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Guideline of Guidelines: Imaging of Localized Prostate Cancer

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Introduction

In the era before the widespread adoption of PSA screening for prostate cancer, most incident cases were already advanced stage. Because treatment options, such as surgery or radiation, are thought mainly to benefit patients with localised disease, prostate cancer imaging was necessary before treatment of almost all patients. However, in the PSA era >90% of incident cases are localised, making the need for routine imaging with CT, MRI, or bone scan obsolete [1]. Numerous studies show a relatively low rate of positive staging imaging in low- and intermediate-risk patients. Recognising these trends, several professional societies issued prostate cancer imaging guidelines in the mid-1990s in an effort to curb the overuse of imaging. However, despite these longstanding guidelines, a great number of patients undergo improper imaging [2]. Given how stubborn this problem has been to eradicate, there has been a renewed interest in finding ways to decrease unnecessary imaging, including a Physician Quality Reporting System (PQRS) quality measure and a highlighting of the problem in the ‘Choosing Wisely’ campaign [3–5]. In addition to the guidelines regarding the staging of incident prostate cancer, some groups have also presented guidelines on the use of imaging to follow men with advanced disease [6]. The purpose of the present article is to summarise the main points from multiple professional society guidelines on imaging in prostate cancer to help clarify when patients with prostate cancer should be imaged and with which modalities.

National Comprehensive Cancer Network

The NCCN Guidelines for Prostate Cancer were most recently updated for 2015 and included a precise recommendation for multimodal staging imaging [6]. After the diagnosis of prostate cancer with ultrasonography (US)-guided biopsy, further imaging may be considered for patients with a life expectancy of >5 years or those who are symptomatic. The guidelines stated that pelvic CT or MRI should be used in patients with T3–T4 disease or those with T1–T2 disease, if their nomogram-predicted probability of lymph node involvement is >10%. Of note, no specific nomogram is discussed for making this decision, but several of the most common include the Memorial Sloan Kettering Cancer Center Prostate Cancer: Pre-Radical Prostatectomy Nomogram, Partin Nomogram, and the University of California, San Francisco (UCSF) Cancer of the Prostate Risk Assessment (CAPRA) score. Bone scan is recommended for all patients with Gleason score 8, T3–T4 disease, or symptoms consistent with bone metastases, as well as for patients with T1 disease who have a PSA level of >20 ng/mL or those with T2 disease who have a PSA level of >10 ng/mL.

The NCCN also recommended imaging in patients with post-treatment recurrence to evaluate for local vs distant recurrence, although the exact type of imaging is not specified. Additionally, more advanced imaging techniques, e.g. multiparametric MRI (mpMRI) and ¹¹C-choline positron emission tomography (PET)/CT were discussed in a positive light in the discussion section, but they were not incorporated into the official guidelines.

American Urological Association

According to the AUA Best Practice Statement on PSA, routine bone scan is not recommended in patients with prostate cancer with PSA levels of <20 ng/mL who have clinically localised disease, given the low risk of metastasis in patients with low PSA levels at diagnosis [7]. Bone scan may be considered in patients with PSA levels of <20 ng/mL, if the tumour is Gleason 8 on biopsy, if the clinical stage is T3, or if the history and physical symptoms suggest possible bony metastasis.

The AUA recommended considering CT/MRI in patients with PSA levels of >20 ng/mL, Gleason score 8, or clinically advanced disease, as few patients without these parameters harbour metastatic lymphadenopathy. Patients with a risk of lymph node metastasis of >20% according to estimates from the Partin tables may benefit from CT/MRI as well. These recommendations were made based upon the poor sensitivity of current cross-sectional imaging for positive lymph nodes, as the methods rely solely on size criteria. The guidelines suggested that novel cross-sectional imaging techniques, such as functional or dynamic studies, may have increased utility in the future.

European Association of Urology

The EAU Guidelines on Prostate Cancer were updated in 2014 to discuss all aspects of prostate cancer screening, diagnosis, staging, and treatment [8]. The EAU discussed the use of mpMRI in both a ‘triage’ (or before biopsy) setting, as well as a trigger for repeat targeted biopsy. Based on current data, mpMRI is recommended only for diagnosis in the latter

situation (Grade B recommendation – based on well-conducted clinical studies without randomised trials).

The recommendations for staging incident disease were divided by T-, N-, and M-stages at diagnosis, with multiple imaging methods considered for each stage category. The EAU recommended against using TRUS or CT to stage the primary lesion (Grade A recommendation – based on clinical studies of good quality with at least one randomised trial). Routine use of MRI among low-stage patients was similarly discouraged (Grade B recommendation), although mpMRI was recommended for local staging in cases where the results might change management (Grade A recommendation).

CT and MRI were the primary methods considered to stage nodal metastases in these guidelines. As these imaging methods use size to detect positive nodes, their sensitivity is low (<40%). Lymph node staging (with either CT or MRI) was recommended only for patients in whom curative treatment is planned (Grade B recommendation) and who have PSA levels of >10 ng/mL, Gleason score 8, or clinical stage T3 (Grade A recommendation).

