

ORIGINAL PAPER

Pixel Prostate Software as a Reliable Tool in Depicting Spatial Distribution and Determination of the Prostate Cancer Volume

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ABSTRACT

Introduction: Cancer of the prostate (PCa) is the second most common cancer-related cause of death among men and the most common non-cutaneous malignancy in Western countries. Numerous papers have been published on the topic of various aspects of this disease; however, rather little has been written on the diagnostic and prognostic value of the prostate cancer obtained from needle biopsy.

Aim: To examine the utility of Pixel Prostate software in determining the volume and topographic distribution cancer of the prostate (PCa), and to analyze it with other variables that are characteristic for PCa. **Methods:** retrospectively, 75 patients data and postoperative prostate specimens were analyzed, after determining topographic distribution and cancer volume (PCa), using PixelProstate software. **Results:** Mean VPCa was 6.99 cm³ (0.14-29.7; median 4.51), and mean percentage cancer volume relative to prostate volume (%VPCa) was 16% (0.1-67.2%; median 13%). 71% of the patients had T2 stage, while the rest had T3 stage. Apex involvement was present in 65% of the patients, while central zone involvement and extraprostatic extension were present in 23.5% and 22.7% of the patients, respectively. Preoperative Gleason score undergrading was present in 27 (36%) patients, while bilateral PCa finding was increased from 51% to 87%, postoperatively. The most discriminant variable according to the prediction of %VPCa > 10% had preoperative bilateral needle biopsy findings, with AUC of 0.75 (<.001), with sensitivity and specificity of 84% and 70%, respectively; (+LR 2.8; PPV of 74%; NPV of 82%). %VPCa showed good correlation with prostate specific antigen (PSA) and PSA-density. **Conclusion:** A possibility of precise spatial orientation and volume characterization of the PCa by PixelProstate software was shown. Simultaneously, with time, a clinician, experienced by PP software feedback, gets better insight for the planning of future prostate biopsy, as an important factor in clinical decision making.

Keywords: Cancer of the prostate, PixelProstate software, Volume of the cancer, Cancer percentage involvement, Topographic cancer distribution.

1. INTRODUCTION

Cancer of the prostate (PCa) is the second most common cancer-related cause of death among men and the most common non-cutaneous malignancy in Western countries. Numerous papers have been published on the topic of various aspects of this disease; however, rather little has been written on the diagnostic and prognostic value of the prostate cancer obtained from needle biopsy (1). Cancer volume in postoperative specimens significantly correlates with the spread of the cancer, and can help in assessing the aggressiveness of the cancer. It was proven that the cancer volume also correlates with other prognostic indicators and

with progression following a radical prostatectomy (2). These observations suggest that a precise assessment of the cancer volume preoperatively may help decide on a choice of treatment (3, 4).

Morphometric studies following a radical prostatectomy (RPE) and their diagrams provide accurate documentation of the tumor extension, as well as the status of surgical margins. At the same time, approximate determination of absolute and relative tumor volumes is obtained, as well as topographic distribution of tumor foci (5). Given that, here, insufficient attention is still paid to predictive parameters, as well as to the precise definition of the final cancer

