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Clinical-Prostate cancer

Do patients who undergo multiparametric MRI for prostate cancer benefit from additional staging imaging? Results from a statewide collaborative

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Abstract

Objectives: Prostate cancer (CaP) staging traditionally includes computed tomography (CT) and technetium-99m bone scintigraphy (BS) for assessment of lymph node (LN) and bone metastases, respectively. In recent years, multiparametric magnetic resonance imaging (mpMRI) has been used in diagnostic assessment of CaP. We sought to compare the accuracy of mpMRI to CT and BS for pretreatment staging.

Materials and methods: Using the Michigan Urological Surgery Improvement Collaborative registry, we identified men undergoing pretreatment mpMRI in addition to CT and/or BS in 2012 to 2018. Imaging reports were classified as positive, negative, or equivocal for detection of LN and bone metastases. A best value comparator (BVC) was used to adjudicate metastatic status in the absence of pathologic data. mpMRI accuracy was calculated using pessimistic (equivocal=positive) and optimistic (equivocal = negative) interpretations. We compared the diagnostic performance of mpMRI, CT, and BS in detecting metastases.

Results: In total, 364 men underwent CT and mpMRI, and 646 underwent BS and mpMRI. Based on the BVC, 52 men (14%) harbored LN metastases and 38 (5.9%) harbored bone metastases. Sensitivity of mpMRI for LN metastases was significantly higher than CT (65−73% vs 38%, $P < 0.005$), and specificity of mpMRI and CT were 97% to 99% and 99% ($P = 0.2−0.4$), respectively. For bone metastases, BS sensitivity was 68% as compared to 42% to 71% ($P = 0.02−0.83$) for mpMRI. Specificity for bone metastases was 95% to 99% across all modalities.

Conclusions: Using statewide data, mpMRI appears superior to CT and comparable to BS for detection of LN and bone metastases, respectively. Pretreatment mpMRI may obviate the need for additional staging imaging.

Keywords: Prostate cancer; Michigan Urological Surgery Improvement Collaborative; Multiparametric magnetic resonance imaging; Best value comparator

1. Introduction

Prostate cancer (CaP) is the second most common cause of cancer-related death in North American men [1]. Localized CaP is curable with definitive intervention such as radical prostatectomy or radiotherapy, but metastatic CaP remains incurable with systemic therapy despite recent therapeutic advances [2-4]. Although less than 10% of men

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harbor metastases at the time of diagnosis, management of metastatic CaP differs substantially from localized CaP [5,6]. Therefore, accurate staging is essential for optimal management of men with newly diagnosed CaP [7,8].

Clinical guidelines from the National Comprehensive Cancer Network (NCCN) recommend abdominopelvic imaging with computed tomography (CT) or multiparametric magnetic resonance imaging (mpMRI) in men with intermediate- and high-risk CaP and increased probability of lymph node (LN) involvement [5,6]. Imaging with technetium-99m bone scintigraphy (BS) is recommended in men diagnosed with high-risk CaP and select patients with intermediate-risk disease [5,6]. In recent years, technological advances have led to more widespread use of mpMRI as part of the diagnostic workup of CaP [9,10]. Limited data have suggested that mpMRI could have superior diagnostic sensitivity to CT and BS in the detection of LN and bone metastases, respectively [11]. Although CT and BS remain widely used in CaP staging, these findings raise the possibility that use of mpMRI alone could replace the need for conventional imaging with CT and BS.

The Michigan Urological Surgery Improvement Collaborative (MUSIC) is a consortium of 44 urologic practices aiming to improve the quality of CaP and urologic care in Michigan. Based on this unique statewide collection of patient-level data, we aimed to assess the performance of mpMRI, CT, and BS for staging of CaP. We herein evaluated the performance of mpMRI as compared to CT and BS for the detection of LN and bone metastases.

2. Methods

2.1. Study population

MUSIC is comprised of 44 diverse academic and community practices throughout Michigan, accounting for approximately 90% of the practicing urologists in the state [12]. All patient-level data are entered into a web-based registry by trained data abstractors. Each MUSIC practice obtained or was exempted approval for collaborative participation from a local ethics review board. In addition, a site visit is performed at least annually in order to assess for and assist with any quality improvement opportunities that are identified. Overall, between January 2012 and September 2018, 32,582 men in the MUSIC registry were diagnosed with CaP. Of these men, 3,595 underwent mpMRI. The final study cohort included men who underwent staging abdominopelvic CT and/or BS within 90 days of mpMRI and had longitudinal clinical follow-up.

