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Research Article

Estimating Bone Metastasis Risk in Prostate Cancer: A Three-Parameter Model Using BSP, ISUP Grading, and Tumor Progression

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Running/Short title: Predicting Bone Metastases in Prostate Cancer using BSP, ISUP, and Tumor Progression

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Keywords: Bone metastasis; Bone sialoprotein; immunohistochemistry; prostate cancer

ABSTRACT

Introduction: Osseous metastasis is the most common site of distant spread in prostate cancer. Several factors contribute to predicting bone metastasis, including elevated PSA levels, short PSA doubling time, advanced ISUP grading, local tumor progression, and novel biomarkers. However, no clinical scoring system currently exists to assess bone metastasis risk at the time of prostate cancer diagnosis. Furthermore, no study has investigated the correlation between predictive factors and bone sialoprotein (BSP) expression in the primary tumor.

Methods: Immunehistochemistry was used to evaluate BSP expression in transrectal ultrasound (TRUS)-guided biopsies from prostate cancer patients. Data from 673 patients were analyzed over a 7–9 year follow-up period to assess the development of bone metastases. BSP expression was also evaluated in patients with benign prostatic hyperplasia (BPH). Additionally, BSP expression was analyzed alongside established risk factors using multivariate logistic regression to determine their combined predictive value for bone metastasis.

Results: Bone metastases developed in 12.5% (84/673) of patients. BSP expression was negative (0–5%) in 23.8% of cases, while 22.2% exhibited high expression (>40%). Patients with bone metastases had significantly higher BSP expression than those without (55.5 ± 19.7% vs. 25.7 ± 24.9%; $p < 0.001$). In contrast, 97% of patients without prostate carcinoma had BSP values below 5%.

Among metastatic patients: 82.9% had BSP expression of at least 40%, and none had values below 20%. As a single predictive parameter, BSP showed a sensitivity of 50% and a specificity of 81.6%. However, using multivariate analysis, a three-parameter scoring model integrating BSP expression, ISUP grading, and the number of affected core needle biopsies achieved 88.6% sensitivity and 81.1% specificity for predicting bone metastases.

Conclusion: BSP expression serves as a potential indicator for bone metastasis development but lacks sufficient sensitivity as a standalone clinical marker. Similarly, local tumor progression and histopathologic grading (ISUP) fail as single predictors. However, integrating BSP expression with established risk factors significantly enhances predictive accuracy. Given that all three parameters are derived from routine histopathological analysis, BSP immunohistochemistry should be considered for integration into clinical practice for early risk stratification in prostate cancer patients.

1. Introduction

As life expectancy increases in Western industrialized nations, the incidence of malignant neoplastic diseases continues to rise [1]. Among men, prostate carcinoma is the most frequently diagnosed malignancy, accounting for approximately one in four newly diagnosed cancers. In 2020 alone, 65,820 new

cases and 15,403 deaths were reported in Germany, while 1.41 million cases and 375,304 deaths were recorded worldwide [2,3].
A key prognostic factor in prostate cancer is the presence or absence of metastases at the time of diagnosis. By far, the most common site of metastasis is bone tissue, occurring in up to 80% of patients with advanced stage prostate carcinoma [4]. Several factors have been associated with an increased risk of bone metastases, including high PSA levels, short PSA doubling time, high pathological grading (ISUP), and local tumor progression [5–7].
One biomarker suspected to play a central role in bone metastasis formation is Bone Sialoprotein (BSP). Originally discovered in bovine cortical bone, BSP belongs to the same protein family as osteonectin and osteopontin and constitutes 12% of the total non-collagenous extracellular protein in bone tissue [8,9]. BSP is involved in apatite crystal deposition and is physiologically expressed in mineralizing cells such as osteoblasts, osteoclasts, osteocytes, chondrocytes, and trophoblasts [10,11].
Since the early 1990s, the role of BSP in bone metastasis formation has been extensively studied [12–14]. BSP has been found to be expressed in multiple tumor types that primarily metastasize to bone, including breast cancer [12], lung cancer [13], prostate cancer [14], and cervical cancer [15]. Recent studies using interleukin-8 (IL-8)-manipulated cellcultures demonstrated that BSP upregulation enhances tumorcell adherence to bone tissue [16].
Additionally, structural differences between physiologically produced BSP and tumor-derived BSP enable tumor-specific BSP antibodies to bind and inactivate metastatic BSP. Animal models have shown that the administration of BSP-specific antibodies alongside tumorcells reduces bone metastasis formation [17].
Given these findings, this study aims to evaluate whether BSP expression in prostate carcinoma can predict the development of bone metastases, either as a single parameter or in combination with other known risk factors. Furthermore, we assess the potential integration of BSP immunohistochemistry into routine histopathological diagnostics.
To achieve this, transrectal ultrasound-guided biopsies (TRUS) were analyzed, as histological confirmation of bone metastases is generally not required in clinical practice. The diagnosis of osseous prostate cancer metastases is primarily based on clinical and radiological findings, with histological confirmation only performed in cases of diagnostic uncertainty or multiple malignancies.
Unlike previous studies that focused solely on serum BSP levels [14], our investigation focuses on BSP expression in prostate carcinoma tissue to determine whether it provides a predictive value for bone metastases. Additionally, we examine BSP expression in benign prostate conditions, as no previous studies have evaluated BSP in prostate tissue from patients without carcinoma or within elderly populations.

2. Material and methods

The patient collective consists of 1,201 individuals diagnosed with prostate cancer following transrectal ultrasound (TRUS)-guided biopsies in the urology unit of the Institute of Pathology, Augusta-Hospital, Bochum, Germany, between 2011 and 2013. At the time of diagnosis, all patients were non-metastatic. Data on osseous metastases were available for 673 patients after a 7–9 year follow-up.
During the follow-up period, 84 patients (12.5%) developed bone metastases, while 589 patients (87.5%) did not. The mean age in the metastasis group was 72.5 years, compared to 69.8 years in the non-metastatic group. None of the patients in this cohort were diagnosed with other malignant tumors.
For correlation analysis, BSP expression was also investigated in 30 patients without carcinoma. The sample included 10 patients aged 50–60 years, 10 patients aged 60–70 years, and 10 patients aged 70–80 years.
The study was conducted in accordance with ethical guidelines, and approval was obtained from the institutional ethics committee (Medical Faculty of the University Duisburg-Essen, 20-9548-BO).
Three antibodies were tested for reliability and stability. Only one antibody, namely Linaris (Linaris Biological Products, Dossenheim, Germany) at a 1:1000 dilution, showed sufficient stability in positive controls on placenta and bone tissue. The other two antibodies yielded unsatisfactory results, even after repeated testing with heat and enzyme pretreatment.
For this study, immunohistochemistry with Linaris (1:1000 dilution) was applied to the entire patient collective. The reaction was performed manually by a laboratory assistant and automated using a Benchmark Ventana device.

