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ORIGINAL ARTICLE

Integration of MRI to clinical nomogram for predicting pathological stage before radical prostatectomy

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Abstract
Background Debate persists regarding whether MRI should be used routinely for preoperative evaluation of prostate cancer.
Objective The aim is to assess the role of prostatic magnetic resonance imaging (MRI) and other preoperative data in extra-prostatic extension (EPE) evaluation.
Patients and methods From 2000 to 2013, 1743 patients operated for radical prostatectomy had a preoperative MRI. Age, clinical stage with digital rectal exam (DRE), PSA, prostate weight, biopsy, MRI and pathological findings of the surgical specimen were noticed. A multiparametric score of the variables independently associated with EPE was built with or without MRI on a random sample test population and internally validated.
Results With mean age of 62.9 years and mean PSA of 9.6 ng/ml, the population was distributed as follows: 1424 DRE T1, 254 T2, 32 T3; on biopsy 990 Gleason score = 6 and 717 ≥ 7; on MRI 1322 iT2, 290 iT3A and 131 iT3B; on prostatectomy 15 pT0, 998 pT2, 548 pT3A, 181 pT3B and 1 pT4A. In multivariate analysis, DRE, PSA, Gleason score, prostate weight and MRI were independently associated with EPE and integrated in a score with an area under curve (AUC) of 0.74 [95% CI 0.71–0.77] (0.72 without MRI, $p < 0.01$) a positive predictive value of 61% and a negative predictive value of 74%, internally validated. The Hosmer–Lemeshow goodness-of-fit test showed good accuracy ($p = 0.77$).
Conclusions Integration of MRI with clinical data for predicting pathological stage before radical prostatectomy permits to exclude accurately EPE in 74% of cases.

Keywords EPE · MRI · Nerve sparing · Preoperative system score · Prostate cancer · Staging

Introduction

Nerve-sparing strategies during radical prostatectomy (RP) for localized prostate cancer (PCa) are associated with preservation of erectile function and urinary continence. Neurovascular bundles (NVB) are localized all-around of the prostate and seminal vesicles especially for cavernous nerves [1]. Nerve-sparing strategy has to be planned depending on the knowledge of the presence and localization of extra-prostatic extension (EPE) and seminal vesicle invasion (SVI) to reduce probability of positive surgical margins associated with a twofold increased hazard of biochemical relapse [2].

Prediction of EPE by digital rectal exam (DRE) or prostate biopsy is known to have low accuracy [3]. Nomograms like "Partin tables" using commonly available preoperative

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data—serum PSA level, clinical stage and biopsy Gleason score—to predict pathological stage at RP can be used [4].

Moreover, debate persists regarding whether MRI should be used routinely for preoperative evaluation of PCa. The millimetre accuracy provided by pathologist is impossible to obtain by MRI, and its performance to investigate the EPE remains notably lower below 0.75 mm or extension at the apex [5]. Recently, Rud et al. [6] have found in a randomized controlled trial that MRI alone prior to RP does not reduce risk for positive surgical margin [8]. Radiologists reached a sensitivity of 33–84% and specificity of 71–92% for T2/T3 differentiation depending on their experience: specialist uroradiologist in academic centre reflects the best diagnostic performance of MRI [7, 8]. However, in general radiologist centres, where the majority of prostate MRIs are conducted, this performance may be lower.

Our objective was to evaluate the place of the "everyday" (or current) prostate MRI in relation to other data in the preoperative staging of EPE and/or SVI and to establish a predictive scoring system combining SVI and EPE.

Methods

Patients

From January 2000 to December 2013, 1743 consecutive patients had RP in an academic centre for localized PCa. All of these have had a pretreatment MRI. For each patient, preoperative data were noted: clinical stage (T1–T3, N0 and M0), biopsy before surgery for evaluation of Gleason score, serum PSA level, MRI as preoperative staging tool of prostatic cancer.

Pathologic specimens

RP specimens were step sectioned and prospectively evaluated by experienced uropathologists of our centre according to Stanford protocol. The T category as defined using the American Joint Committee on Cancer categorization and the Gleason score original or on International Society of Urological Pathology (ISUP) 2005 Gleason score, and ISUP 2010 for specimens after these years was noted.