2.2. Imaging

CT assessment of LNs consisted of contrast-enhanced imaging of the pelvis, abdomen, and/or thorax. LNs were considered positive on CT and mpMRI when >8 mm in the short-axis and/or there was specific mention of "suspicious" morphological features [13]. BS was performed according to practice parameters established by the American College of Radiology and the Society for Pediatric Radiology [14]. The most common protocol included intravenous injection of technetium-99m medronate (methylene diphosphonate) with dose determined by local practice standards (typically 15−30 mCi). A gamma camera was used to obtain anterior and posterior delayed whole-body imaging at 2 hours with additional spot images as needed.

Prostate mpMRI was performed on 3T or 1.5T MRI scanners according to local protocols. The most common protocol employed 3.0 GE Discovery MR750 scanners utilizing an 8-channel phased array coil without an endorectal coil. Recommended series included full field of view T2 axial images from the pelvis up to the aortic bifurcation to assess for LN involvement; diffusion-weighted imaging (DWI) utilizing b-values of 800, 1,400, and 2,000; and axial dynamic-contrast-enhanced images with a temporal resolution of 14 seconds per phase. Lesions noted as "enlarged" or "indeterminate" on mpMRI, but not meeting size criteria (>8 mm in short-axis) were classified as equivocal. Patient charts were retrospectively reviewed, and imaging interpretations were recorded as positive, negative, or equivocal based on the attending radiologist.

2.3. Best value comparator

Patients were managed at the discretion of their physicians and follow-up data were abstracted as previously described [15]. Because LN and bone biopsies are not routinely performed to confirm positive imaging findings, a best value BVC was used to determine metastatic status in the absence of a histologic gold standard [16-18]. As described by Lecouvet et al. [18], the BVC consisted of review of all imaging tests, treatments administered, and clinical outcomes to date, and; thus, a determination of metastatic status was performed based on a comprehensive assessment of all available clinical data. These data were independently reviewed by study physicians (J.J.T. and B.R.L.) who, based on these data, determined in consensus a final diagnosis of positive or negative for LN and bone metastases at time of staging. In cases of concordance, the BVC was as determined. In cases of discordance ($n = 7$), the final determination was made by a third study physician (J.E.M.).

2.4. Statistical analysis

Demographic and clinical features of the study population were compared across imaging modalities. The primary analysis compared interpretation of imaging findings (i.e., positive or negative) with LN and bone metastatic status as determined by BVC adjudication. Prostate mpMRI and abdominopelvic CT were compared for detection of LN metastases; mpMRI and BS were compared for detection

Table 1
Study population.

	MRI alone	MRI with additional imaging (CT or BS)	*P*	MRI, CT, and BS	MRI and BS	MRI and CT	*P*
No. patients	2913	681		329	317	35	
Age, median (IQR)	64.9 (59.5-69.7)	66.7 (61.3-71.3)	<.001	66.2 (61.1-70.5)	67.2 (61.7-72.0)	67.0 (59.1-70.3)	0.07
PSA, median (IQR)	5.9 (4.5-8.1)	8.6 (5.7-16.2)	<.001	8.6 (5.8-18.7)	8.6 (5.4-16.0)	7.9 (5.5-12.9)	0.34
Initial PSA							
<10	2422 (85%)	383 (58%)	<.001	177 (55%)	182 (59%)	24 (69%)	0.11
10–20	355 (13%)	152 (23%)		68 (21%)	76 (25%)	8 (23%)	
>20	66 (2.3%)	130 (20%)		75 (23%)	52 (17%)	3 (8.6%)	
Clinical T-stage							
T1	2480 (85%)	381 (56%)	<.001	175 (53%)	181 (57%)	25 (71%)	0.28
T2	364 (13%)	247 (36%)		125 (38%)	113 (36%)	9 (26%)	
T3/T4	14 (0.5%)	39 (5.7%)		20 (6.1%)	19 (6.0%)	0 (0%)	
Unknown	55 (1.9%)	14 (2.1%)		9 (2.7%)	4 (1.3%)	1 (2.9%)	
Biopsy GS (Grade Group)							
6 (GG1)	1531 (59%)	64 (10%)	<.001	22 (7.2%)	32 (11%)	10 (31%)	<.001
3 + 4 = 7 (GG2)	741 (29%)	104 (17%)		47 (15%)	48 (17%)	9 (28%)	
4 + 3 = 7 (GG3)	226 (8.8%)	117 (19%)		53 (17%)	60 (21%)	4 (13%)	
8 (GG4)	54 (2.1%)	159 (26%)		77 (25%)	81 (29%)	1 (3.1%)	
9–10 (GG5)	30 (1.2%)	175 (28%)		105 (35%)	62 (22%)	8 (25%)	
NCCN risk group							
Low	1307 (49.8%)	43 (6.6%)	<.001	18 (5.6%)	19 (6.3%)	6 (17%)	<.001
Intermediate	1129 (43.0%)	179 (27%)		72 (23%)	90 (30%)	17 (49%)	
High	188 (7.2%)	432 (66%)		228 (72%)	192 (64%)	12 (34%)	

