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Role of Multiparametric Magnetic Resonance Imaging of the Prostate in Surgical Planning of Radical Prostatectomy

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Abstract

The nerve sparing technique offers better functional outcomes (urinary continence and erectile function) at cost of arguably higher risk of positive surgical margins. The EAU guidelines affirm there is no conclusive data to recommend for or against nerve sparing. Therefore, the preoperative available factors (e.g. digital-rectal-examination and bioptic findings, and multiparametric MRI) are discretionarily used by the urologist while counselling patients undergoing radical prostatectomy regarding a nerve sparing technique. Although the prostate multiparametric MRI is routine practice to guide nerve sparing nowadays, its accuracy performance for local staging is far from consistent among the literature, ranging 0% to 100%. Our study aims at assessing its role in surgical planning in a real-world workframe. 356 consecutive patients undergone radical prostatectomy were enrolled at two institutions. Their preoperative local staging was compared to their wholemount pathological findings to assess whether being confirmed as localized or locally advanced. Local staging was correct in only 37% of overall population, in 28% of patients with positive surgical margins, in 37% of those with multifocal positive surgical margins and in 33% of high-risk patients with positive surgical margins. We confirm an important role of multiparametric MRI of the prostate in surgical planning of radical prostatectomy; nevertheless, our results also demonstrate that a peripherally performed mpMRI is not reliable enough to guide nerve sparing as a stand-alone technique. Finally, we reiterate the importance of rectal-examination and bioptic findings in surgical planning. An individualized combination of multiparametric MRI, rectal examination and bioptic findings can accurately select patients for a safe nerve sparing technique, both in every-risk and high-risk subsets of patients.

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Introduction

Prostate Cancer (PCa) is the most common malignancy and the second leading cause of cancer-related death among men [1].

When surgery for PCa is advised, a Radical Prostatectomy (RP) is the only curative procedure to be offered among surgical options.

Despite providing high rates of cancer control, RP is associated with a nonnegligible risk of erectile dysfunction and urinary incontinence. Nerve Sparing (NS) RP allows for the preservation of the neurovascular bundles, with the aim to preserve erectile function and urinary continence [2,3]. A concern with NS is that close surgical preparation along the prostatic capsule may inadvertently lead to a Positive Surgical Margin (PSM) and potentially a noncurative resection. PSMs are associated with an increased risk of biochemical recurrence [4], [5], and Cancer-Specific (CSM) and Overall Mortality (OM) when multifocal [6]. Surgeons must plan NS by balancing the competing functional and oncological outcomes. Therefore, it is optimally important to risk-stratify patients who opt RP for (side-specific) NS or non-NS [4]. The evolution of imaging-guided technology is an increasing need to improve the surgical dissection for a tailored surgery of PCa. Some authors believe that prostate multiparametric Magnetic Resonance Imaging (mpMRI) is a useful tool for interrogating the prostate, and it represent as routine practice to guide NS surgery nowadays [7]. Nevertheless, the EAU guidelines state that there is no conclusive data to recommend in favor or against NS. The literature, indeed, is far from solidly consistent regarding mpMRI's accuracy for PCa local staging, with sensitivity for a locally advanced stage ranging 0% to 100% [8,9] mainly depending on experience of readers and radiologic centers, with those dedicated to prostate mpMRI achieving better results and those located peripherally, non-academic and addressing a broad spectrum of techniques other than prostate mpMRI performing worse.

The aim of the present study is to assess the role of a peripherally performed, real-world everyday practice mpMRI in planning radical prostatectomy for PCa.

Materials and Methods

Study population

Patients undergoing RP at two high-volume European institutions (Centre 1 and Centre 2) between January and December 2023 were recruited. All RP were performed with a four-arm da Vinci Xi Surgical System (Intuitive Surgical, Sunnyvale, CA, USA), by 6 experienced robotic surgeons (i.e., surgical experience ≥ 500 cases at the moment of the surgery).

Inclusion criteria consisted of available report of preoperative mpMRI (both 1.5 and 3 Tesla were accepted, regardless of the previous experience of the radiologist and the type of radiological institution – both "hub" and "spoke" centers), written consent to be enrolled in the study, and absence of systemic disease. Exclusion criteria consisted of refusal of consenting to be enrolled and mpMRI performed >3 months before surgery. This translated into overall 356 patients.