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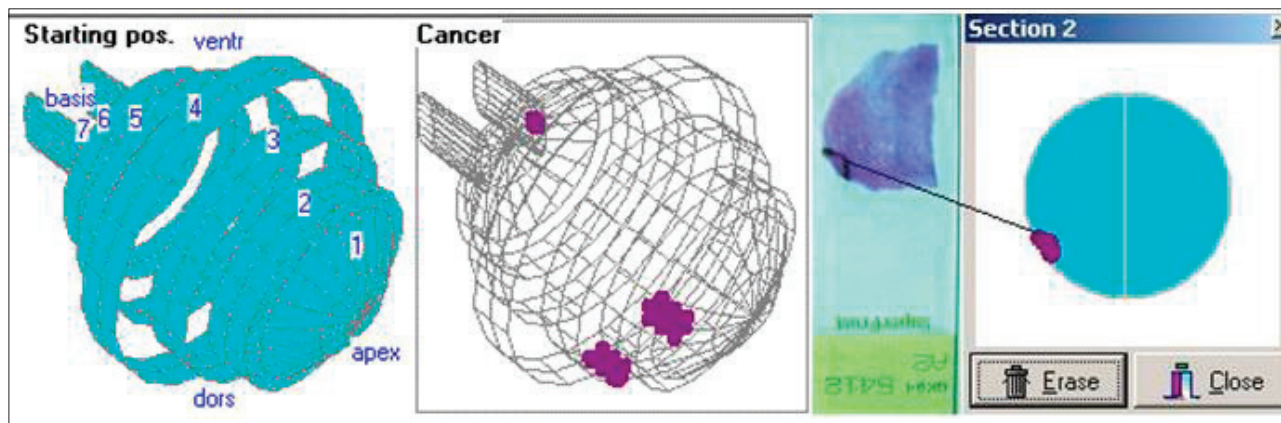


Figure 1. Pixel Prostate provides insight into spatial orientation and volume of the prostate cancer (6)

volume (following RRP) and the spatial distribution of cancer – which would have positive impact on future diagnostic and therapeutic protocols – it becomes essential to have a clear and high quality mapping of tumor on the postoperative pathological sample.

2. AIM

The aim of this study is to determine the utility of PixelProstate Software (6) as a effective tool to determine the final volume of prostate cancer (VPCa) or the percentage of the total prostate volume (%VPCa), and to analyze it with other characteristics of PCa.

3. METHODS

This retrospective study evaluates the data on the final sample of 75 patients, hospitalized at the Urology Clinic of the Sarajevo University Clinical Center, diagnosed with localized prostate cancer and RRP performed in period 2009-2012. Data were obtained from the patients’ medical histories and using PixelProstate Software. The processing of histopathological material, by PixelProstate / PP software, ver. 3.01 (freeware since 2010)/, provided data on prostate volume, prostate cancer volume (cm³), as well as spatial distribution of cancer, and they were compared with preoperative histopathological findings and other variables. All patients had TRUS-guided 12 needle core prostate biopsy findings. 33 patients were excluded from the study due to incomplete data.

PP software provides a simple method for calculating cancer volume with 3D visualization of the area affected by the cancer. After a routine treatment of postoperative specimens, all 3 prostate dimensions are entered into the PP program, as well as the number of cross sections (5-12) and the program automatically calculates the value of prostate volume (cm³). Total prostate volume is calculated using the ellipsoidal formula: $\frac{4}{3} \times \Pi \times (\text{length}/2 \times \text{width}/2 \times \text{height}/2)$. The cancer area is delineated on histopathological glass and the same area is “copied” onto the PP working surface, i.e. using pathologist’s visual memory, an identical tumor area is painted with the mouse on the virtual slide (6). Once completed, the Pixel software automatically calculates the cancer volume,

which represents the sum of all cancer areas painted into the PP, multiplied by the thickness of each cross section, previously calculated by the program. Once the results of cancer volume are obtained (in cm³ and %), the image is automatically generated, and the spatial distribution of cancer can be visualized by a 3D image (Figure 1).

Statistical analysis was performed through one- and two-way analyses of variance (ANOVA test), Spearman correlation coefficient, Kruskal-Wallis test for the rank-ordering data and calculation of area under the receiver operating characteristic (ROC) curve. Statistical analysis was made using Medcalc program for Windows version 12. The level of significance (two-tailed) was set at $p < 0.05$.

4. RESULTS

The average patient age in the observed sample was 69 years (56-81), mean total PSA-t value 7.8 ng/mL (1,5-23,9), mean PSA-density 0.26 (0.02-0.96). Using the Pixel Software, the following data were obtained: mean prostate volume (VP) was 40.5cm³, (24.7-131), mean VPCa was 6.99 cm³ (0.14-29.7; median 4.51), while the average cancer volume percentage relative to prostate volume (%VPCa) was 16% (0.1-67.2%; median 13%).