BS = bone scintigraphy; CT = computed tomography; MRI = magnetic resonance imaging; IQR = interquartile range.

of bone metastases. Given a proportion of mpMRI findings were equivocal, the accuracy of mpMRI was calculated using both an optimistic (equivocal = nonmetastatic) and pessimistic (equivocal = metastatic) reading [18]. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each imaging modality was determined. Sensitivity and specificity were compared between different imaging modalities using McNemar test. Statistical analyses were performed using with SAS 9.4 and statistical significance was considered at $P < 0.05$.

3. Results

3.1. Study population

Overall, 3,595 patients with newly diagnosed CaP underwent prostate mpMRI as part of a diagnostic or staging workup. Of these, 329 (9.2%) also underwent CT and BS, 317 (8.8%) underwent BS only, and 35 (1.0%) underwent CT only, yielding the overall study cohort of 681 men who received mpMRI and at least one additional imaging study. As compared to men who underwent mpMRI alone, men who had additional imaging with CT and/or BS had higher serum prostate-specific antigen (PSA) (median 8.6 ng/ml vs. 5.9 ng/ml, $P < 0.001$), higher biopsy Gleason score ($P < 0.001$), and were of higher NCCN risk classification ($P < 0.001$; Table 1). Similarly, men who underwent mpMRI with both CT and BS tended to harbor higher-risk disease than those who underwent mpMRI with either CT or BS ($P < 0.001$).

3.2. CT vs. mpMRI

There were 364 men (329 + 35) who underwent CT in addition to mpMRI. CT assessment of LNs was positive in 24 patients (6.6%) and negative in 340 patients (93%), and mpMRI assessment of LNs was positive in 36 patients (10%), equivocal in 11 (3.0%), and negative in 317 (87%; Table 2A). Based on BVC adjudication, 52 men (14%) who underwent CT and mpMRI were determined to be positive for LN metastases (Table 3A). In this population, LN metastases were detected by CT in 20 men (38%). Considering equivocal mpMRI findings as positive (pessimistic reading), mpMRI was positive for LN metastases in 38 men, demonstrating significantly higher sensitivity than CT (73% vs. 38%, $P < 0.001$). When equivocal mpMRI

Table 2
Correlation of MRI findings with (A) CT scan for lymph node metastases and (B) bone scan for bone metastases.

		Multiparametric MRI			
		Positive	Equivocal	Negative	Total
(A)					
CT Scan	Positive	16	1	7	24
	Negative	20	10	310	340
	Total	36	11	317	364
(B)					
Bone scan	Positive	13	4	24	41
	Negative	11	30	564	605
	Total	24	34	588	646

Table 3
Imaging findings and BVC assessment of (A) LN metastases and (B) bone metastases.

(A)

		BVC for LN metastases[a,b]		
		Positive ($n = 52$)	Negative ($n = 312$)	Total ($n = 364$)
CT	Positive	20	4	24
	Negative	32	308	340
mpMRI (pessimistic)	Positive	38	9	47
	Negative	14	303	317
mpMRI (optimistic)	Positive	34	2	36
	Negative	18	310	328

(B)

		BVC for bone metastases[b,c]		
		Positive ($n = 38$)	Negative ($n = 608$)	Total ($n = 646$)
CT	Positive	26	15	41
	Negative	12	593	605
mpMRI (pessimistic)	Positive	27	31	58
	Negative	11	577	588
mpMRI (optimistic)	Positive	16	8	24
	Negative	22	600	622

