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# Head to head comparison of three generations of Partin tables to predict final pathological stage in clinically localised prostate cancer

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## ABSTRACT

**Objective:** To perform a head to head comparison between three generations of Partin tables, namely from 1997, 2001 and the last updated version of 2007.

**Material and methods:** The external validations were based on clinical and pathological data of 687 consecutive patients undergoing radical prostatectomy for clinically localised prostate cancer between 2003 and 2008. Three versions of the Partin tables were compared for their accuracy and performance to predict final pathological stage using receiver operating characteristic (ROC) curve and Loess plots analyses.

**Results:** Of the whole cohort, 76.2% of men were presented with organ-confined disease (OC), 17.0% had extraprostatic extension (ECE), 6.0% showed seminal vesicle involvement (SVI) and 1.2% had lymph node involvement (LNI). The area under the receiver operating characteristic curve (AUC) of the Partin Tables 1997, 2001 and 2007 was 0.731, 0.727 and 0.722 for OC; 0.671, 0.662 and 0.650 for ECE; 0.795, 0.788 and 0.779 for SVI as well as 0.826, 0.786 and 0.746 for LNI, respectively.

**Conclusion:** All three generations of the Partin tables showed a good accuracy to predict OC, SVI and LNI. However, the predictive accuracy for ECE was only modest. Overall, the newer versions of the Partin tables could not exceed the version of 1997 in their predictive accuracy for any pathological stage and they failed to demonstrate a clear advantage. Our results underline the necessity to perform external validations before the implementation of a new predicting tool.

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## 1. Introduction

In European and North American men, prostate cancer (PC) has been established as the most common malignancy. Unfortunately, treatment decisions are hampered by a biolog-

ical heterogeneous tumour characteristic. Basically, counselling and proper treatment selection require precise clinical staging and accurate prediction of final pathological stage. Traditionally, a physician's judgment was based on knowledge and experience about preceding similar courses.

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However, clinical judgment may be biased by several confounders (e.g. recall bias) and a tendency exists to predict the preferred outcome rather than that with the highest actual probability.<sup>1</sup> To overcome individual bias, prediction tools like look-up tables, nomograms or artificial neuronal networks, which are based on data of hundreds of patients, were developed.<sup>2</sup>

Partin and colleagues pioneered the field of predictive tools with the development of their probability tables. In 1993, Partin and colleagues published a statistical model based on pre-treatment prostatic-specific antigen (PSA), digital rectal examination (DRE) and biopsy Gleason score.<sup>3</sup> The common availability of these basic clinical parameters and the uncomplicated handling of the look-up tables may have contributed to its popularity and widespread use. However, a validation study performed by Kattan and colleagues showed only moderate reliability of these tables.<sup>4</sup> Subsequently, in 1997 the tables were updated based on a multi-institutional dataset.<sup>5</sup> This modified version demonstrated a good performance and reliability not only with other United States (US) patients but also with European patients.<sup>6,7</sup> Partin and colleagues modified and updated their look-up tables in series in 2001 and finally in 2007.<sup>8,9</sup> These versions of the tables were sequentially based on more contemporary patient cohorts as a consequence of stage and Gleason score migration over the last decade.<sup>10,11</sup>

The aim of these continuous modifications and updates was to increase the predictive accuracy. However, to our knowledge none of the last three versions of the Partin tables have ever undergone a direct head to head comparison to confirm the superiority of the newer versions. Therefore, we determined the overall predictive accuracies and estimated the performance characteristics with the same external validation sample and compared those directly.

## 2. Materials and methods

### 2.1. Study population

Between January 2003 and December 2008, a consecutive series of 840 patients underwent radical retropubic prostatectomy (RP) and limited pelvic lymph node dissection (IPLND) for clinically localised PC at the Department of Urology, Medical University of Graz. A total of 153 patients were excluded due to neoadjuvant endocrine therapy ( $n = 11$ ), missing information on clinical stage ( $n = 60$ ), pretreatment PSA level ( $n = 2$ ) or biopsy Gleason score ( $n = 80$ ). Overall, 687 consecutive patients were eligible for analysis.