A correlation table for observed characteristics was created and very good correlations were found between VPCa and %VPCa with postoperative Gleason Score (GS), with PSA-t, and

	Age	V. prost.	V. CaP	V. CaP / V. prost.	GS-b	GS-op	PSA-t	PSA-d	Apex	CZ	EPE	R
Age		0.1* 0.4**	0.08 0.5	0.02 0.9	0.1 0.4	0.04 0.7	-0.03 0.8	-0.03 0.8	-0.18 0.13	0.09 0.4	0.14 0.23	0.0 1
V. prost.			0.29 0.01	-0.21 0.07	-0.03 0.8	-0.03 0.8	0.19 0.09	-0.51 <0.0001	-0.11 0.4	-0.11 0.36	0.10 0.4	0.02 0.71
V. CaP				0.84 <0.0001	0.21 0.06	0.29 0.009	0.43 0.0001	0.18 0.12	0.314 0.006	0.5 <0.0001	0.45 0.0001	0.28 0.01
V. CaP / V. prost.					0.30 0.008	0.39 0.0005	0.41 0.0002	0.49 <0.0001	0.37 0.0013	0.59 <0.0001	0.41 0.0003	0.22 0.06
GS-b						0.6 <0.0001	0.15 0.21	0.18 0.11	0.08 0.5	0.08 0.5	-0.0 0.94	0.08 0.52
GS-op							0.25 0.03	0.24 0.04	-0.03 0.83	0.26 0.02	0.15 0.21	0.14 0.22
PSA-t								0.7 <0.0001	0.06 0.6	0.35 0.0018	0.23 0.05	-0.09 0.4
PSA-d									0.21 0.08	0.43 0.0001	0.15 0.20	-0.1 0.37
Apex										0.3 0.01	-0.07 0.52	0.08 0.48
CZ											0.34 0.003	0.18 0.13
EPE												0.14 0.22

Table1. Correlations for observed characteristics. V. prost. Prostate volume; V. CaP. Cancer volume; Vol. CaP / Vol. Prost. ratio of the CaP. and V. prost. (%); GS-b Preoperative Gleason score, GS-op Postoperative Gleason score, PSA-t total PSA, PSA-d PSA density; Apex involvement of prostatic apex; CZ Involvement of prostatic central zone; R positive margin; EPE extraprostatic extension

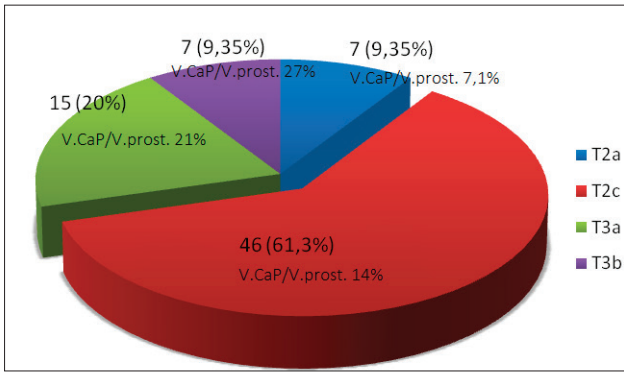


Figure 2. T stage after RRP and mean %VcAP (No 75 pats.)

Gleason Score	GS preoperative	GS postoperative	χ^2 ; p	Preoperative bilat. finding	Postoperative bilat. finding	χ^2 ; p
3+3	19(25%)	9 (12%)	5; 0,02	4/21 (19%)	16/21 (76%)	11,5; 0,001
3+4	38(51%)	31 (41%)	0,4; 0,5	21/36 (58%)	31/36 (86%)	5; 0,02
4+3	11 (15%)	23 (31%)	4,6; 0,03	6/11 (55%)	11/11 (100%)	4; <0,05
4+4 (4+5)	7 (9%)	12 (16%)	0,9; 0,3	7/7	7/7	

Table 2. Preoperative versus postoperative Gleason score and preoperative versus postoperative prostate bilateral (bilobar) involvement