MRI

Prostate MRI was performed without any restriction of technique (it depended on the MRI technology available at the time of examination). Patient with MRI which is technically insufficient was not included. All MRI imaging were prospectively evaluated preoperatively for the presence of EPE by four urologists experienced in prostate cancer evaluation and radical prostatectomy. Presence of EPE on MRI was concluded based on personal training and knowledge of the radiologist's report. Results were categorized using a scale for suspicion of EPE at MRI: iT2 if there was no EPE, iT3A if EPE was suspected or iT3B in case of seminal vesicle invasion (SVI).

Statistical analysis

The population of 1743 patients was randomly divided in two groups: (1) the training group of 1054 patients and (2) the validation group of 689 patients.

Characteristics of patients included in the two groups of analysis are presented as numbers and percentages, mean ± 1 standard deviation or median [interquartile range], depending of the distribution of the variable. Serum PSA was transformed in ordinal categorical variable with the following cut-offs: ≤5,]5–10],]10–15], >15 ng/ml. Gleason score was considered ≤6 or ≥7. Prostatic weight was divided as ≤50 or >50 g.

Factors associated with EPE were tested in the training group by means of Chi-squared test or Fisher's exact test, where appropriate. All variables significant in univariate analysis at a $p \leq 0.05$ level were tested in a stepwise logistic regression model that estimated the β coefficients, the odds ratios (ORs) with their 95% confidence intervals of the variables independently associated with EPE at a $p \leq 0.05$ value. The goodness-of-fit of the model was assessed by the Hosmer–Lemeshow test.

A score of risk of EPE was calculated for each patient as the sum $\beta_i x_i$, where β_i designed the β coefficient of each class of a variable, and corresponded to the variables with the value 0 for the category of reference and 1 otherwise. Performance of the score was assessed by the area under curve (AUC). Several cut-offs derived from the ROC curve were tested according to a better value of negative (NPV) or positive predictive value (PPV).

A simplified, user-friendly version of the model has been built. It was derived from the original model by linear transformation of the β coefficient. This simplified model was compared to the original one in terms of performance. The score was then applied to the validation population.

Results

Patients' characteristics are shown in Table 1. Clinical, radiological and biological aspects were not different between the two groups. Overall 549 patients (31.5%) had EPE in their RP specimen (95% CI 29.3–33.7). SVI was reported in 182 patients (10.5%; 95% CI 9.0–11.8).

Table 1 Patients' characteristics $N = 1743$; random sample: test population $n = 1054$; validation population $n = 689$

	Test *n* (%)	Validation *n* (%)	Total *n* (%)	*p*
Clinical stage				
T1	853 (80.9)	582 (84.5)	1435 (82.3)	0.16
T2	180 (17.1)	97 (14.1)	277 (15.9)	
T3	21 (2.0)	10 (1.5)	31 (1.8)	
MRI				
iT2	812 (77.0)	510 (74.0)	1322 (75.8)	0.33
iT3A	165 (15.7)	125 (18.1)	290 (16.6)	
iT3B	77 (7.3)	54 (7.8)	131 (7.5)	
Pathological stage				
pT0	10 (0.9)	5 (0.7)	15 (0.9)	0.24
pT2A	104 (9.9)	74 (10.7)	178 (10.2)	
pT2B	12 (1.1)	17 (2.5)	29 (1.7)	
pT2C	479 (45.5)	310 (45.0)	789 (45.3)	
pT3A	329 (31.2)	220 (31.9)	549 (31.5)	
pT3B/4A	119 (11.3)	63. (9.1)	182 (10.5)	
Lymph node				
N+	34 (3.2)	17 (2.5)	51 (2.9)	0.36
Age (years)				
>60	707 (67.1)	470 (68.2)	1177 (67.5)	0.62
Serum PSA level (ng/ml)				
<5	241 (23.0)	153 (22.3)	394 (22.7)	0.41
]5–10]	544 (51.9)	377 (55.0)	921 (53.1)	
]10–15]	144 (13.7)	77 (11.2)	221 (12.8)	
>15	119 (11.4)	78 (11.4)	197 (11.4)	
Biopsy Gleason score				
6	603 (57.2)	422 (61.4)	1025 (58.9)	0.081
≥7	451 (42.8)	265 (38.6)	716 (41.4)	
Final Gleason score				
6	251 (24.0)	179 (26.1)	430 (24.9)	0.33
≥7	793 (76.0)	506 (73.9)	1299 (75.1)	