### 2.2. Clinical and pathological assessment

Patients were not part of an organised screening programme. Commonly, PC was detected by opportunistic screening. Routine staging work-up included the assessment of PSA level and DRE. Serum PSA determinations were performed before DRE or transrectal ultrasound guided biopsy with the Roche PSA immunoassay (Roche Diagnostics, Mannheim, Germany). In referred patients with only previous transrectal biopsy, serum PSA levels were assessed at least 6 weeks afterwards. A bone scan was only performed in patients with a PSA higher

than 20 ng/ml. Clinical and pathological staging were performed according to the 6th edition of TNM Classification of Malignant Tumours.<sup>12</sup> No imaging information was used to determine clinical stage. All prostatectomy specimens were inked entirely on their surfaces and processed according to the Stanford protocol using serial transverse sections at 3 mm.<sup>13</sup> Histological grading was assessed according to the Gleason grading system.<sup>14</sup> The stratification into organ-confined (OC), extraprostatic extension (ECE), seminal vesicle invasion (SVI) and lymph node involvement (LNI) goes along with the criteria used by Partin and colleagues.<sup>5,8,9</sup>

### 2.3. Statistical analysis

The SPSS software package, version 14 (SPSS Inc., Chicago, IL), and the S-Plus Professional (MathSoft Inc., Seattle, WA) were used for statistical calculations. The predictive accuracy of the Partin tables' OC, ECE, SVI and LNI relative to observed pathological stage was quantified with receiver operating characteristics (ROC) which derived area under the curve (AUC) estimates. To compare the associations of the actual pathological stages with the predicted pathological stages for different probability areas of the Partin tables, the actual percentage with a given pathological stage was plotted versus the mean predicted value as a percentage for each of these areas. Hereby, the extent of underestimation or overestimation was analysed graphically with non-parametric, local

**Table 1 – Cancer characteristics of the validation cohort who had undergone radical prostatectomy between January 2003 and December 2008.**

Characteristics	% Validation cohort(687pts.)
<b>Clinical stage</b>	
T1c	71.5
T2a	9.5
T2b	15.4
T2c	2.8
T3	0.8
<b>PSA (ng/ml)</b>	
0–2.5	3.5
2.6–4.0	8.9
4.1–6.0	26.1
6.1–10	39.6
10.1–20	18.0
>20.0	3.9
<b>Biopsy Gleason score</b>	
2–4	9.6
5	7.7
6	54.1
3 + 4 = 7	14.6
4 + 3 = 7	5.4
8–10	8.6
<b>Pathological stage</b>	
OC	76.2
ECE	17.8
SVI	6.0
LNI	1.2

Abbreviations: OC, organ-confined; ECE, extracapsular extension; SVI, seminal vesicle invasion; LNI, lymph node involvement.

regression Loess smoothing technique.<sup>4</sup> A probability (*p*) level of less than 0.05 was considered statistically significant. All statistical tests were two sided.

### 3. Results

#### 3.1. Study cohort

Table 1 presents the detailed clinical and pathological characteristics of the validation cohort. The mean age of the whole study cohort (*n* = 687) was  $62.1 \pm 6.4$  (range 41–76) years and the men showed a mean preoperative serum PSA level of  $8.2 \pm 5.2$  (range 1.3–48.6) ng/ml. The majority of patients were clinically diagnosed with T1c disease (71.5%) and showed biopsy Gleason score 6 (54.1%). On final pathological examination 76.2% of all men were presented with OC disease. More specifically, 3.2% of patients were diagnosed with pT2a, 26.9%

with pT2b and 46.1% with pT2c, respectively. The positive surgical margin rate was 16.2% for all stages and 11.6% for pT2 tumours.