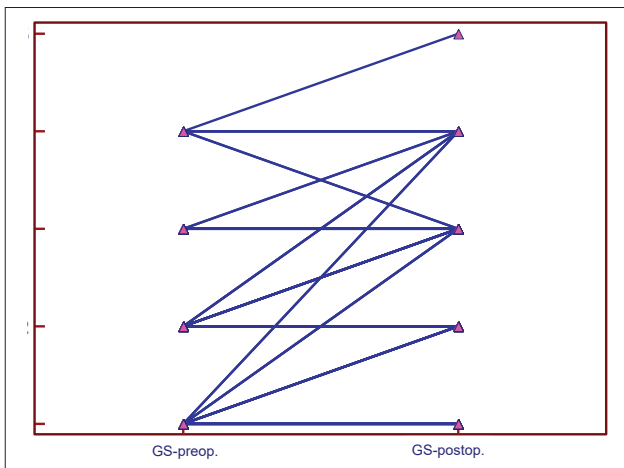


Figure 3. Multiple variables graph shows the changes in the postoperative GS comparing with preoperative biopsy GS (Wilcoxon test; $p < .0001$)

PSA-d with only %VcA ($p < .001$). Preoperative GS correlates less with VcA, but it correlates well with %VcA. As expected, there is a good correlation of %VcA with the invasion of apex, central zone (CZ), and extraprostatic extension (EPE); while PSA-t and PSA-d show good correlation only with the invasion of CZ ($p < .002$); Other clinically significant correlations are shown interchangeably (VP and %VcA; $p > 0.05$; VP and VcA; $p = 0.01$) (Table 1).

The final postoperative findings showed, according to TNM classification, that 9.35% of the patients had T2a stage, with the mean percentage of VcA of 7.1%; 61.3% of the patients had T2c with the mean VcA of 14%, and T3a and 20% and 9.35% of the patients had T3b, with the mean VcA of 21% and 27%, respectively (Figure 2). ANOVA test showed, as expected, that there was a statistically significant difference in %VcA as well, with a higher stage ($F = 4.9$; $p = .004$), while T stage correlates very poorly with PSA-t and its fractions ($p = 0.05$).

So, 70.65% of the patients had organ-confined disease (T2a and T2c group had lower mean %VcA than the mean %VcA for the entire observed group of 16%), while the remaining patients had some form of cancer expansion beyond the prostate