Population test analysis

Univariate analysis

In the population test, 329 patients had EPE in their RP specimen, accounting for an overall prevalence of EPE of 31.2%. SVI was reported in 119 patients accounting for an overall 11.3% prevalence of SVI. As shown in Table S1, in univariate analysis PSA, clinical stage (DRE), biopsy Gleason score, prostate weight and stage at MRI were significantly associated with EPE at RP ($p < 0.05$).

The crude results of MRI in that population were a sensibility of 34.8%, a specificity of 85.7%, a negative predictive value (NPV) of 63.6% and a positive predictive value (PPV) of 64.7%. For clinical exam, the DRE has a sensibility of 4.0%, a specificity of 99.5%, a NPV of 57.9% and a PPV of 85.7%.

Multivariate analysis and EPE score system development

All significant variables in univariate analysis were tested in a logistic regression model. As shown in Table 2Aa, multivariate analysis identified PSA > 5 ng/ml, clinical stage DRE T2 or T3, biopsy Gleason score ≥7, prostate weigh >50 g and stage at MRI iT3A or iT3B as factors independently associated with EPE at RP ($p < 0.05$).

Fitness of the model was assessed by the Hosmer–Lemeshow goodness-of-fit statistic showing that there was good concordance between observed and predicted EPE with a $p = 0.77$.

On the other hand, we have built a model without MRI (Table 2Ab). Addition of MRI with clinical parameters improved this fitness from 0.49 to 0.77.

As shown in Table 2B, the EPE scoring system was then produced by multiplying the coefficients β by 3 and rounding them to the nearest integer value. The score ranges from −1.5 to 13 points and −1.5 to 11.5 for the model without MRI.

The ROC curves are shown in Fig. 1. The AUC is 0.74 (IC 95% [0.71–0.77]; SE 0.0156), for the score with MRI. For the model without MRI, the AUC is 0.72 (IC 95% [0.69–0.75]; SE 0.0160).

There is a statistical difference between models with or without MRI (χ^2; $p = 0.0039$).

Its prognostic value was tested using several threshold values (2, 2.5 and 3). Although several cut-off values were significantly associated with EPE, the value of 3 was selected as optimal. The cut-off value of 3 separated the population into two subgroups: less probability of EPE (≤3) and high probability of EPE (>3).

Sensitivity, specificity, PPV and NPV of the EPE scoring system with MRI and a threshold of three were 67.6, 69.5, 62.7 and 73.9%, respectively.

Validation population

In the validation population of 689 patients, 220 patients (31.9%) had EPE in their RP specimen. SVI was reported in 63 patients (9.1%). Informational indices sensitivity, specificity, PPV and NPV at the threshold of three were, respectively, 65.4, 71.1, 61.4 and 74.5%.

Discussion

It has been well established that the prevalence of EPE is influenced by several established parameters such as PSA,

Table 2 (A) Multivariate analysis of preoperative parameters predicting extra-prostatic extension (EPE) and/or seminal vesicle invasion (SVI): (a) with MRI (b) without MRI; (B) extra-prostatic extension (EPE) and/or seminal vesicle invasion (SVI) preoperative system score with or without MRI