BVC = best value comparator; CT = computed tomography; LN = lymph node; mpMRI = multiparametric magnetic resonance imaging.
[a] Pessimistic: equivocal lesions classified as positive/metastatic.
[b] Optimistic: equivocal readings classified as negative/nonmetastatic.
[c] Pessimistic: equivocal readings classified as positive/metastatic.

findings were considered negative (optimistic reading), mpMRI sensitivity for LN metastases remained significantly higher than CT (65% vs. 38%, $P = 0.003$). Among the 312 patients negative for LN metastasis, CT was negative in 308 (98.7%), pessimistic mpMRI reading was negative in 303 (specificity 97.1% vs. 98.7%, $P = 0.13$), and optimistic mpMRI reading was negative in 310 (specificity 99.4% vs. 98.7%, $P = 0.41$). The sensitivity, specificity, PPV, and NPV of CT and mpMRI for detection of LN metastases are listed in Table 4.

3.3. BS vs. mpMRI

There were 646 men (329 + 317) who underwent BS and mpMRI. Overall, BS imaging was positive for metastases in 41 patients (6.3%) and negative in 605 patients (94%; Table 2B). Assessment of bone metastases on mpMRI was positive in 24 patients (3.7%), equivocal in 34 patients (5.3%), and negative in 588 (91%). After BVC adjudication, 38 patients (5.9%) were determined to be positive for bone metastasis (Table 3B). Among them, BS was

Table 4
Sensitivity, specificity, PPV, and NPV of imaging modalities.

	LN metastases			Bone metastases		
	CT	mpMRI (pessimistic)	mpMRI (optimistic)	BS	mpMRI (pessimistic)	mpMRI (optimistic)
Sensitivity (%)	38	73*	65*	68	71	42**
Specificity (%)	98.7	97.1	99.4	97.5	95**	98.7
PPV (%)	83	81	94	63	47	67
NPV (%)	91	95.6	95	98.0	98.1	96.5

BS = bone scintigraphy; CT = computed tomography; LN = lymph node; mpMRI = multiparametric magnetic resonance imaging; NPV = negative predictive value; PPV = positive predictive value.
Pessimistic: equivocal readings classified as positive/metastatic.
Optimistic: equivocal readings classified as negative/nonmetastatic.
* $P < 0.05$ for comparison to CT.
** $P < 0.05$ for comparison to BS.

classified as positive in 26 men (68%), and mpMRI was classified as positive in 27 (71%) and 16 men (42%) based on pessimistic and optimistic mpMRI readings, respectively. Thus, the sensitivity of pessimistic mpMRI was comparable to BS (71% vs. 68%, $P = 0.83$), and optimistic mpMRI was significantly inferior to BS (42% vs. 68%, $P = 0.018$). As compared to 97.5% using BS, the specificity of pessimistic and optimistic mpMRI was 95% ($P = 0.014$) and 98.7% ($P = 0.13$), respectively. The sensitivity, specificity, PPV, and NPV of BS and mpMRI for bone metastases are listed in Table 4.

4. Discussion

Appropriate staging of newly diagnosed CaP is critical to guiding patient management. Among intermediate- and high-risk patients at risk for metastases, staging has traditionally included abdominopelvic CT and BS [5,6]. The diagnostic approach to CaP has evolved; however, and a substantial number of men undergo mpMRI during the initial diagnostic evaluation [9,10]. While several studies have evaluated the use of mpMRI for detection of localized CaP [18-22], the accuracy of mpMRI in detecting LN and bone metastases remains poorly characterized. In particular, it is unclear whether CT and/or BS remain necessary for staging in men who previously underwent mpMRI.

Using prospective data from the statewide MUSIC registry, we found that the performance characteristics of mpMRI varied based on the interpretation of a minority of equivocal cases. For detection of LN metastases, when equivocal cases were classified as positive (pessimistic reading), mpMRI had greater sensitivity than CT (73% vs. 39%, $P < 0.001$) and maintained comparable specificity (97.1% vs. 98.7%, $P = 0.17$). When equivocal LN lesions were classified as negative (optimistic reading), mpMRI again demonstrated improved sensitivity (65% vs. 39%, $P = 0.003$) to CT, with similar specificity (99.4% vs. 98.7%, $P = 0.41$). For bone metastases, the pessimistic mpMRI reading had comparable sensitivity to BS (71% vs. 68%, $P = 0.83$). Although specificity was slightly reduced with this approach (95% vs. 97.5%, $P = 0.014$), the absolute difference of 2.5% is likely to be of limited clinical significance. The optimistic mpMRI reading demonstrated decreased sensitivity (42% vs. 68%, $P = 0.018$) and comparable specificity (98.7% vs. 97.5%, $P = 0.13$) to BS. Ultimately, these data suggest that mpMRI may be superior to CT for detection of LN metastases, and, when considered using a pessimistic approach where equivocal cases are classified as metastatic [18], mpMRI appears to be at least comparable to BS for detection of bone metastases.