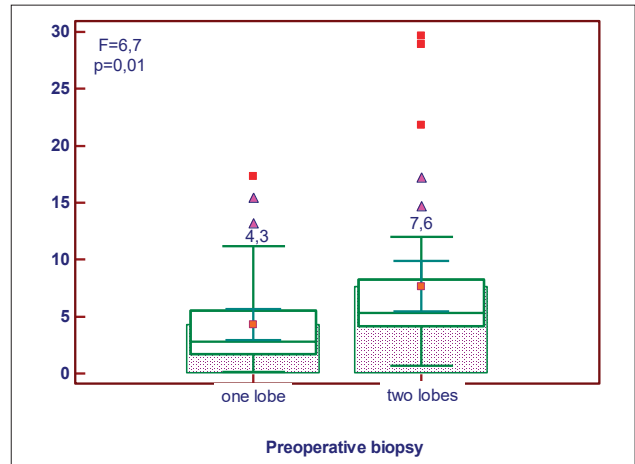


Figure 4. Uni or bilobar preoperative biopsy finding depending on VcA

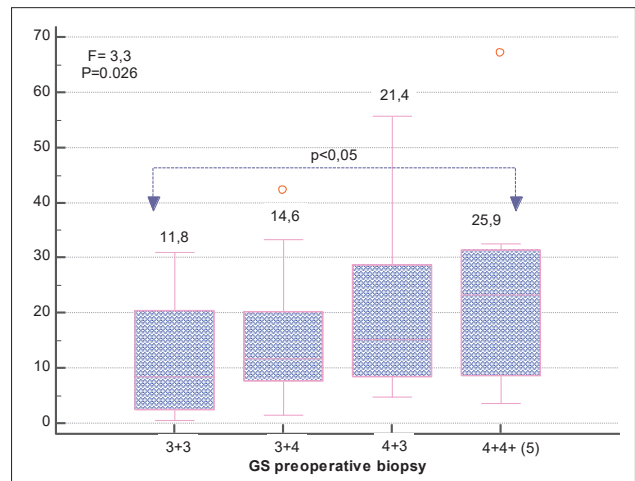


Figure 5. Preoperative biopsy GS grades finding depending on %VcA

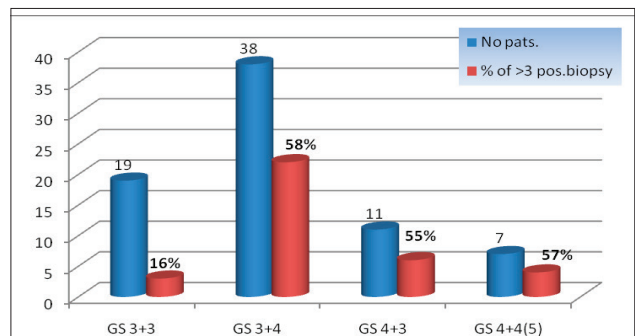


Figure 6. Percentage of more than 3 positive preoperative biopsy findings depending on GS grade

(EPE 22.7%; positive margin 24%), in addition to seminal vesicle invasion of 9.35%. Six patients had concurrent EPE and +R (6/22 or 27.3%), while two patients had EPE and seminal vesicle invasion. Seven patients (12%) had LVI, and 57 (76%) patients had PNI. ASAP and HGPIN were found on the final specimen of 18% and 76% of the patients, respectively. Only LVI showed good correlation with %VcA and VcA ($\rho = 0.35$, $p = 0.002$; $\rho = 0.32$, $p = 0.005$, respectively). Five patients (6.7%) had a spread into regional lymph nodes (mean VcA and %VcA of 18.9 cm^3 and 40.2%, respectively).

Following GS changes compared with preoperative finding, GS undergrading can be observed for GS grades 3+3 and 4+3, respectively, on account of increased GS 4+3, and 4+4 (Table 2). Only one patient had preoperative GS 4+5, and this remained