#### 3.2. Comparison of accuracy and performance

To analyse the discriminative ability of the three generations of Partin tables, ROC analyses for OC, ECE, SVI and LNI were performed. Fig. 1 graphically shows ROC derived AUCs of the predictive accuracy of the Partin tables' pathological stage predictions, relative to the observed stage. Table 2 lists the AUC separately for each stage and each version of the Partin tables. Fig. 2 shows the Loess plots of the look-up tables' performance relative to the observed pathological stage.

For OC, the Partin tables presented an almost similar AUC (1997: 0.731; 2001: 0.727 and 2007: 0.722). All three versions underestimated the observed OC covering nearly the whole

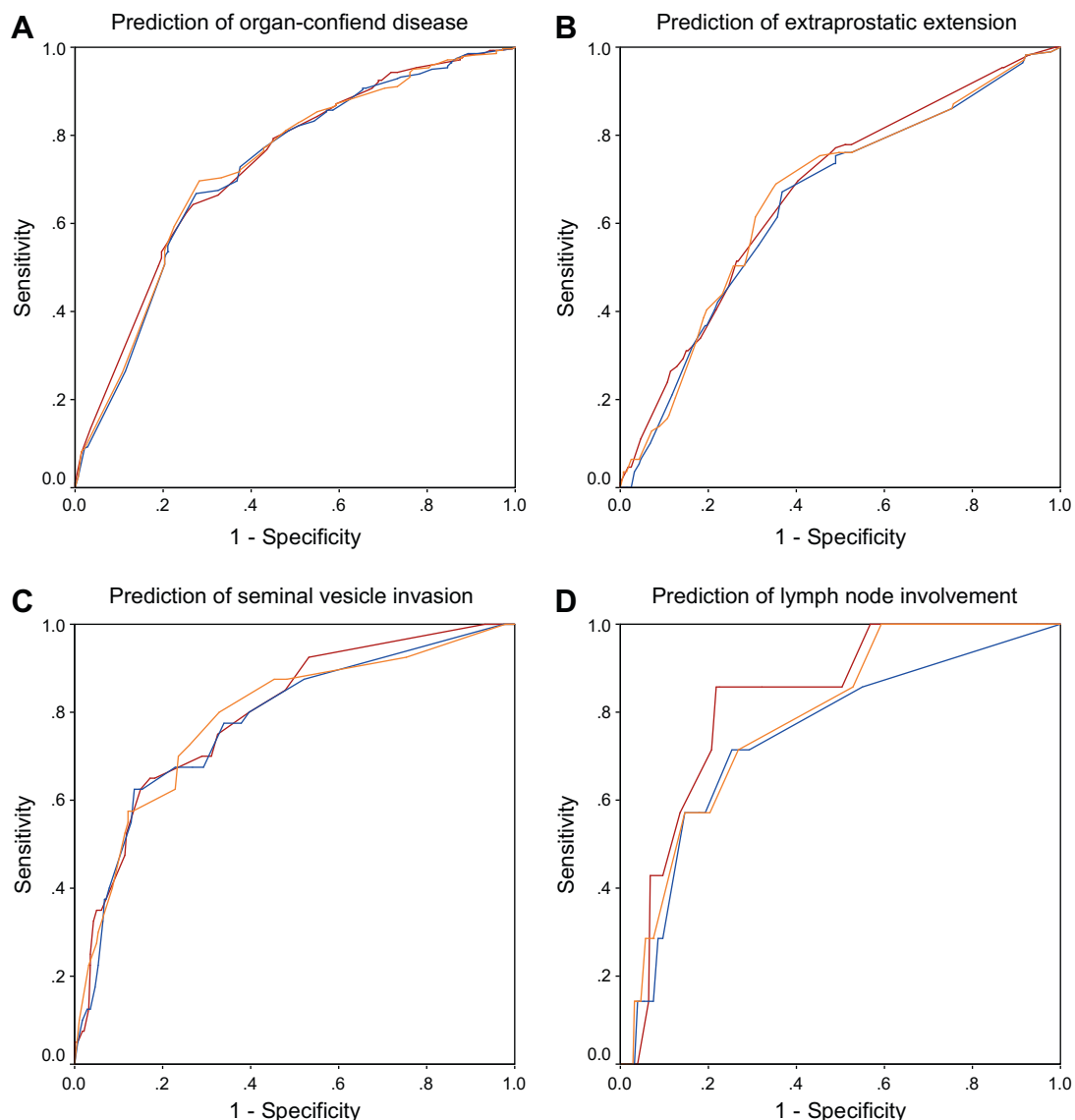


Fig. 1 – Each panel demonstrates the receiver operating characteristic (ROC) curves of the 1997 (brown), 2001 (orange) and 2007 (blue) Tables for OC (A), ECE (B), SVI (C) and LNI (D). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

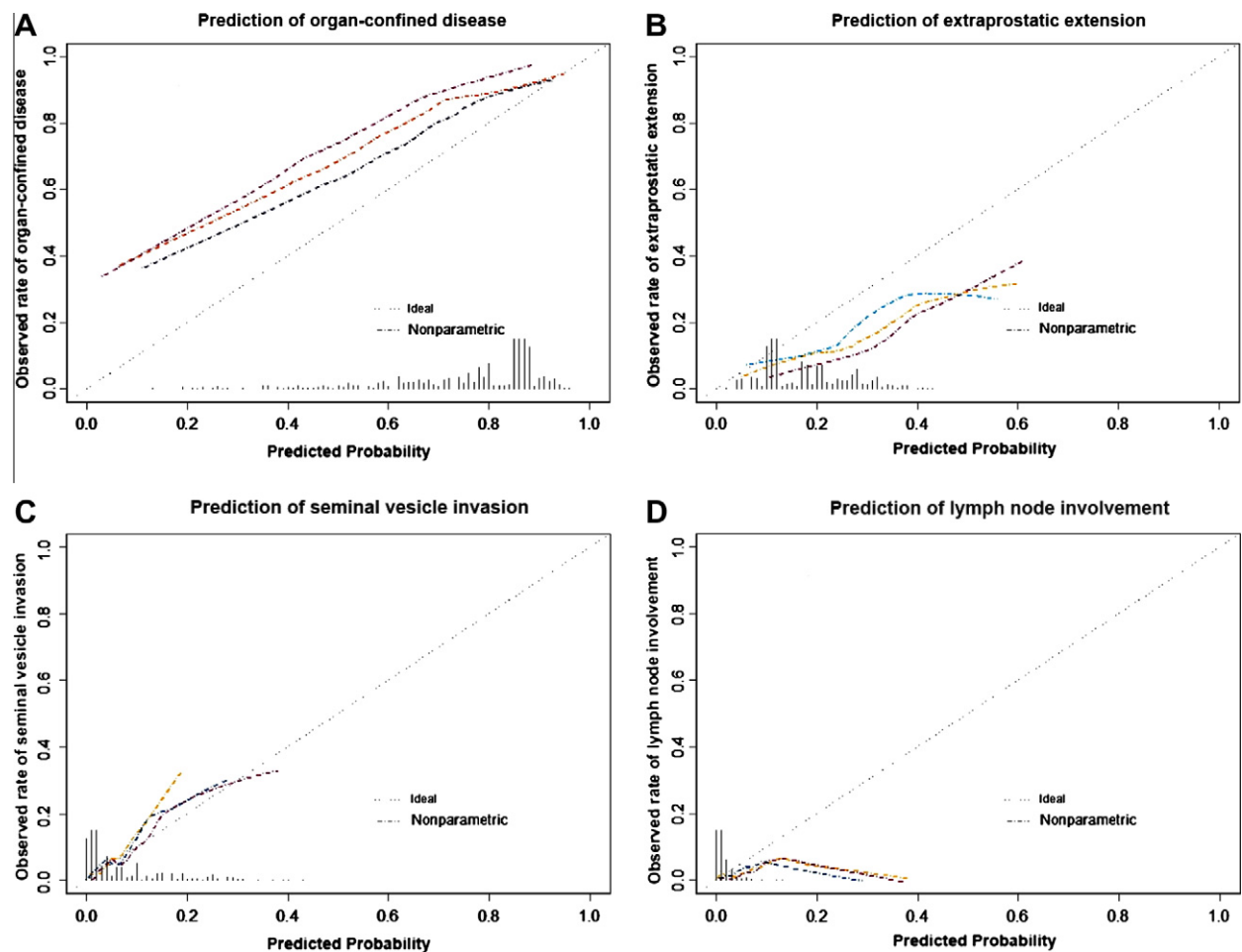
**Table 2 – Areas under the curve (AUC) accompanied by their respective 95% confidence intervals.**