Preoperative parameters		Logistic regression			
A. a. With MRI		β*	OR	IC 95%	*p*
Serum PSA level (ng/ml)	≤5	0	1		
	[5–10]	0.371	1.450	1.021–2.059	0.038
	[10–15]	0.824	2.280	1.425–3.648	0.001
	>15	1.344	3.836	2.258–6.516	<0.001
MRI	iT2	0	1		
	iT3A	0.903	2.468	1.688–3.608	<0.001
	iT3B	1.047	2.850	1.631–4.979	<0.001
Biopsy Gleason score	6	0	1		
	≥7	1.119	3.063	2.322–4.041	<0.001
Prostate weight	≤50 g	0	1		
	>50 g	−0.470	0.625	0.465–0.840	0.002
Clinical stage	T1	0	1		
	T2	0.411	1.509	1.048–2.172	0.027
	T3	0.898	2.456	0.661–9.128	0.180
A. b. Without MRI					
Serum PSA level (ng/ml)	≤5	0	1		
	[5–10]	0.347	1.415	1.002–1.999	0.049
	[10–15]	0.841	2.319	1.462–3.679	<0.001
	>15	1.331	3.786	2.245–6.383	<0.001
Biopsy Gleason score	6	0	1		
	≥7	1.185	3.271	2.492–4.294	<0.001
Prostate weight	≤50 g	0	1		
	>50 g	−0.439	0.644	0.482–0.861	0.003
Clinical stage	T1	0	1		
	T2	0.530	1.699	1.193–2.419	0.003
	T3	1.426	4.161	1.146–15.116	0.030

B		Score with MRI	Score without MRI
Serum PSA level (ng/ml)	≤5	0	0
	[5–10]	1	1
	[10–15]	2.5	2.5
	>15	4	4
MRI	iT2	0	–
	iT3A	2.5	–
	iT3B	3	–
Biopsy Gleason score	6	0	0
	≥7	3.5	3.5
Prostate weight	≤50 g	0	0
	>50 g	−1.5	−1.5
Clinical stage	T1	0	0
	T2	1	1.5
	T3	2.5	4

Score is calculated after a linear transformation: rounded ($\beta \times 3$); threshold = 3

* The β coefficient derived from the logistic regression model. OR = expβ

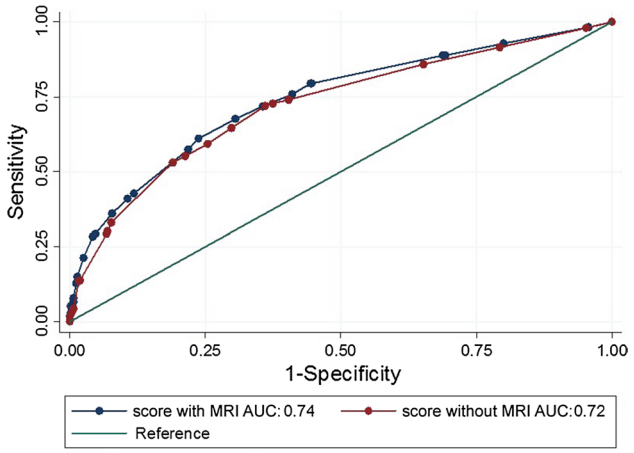

Fig. 1 Validation data set ROC curve for extra-prostatic extension (EPE) with preoperative data using the EPE evaluation scoring system. Comparison of ROC curves and AUC with or without MRI

clinical stage and biopsy Gleason score [9–12]. Because of the high incidence of PCa and the high cost of MRI, debate persists regarding whether MRI should be used routinely for preoperative evaluation of PCa. European Association of Urology (EAU) and French Association of Urology (AFU) have established recommendations for the evaluation of tumour extension before RP [13, 14]. For the EAU, the extent of PCa is evaluated by DRE and PSA and may be supplemented with bone scanning and computed tomography (CT) or multiparametric MRI (mp-MRI). For the AFU, the prostate MRI is optional and easily proposed to evaluate the indication of nerve preservation during RP.

Various nomograms have been developed to predict pathological characteristics [15, 16] (Table S2). Without MRI, the AUC of preoperative clinical parameter to predict EPE varied from 0.702 to 0.84 [4, 17–19].

Some authors have evaluated the MRI to predict risk and location of EPE. MRI with other associated parameters has little result.

- For Billing et al. [20] (106 patients), the accuracy of diagnosing EPE was 72.2%, with an overall sensitivity and specificity of 30.0 and 93.3%, respectively. The negative predictive value was 72.7%.
- For Wang et al. [21] (612 patients), in the combined endorectal MR imaging–MR spectroscopic imaging group, the areas under the ROC curves were 0.81 for the staging nomograms and 0.90 for the staging nomograms plus MR findings.
- Pak et al. [22] (944 patients) have developed a scoring system for the prediction of posterolateral EPE with an AUC of 0.810 for discrimination ability of the scoring system. The Hosmer–Lemeshow goodness-of-fit test is low ($p = 0.396$).
- Feng et al. [23] with a limited population of 112 patients have shown that mp-MRI improved accuracy of existing clinical nomograms with an AUC of 0.93 with Partin table plus MRI and 0.94 with MSK nomogram plus MRI.