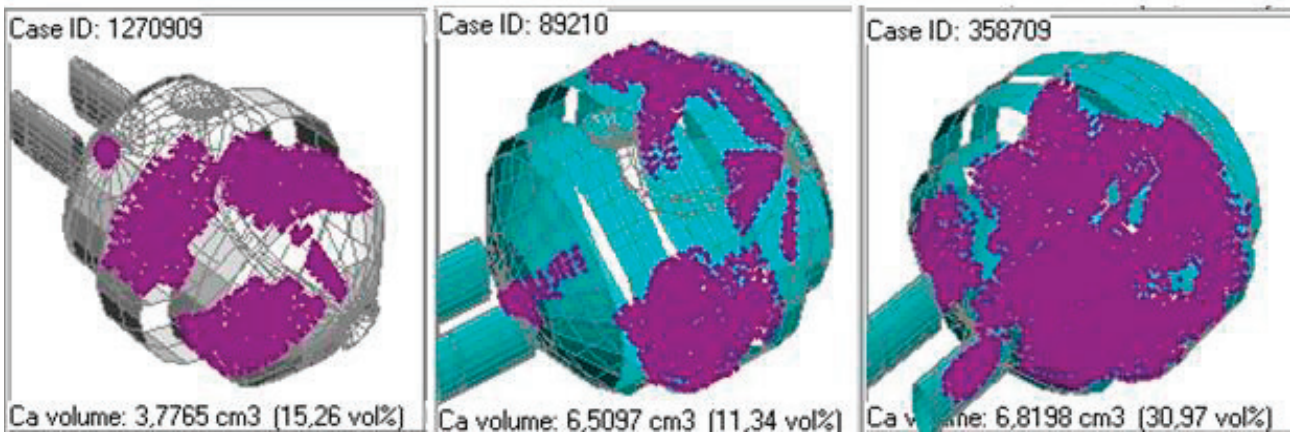


Figure 7. Apex and CZ free of CaP Apex involvement Apex and CZ involvement

	APEX (No 49) M±SD (range) Median	CZ (No 19) M±SD (range) Median	EPE (No 17) M±SD (range) Median	F/H/x ²	p
Age	68±6,9 (56-78) 69	70±6,8 (56-80) 69	70,8±5,3 (60-80) 71	2,3 ¹	n.s.
PSA-t (ng/mL)	7,9±5,1 (1,7-23,9) 7,4	11,2 ±6,3 (3,7-23,9) 8,9	10,3±6,2 (3-22,6) 8,3	5,9 ¹	n.s.
PSA-d (%)	0,26±0,2 (0,03-0,96) 0,21	0,36±0,24 (0,13-0,96) 0,13	0,26±0,2 (0,05-0,96) 0,25	5 ¹	n.s.
Vol.Prost.(cm ³)	36,5±15,6 (14,7-84,2) 31,8	33,9±13,7 (18,3-57,6) 29,5	48,3±33,4 (18,8-131) 34	1,3 ¹	n.s.
Vol. PCa (cm ³)	6,6±5,5 (0,3-29,7) 5,3	10±7 (2,8-29,7) 7,4	11,3±8,3 (2,8-29,7) 8,23	11 ¹	< 0,005
Vol. PCa /Vol.Prost. (%)	19,5±13,6 (0,1-67,2) 18,2	29,2±13,9 (11,2-67,2) 11,2	24,3±11,1 (11,2-67,2) 22,3	3,9 ¹	0,02
CZ	17/49 (35%)	%	9/17 (53%)	1,7 ²	n.s.
LVI	6/49 (12%)	6/19 (32%)	4/17 (24%)	0,4 ²	n.s.
R	13/49 (27%)	7/19 (37%)	6/17 (35%)	0,6 ²	n.s.
APEX	%	17/19 (89%)	10/17 (59%)	4,5 ²	n.s.
>3 positive preop. biopsy	24/49 (49%)	8/19 (42%)	10/17 (59%)	0,11 ²	n.s.
Bilobar positive preop. biopsy	20/49 (41%)	11/19 (58%)	9/17 (53%)	0,09 ²	n.s.

Table 3. Differences in main characteristics, depending on specific prostatic site involvement

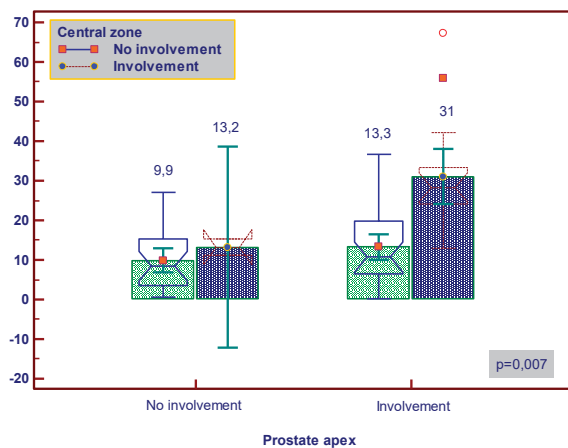


Figure 8. Difference of %VPCa in the patients with apex involvement with or without central zone simultaneous involvement

unchanged after surgery. Wilcoxon paired test showed 27 positive differences ($Z_{st} = -4.2; p < .0001$), i.e. postoperative GS overgrading of 36%. (Figure 3).