Versions of the Partin tables	Pathological stage variables AUC (95% confidence interval (CI))			
	OC	ECE	SVI	LNI
1997	0.731 (0.683–0.779)	0.671 (0.617–0.726)	0.795 (0.725–0.865)	0.826 (0.707–0.946)
2001	0.727 (0.678–0.776)	0.662 (0.606–0.718)	0.788 (0.711–0.866)	0.786 (0.646–0.926)
2007	0.722 (0.673–0.771)	0.650 (0.594–0.706)	0.779 (0.702–0.856)	0.746 (0.707–0.946)

Abbreviations: OC, organ-confined; ECE, extracapsular extension; SVI, seminal vesicle invasion; LNI, lymph node involvement.

probability range. Hereby, the 2007 table showed a calibration line distinctly closer to the 45 degree ideal line compared to both other versions (Fig. 2A). For ECE, the AUCs of all three versions were also similar, but they only revealed a modest overall accuracy (Table 2). This decrement was the result of a general overestimation, which was especially more pronounced in the high probability ranges (Fig. 2B). The accuracies of all three versions for SVI were generally high. More

specifically, the 1997 version showed a small advantage with an AUC of 0.795 compared to 0.788 for the 2001 and 0.779 for the 2007 version, respectively. Both the 1997 and 2007 versions were close to the ideal line, whereas the 2001 version tended to underestimate the observed rate (Fig. 2C). For LNI, the 1997 version distinctly showed the highest accuracy with an AUC of 0.826. The newer versions were inferior with 0.786 for the 2001 and 0.746 for the 2007 version, respectively. Over-



**Fig. 2 – Calibration plots, graphically depicting the relationship between the Partin tables’ predicted and actually observed rates of OC (A), ECE (B), SVI (C) and LNI (D). The brown broken line refers to the 1997 version of the Partin tables, the orange line to the 2001 version and the blue line to the 2007 version. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)**

all, all three versions overestimated the observed probability of LNI. This performance was clearly more pronounced when the probability of LNI rose above 10% (Fig. 2D).

#### 4. Discussion

In the field of PC, predictive statistical tools play an important part. Consequently, a large range of models for different purposes are available.<sup>2</sup> Generally, the intent of these tools is to overcome the subjectivity of a physician's judgment and to provide a basis for an evidence-based medical decision-making process. In general, predictive models demonstrate predicting clinical outcome more accurately than physicians.<sup>15</sup> However, predictive tools are not perfect and may show limitations. In particular, these instruments may lower their accuracy in patients with extreme characteristics. Moreover, they may deteriorate when applied to a new and heterogeneous dataset separate from the training dataset. Subsequently, internal and particularly external validation is an essential process to become familiar with the specific shortcomings of statistical models. Validation is basically based on the evaluation of predictive accuracy and calibration.<sup>2</sup> The accuracy to discriminate between two different characteristics is mostly quantified by the ROC derived AUC. An AUC of 0.500 represents the probability of flipping a coin to discriminate between two possibilities. Generally, an AUC beyond 0.700 represents an acceptable discriminative ability. The predictive accuracy represents the discriminate ability for all risk ranges. The calibration estimates the discriminative ability for specific risk ranges and illustrates it graphically. Therefore, over- and underestimation of a statistical model for specific risk ranges are displayed related to the 45 degree ideal line.<sup>4</sup>