Variable definition

For each patient, the following variables were collected: Age (continuously coded; years), prostate specific antigen at diagnosis (PSA; ng/ml), and ISUP grade at prostate biopsy (from 1 to 5) [10]. Prostate biopsies included both systematic and targeted specimens, either with transperineal or transrectal approach, based upon either center's protocol.

Clinical T stage (cT stage; ≤ cT2b, cT2c-3) was assessed based on preoperative mpMRI. The assessment of mpMRI was based on the latest version of the PI-RADS scoring system [8].

Pathological T (pT) as well as pathological ISUP grade were retrieved from pathological charts. The Tumor, Node, Metastasis (TNM) Classification (2017) was used according to the eighth edition [11].

For each patient, the concordance between mpMRI and final pathology in terms of PCa location was assessed. The partial correspondence between mpMRI and final pathology (*e.g.*, unilateral lesion at mpMRI and bilateral tumor, or absence of extracapsular extension at mpMRI and locally advanced tumor at final pathology) was considered as "no concordance".

Study endpoints

First, the study aimed to test the association between the concordance mpMRI/pTstage and PSM. PSM were defined as the presence of inked cells at the edge of the surgical specimen [5].

Second, the study aimed to test the association between the concordance mpMRI/pTstage and multifocal PSM (i.e., at least 2 PSM).

Third and last, the study aimed to test the association between the concordance mpMRI/pTstage and PSM in high-risk PCa patients (according to D'Amico risk classification [12]).

Statistical analyses

First, univariable and multivariable logistic regression models tested the impact of concordance mpMRI/pTstage on PSM. Covariates consisted of bioptic ISUP grade (1-3 *vs.* 4-5, cT stage (organ-confined *vs.* non-organ-confined), PiRADS score (3 *vs.* 4 *vs.*

Table 1: Preoperative data.

Variable		Classes	Result (% overall population)
Patient origin		Centre 1	249 (69.94%)
		Centre 2	107 (30.06%)
Age, years, mean (range)		65.17 (39-77)	
Preoperative PSA, ng/ml, mean (range)		8.87 (0.32-59.65)	
DRE status	Overall population	Negative	214 (60.11%)
		Right	82 (23.034%)
		Left	52 (14.61%)
		Bilateral	8 (2.25%)
	Multifocal PSM patients	Negative	12 (3.37%)
		Right	9 (2.53%)
		Left	16 (4.49%)
		Bilateral	1 (0.28%)
	High-risk patients	Negative	48 (13.48%)
		Right	30 (8.43%)
		Left	24 (6.74%)
		Bilateral	3 (0.84%)
Side of positive biopsy	Overall population	Left	77 (21.63%)
		Right	80 (22.47%)
		Bilateral	199 (55.90%)
	Multifocal PSM patients	Left	8 (2.25%)
		Right	1 (0.28%)
		Bilateral	29 (8.15%)
	High-risk patients	Left	21 (5.90%)
		Right	23 (6.46%)
		Bilateral	61 (17.13%)
Maximum ISUP at biopsy		1	39 (10.96%)
		2	158 (44.38%)
		3	110 (30.90%)
		4	41 (11.52%)
		5	8 (2.25%)
mpMRI maximum PIRADS		Negative	23 (6.46%)
		Left PIRADS 3	25 (7.02%)
		Right PIRADS 3	26 (7.30%)
		Left PIRADS 4	72 (20.22%)
		Right PIRADS 4	61 (17.13%)
		Left PIRADS 5	45 (12.64%)
		Right PIRADS 5	39 (10.96%)
		Bilateral PIRADS 3	15 (4.21%)
		Bilateral PIRADS 4	34 (9.55%)
		Bilateral PIRADS 5	26 (7.30%)
mpMRI local staging		Organ confined	264 (72.16%)
		Left capsular abutment	4 (1.12%)
		Right capsular abutment	4 (1.12%)
		Anterior capsular abutment	2 (0.56%)
		Bilateral capsular abutment	3 (0.84%)