Our study has developed a scoring system including PSA, DRE, biopsy Gleason score, prostate weight and MRI for the prediction of EPE having an AUC of 0.74 for discrimination ability of the scoring system for EPE. With a Hosmer–Lemeshow goodness-of-fit test of 0.77, the preoperative scoring system has a good accuracy and the best one of the literature. A model with MRI had a better AUC and accuracy than a model without MRI justifying the contribution of MRI in the preoperative plan.

Clinical stage T2 was shown to be associated with presence of EPE ($p = 0.027$ in the multivariate analysis). This is unexpected and underlined the fact that DRE with low sensibility but high positive predictive value needs to be taken in consideration before RP. Prostate weight >50 g is a protective factor (OR 0.64 [0.48–0.86]). This is described in the literature [24–26].

Larger glands may produce more PSA due to the presence of benign prostatic hyperplasia, causing a lead time bias or diagnosis of prostate cancer at an earlier point in the progression of disease. But, this has to be confirmed in a prospective study.

Compared to our cohort, some studies have better AUC even without MRI but our score has the best accuracy with the largest sample and an internal validation.

If we resume our study and others publications (Table S3), predictive models are more performing with MRI (mean of performance index values = 0.793) versus without MRI (mean of performance index values = 0.734). We have to take in consideration that MRI not only predicts EPE but also provides an anatomical view of the localization of the PCa [27].

Limitations of our study are that we did not standardize the patients who underwent MRI that introduce bias in evaluation. Additionally, because of "real life" condition, we were unable to obtain the training and experience profiles of the radiologists who conducted the MRIs. The MRI evaluation was heterogeneous by nonspecialized radiologists providing of multiple radiology centres. The performance of specialized radiologist MRI reading for EPE prediction is an incremental benefit [28]. MRI radiologist report homogenization was approached by evaluation of four urologists experienced in prostate cancer evaluation and radical prostatectomy. It is possible that our findings underestimate the true diagnostic accuracy of MRI and its added value.

Other limitation of our study is that the inclusion of preoperative parameters of our cohort lasted 13 years; this

long period includes the development of MRI techniques. A recent meta-analysis by De Rooij et al. [29] analysed the accuracy of MRI with different technical features to detect EPE. Their conclusion is that functional imaging in addition to T2-weighted imaging improved sensitivity for EPE, while the sensitivity was not improved by endorectal coil use. There is a lack of sector-based comparison between MRI and histopathology. Neither the side nor the level of EPE was consistently reported in the prospectively recorded data.

This study has several strengths. Patient populations influence staging accuracy, as a high rate of organ-confined disease may obscure a poor detection of locally advanced disease, and small study populations may result in higher staging performance [30]. Our study population was large ($n = 1743$) and consisted of 41.9% with stage pT3 disease.

Our study "everyday" prostate MRI has a good calibration and is internally validated. So, this user-friendly score could be used in clinical practice.

Conclusions

Analysis of MRI associated with conventional preoperative data allows good staging prior to radical prostatectomy. A scoring system including PSA, DRE, biopsy Gleason score, prostate weight and MRI allows to exclude an EPE and/or VSI in 74% of localized PCa accurately.

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Author's contribution CL and LS involved in project development, data collection and management, data analysis and manuscript writing and editing; FR-T performed data management, data analysis and manuscript editing; AM and MB edited the manuscript; ADLT contributed to project development, data collection and management and manuscript editing.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Informed consent For this type of study, formal consent is not required.