Quantification was conducted under a light microscope by two independent observers. The immunohistochemistry and quantification process was repeated for metastatic patients to ensure accuracy of BSP expression.
Any reaction of tumor cells was classified as positive. All tumor cells in the biopsy cylinders were examined, and the percentage of positive tumor cells was calculated.
For statistical analysis, BSP expression was categorized as follows:

- 0–5% BSP expression = BSP-negative tumors
- Tumors were further classified into 10 percentile groups (e.g., 5–15%, 15–25%, 25–35%, etc.).

In addition to BSP expression in the primary tumor, other known risk factors were evaluated, including: Number of affected biopsies, Patient age, Serum PSA level at the time of core needle biopsy, Histopathological grading (ISUP) and Tumor stage (TNM system) in patients who underwent radical prostatectomy
Furthermore, BSP expression in patients without carcinoma but with benign prostatic hyperplasia (BPH) was examined.
All variables were analyzed descriptively, including: Sample size, Mean and standard deviation, Median and quartiles and range.
Group differences were assessed using the Mann-Whitney U test, with a significance threshold of $p < 0.05$.
Bivariate correlations between variables were analyzed using the non-parametric Spearman-Rho correlation.
To evaluate the influence of risk factors, a multiple logistic regression model was applied. Based on these models, easily manageable score-based classification systems were developed.

3. Results

In the group of patients without carcinoma, the vast majority exhibited BSP expression of less than 1%. Twenty-nine out of thirty patients had a value below 5% (Table 1). One patient showed a BSP expression of 9%; however, the expression was observed only in basal cells in a condition of basal cell hyperplasia combined with chronic inflammation (Figure 1). BSP expression in prostate tissue without carcinoma and without basal cell hyperplasia is shown in Figure 2.
Among the 673 patients with prostate cancer, 12.5% (84/673) developed bone metastases. The metastatic patients were, on average, older than the non-metastatic patients ($p = 0.003$, Table 2). Furthermore, there was a statistically significant correlation between BSP expression and age in the non-metastatic group ($N = 567$, $r = 0.088$; $pSR = 0.037$), whereas no correlation was observed in the metastatic group ($N = 82$, $r = 0.162$; $pSR = 0.147$, Table 2a).
The average BSP expression in the metastatic group was 55.5%, while in the non-metastatic group, it was 25.7%. This difference was statistically significant ($Z = -9.429$; $pU < 0.001$, Table 3). Notably, all patients in the metastatic group had a BSP value of at least 20%, whereas in the non-metastatic group, 23.8% (135/567) had BSP values between 0-5%, and 43.7% (248/567) had BSP values below 20% (Figure 3). In the entire patient cohort:

- 23.8% were BSP-negative (0-5% expression).

- 22.2% had high BSP expression (>40%).
- 82.9% of metastatic patients exhibited BSP expression of at least 40%.
- No metastatic patient had BSP values below 20%.

These results are summarized in Table 3, and Figures 3 & 4 & 5.

To avoid bias, calculations were repeated after excluding all non-metastatic patients with BSP values below 20%, and the results were confirmed. The difference in BSP expression remained statistically significant (Z = −5.054; pU < 0.001, Table 4).

Using BSP as a single predictive parameter with a cut-off value of 50%, the model achieved (Table 5):

- Sensitivity: 50% (correctly predicting 41/82 metastatic patients).
- Specificity: 81.6% (correctly predicting 464/567 non-metastatic patients).

These findings suggest that BSP alone is insufficient as a predictive factor. Therefore, additional risk factors and their correlations were analyzed.

Most patients (84.5%) presented with clinically advanced tumors (pT3a or pT3b, Table 5a). Additionally, 83.3% of metastatic patients had high-grade carcinomas (ISUP groups 4 or 5). Even among less advanced tumors (pT2b or pT2c), the majority (69.3%) were classified as ISUP group 4 or 5 (Table 5b).

The study did not demonstrate a correlation between tumor stage and BSP expression (Table 5c). However, an analysis of serum PSA levels at the time of core needle biopsy revealed a significant correlation between PSA levels, disease progression, and tumor burden (Table 5d).

A comparison of the last recorded PSA level vs. the initial PSA value showed a 200-fold increase in serum PSA levels in patients with pT3a tumors (Table 5e). Additionally, the number of affected biopsies served as a strong indicator of local tumor progression and a risk factor for bone metastasis. The difference between metastatic and non-metastatic tumors was significant:

- Metastatic tumors: 74.1% affected biopsies
- Non-metastatic tumors: 47.4% affected biopsies

These results are presented in Table 5f.

The relationship between ISUP grading and BSP expression is illustrated in Table 6 and Figure 6:

- In the non-metastatic group, BSP expression correlated significantly with ISUP grade (r = 0.329; pSR < 0.001).
- In the metastatic group, no correlation was found (r = 0.011; pSR = 0.919).

Mean BSP values per ISUP group further illustrate this trend.

Using logistic regression, the predictive value of several parameters for bone metastasis formation was analyzed (Table 7):

- Initial serum PSA level at core needle biopsy: Sensitivity 58.1%
- Number of affected biopsies: Sensitivity 50.6%
- BSP expression alone: Sensitivity 50.0%
- ISUP histopathological grading: Shows despite a low sensitivity the highest specificity in predicting non-metastatic patients, since none of the patients with well-differentiated carcinoma developed metastases.

Using a two-factor model (Table 8):

- BSP expression + number of affected biopsies → Sensitivity 81.0%
- BSP expression + initial PSA level → Sensitivity 61.1% (failed to provide strong predictive power).

By combining three key risk factors—BSP expression, number of affected biopsies, and ISUP grading a scoring system was developed (Table 9).