Previous studies have directly compared CT and mpMRI for LN metastases in a limited number of patients [18,23]. Heck et al. assessed patient- and field-based performance of CT and diffusion-weighted MRI (DWI) for LN staging in 33 men who underwent radical prostatectomy and extended pelvic LN dissection [23]. On patient-level analysis, they found that DWI had equivalent sensitivity (57.1% vs. 57.1%) and improved specificity (78.9% vs. 68.4%) compared to CT. Similarly, Lecouvet et al. prospectively compared CT and whole-body MRI (wbMRI) findings to the BVC in 100 men with CaP [18]. Interestingly, they observed similar sensitivities of CT and wbMRI (ranging from 77% to 82% for both modalities), while we observed greater sensitivity with mpMRI. Such findings may be secondary to the era of their study (2007–2010), and it is likely that advances in MRI in the last decade have improved detection of LN metastases relative to CT. It is also notable that the sensitivities of 77% to 82% the authors observed for CT and wbMRI are higher than those observed in our experience. This is likely due to differences in study populations, as their cohort included only high-risk CaP, while ours included low- and intermediate-risk disease.

Previous studies have suggested that wbMRI may modestly improve upon BS for the detection of bone metastases. For example, Lecouvet et al. observed sensitivity/specificity of 98% to 100%/98% to 100% for wbMRI as compared to 86%/98% for BS [18]. Similarly, in a cohort of 30 consecutive patients with newly diagnosed high-risk CaP, Pasoglou et al. observed sensitivity/specificity of 100%/100% for wbMRI as compared to 89%/100% for BS [24]. It is notable that the sensitivities observed in these studies for wbMRI and BS were higher than we determined. Again, this is likely due to the fact that these cohorts were exclusively composed of high-risk patients. Nonetheless, we observed a similar relationship between modalities, as the mpMRI-pessimistic approach demonstrated a slightly higher but ultimately similar sensitivity to BS (71% vs. 68%, $P = 0.83$). Notably, diagnostic mpMRI in our cohort was generally limited to the pelvis, as compared to wbMRI in these studies. Thus, lower sensitivity of mpMRI we observed is likely secondary to bone metastases located outside the imaging field of view. Nonetheless, mpMRI appears to be at least comparable to BS for detecting bone metastases and potentially superior in the higher-risk population most frequently indicated for staging.

Our findings draw attention to several points. First, the classification of equivocal or “borderline” cases appears to impact the performance of mpMRI considerably. The pessimistic interpretation, in which mpMRI-indeterminate lesions were considered positive, demonstrated superior sensitivity and comparable specificity to optimistic readings. Thus, consistent with previous analyses [18,25], the optimal approach to such cases may depend on specific clinical settings. As such, subsequent studies should clearly define “equivocal” readings and provide performance characteristics based on differing approaches. At the same time, irrespective of the use of mpMRI, it appears that some men diagnosed with CaP undergo unnecessary imaging studies. For example, among the 329 men who underwent all 3 imaging modalities, 55% had a PSA <10 ng/ml, 53% were clinical stage T1, and 17% harbored primary Gleason pattern 3 cancer. While our study approach cannot assess the

unique context of each clinical decision, it is likely that most patients not meeting guideline-based criteria lacked a specific clinical indication for staging. Similar observations from previous authors have led to resource-conscious initiatives such as the Choosing Wisely campaign [26,27], which recommends against CT or BS for newly diagnosed low-grade CaP. Although only 6.6% of our cohort harbored NCCN low-risk CaP, it is likely that increased awareness can help to further reduce this phenomenon, limiting the cost and morbidity associated with unnecessary testing.