Unfortunately, some of the statistical models may be hampered in their use as they are based on clinical parameters which are cumbersome and/or time consuming to assess. One of the pioneers, Partin and colleagues, published a model to predict pathological stages in clinically localised PC which gained widespread popularity due to its easy usability and limitation to routinely performed predictor variables.<sup>3</sup> The Partin tables were modified and updated in 1997. Hereby, data from 4133 patients who had undergone radical prostatectomy between 1982 and 1996 in three different highly reputed US institutions were used.<sup>5</sup> As a result of stage migration with a distinct trend towards earlier stage diseases and with an aim to increase the predictive accuracy, the Partin tables were updated and modified repeatedly. In contrast to the 1997 version, the 2001 and 2007 updates were based solely on single institution data. Moreover, in the 2001 version the preoperative PSA ranges were stratified into narrower intervals and the Gleason categories were redefined with a Gleason sum 7, separated into 3 + 4 and 4 + 3. This update was based on data of 5079 men treated between 1994 and 2000.<sup>8</sup> In the 2007 version the Gleason category 2–4 was abandoned and clinical stages 2b and 2c were merged.<sup>9</sup> The latter update was based on data of 5730 men who had undergone surgery between 2000 and 2005.

Shortly, Karakiewicz and colleagues externally validated the 2007 version of the tables based on 1838 patients treated

by RP between 2001 and 2005 at the Cleveland Clinic Foundation.<sup>16</sup> They found an AUC of 0.708 for ECE, 0.800 for SVI and 0.752 for LNI which were comparable with the original development cohort. However, the similarity between these two US cohorts, namely the development and the external validation cohort, may impair the ability to generalise. In a recent report, Yu and colleagues analysed the 2007 Partin table based on 11,185 US men of the National Cancer Institute Surveillance, Epidemiology and End Results (SEER) database who underwent RP between 2004 and 2005.<sup>17</sup> They assessed an AUC of 0.620 for ECE and 0.740 for SVI which were in line with the present study (Table 3).

A main requisite for a predictive tool is generalisability which means better applicability for different target populations.<sup>2</sup> Notably, most external validations were performed with datasets of high volume centres with a potentially higher homogeneity of their cohorts than low volume centres have. Hence, the homogeneity may represent a limitation, as smaller institutions may show a greater heterogeneity due to a higher proportion of clinically intermediate and high risk patients.<sup>18</sup> Therefore, the present analysis might account for this aspect as it was based on data from a standard referral European centre with about 140 RP per year.

In the presented study, we performed a head to head comparison of the last three versions of the Partin tables. Generally, all three versions showed a good accuracy to predict OC, SVI and LNI, but their predictive accuracy for ECE was only moderate. However, the predictive accuracies of the 1997 version for all categories were still superior to those of the versions from 2001 and 2007 (Table 2). Interestingly, the AUC of all categories even decreased slightly from versions 1997 and 2001 through to version 2007 (Table 2). With emphasis on the calibration, the differences were generally small (Fig. 2), with no pronounced advantage of one over the other. Thus, we could not observe an increase in the predictive accuracy by the newer and modified versions. However, it might be hypothesised that the development cohort of the 1997 version, based on data from three different institutions, may better reflect the heterogeneity of a standard centre than the later single institution updates.

In 2004, a similar comparison between the 1997 and 2001 tables was performed with data of a reputable European high volume centre in Hamburg-Eppendorf.<sup>19</sup> The AUCs for OC, SVI and LNI were comparable with the present analysis, whereas the AUC for ECE was clearly higher with 0.766 and 0.728 for the 1997 and 2001 versions, respectively. Furthermore, in contrast to the present analysis the calibration of both versions showed a distinctly different plot. The curve reflected an s-shape indicating overestimation for the low probability ranges and underestimation for the high probability ranges. The reasons for these differences might be manifold. Besides higher homogeneity of the cohort, another reason may be contributed to the differences of the pathological evaluation by excluding the inter-observer variability.<sup>20</sup> Therefore, the biopsies of the aforementioned European high volume centre are ideally reviewed by one single dedicated uro-pathologist, whereas several pathologists assessed the Gleason score of the biopsies at our institution. However, this optimal infrastructure of high volume centres might not be standard in smaller units. Consequently, validation results of centres of