- A maximum score of 9 was assigned.
- A score <5 indicated low risk, while ≥5 indicated high risk.
- Using a cutoff score of 5, the model achieved:
    - Sensitivity: 88.6% (70/79 metastatic patients identified).
    - Specificity: 80.0% (458/565 non-metastatic patients correctly classified).

4. Discussion

Bone sialoprotein (BSP) plays a key role in the pathogenesis of osseous metastases. BSP expression has been demonstrated in several malignancies with a known tropism for bone metastases, including lung cancer [18], cervical cancer [15], breast cancer [12], and prostate cancer [14]. However, to the best of our

knowledge, no study has explicitly established a correlation between BSP expression and the occurrence of osseous metastases in prostate cancer patients.
In our study, immunohistochemical staining of paraffin-embedded tissue samples was used to assess BSP expression, following methodologies similar to those employed by other authors [14], [15]. Furthermore, a recent in vitro study from 2019 [19] demonstrated that IL-8 upregulates BSP expression, increasing the adherence of prostate carcinoma cells to bone tissue. Their findings showed a significant reduction in cell adherence to bone following treatment with IL-8-specific antibodies.
In our analysis of prostate tissue from carcinoma-free patients, 29 out of 30 individuals (96.7%) exhibited BSP expression below 5%, which was classified as BSP-negative for statistical purposes. Among prostate cancer patients, 23.8% also had BSP-negative values (0–5%).
A study from 2013 [20] is the only known research comparing serum BSP levels between carcinoma patients and those with benign prostatic hyperplasia. Their findings showed that serum BSP levels were significantly higher in prostate cancer patients with bone metastases than in those without metastases, as well as in benign prostatic hyperplasia patients and healthy controls.
One of the most relevant comparisons is a study conducted in 1998 [14], which examined histological samples from 180 patients with localized prostate cancer and correlated BSP expression with clinical and biochemical parameters (Gleason score, PSA levels, and capsular rupture). Their study found immunohistochemical BSP expression in 78.9% of cases, concluding that increased BSP expression in the primary tumor is associated with a higher risk of osseous metastases and tumor progression. However, no specific cut-off value was determined.
Similarly, in our study, 76.2% of patients exhibited BSP expression in tumor cells, aligning with the previously described findings. Importantly, the authors used prostate tissue obtained after radical prostatectomy, whereas our study analyzed TRUS-guided biopsy samples at the time of initial diagnosis. Despite the differences in methodology and sample size (673 patients in our study vs. 180 in 1998´s study), the slight variation in BSP positivity rates further supports the robustness of immunohistochemical staining techniques in both studies.

BSP as a Predictor of Bone Metastasis

Our study provides strong evidence that BSP expression correlates with the development of bone metastases in prostate cancer. Notably:

- All patients with bone metastases had BSP expression of at least 20%.
- None of the metastatic patients had BSP-negative tumors (0–5%).
- BSP expression in metastatic tumors varied between 20–80%.

Over a 7–9 year follow-up period, no patient with a BSP expression below 20% at the time of initial biopsy developed bone metastases, highlighting BSP's potential as a prognostic biomarker.
The classification model of BSP-expression varies across studies. For example:
The authors of 1998´s study [14] reported that 78.9% of prostate carcinoma patients had detectable BSP expression, with low or no expression in adjacent normal glandular tissue findings that align with our results.
Reference [11] categorized BSP expression based on staining intensity (0, 1+, 2+, 3+) and the percentage of positive neoplastic glands. They divided patients into two groups: low BSP expression (0, 1+) and high BSP expression (2+, 3+) and found that high BSP expression correlated with an increased risk of PSA relapse.
In contrast, our study classified BSP expression into 10-percentile increments (0–10%, 10–20%, 20–30%, etc.), allowing for a more granular analysis of expression patterns.

Development of a Predictive Scoring Model

Identifying patients at increased risk of developing bone metastases at the time of initial diagnosis is crucial for optimizing follow-up strategies and initiating early treatment. While BSP expression alone does not achieve sufficiently high sensitivity, its combination with other known risk factors enhances predictive accuracy.
Using a multivariate analysis, we developed a three-parameter scoring system incorporating:
BSP expression in the primary tumor, Number of affected core needle biopsies and ISUP grading
This model achieves:

- Sensitivity: 88.6% for predicting bone metastasis development in the years following initial prostate cancer diagnosis.
- High specificity of 81,1% for predicting which patient will not develop bone metastasis in the years following initial prostate cancer diagnosis.

5. Conclusion

Our study provides the largest patient dataset (N = 673) assessing BSP expression at the time of first prostate cancer diagnosis using TRUS-guided biopsies. It is the first to establish a strong correlation between BSP expression and bone metastases in a large, well-characterized patient cohort.

BSP can serve as an indicator for the development of bone metastases in prostate cancer. While it demonstrates high specificity (81.6%), its sensitivity (50%) is insufficient for BSP to be used as a standalone predictive marker in clinical practice. Similarly, other known risk factors, such as local tumor progression and histopathologic grading (ISUP), also fail to provide sufficient predictive value when considered independently.

However, by applying multivariate logistic regression analysis, we developed a three-parameter scoring system that combines:

1. BSP expression in the primary tumor
2. Extent of local tumor progression (affected core needle biopsies)
3. Histopathologic grading (ISUP classification)

This combined approach enables the detection of 88.6% of patients who will develop bone metastases following their initial prostate carcinoma diagnosis via core needle biopsy.

Since all three parameters are derived from standard histopathological analysis, these findings highlight the potential integration of BSP immunohistochemistry into routine clinical practice. Further studies and clinical validation are warranted to assess its practical application in risk stratification and treatment planning for prostate cancer patients.

Word Count: 2597

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Statements

Ethics Statement
The vote of the institutional ethics committee (29th September 2020, University Duisburg-Essen, No. 20-9548-BO) has been obtained before the start of the study. In correspondence with the decision of the ethics committee, the evaluation of the data was anonymized and only retrospective data have been used.Thus written consent was not needed. The study was conducted in accordance with the World MedicalAssociation and Declaration of Helsinki. The decision of the ethics committee is attached.

Conflictsof Interest
The authors declare to have no conflicts of interest to declare.