References

1. Alsaid B, Karam I, Bessede T, Abdlsamad I, Uhl JF, Delmas V et al (2010) Tridimensional computer-assisted anatomic dissection of posterolateral prostatic neurovascular bundles. Eur Urol 58:281–287. doi:10.1016/j.eururo.2010.04.002
2. Yossepowitch O, Briganti A, Eastham JA, Epstein J, Graefen M, Montironi R et al (2014) Positive surgical margins after radical prostatectomy: a systematic review and contemporary update. Eur Urol 65:303–313. doi:10.1016/j.eururo.2013.07.039
3. Ristau BT, Tomaszewski JJ, Chen Y-F, Bertolet M, Woldemichael E, Nelson JB (2014) Prostate biopsy perineural invasion is not independently associated with positive surgical margins following radical retropubic prostatectomy. World J Urol. doi:10.1007/s00345-014-1430-2
4. Eifler JB, Feng Z, Lin BM, Partin MT, Humphreys EB, Han M et al (2013) An updated prostate cancer staging nomogram (Partin tables) based on cases from 2006 to 2011. BJU Int 111:22–29. doi:10.1111/j.1464-410X.2012.11324.x
5. Bloch BN, Genega EM, Costa DN, Pedrosa I, Smith MP, Kressel HY et al (2012) Prediction of prostate cancer extracapsular extension with high spatial resolution dynamic contrast-enhanced 3-T MRI. Eur Radiol 22:2201–2210. doi:10.1007/s00330-012-2475-5
6. Rud E, Baco E, Klotz D, Rennesund K, Svindland A, Berge V et al (2015) Does preoperative magnetic resonance imaging reduce the rate of positive surgical margins at radical prostatectomy in a randomised clinical trial? Eur Urol. doi:10.1016/j.eururo.2015.02.039
7. Cornud F, Rouanne M, Beuvon F, Eiss D, Flam T, Liberatore M et al (2012) Endorectal 3D T2-weighted 1 mm-slice thickness MRI for prostate cancer staging at 1.5 Tesla: Should we reconsider the indirects signs of extracapsular extension according to the D'Amico tumor risk criteria? Eur J Radiol 81:e591–e597. doi:10.1016/j.ejrad.2011.06.056
8. Ruprecht O, Weisser P, Bodelle B, Ackermann H, Vogl TJ (2012) MRI of the prostate: interobserver agreement compared with histopathologic outcome after radical prostatectomy. Eur J Radiol 81:456–460. doi:10.1016/j.ejrad.2010.12.076
9. Ward JF, Slezak JM, Blute ML, Bergstralh EJ, Zincke H (2005) Radical prostatectomy for clinically advanced (cT3) prostate cancer since the advent of prostate-specific antigen testing: 15-year outcome. BJU Int 95:751–756. doi:10.1111/j.1464-410X.2005.05394.x
10. Yossepowitch O, Eggener SE, Bianco FJ, Carver BS, Serio A, Scardino PT et al (2007) Radical prostatectomy for clinically localized, high risk prostate cancer: critical analysis of risk assessment methods. J Urol 178:493–499. doi:10.1016/j.juro.2007.03.105 **(discussion 499)**
11. Joniau S, Hsu CY, Lerut E, Van Baelen A, Haustermans K, Roskams T et al (2007) A pretreatment table for the prediction of final histopathology after radical prostatectomy in clinical unilateral T3a prostate cancer. Eur Urol 51:388, 394–396. doi:10.1016/j.eururo.2006.06.051
12. Nakanishi H, Troncoso P, Babaian RJ (2008) Prediction of extraprostatic extension in men with biopsy Gleason score of 8 or greater. J Urol 180:2441, 2445–2446. doi:10.1016/j.juro.2008.08.023
13. Heidenreich A, Bellmunt J, Bolla M, Joniau S, Mason M, Matveev V et al (2011) EAU guidelines on prostate cancer. Part 1: screening, diagnosis, and treatment of clinically localised disease. Eur Urol 59:61–71. doi:10.1016/j.eururo.2010.10.039
14. Salomon L, Bastide C, Beuzeboc P, Cormier L, Fromont G, Hennequin C et al (2013) CCAFU Recommendations 2013: prostate cancer. Prog Urol 24:S69–S101
15. Chun FK-H, Karakiewicz PI, Briganti A, Gallina A, Kattan MW, Montorsi F et al (2006) Prostate cancer nomograms: an update. Eur Urol 50:914–926. doi:10.1016/j.eururo.2006.07.042 **(discussion 926)**
16. Guillonneau B (2007) Ceteris paribus and nomograms in medicine. Eur Urol 52:1287–1289. doi:10.1016/j.eururo.2007.04.085
17. Ohori M, Kattan MW, Koh H, Maru N, Slawin KM, Shariat S et al (2004) Predicting the presence and side of extracapsular extension: a nomogram for staging prostate cancer. J Urol