mpMRI local staging		Left EPE	20 (5.62%)
		Right EPE	19 (5.34%)
		Anterior EPE	0 (0%)
		Bilateral EPE	4 (1.12%)
		Left SVI	7 (1.97%)
		Right SVI	25 (7.02%)
		Bilateral SVI	4 (1.12%)
Radiologic staging	Overall population	Organ confined	277 (77.81%)
		Locally advanced	79 (22.19%)
	Multifocal PSM	Organ confined	17 (4.78%)
		Locally advanced	21 (5.90%)
	High-risk patients	Organ confined	27 (7.58%)
		Locally advanced	78 (21.91%)
High-risk (D'Amico classification)		Yes	105 (29.49%)
		No	251 (70.51%)

5), number of lesions at mpMRI (single *vs.* bilateral), NS technique (NS *vs.* no-NS).

Second, the above-described methodology reapplied specifically focusing on multifocal PSM as dependent variable of interest.

Third, sensitivity analyses addressed the impact of concordance mpMRI/pTstage on PSM within a population of high-risk PCa patients.

In all statistical analyses, R software environment for statistical computing and graphics (R version 4.1.2; R Foundation for Statistical Computing, Vienna, Austria) was used. All tests were two sided, with a level of significance set at $p<0.05$.

Surgical planning

The decision whether to perform a NS RP was based on a single patient basis, after a thorough preoperative counselling which took into comprehensive consideration 1) clinical data: PSA, age, preoperative functional scores (IPSS and IIEF-5 questionnaires were systematically administered), patients' expectations and desire; 2) pathological data: Biopsy findings (number and location of positive cores, maximum ISUP grade); 3) local staging: mpMRI findings, DRE status. In all cases, the surgeon's preference was the most important decision-driver.

Results

Concordance was observed in 133 of 356 overall patients (37%); 28 of 99 patients with PSM (28%); 14 of 38 patients with multifocal PSM (37%); 18 of 54 high-risk patients with PSM (33%) (Tables 1-4).

Concordance was independently associated with a higher risk of overall PSM (OR: 1.85; 95% CI 1.14-3.84; p=0.033), as well as a locally advanced disease at clinical staging (OR: 3.46; 95% CI 1.57-7.84; p=0.002) and a PIRADS 5 (OR: 2.56; 95% 1.12-6.20; p=0.030). Receiving a nerve sparing technique was an independent predictive factor for lower risk of PSM (OR: 0.54; CI 0.31-0.94; p=0.029) (Table 5).

A locally advanced clinical stage and a PIRADS 5 were independently associated with a higher risk of multifocal PSM (OR: 5.02; 95% CI 2.05-12.16; p<0.001 and OR 9.81; 95% CI 1.74-18.63; p=0.035) (Table 6).

Table 2: Surgical data.

Variable		Classes	Result (% overall population)
Surgeon's volume		500 – 1000 cases	162 (45.51%)
		1000 – 2000 cases	13 (3.65%)
		2000 – 3000 cases	100 (28.09%)
		>3000 cases	81 (22.75%)
Nerve sparing technique	Overall population	No nerve sparing	119 (33.43%)
		Left nerve sparing	56 (15.73%)
		Right nerve sparing	56 (15.73%)
		Bilateral nerve sparing	125 (35.11%)
	Multifocal PSM patients	No nerve sparing	19 (5.34%)
		Left nerve sparing	3 (0.84%)
		Right nerve sparing	4 (1.12%)
		Bilateral nerve sparing	12 (3.37%)
	High risk patients	No nerve sparing	55 (15.45%)
		Left nerve sparing	7 (1.97%)
		Right nerve sparing	23 (6.46%)
		Bilateral nerve sparing	20 (5.62%)

Table 3: Final pathology.