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Author Contributions
Christos Philippou: conceptualization, writing, visualization, methodology, data curation, supervision, validation, investigation, resources, review and editing;
Simon Gloger: investigation, resources, review and editing;
Burkhard Ubrig: investigation, resources, review and editing;
Norman Bitterlich: methodology, review, editing, statistical evaluation, visualization;
Emilia KrassimirovaNaseva: methodology, review, editing, statistical evaluation, visualization;
Hans-Joerg Sommerfeld: investigation, resources, review and editing;
Andreas Wiedemann: investigation, resources, review and editing;
Dirk Theegarten: conceptualization, methodology, investigation, review and editing, Validation, project administration;
Haji Abdulla: investigation, review and editing;
Stathis Philippou: conceptualization, methodology, project administration, investigation, writing, Validation, supervision, formal analysis, resources, review and editing;

Data Availability Statement
All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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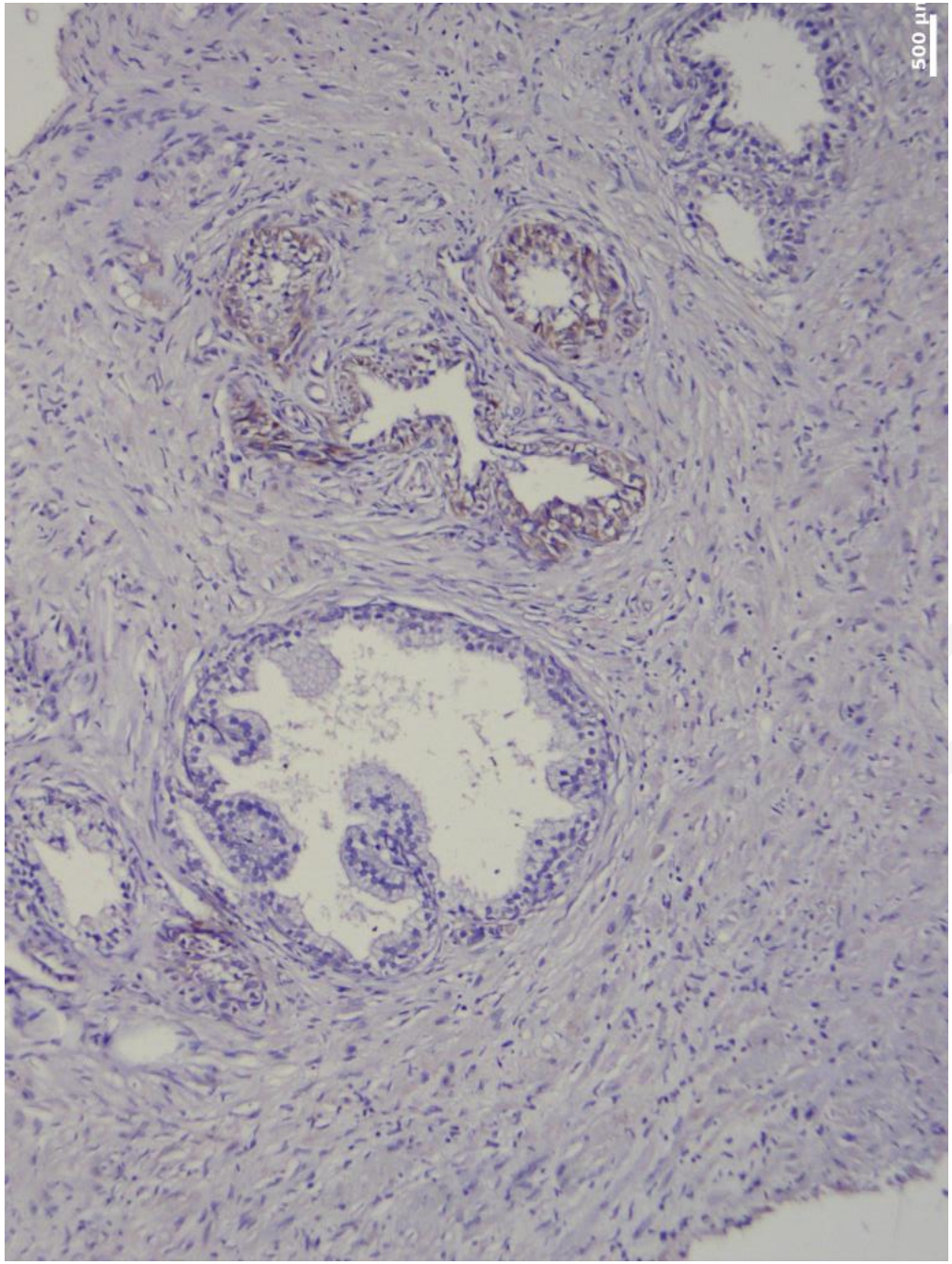
Figures

