most influential predictive factor, followed by erMRI results and then PSA levels. Several studies have documented that erMRI is most successful in men with intermediate-risk prostate cancer based on Partin’s tables. In these men, erMRI staging was highly predictive of PSA recurrence [56-58]. In a study involving 344 patients, Wang et al [58] demonstrated that erMRI added statistically meaningful staging data regarding ECE. Endorectal MRI has also proven helpful in directing 3D conformal radiotherapy and improving outcomes [59].

#### *Magnetic Resonance Spectroscopy*

Coakley et al demonstrated that prostate cancers have a characteristic loss of the citrate peak and gain in the choline/creatine peak on MR spectroscopic imaging [60,61]. Moreover, the ratio of choline to citrate is related to the Gleason score, suggesting that MRSI may provide information about tumor aggressiveness [61]. Improvements in diagnostic accuracy and staging have been reported [60,62]. However, a recent clinical trial under the auspices of the American College of Radiology Imaging Network® (ACRIN®) showed no benefit of MR spectroscopy for localizing prostate cancer over standard MRI alone [63]. Thus, MRSI cannot yet be considered a routine diagnostic tool.

#### *Dynamic Contrast-Enhanced Magnetic Resonance Imaging*

Prostate cancers, like many tumors, demonstrate angiogenesis that can be detected on DCE-MRI. DCE-MRI demonstrates earlier and more intense enhancement in sites of tumor compared with the normal peripheral zone. Jager et al [64] found minimal improvements in diagnostic accuracy over conventional T2-weighted scans using DCE-MRI. Padhani et al [65] showed that tumors could be distinguished from noncancerous prostate with high reliability, although the study did not specifically

address staging. DCE-MRI can improve staging performance when used in conjunction with T2-weighted images for less experienced readers when compared to more experienced readers [53]. Bloch et al [66] has demonstrated that the combination of high-spatial-resolution DCE-MRI and T2-weighted images improved assessment of extracapsular extension and yielded better results for prostate cancer staging compared with either technique independently. However, this method still suffers from a lack of a uniformly accepted analytic method and has not been tested in multi-institutional trials. Thus, it is still of unproven benefit.

#### *Nodal Staging with Magnetic Resonance Imaging*

MRI has been shown to be at least equivalent to computed tomography (CT) for detecting abnormal lymph nodes in men with prostate cancer [67]. Neither MRI nor CT scans are as accurate as laparoscopic node dissection [68]. Unfortunately, metastatic lymph nodes in prostate cancer are often small, so that conventional size criteria underestimate the extent of nodal disease. Thus, low sensitivities are observed, even in high-risk patients. Ultrasmall particles of iron oxide (USPIO) have been shown to dramatically improve sensitivity of MRI for nodal metastasis; however, the iron-based contrast agent ferumoxtran (trade name Combidex) is not yet approved by the FDA. The role of MRI for nodal staging will need to be reassessed if the FDA approves Combidex.

#### *Computed Tomography*

CT of the abdomen and pelvis suffers from poor sensitivity in detecting capsular penetration, SV+, and lymph node extension and should be reserved for use in patients with a high probability of LN+. Overall accuracy in staging was reported as 65% by Hricak et al [67] and as 67% by Platt et al [69]. For locoregional staging, such as extracapsular penetration, the accuracy has been reported as low as 24% [70]. Even with refined techniques in performing CT (3 mm slice thickness and 5 mm table increments with both IV and oral contrast), it is generally felt that CT is of little value in staging the local extent of prostatic carcinoma [69]. However, one study reports 93.7% accuracy for CT in detecting positive lymph nodes, which increases to 96.5% if CT-guided fine-needle aspiration biopsy is added [70]. This degree of accuracy was only achieved by using a threshold of 6 mm or larger as pathologic. Thus, CT of the abdomen and pelvis is of limited value in local staging and nodal staging and should be reserved for intermediate- and high-risk patients.

#### *ProstaScint (Indium Capromab)*

The reliability and usefulness of ProstaScint scan based on indium-111 radiolabeled capromab pentetide (a first-generation monoclonal antibody against prostate-specific membrane antigen [PSMA]) as a method to help initial staging in prostate cancer remain unproven at this time. Initial studies suggested that this technology may improve the detection of metastatic lymph nodes when applied to patients estimated to have a risk of LN+ of >20% [30]. Studies are needed with a sufficient number of patients with histopathological correlation [71] to document

sensitivity, specificity, positive predictive value, negative predictive value, and accuracy. Bermejo et al [71] conducted histopathological correlation in lymph nodes after ProstaScint scan in 31 patients (43 samples). The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy value were 94%, 42%, 53%, 92%, and 65%, respectively. Its limitations appear to be due to the intracellular binding site of the antibody [72] as well as nonprostatic expression of PSMA [73]. Routine ProstaScint scanning as an initial staging procedure is not justified based on evidence at this time. However, many studies show its utility in postoperative failure settings, especially to guide radiotherapeutic decisions [74-78]. New methods to suppress normal uptake as well as coregistration and fusion with CT or MRI seem to improve its utility in defining target volumes in radiotherapeutic settings [74,79,80].

#### *Bone Scan*

The radionuclide bone scan is a standard component of the evaluation for many patients diagnosed with prostate cancer. However, original work by Oesterling and others has shown that in patients with low PSA level (<10 ng/ml) who have no pain, the yield of a staging bone scan is too low to warrant its routine use [81,82]. In their experience, no patient with a PSA  $\leq$ 10 ng/ml had a positive bone scan, and only one patient in 300 with a PSA level  $\leq$ 20 ng/ml had a positive radionuclide bone scan. Such observations have been confirmed by more recent studies as well [83,84]. These studies suggest that for patients with no skeletal symptoms and a serum PSA level of 10 ng/ml or less, a staging radionuclide bone scan is not necessary; however, this recommendation has to be modified under specific circumstances such as T3 or T4 disease or a high Gleason score.