Variable	Classes	Result (% overall population)
Wholemount pT stage	pT2a	19 (5.34%)
	pT2b	6 (1.69%)
	pT2c	221 (62.08%)
	pT3a	73 (20.51%)
	pT3b	37 (10.39%)
	pT4	0 (0%)
Max wholemount ISUP grade group	1	17 (4.78%)
	2	193 (54.21%)
	3	117 (32.87%)
	4	18 (5.06%)
	5	11 (3.09%)
Surgical margins	Negative	257 (72.19%)
	Unifocal PSM	61 (17.14%)
	Multifocal PSM	38 (10.67%)
Side of PSM	Left	43 (12.08%)
	Right	35 (9.83%)
	Bilateral	21 (5.90%)
Pathologic staging	Organ confined	246 (69.10%)
	Locally advanced	110 (30.90%)

Bilaterally positive findings at mpMRI (OR: 3.19; 95% CI 1.18-9.44; p=0.027) and NS technique (OR: 0.39; 95% CI 0.17-0.90; p=0.027) were independently associated with the risk of PSM in high-risk patients. Patients with high-risk PCa were 105 (29% of overall population); MpMRI, DRE and bioptic findings (*i.e.* clinical local staging taken together) was negative for disease or unilaterally

Table 4: Population distribution according to mpMRI - final pathology concordance.

Characteristic	Overall, N=356	Concordance, N=133 (37.36%)	No Concordance, N=223 (62.64%)	p-value
Age, median (IQ[1] range)	67 (61, 70)	65 (61, 69)	67 (62, 71)	0.15
PSA, median (IQ[1] range)	7.4 (5.2, 10)	7.7 (5.0, 10.6)	7.2 (5.3, 9.9)	0.6
Surgical volume				0.9
≤ 1000	168 (47%)	62 (37%)	106 (63%)	
>1000	188 (53%)	71 (38%)	117 (62%)	
DRE				0.054
Negative	211 (59%)	70 (33%)	141 (67%)	
Positive	145 (41%)	63 (43%)	82 (57%)	
ISUP at prostate biopsy				0.11
1-3	307 (86%)	108 (35%)	199 (65%)	
4-5	49 (14%)	24 (49%)	25 (51%)	
Side of positive bioptic cores				0.2
Single side	157 (44%)	52 (33%)	105 (67%)	
Bilateral	199 (56%)	80 (40%)	119 (60%)	
mpMRI local staging				0.002
cT2	275 (77%)	89 (32%)	186 (68%)	
cT3a	45 (13%)	23 (51%)	22 (49%)	
cT3b	36 (10%)	21 (58%)	15 (42%)	
Pathologic stage				<0.001
pT2	245 (69%)	76 (31%)	169 (69%)	
pT3a	75 (21%)	36 (49%)	38 (51%)	
pT3b	36 (10%)	20 (56%)	16 (44%)	
PIRADS score				<0.001
3	62 (17%)	14 (23%)	48 (77%)	
4	176 (50%)	41 (23%)	135 (77%)	
5	118 (33%)	77 (65%)	41 (35%)	
Laterality of mpMRI lesions				<0.001
Unilateral	266 (75%)	58 (22%)	208 (78%)	
Bilateral	90 (25%)	75 (83%)	15 (17%)	
Nerve sparing technique				0.088
No NS	120 (34%)	55 (46%)	65 (54%)	
NS unilateral	113 (32%)	40 (35%)	73 (65%)	
NS bilateral	123 (35%)	38 (31%)	85 (69%)	
Focality of PSM				0.022
Negative margins	255 (72%)	91 (36%)	164 (64%)	
Unifocal	57 (16%)	17 (30%)	40 (70%)	
Multifocal	44 (12%)	25 (57%)	19 (43%)	

[1]IQ range: Inter-Quartile range

positive in 74%, 97% and 42% of them, respectively; 50 patients within this subpopulation underwent a NS technique (30 unilaterally, 20 bilaterally) (Table 7).

Discussion and Conclusion

Our results show that mpMRI's reliability for PCa local staging is low (its findings were only confirmed in roughly 1 patient in 3). A non-concordant local staging exposed the 63% of our patients to an 85% higher risk of PSM, which are associated with a higher risk of biochemical recurrence.

Furthermore, a mistaken local staging was observed in 63% of patients with multifocal PSM, which are associated with worse CSM (HR=4.68) and OM (HR=1.82) [6]. Concordance didn't reach

Table 5: Multivariable logistic regression testing the association between the concordance between tumor location at final pathology and mpMRI and overall presence of PSM.