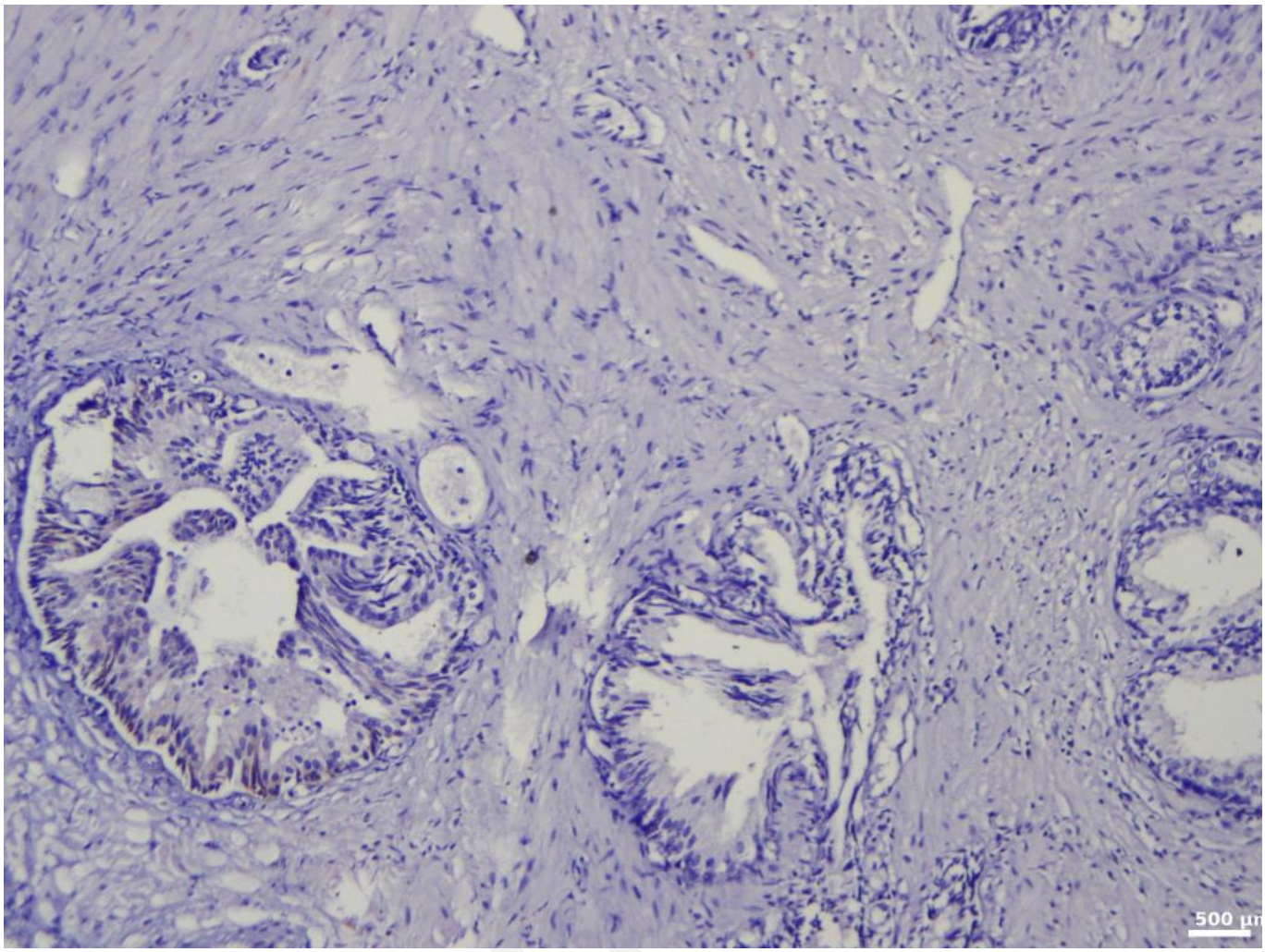
Figure 1– Immunhistochemistry in prostate tissue without carcinoma and with basal cell hyperplasia
Figure 2- Immunhistochemistry in prostate tissue without carcinoma and without basalcell hyperplasia
Figure 3 –BSP expression in the patient collective (649).
Figure 4 – Strong BSP expression of 90% in poorly differentiated prostate carcinoma, (G3, ISUP 5), with capsular and perineural invasion. Immunohistochemistry BSP
Figure 5 – Low BSP expression (20%) in a moderate differentiated acinar prostate carcinoma (G2, ISUP 2). Immunohistochemistry BSP.
Figure 6- BSP per ISUP Group