There are notable limitations of our study. First, although use of the BVC adjudication method has been supported in several previous studies [17,18,28], it is important to acknowledge that this approach includes subjective assessment of clinical data and is not equivalent to histologic verification of metastatic status. Second, as described, a proportion of lesions were reported as equivocal on mpMRI. We, therefore, measured the performance of mpMRI when classifying these lesions as positive (pessimistic) or negative (optimistic), providing the range of performance metrics. Third, prostate mpMRI at most centers includes focused imaging of the pelvis and, thus did not capture metastases outside of this template (that would be captured in a standard skeletal survey). Furthermore, our data did not capture the location of metastases that were detected by BS, but not mpMRI. Thus, it is unclear how often false-negative mpMRI readings were secondary to lesion location outside the imaging field of view. Therefore, in the absence of expanding the template from pelvic mpMRI to MRI of the whole skeleton, it is unlikely that mpMRI can replace full skeletal BS in patients at high risk of metastasis. Finally, this multi-center study did not have centralized radiologic review, and imaging reads are subject to intrareader variability. Still, such limitations represent the reality of urologic practice and may be more representative of real-world findings.

5. Conclusions

These data suggest that mpMRI offers superior performance to CT and comparable performance to BS for detection of LN and bone metastases, respectively. Importantly, the overall accuracy of mpMRI is dependent on the classification of equivocal lesions, and a pessimistic reading appeared to yield a more optimal balance of sensitivity and specificity. Further studies should aim to better characterize the optimal approach to equivocal cases. Nonetheless, more widespread use of mpMRI could obviate the need for additional staging imaging in men who undergo mpMRI as part of their diagnostic evaluation.

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References

[1] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin. 2018;68:7–30.
[2] Sweeney CJ, Chen YH, Carducci M, Liu G, Jarrard DF, Eisenberger M, et al. Chemohormonal therapy in metastatic hormone-sensitive prostate cancer. N Engl J Med 2015;373:737–46.
[3] James ND, de Bono JS, Spears MR, Clarke NW, Mason MD, Dearnaley DP, et al. Abiraterone for prostate cancer not previously treated with hormone therapy. N Engl J Med 2017;377:338–51.
[4] Smith MR, Saad F, Chowdhury S, Oudard S, Hadaschik BA, Graff JN, et al. Apalutamide treatment and metastasis-free survival in prostate cancer. N Engl J Med 2018;378:1408–18.
[5] Mohler J, Bahnson RR, Boston B, Busby JE, D'Amico A, Eastham JA, et al. NCCN clinical practice guidelines in oncology: prostate cancer. J Natl Compr Canc Netw 2010;8:162–200.
[6] Thompson I, Thrasher JB, Aus G, Burnett AL, Canby-Hagino ED, Cookson MS, et al. Guideline for the management of clinically localized prostate cancer: 2007 update. J Urol 2007;177:2106–31.
[7] Andriole GL, Crawford ED, Grubb RL 3rd, Buys SS, Chia D, Church TR, et al. Mortality results from a randomized prostate-cancer screening trial. N Engl J Med 2009;360:1310–9.
[8] Fueger BJ, Helbich TH, Schernthaner M, Zbyn S, Linhart HG, Stiglbauer A, et al. Diagnose importance of multiparametric magnetic resonance tomography for prostate cancer. Radiology 2011;51:947–54.
[9] Rosenkrantz AB, Hemingway J, Hughes DR, Duszak R Jr., Allen B Jr., Weinreb JC. Evolving use of prebiopsy prostate magnetic resonance imaging in the medicare population. J Urol 2018;200:89–94.
[10] Kim SP, Karnes RJ, Mwangi R, Van Houten H, Gross CP, Gershman B, et al. Contemporary trends in magnetic resonance imaging at the time of prostate biopsy: results from a large private insurance database. Eur Urol Focus 2019; pii: S2405-4569(19)30102-6. https://doi.org/10.1016/j.euf.2019.03.016.
[11] De Visschere PJL, Standaert C, Futterer JJ, Villeirs GM, Panebianco V, Walz J, et al. A systematic review on the role of imaging in early recurrent prostate cancer. Eur Urol Oncol 2019;2:47–76.
[12] Ginsburg KB, Arcot R, Qi J, Linsell SM, Kaye DR, George AK, et al. Confirmatory magnetic resonance imaging with or without biopsy impacts decision making in newly diagnosed favorable risk prostate cancer. J Urol 2019;201:923–8.
[13] Meijer HJ, Debats OA, van Lin EN, Witjes JA, Kaanders JH, Barentsz JO. A retrospective analysis of the prognosis of prostate cancer patients with lymph node involvement on MR lymphography: who might be cured. Radiat Oncol 2013;8:190.
[14] Radiology ACo. ACR–SPR Practice parameter for the performance of skeletal scintigraphy (bone scan). 2018.
[15] Womble PR, Dixon MW, Linsell SM, Ye Z, Montie JE, Lane BR, et al. Infection related hospitalizations after prostate biopsy in a statewide quality improvement collaborative. J Urol 2014;191:1787–92.
[16] Venkitaraman R, Cook GJ, Dearnaley DP, Parker CC, Khoo V, Eeles R, et al. Whole-body magnetic resonance imaging in the detection of skeletal metastases in patients with prostate cancer. J Med Imaging Radiat Oncol 2009;53:241–7.
[17] Lecouvet FE, Geukens D, Stainier A, Jamar F, Jamart J, d'Othee BJ, et al. Magnetic resonance imaging of the axial skeleton for detecting bone metastases in patients with high-risk prostate cancer: diagnostic and cost-effectiveness and comparison with current detection strategies. J Clin Oncol 2007;25:3281–7.
[18] Lecouvet FE, El Mouedden J, Collette L, Coche E, Danse E, Jamar F, et al. Can whole-body magnetic resonance imaging with diffusion-weighted imaging replace Tc 99m bone scanning and computed