Bone scan is typically used to stage metastatic disease, but the performance of this imaging method is highly dependent on disease characteristics. The EAU guidelines recommended using bone scan to stage patients with PSA levels of >10 ng/mL, Gleason score 8, or clinical stage T3, along with patients with symptoms consistent with bone metastasis (Grade A recommendation).

These guidelines avoided the question of imaging patients on active surveillance, although they recommended avoiding routine imaging in the management of stable patients after they have undergone treatment of any kind (Grade B recommendation).

National Institute for Health and Care Excellence

NICE issued a significantly updated clinical guideline on the diagnosis and treatment of prostate cancer in 2014 [9]. The guideline recommended consideration of mpMRI (using T2- and diffusion-weighted imaging) for men with a negative US-guided biopsy and continued suspicion for undiagnosed prostate cancer. If negative, repeat biopsy is discouraged unless the patient had high-grade prostatic intraepithelial neoplasia/atypical small acinar proliferation on initial biopsy or abnormal DRE on physical examination. A baseline MRI was also recommended before the initiation of active surveillance.

The NICE guidelines suggested that patients who are not candidates for curative treatment should not undergo routine staging with the above imaging methods. The guideline also discouraged use of CT to stage men with low- or intermediate-risk localised prostate cancer (PSA level <20 ng/mL, Gleason score 7, and clinical stage T2b) and recommended against routine bone scan in patients with low-risk disease (PSA level <10 ng/mL, Gleason score 6, and stage T1–T2a). PET was discouraged in routine clinical practice.

NICE suggested that routine MRI should not be performed in patients with biochemical relapse after radical treatment, although they felt bone scan can be useful in this situation if symptoms or PSA trends are consistent with metastatic disease.

American Board of Internal Medicine (ABIM) ‘Choosing Wisely’

‘Choosing Wisely’ is an initiative launched by Consumer Reports and the ABIM Foundation in 2012 to start conversations between patients and their doctors regarding stewardship of healthcare resources and the proper delivery of care. Various professional societies participated in Choosing Wisely by creating lists of procedures or tests that could be eliminated, both improving care and saving money simultaneously.

The AUA ‘Top Five’ list, released in 2013, focused on decreasing the inappropriate use of bone scan to stage incident prostate cancer as an area for improvement [4]. The statement suggested that bone scans should not be used routinely in patients with PSA levels of <20 ng/mL and Gleason score ≤ 6, as long as bony involvement is not suspected based on clinical examination. The American Society of Clinical Oncology (ASCO) also released their own Choosing Wisely document in 2012, which recommended against CT, PET, or bone scan evaluation of low-risk prostate cancer (clinical stage T1c/T2a, PSA level <10 ng/mL, Gleason score ≤ 6) [5]. According to their data, performing these imaging studies on low-risk patients may lead to misdiagnosis and over-treatment.

Physician Quality Reporting System

The Centers for Medicare and Medicaid Services (CMS) PQRS measures are a tool for improving quality of care through financial incentives. A component of the American College of Radiology (ACR) PQRS measures released in 2013 brought attention to the overuse of bone scan for low-risk prostate cancer [3]. Through this measure, the percentage of patients who underwent treatment for low-risk prostate cancer (PSA level ≤ 10 ng/mL, Gleason score ≤ 6, clinical stage T1c or T2a) who did not receive bone scan staging can be reported to document improved performance.

American College of Radiology

The ACR Appropriateness Criteria for specific clinical conditions are reviewed every 2 years and were most recently updated for prostate cancer in 2013 [10]. The multidisciplinary committee reviewed the evidence for each prostate cancer imaging method, including US, MRI, CT, bone scan, and PET. US (with and without colour/power Doppler) was deemed to be unable to improve staging accuracy, although investigational techniques like contrast-enhanced and three-dimensional US may improve performance. Imaging with Indium Capromab (a monoclonal antibody against prostate-specific membrane antigen) and PET were not recommended for initial staging due to insufficient evidence at this time.

ACR recommended that for patients with low-risk disease (defined as PSA level ≤ 10 ng/mL, Gleason score ≤ 6, and clinical stage T1 or T2a), CT is usually not appropriate for staging. For intermediate-risk patients (PSA level 10–20 ng/mL, Gleason score 7, clinical stage T2b) CT may be appropriate, while high-risk patients (PSA level > 20 ng/mL, Gleason score 8–10,

clinical stage T2c) are good candidates. These recommendations were based on data suggesting CT for locoregional and nodal staging suffers from very poor accuracy (12–55%), and yet it is widely overused. CT is not sensitive for detecting extraprostatic extension or seminal vesicle invasion.

The ACR only recommends bone scan in high-risk patients (as defined above) with the caveat that it may be appropriate in intermediate-risk patients as well. Studies have shown that patients with a low PSA level, Gleason score, and clinical stage have a very low probability of positive bone scan.