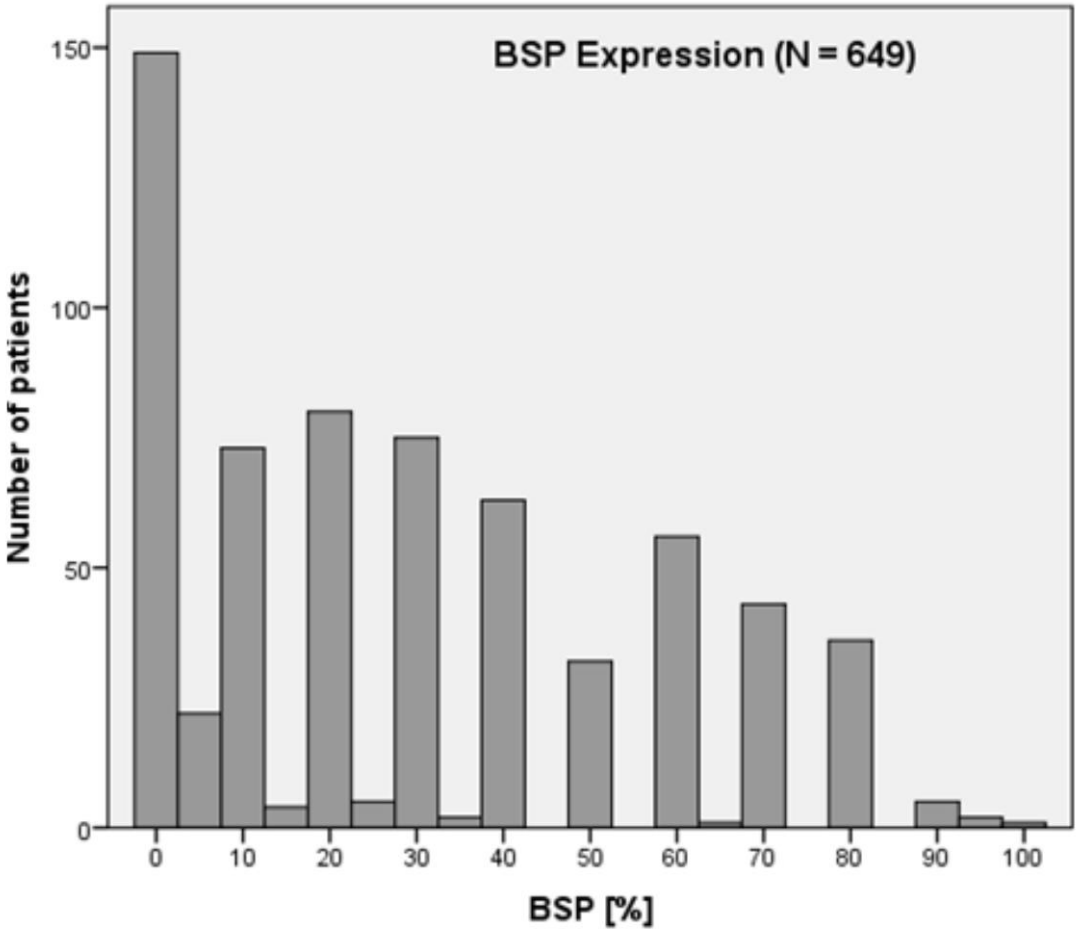
Abbreviations

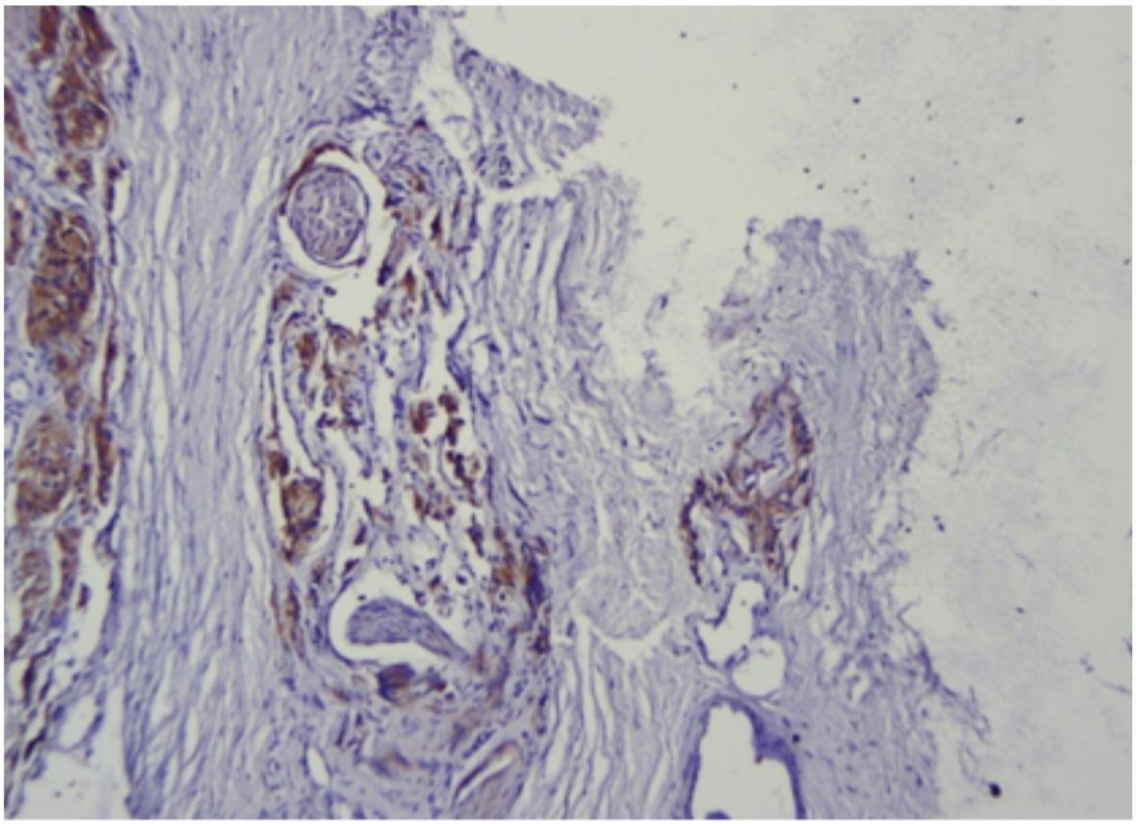
BSP	Bone sialoprotein
ISUP	International Society ofUrologicalPathology
MAX/MIN	Maximum/Minimun
Mm	Group with metastasis
Mo	Group without metastasis

MW	Mean value
PSA	Prostate specificantigen
Q1/Q3	First/ThirdQuartile
SD	Standard deviation
p_U	p-value of Mann-Whitney-U
p_{SR}	p-value of Spearman-Rho
r	Correlation coefficient
Z	Test size of Mann-Whitney-U









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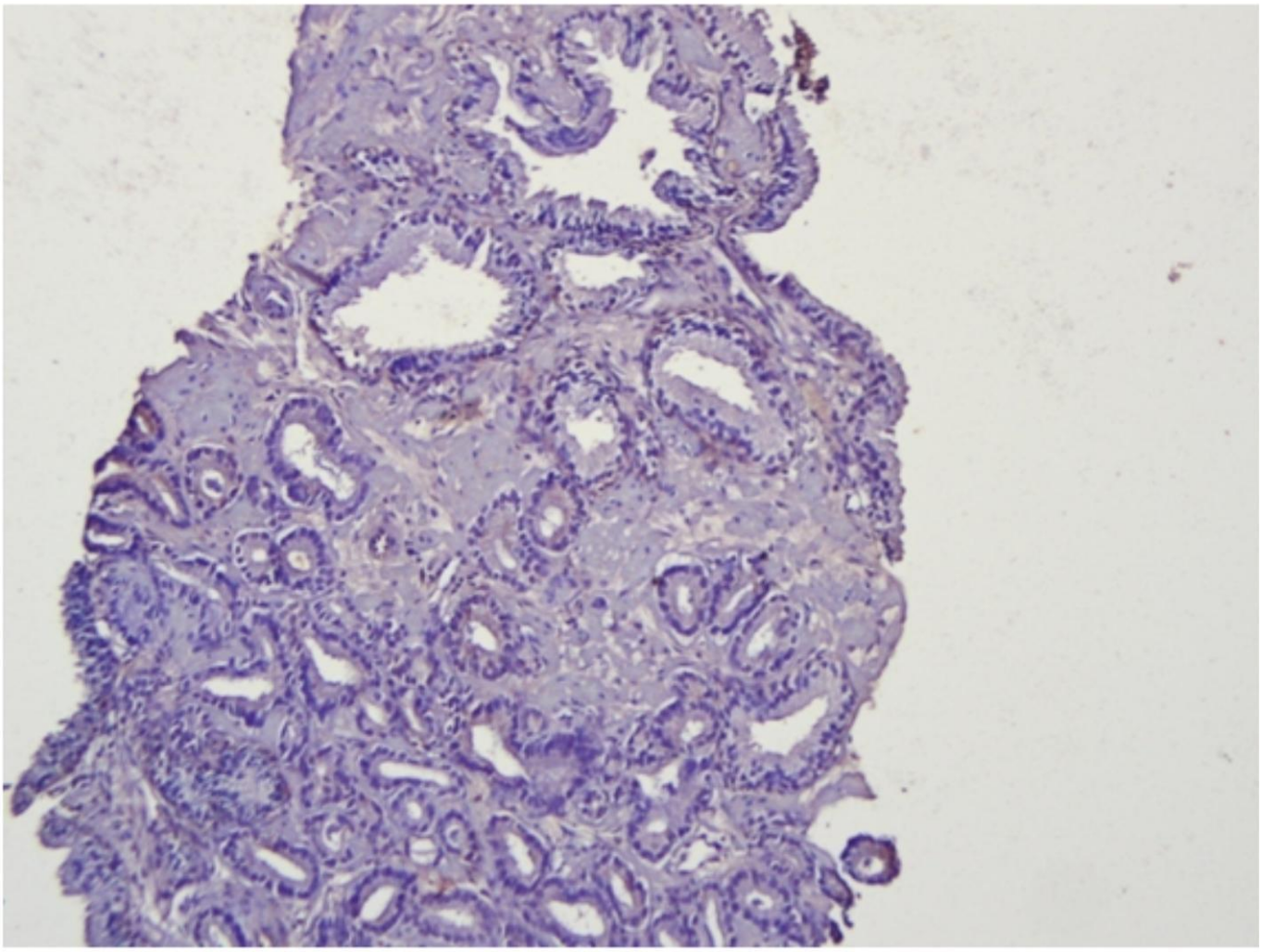