The rate of positive bone scans depends on the PSA value and Gleason score. Patients with PSA  $\leq$ 20 ng/ml and Gleason Score <8 have a 1%-13% rate of positive bone scans [85,86]. For this reason only patients with a PSA  $\geq$ 20 ng/ml (with any T stage or Gleason score), locally advanced disease (T3 or T4 with any PSA or Gleason score), or Gleason score  $\geq$ 8 (with any PSA or T stage) should be considered for a radionuclide bone scan [83,85,87]. Patients with skeletal symptoms or advanced stage disease should also be considered candidates for bone scans.

#### *Positron Emission Tomography*

The role of positron emission tomography (PET) in the staging workup of newly diagnosed and recurrent prostate cancer is still being evaluated [88-91]. It has the potential to play an important role in detecting early metastatic spread and monitoring post-therapy response. PET using the most commonly available tracer, fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG), has proved disappointing in the initial staging of prostate cancer [92]. In that study 23 of 24 primary prostate cancer lesions were not detected by FDG-PET. FDG-PET can play a role in the detection of local recurrence and/or distant metastases with increasing PSA after initial treatment failure [91]. Several additional radiotracers have been extensively studied, including C11

or F18 choline and acetate, C11 methionine, F18 fluoride, gallium-68-labeled peptides, and fluorodihydrotestosterone [88-91,93,94]. PET scans using these radiotracers can have advantages over traditional agents and may help in the clinical decision-making process, especially in patients with high-risk primary disease. For instance, the use of C11 choline or acetate PET appears to be promising for detecting nodal metastases. But such agents remain experimental or are not widely available, and so PET scanning has a limited role in the staging of prostate cancer at present.

#### *Chest Radiography*

There are no data in the literature documenting the yield of a chest radiograph. Therefore, it should be performed as part of the initial staging only with suspected metastatic disease (eg, PSA >100 ng/ml) or in patients who are heavy smokers with clinically localized disease.

#### **Summary**

- Pretreatment staging of prostate cancer should be individualized based on consideration of the clinical parameters that are predictive of the likelihood of ECE, SV+, and LN+. These clinical parameters should include: the pretreatment PSA level and the rate of rise or doubling time, the Gleason score, the palpation T stage, the number of positive biopsies, and the percentage of the specimen involved.
- Imaging in low-risk patients is controversial.
- In intermediate-risk and high-risk individuals, imaging may play a role in staging and thus in directing therapy. MRI using endorectal coil techniques appears to be the most accurate imaging test available for local staging of the prostate, providing both locoregional and nodal evaluation. The accuracy of the technique appears related to the experience of the radiologists. MR spectroscopy and dynamic contrast-enhanced MRI may be useful adjuncts in the future but are, as yet, unproven in multi-institutional trials.
- In truly high-risk patients (clinical T3, very high PSA levels, and Gleason score  $\geq$ 8), radionuclide bone scans and CT may be useful for detecting bony metastases and lymph nodes, respectively. ProstaScint scans may also play a role in detecting nodal metastases in selected high-risk patients, but the modest accuracy of this test has led most experts to consider its value dubious. PET scans with FDG are of limited value in initial staging but may be more useful in recurrent and metastatic disease.

#### **Anticipated Exceptions**

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It appears to be related to both underlying severe renal dysfunction and the administration of gadolinium-based contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR)

(ie, <30 mL/min/1.73m<sup>2</sup>), and almost never in other patients. There is growing literature regarding NSF. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates <30 mL/min/1.73m<sup>2</sup>. For more information, please see the [ACR Manual on Contrast Media](#) [95].

### Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria<sup>®</sup> [Radiation Dose Assessment Introduction](#) document.

Relative Radiation Level Designations		
Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
☼	<0.1 mSv	<0.03 mSv
☼☼	0.1-1 mSv	0.03-0.3 mSv
☼☼☼	1-10 mSv	0.3-3 mSv
☼☼☼☼	10-30 mSv	3-10 mSv
☼☼☼☼☼	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as NS (not specified).		

### Supporting Document(s)

- [ACR Appropriateness Criteria<sup>®</sup> Overview](#)
- [Procedure Information](#)
- [Evidence Table](#)

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

## Appendix 1. Staging of Prostate Cancer [29]

### *Primary Tumor (T)*

Stage	Sub-Stage	Definition
T1		Clinically unapparent tumor, neither palpable nor visible by imaging
	T1a	Incidental histologic finding; <5% of tissue resected during TURP
	T1b	Incidental histologic finding; >5% of tissue resected during TURP
	T1c	Tumor identified by needle biopsy (eg, due to elevated PSA)
T2		Tumor confined within the prostate
	T2a	Tumor involves half of one lobe or less
	T2b	Tumor involves more than half of one lobe but not both lobes
	T2c	Tumor involves both lobes
T3		Tumor extends through the prostate capsule
	T3a	Extracapsular extension (unilateral or bilateral)
	T3b	Tumor invades seminal vesicle(s)
T4		Tumor is fixed or invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles, and/or pelvic wall

### *Regional Lymph Nodes (N)*

Stage	Sub-Stage	Definition
	N0	No lymph node metastasis
	N1	Metastasis in regional lymph node(s)

### *Distant Metastasis (M)*

Stage	Sub-Stage	Definition
	M0	No distant metastasis
	M1	Distant metastasis
	M1a	Nonregional lymph node metastasis
	M1b	Bone metastasis
	M1c	Metastasis at other sites with or without bone disease