171:1844–1849. doi:10.1097/01.ju.0000121693.05077.3d **(discussion 1849)**
18. Steuber T, Graefen M, Haese A, Erbersdobler A, Chun FK-H, Schlom T et al (2006) Validation of a nomogram for prediction of side specific extracapsular extension at radical prostatectomy. J Urol 175:939–944. doi:10.1016/S0022-5347(05)00342-3 **(discussion 944)**
19. Kattan MW, Stapleton AM, Wheeler TM, Scardino PT (1997) Evaluation of a nomogram used to predict the pathologic stage of clinically localized prostate carcinoma. Cancer 79:528–537
20. Billing A, Buchner A, Stief C, Roosen A (2014) Preoperative mp-MRI of the prostate provides little information about staging of prostate carcinoma in daily clinical practice. World J Urol. doi:10.1007/s00345-014-1448-5
21. Wang L, Hricak H, Kattan MW, Chen H-N, Scardino PT, Kuroiwa K (2006) Prediction of organ-confined prostate cancer: incremental value of MR imaging and MR spectroscopic imaging to staging nomograms. Radiology 238:597–603. doi:10.1148/radiol.2382041905
22. Pak S, Park S, Ryu J, Hong S, Song SH, You D et al (2013) Preoperative factors predictive of posterolateral extracapsular extension after radical prostatectomy. Korean J Urol 54:824–829. doi:10.4111/kju.2013.54.12.824
23. Feng TS, Sharif-Afshar AR, Wu J, Li Q, Luthringer D, Saouaf R et al (2015) Multiparametric MRI improves accuracy of clinical nomograms for predicting extracapsular extension of prostate cancer. Urology 86:332–337. doi:10.1016/j.urology.2015.06.003
24. Newton MR, Phillips S, Chang SS, Clark PE, Cookson MS, Davis R et al (2010) Smaller prostate size predicts high grade prostate cancer at final pathology. J Urol 184:930–937. doi:10.1016/j.juro.2010.04.082
25. Briganti A, Chun FK-H, Suardi N, Gallina A, Walz J, Graefen M et al (1990) Prostate volume and adverse prostate cancer features: fact not artifact. Eur J Cancer Oxf Engl 2007(43):2669–2677. doi:10.1016/j.ejca.2007.09.022
26. Freedland SJ, Isaacs WB, Platz EA, Terris MK, Aronson WJ, Amling CL et al (2005) Prostate size and risk of high-grade, advanced prostate cancer and biochemical progression after radical prostatectomy: a search database study. J Clin Oncol Off J Am Soc Clin Oncol 23:7546–7554. doi:10.1200/JCO.2005.05.025
27. Kayat Bittencourt L, Litjens G, Hulsbergen-van de Kaa CA, Turkbey B, Gasparetto EL, Barentsz JO (2015) Prostate cancer: the European Society of Urogenital Radiology prostate imaging reporting and data system criteria for predicting extraprostatic extension by using 3-T multiparametric MR imaging. Radiology 276:479–489. doi:10.1148/radiol.15141412
28. Tay KJ, Gupta RT, Brown AF, Silverman RK, Polascik TJ (2016) Defining the incremental utility of prostate multiparametric magnetic resonance imaging at standard and specialized read in predicting extracapsular extension of prostate cancer. Eur Urol 70:211–213. doi:10.1016/j.eururo.2015.10.041
29. de Rooij M, Hamoen EHJ, Witjes JA, Barentsz JO, Rovers MM (2015) Accuracy of magnetic resonance imaging for local staging of prostate cancer: a diagnostic meta-analysis. Eur Urol. doi:10.1016/j.eururo.2015.07.029
30. Brajtbord JS, Lavery HJ, Nabizada-Pace F, Senaratne P, Samadi DB (2011) Endorectal magnetic resonance imaging has limited clinical ability to preoperatively predict pT3 prostate cancer. BJU Int 107:1419–1424. doi:10.1111/j.1464-410X.2010.09599.x