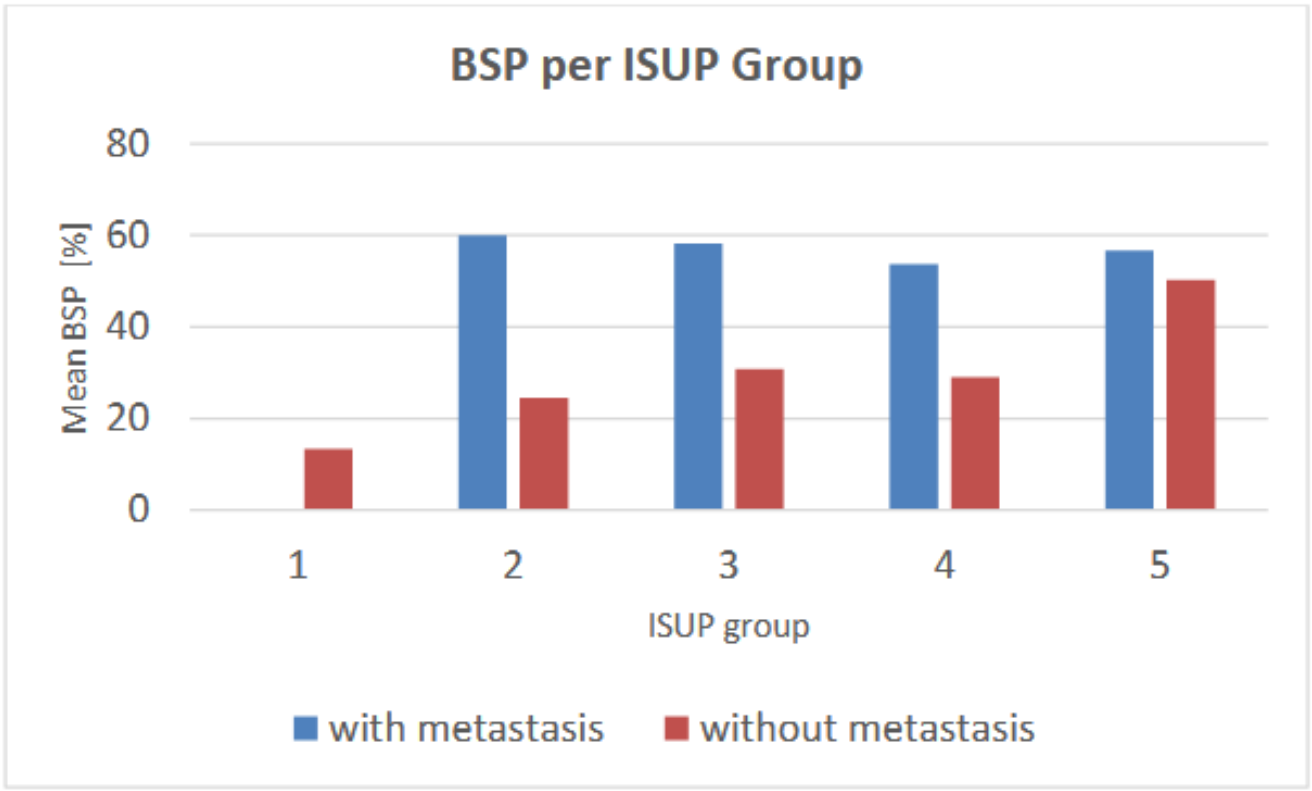
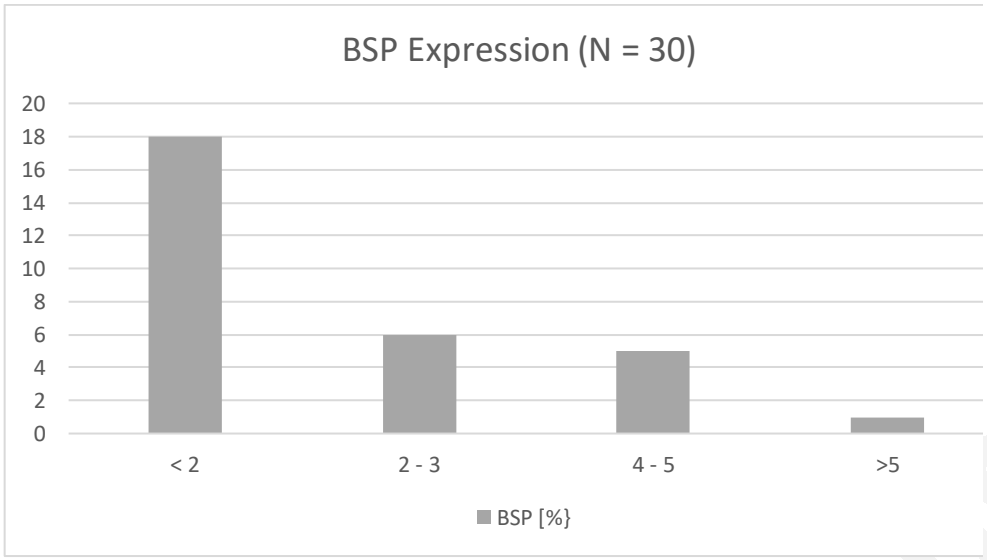


Table 1- BSP expression in prostates without carcinoma



< 2	2 - 3	4 - 5	>5
18	6	5	1
60,0%	20,0%	16,7%	3,3%

Table 2 – Statistically significant difference in age between metastatic (84) and non-metastatic groups (n = 589, Z = −2, 0.933; p_U= 0.003).