A significant portion of this update was focused on the use of MRI in the local staging of prostate cancer. The ACR recommended that patients with low-risk prostate cancer (defined above) may benefit from MRI with and without contrast for local staging. Patients with intermediate- or high-risk cancer (defined above) are usually appropriate for local MRI staging, along with patients with a clinical concern for undetected prostate cancer who have already undergone multiple negative biopsies. MRI appears to be only as accurate as CT to evaluate metastatic lymphadenopathy, thus it was discouraged for this indication alone.

Prior literature demonstrates that increased magnet strength improves accuracy, although the use of an endorectal coil is not universally recommended by the ACR. Each MRI method (T2-weighted, MR spectroscopy, diffusion-weighted, and contrast-enhanced) was discussed in depth, with MR spectroscopy and contrast-enhanced MRI singled out as likely low-utility studies when performed alone. The ACR suggested that mpMRI incorporating multiple techniques (e.g. T2-weighted and diffusion-weighted imaging) has emerged as the best available method for imaging the prostate.

Conclusion

Most patients with prostate cancer continue to undergo unnecessary imaging to stage their disease. Each of the above guidelines, including those from the AUA, EAU, and NCCN, focused on discouraging the use of inappropriate imaging among low- and/or intermediate-risk patients, although the exact definitions of each risk category vary between organisations. Bone scan was typically only recommended for high-risk patients or those with symptoms consistent with bony disease. The guidelines consistently recommended against CT staging for low-risk patients but recommended consideration for intermediate- and high-risk patients. MRI was not routinely recommended, although multiple guidelines suggest that, if it is to be performed, a mpMRI appears to be the most accurate of the MRI modalities for staging local tumour extent. Additional imaging, such as PET, were occasionally discussed but were not recommended, probably because of poor clinical performance or insufficient evidence. Clearly, the current health policy environment favours decreased use of inappropriate staging imaging among low-risk patients, although use of CT, MRI, and bone scan in the appropriate higher-risk patient can be very helpful in clinical staging and other evaluations of prostate cancer (Tables 1 and 2). As professional societies develop guidelines statements and policy makers implement strategies to optimise utilisation of healthcare resources, it is important that clinicians focus on assessing each patient

individually and appropriately, lest patients fall victim to the unintended consequences of the best laid plans [11,12].

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Conflicts of Interest

Danil V. Makarov is a consultant for Castlight Health and a consultant for the USA Food and Drug Administration.

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Abbreviations

ABIM	American Board of Internal Medicine
ACR	American College of Radiology
ASCO	American Society of Clinical Oncology
EAU	European Association of Urology
mpMRI	multiparametric MRI
NCCN	National Comprehensive Cancer Network
NICE	National Institute for Health and Care Excellence
PET	positron emission tomography
PQRS	Physician Quality Reporting System
US	ultrasound/ultrasonography

Key points

- TRUS is the current standard for local imaging at time of biopsy, although it performs poorly in evaluating stage.
- CT should be used for local/distant staging only among patients with intermediate- or high-risk disease.
- Bone scan should be used to evaluate for metastatic disease only among patients with high-risk prostate cancer or symptoms consistent with bony involvement.
- mpMRI is investigational but may prove useful before initiation of active surveillance and when considering repeat biopsy after initial negative biopsy.
- Additional imaging techniques are being evaluated for more accurate staging but are not recommended at this time.

Table 1
Guidelines for prostate cancer imaging use in specific clinical situations by organisation.

	NCCN	AUA	EAU	NICE	Choosing Wisely	PQRS	ACR
Pre-biopsy			✓				
After negative biopsy			✓	✓			✓
Staging after diagnosis	✓	✓	✓	✓	✓	✓	✓
Active surveillance				✓			
Post-treatment	✓		✓	✓			

Table 2

Summary of guidelines for use of CT/MRI and bone scan by organisation.

	NCCN	AUA	EAU	NICE	AUA Choosing Wisely	ASCO Choosing Wisely	PQRS	ACR
CT/MRI	Stage T3 Chance of LN involvement >10%	Gleason 8 PSA level >20 ng/mL	Stage T3 Gleason 8	NOT IF Stage T2b		NOT IF Stage T2a		Stage T2b Gleason 7
		Chance of LN involvement >20%	PSA level >10 ng/mL	Gleason 7		Gleason 6		PSA level >10 ng/mL
				PSA level <20 ng/mL		PSA level <10 ng/mL		
Bone scan	Stage T3 Gleason 8	Stage T3 Gleason 8	Stage T3 Gleason 8 ng/mL	NOT IF Stage T2a	NOT IF Gleason 6	NOT IF Stage T2a	NOT IF Stage T2a	Stage T2c Gleason 8
	T1 with PSA level >20 ng/mL	PSA level >20 ng/mL	PSA level >10 ng/mL	Gleason 6	PSA level <20 ng/mL	Gleason 6	Gleason 6	PSA level >20 ng/mL
	T2 with PSA level >10 ng/mL Bony symptoms	Bony symptoms	Bony symptoms	PSA level <10 ng/mL	[Unless bony symptoms]	PSA level <10 ng/mL	PSA level <10 ng/mL	

LN, lymph node.