**Table 3 – Predictive accuracies of 2007 tables in different study populations.**

Pathological stage variables	2007 version of the Partin tables (source of cohort)					
	Karakiewicz <sup>16</sup> (US)	YU <sup>17</sup> (US)	Bhojani <sup>22</sup> (French)	Bhojani <sup>22</sup> (Italian)	Bhojani <sup>21</sup> (German)	Present study (Austrian)
ECE	0.708	0.620	0.613	0.663	0.798	0.650
SVI	0.800	0.740	0.706	0.924	0.805	0.779
LNI	0.752	0.800	0.816	0.748	0.762	0.746

Abbreviations: ECE, extracapsular extension; SVI, seminal vesicle invasion; LNI, lymph node involvement.

excellence with high volumes could be transferred to standard institutions with caution.

Similarly, Bhojani and colleagues compared the accuracies and performances of the Partin tables of 2001 and 2007.<sup>21</sup> For their external validation, the authors used the data of 3105 men treated by RP between 2000 and 2005 from the same aforementioned high volume centre. For the 2001 and 2007 versions of the Partin tables they found an AUC of 0.799 versus 0.798 for ECE, 0.778 versus 0.805 for SVI and 0.730 versus 0.762 for LNI, respectively. The performance plots were quite similar to the evaluation in the year 2004 based on data of 2139 men undergoing RP between 1992 and 2002.<sup>19</sup> Accordingly, the plots of Bhojani and colleagues showed the same differences to the present analysis.

In another recent study by Bhojani and colleagues, the authors externally validated the 2007 version based on data of 839 French and 225 Italian men.<sup>22</sup> For the French men they assessed an AUC of 0.613 for ECE, 0.706 for SVI and 0.816 for LNI. In comparison, they found for the Italian cohort an AUC of 0.663 for ECE, 0.924 for SVI and 0.748 for LNI, respectively. In addition, the performance plots were also quite different between the cohorts. It is interesting to compare these data with the preceding analysis by the same authors, as distinct variations of the AUCs exist in relation to the German validation cohort. In these smaller series the AUC for ECE was comparable to our study. However, the performance plots were clearly different. For example, when the 2007 version predicted a 40% probability of ECE, the observed rate was less than 20% in the Italian cohort but it was very close to 40% in the French group. In our analysis the observed rate for the 2007 version was near to 30% and about 20% for the 1997 version, the 2001 version was roughly positioned between both. An overview on recent external validations of the 2007 version is provided in Table 3.

Nerve-sparing techniques may preserve erectile function in a considerable part of patients and enhance postoperative health-related quality of life. Unfortunately, in the presence of ECE, surgery may carry a substantial risk of positive surgical margins and subsequently compromise cancer control.<sup>23</sup> Thus, an accurate prediction of ECE represents a cornerstone to indicate nerve-sparing surgery as the preservation of the neurovascular bundles appears to be safe in patients without ECE. However, as outlined above in our analysis, the AUCs were only modest for the prediction of ECE and all three tables overestimated the probability for ECE. Hence, according to the tables' probabilities a higher portion of men would be spared from nerve-sparing RP than necessary. In a recent analysis we compared in a small series the accuracies between the 2001 version and 3-Tesla magnetic resonance imaging (MRI).<sup>24</sup> In

contrast to the tables, MRI predicted ECE significantly more accurately than the Partin tables and they also provided side-specified information, making unilateral nerve-sparing surgery possible in men with single-sided ECE and a desire for the preservation of their erectile function.

Finally, looking at the present knowledge about this exciting topic, an external validation should ideally be performed for each target cohort with its particular characteristics to assess the specific performance and also the shortcomings of any statistical tool.<sup>25</sup>

### Conflict of interest statement

None declared.

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