Statistical parameter Age [years]								
Group	**N**	**Mean**	**SD**	**Min**	**Q1**	**Median**	**Q3**	**Max**
Metastatic	84	72.5	7.6	51	67.0	74.0	78.0	89
Non metastatic	589	69.8	8.0	46	65.0	71.0	75.0	92

Table 2a – Non-parametric correlation by Spearman-rho

Correlation between BSP [%] and Age [years] depending on metastasis			
Group	**N**	**correlation**	**p-value**
Metastatic	82	-0.162	0.147
Non metastatic	567	0.088	0.037

Table 3 –Statistical parameters of bone sialoprotein expression (BSP) ($Z = -9.429$; $p_U < 0.001$)

Statistical parameter BSP [%]								
Group	**N**	**Mean**	**SD**	**Min**	**Q1**	**Median**	**Q3**	**Max**
Metastatic	82	55.5	19.7	20	40.0	55.0	70.0	95
Non metastatic	567	25.7	24.9	0	1.0	20.0	40.0	100

Table 4 – Statistical parameters for BSP expression of ≥20% ($Z = -5.054$; $p_U < 0.001$)

Statistical Parameter BSP, minimum 20% [%]								
Group	**N**	**Mean**	**SD**	**Min**	**Q1**	**Median**	**Q3**	**Max**
Metastatic	82	55.5	19.7	20	40.0	55.0	70.0	95
Non metastatic	319	42.8	20.3	20	25.0	40.0	60.0	100

Table 5 – BSP as a single parameter. Sensitivity and Specifity using logistic regression.

		Sensitivity		Specifity
BSP	N = 82	50.0%	N = 567	81.6%

Table 5a – Frequency distribution of TNM classification

	Total	**pT2b**		**pT2c**		**pT3a**		**pT3b**	
	N	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Patients with metastasis	84	3	3.6	10	11.9	59	70.2	12	14.3

For all patients without metastasis the TNM classification is not known.

	ISUP 2/3		ISUP 4/5	
TNM	**N**	**%**	**N**	**%**
pT2b/pT2c	4	30.8	9	69.2
pT3a	9	15.3	50	84.7
pT3b	1	8.3	11	91.7
Total	14	16.7	70	83.3

Table 5b– Frequency distribution of risk factor ISUP depending on the TNM classification

Table 5c

Statistical parameter BSP [%]						
TNM classification	**N**	**Mean**	**SD**	**Min**	**Median**	**Max**
pT2b	3	83.3	28.9	30	80.0	80
pT2c	10	66.0	19.0	30	70.0	90
pT3a	58	54.2	19.2	20	50.0	95
pT3b	11	50.5	20.1	20	50.0	80
Total	82	55.6	19.7	20	55.0	95

Table 5d Initial PSA

TNM_q	N	Mean	SD	Minimum	Median	Maximum
pT2c	4	9.1750	3.31298	5.30	9.0000	13.40
pT3a	28	14.5461	7.39731	5.91	12.5000	36.00
pT3b	4	24.7075	8.03942	16.50	23.4650	35.40
Total	36	15.0783	7.96866	5.30	12.9500	36.00

Statistical parameter: number of affected core needle biopsies in relation to number of collected biopsies[%]. Distribution in metastatic and non-metastatic group.								
Group	N	Mean	SD	Min	Q1	Median	Q3	Max
Mm	81	74.1	26.6	7.7	50.0	77.8	100.0	100.0
Mo	586	47.4	28.6	8.3	25.0	41.7	66.7	100.0

Table 5f

Table 6 – BSP expression in relation to ISUP group

BSP – Value [%]						
ISUP-Group	Mm - Group			Mo - Group		
	N	Mean (SD)	Median	N	Mean (SD)	Median
1	-			149	13.4 (17.6)	5.0
2	1	60.0 (-)	60.0	108	24.5 (23.9)	20.0
3	11	58.2 (21.4)	60.0	136	30.8 (25.5)	22.5
4	40	53.8 (21.1)	50.0	139	29.1 (23.6)	30.0
5	30	56.7 (18.0)	55.0	34	50.3 (30.2)	65.0

Table 7- Multivariance analysis using logistic regression for single parameters

Parameter	Sensitivity		Specifity	
BSP	N = 82	50.0%	N = 567	81.6%
ISUP-Group	N = 84	35.7%	N = 588	94.0%[1]
Affected core needle Biopsies	N = 81	50.6%	N = 588	81.2%
Initial serum PSA	N = 74	58.1%	N = 587	93.9%

Table 8- Multivariance analysis with logistic regression using 2 parameters

Parameter	Sensitivity		Specifity	
BSP & ISUP	N = 82	80.5%	N = 566	82.9%
BSP & number of affected core-needle biospies	N = 79	81.0%	N = 566	81.4%
BSP & Initial serum PSA	N=72	61,1%	N=565	81,1%

Table 9- Multivariance analysis with logistic regression using 3 score

3 Parameter Score-System:BSP, ISUP, affected Specimen
<5 low risk for bone metastasis formation
=/>5 high risk for bone metastasis formation

Score	BSP %	ISUP	Ratio affected/collected Specimen %
0	0-20	1	0-50
1	21-35	2-3	50<75
2	36-60	4	75<95
3	>61	5	95-100

Table 5e PSA_last

TNM_q	N	Mean	SD	Minimum	Median	Maximum
pT2c	4	31.8975	39.86543	6.99	14.8000	91.00
pT3a	25	298.8789	502.27537	.08	110.0000	2275.00
pT3b	3	116.9033	165.41907	4.20	39.7000	306.81
Total	32	248.4460	454.98310	.08	88.7000	2275.00