tomography for single-step detection of metastases in patients with high-risk prostate cancer. Eur Urol. 2012;62:68–75.

[19] Siddiqui MM, Rais-Bahrami S, Turkbey B, George AK, Rothwax J, Shakir N, et al. Comparison of MR/ultrasound fusion-guided biopsy with ultrasound-guided biopsy for the diagnosis of prostate cancer. JAMA 2015;313:390–7.

[20] Curci NE, Lane BR, Shankar PR, Noyes SL, Moriarity AK, Kubat A, et al. Integration and diagnostic accuracy of 3T nonendorectal coil prostate magnetic resonance imaging in the context of active surveillance. Urology 2018;116:137–43.

[21] Emmett L, Metser U, Bauman G, Hicks RJ, Weickhardt A, Davis ID, et al. A prospective, multi-site, international comparison of F-18 fluoro-methyl-choline, multi-parametric magnetic resonance and Ga-68 HBED-CC (PSMA-11) in men with high-risk features and biochemical failure after radical prostatectomy: clinical performance and patient outcomes. J Nucl Med 2018.

[22] Li M, Huang Z, Yu H, Wang Y, Zhang Y, Song B. Comparison of PET/MRI with multiparametric MRI in diagnosis of primary prostate cancer: a meta-analysis. Eur J Radiol 2019;113:225–31.

[23] Heck MM, Souvatzoglou M, Retz M, Nawroth R, Kubler H, Maurer T, et al. Prospective comparison of computed tomography, diffusion-weighted magnetic resonance imaging and [11C]choline positron emission tomography/computed tomography for preoperative lymph node staging in prostate cancer patients. Eur J Nucl Med Mol Imaging 2014;41:694–701.

[24] Pasoglou V, Larbi A, Collette L, Annet L, Jamar F, Machiels JP, et al. One-step TNM staging of high-risk prostate cancer using magnetic resonance imaging (MRI): toward an upfront simplified "all-in-one" imaging approach? Prostate 2014;74:469–77.

[25] Even-Sapir E, Metser U, Mishani E, Lievshitz G, Lerman H, Leibovitch I. The detection of bone metastases in patients with high-risk prostate cancer: 99mTc-MDP planar bone scintigraphy, single- and multi-field-of-view SPECT, 18F-fluoride PET, and 18F-fluoride PET/CT. J Nucl Med 2006;47:287–97.

[26] Makarov DV, Desai RA, Yu JB, Sharma R, Abraham N, Albertsen PC, et al. The population level prevalence and correlates of appropriate and inappropriate imaging to stage incident prostate cancer in the medicare population. J Urol 2012;187:97–102.

[27] Wu LM, Gu HY, Zheng J, Xu X, Lin LH, Deng X, et al. Diagnostic value of whole-body magnetic resonance imaging for bone metastases: a systematic review and meta-analysis. J Magn Reson Imaging 2011;34:128–35.

[28] Venkitaraman R, Cook GJ, Dearnaley DP, Parker CC, Huddart RA, Khoo V, et al. Does magnetic resonance imaging of the spine have a role in the staging of prostate cancer. Clin Oncol (R Coll Radiol) 2009;21:39–42.