Characteristic	OR[1]	95% CI[1]	p-value
Concordance			
Concordance	Reference		
No concordance	1.85	1.14, 3.84	**0.033**
Maximum ISUP grade at prostate biopsy			
1-3	Reference		
4-5	1.84	0.89, 3.77	0.09
Clinical stage			
Organ confined	Reference		
Locally advanced	3.46	1.57, 7.84	**0.002**
PIRADS score			
3	Reference		
4	1.35	0.63, 3.06	0.4
5	2.56	1.12, 6.20	**0.03**
Laterality of lesions at mpMRI			
Single	Reference		
Bilateral	1.84	0.90, 3.75	0.1
Nerve sparing technique			
No NS	Reference		
NS	0.54	0.31, 0.94	**0.029**

Table 5: Multivariable logistic regression testing the association between the concordance between tumor location at final pathology and mpMRI and overall presence of PSM.

statistical significance as a predictive factor for multifocal PSM nor for PSM in high-risk patients, probably due to the low number of outcome events (38 and 54, respectively). Other mpMRI related variables (locally advanced stage and PIRADS 5), though, were associated with higher risk of multifocal PSM, and bilateral lesions in high-risk patients.

Our results, hence, confirm an important role of mpMRI local staging in surgical planning of RP; at the same time, though, our results underline its low accuracy when performed peripherally (roughly 1 staging in 3 was confirmed at final pathology in our real-world cohort).

Surgical planning proved crucial for the occurrence of PSM. Regardless of radiologic local staging (mistaken in 63% and 67% of overall population and high-risk patients, respectively), being selected for a NS RP exposed to a 46% lower risk of overall PSM and 61% lower risk of PSM in high-risk patients.

Such protective association certainly derives from appropriate selection of patients undergone NS RP.

Considering that the decision whether to perform a NS RP was based on a combination of preoperative factors besides mpMRI (*i.e.* DRE and bioptic findings), we also underline the importance these local, "old fashion" but "real world" factors still have in the evolving field of precision medicine.

Conclusion

We confirm an important role of mpMRI of the prostate in surgical planning of radical prostatectomy; nevertheless, our results also demonstrate that the findings of a peripherally performed mpMRI are not reliable enough to guide NS surgery as a stand-alone technique. Finally, we reiterate the importance of DRE and bioptic findings in surgical planning. An individualized combination of mpMRI, DRE and bioptic findings can accurately select patients for a safe NS technique, both in every-risk and high-risk subsets of patients.

Table 6: Multivariable logistic regression testing the association between the concordance between tumor location at final pathology and mpMRI and multifocal PSM.

Characteristic	OR[1]	95% CI[1]	p-value
Concordance			
Concordance	Reference		
No concordance	0.98	0.38, 2.56	0.9
Maximum ISUP grade at prostate biopsy			
1-3	Reference		
4-5	1.64	0.65, 3.88	0.3
Clinical stage			
Organ confined	Reference		
Locally advanced	5.02	2.05, 12.16	**<0.001**
PIRADS score			
3	Reference		
4	7.44	1.42, 13.22	0.057
5	9.81	1.74, 18.63	**0.035**
Laterality of lesions at mpMRI			
Single	Reference		
Bilateral	2.05	0.85, 4.98	0.1
Nerve sparing technique			
No NS	Reference		
NS	0.67	0.31, 1.47	0.3

[1]OR: Odds Ratio; CI: Confidence Interval

Table 7: Multivariable logistic regression testing the association between the concordance between tumor location at final pathology and mpMRI and PSM in only high-risk patients.

Characteristic	OR[1]	95% CI[1]	p-value
Concordance			
Concordance	Reference		
No concordance	0.49	0.06, 2.49	0.4
PIRADS score			
3	Reference		
4	1.57	0.21, 4.84	0.7
5	0.64	0.04, 9.17	0.7
Laterality of lesions at mpMRI			
Single	Reference		
Bilateral	3.19	1.18, 9.44	0,027
Nerve sparing technique			
No NS	Reference		
NS	0.39	0.17, 0.90	0.029

[1]OR: Odds Ratio; CI: Confidence Interval

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