TRUS-guided needle biopsy of the prostate showed bilateral cancer localization in 38/75 patients (51%), while the finding following radical prostatectomy confirmed bilateral localization in 87% (65/75) of the patients (Table 2). The mean %VcaP in the postoperative bilateral finding was 17.3%, while in the

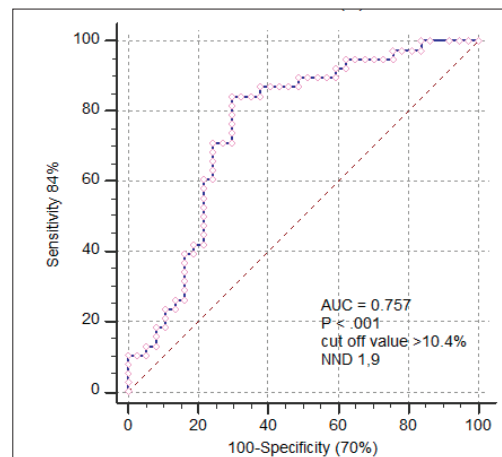


Figure 9. AUC for prediction of %PCa, depending on bilobar preoperative biopsy finding

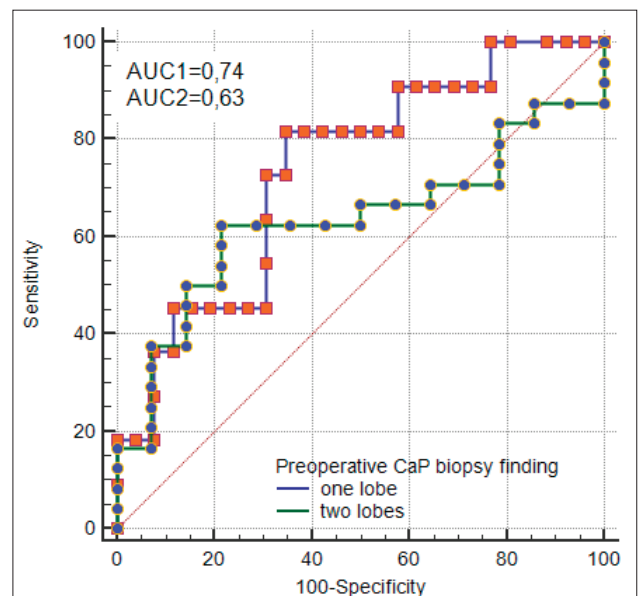


Figure 10. Comparison of independent ROC curves; grouping variable: preoperative uni/bilobar findings; classification variable: more than >3 positive preoperative needle biopsy

unilateral one it was 6.5%. Most changes in the bilateral preoperative PCa finding were shown at the level of GS 3+3, and GS 4+3 (they moved to a higher grade) (Table 2).

In order to examine the influence of PCa volume on uni/bilobar preoperative needle biopsy findings, two-way analysis of variance was performed, which showed a statistically sig-

nificant difference in mean VPCa, depending on whether positive findings of PCa were found in one or both prostate lobes (mean VPCa of 4.3 cm³ and 7.6 cm³, respectively, $p=0.01$) (Figure 4). At the same time, a statistically significant difference was shown in mean %VPCa, depending on preoperative GS grade. Namely, GS 3+3 had mean %VPCa of 11.8, while GS 3+4, 4+3 and 4+4 had mean %VPCa of 14.6, 21.4 and 25.9, respectively ($F=3.3$; $p=0.026$) (Figure 5). Furthermore, %VPCa shows good correlation with bilobar biopsy finding ($\rho=0.42$; $p<.001$), and with preoperative GS ($\rho=0.31$, $p<.007$). VPCa shows a somewhat lower correlation with bilobar preoperative biopsy findings ($\rho=0.37$, $p<.001$), and VPCa shows no correlation with preoperative GS ($\rho=0.21$, $p>0.05$) (Table 1).

Analyzing the number of positive needle biopsies, it was shown that most patients had one positive specimen—31%; 22% of the patients had four positive specimens; 20% of the patients had two positive specimens; 9% of the patients had three and five positive specimens, while remaining 9% of the patients had more than five positive needle biopsy specimens. According to the number of positive needle biopsies, the patients were divided into two groups (≤ 3 and >3 positive needle biopsy). ANOVA test did not show statistically significant difference between the number of positive biopsies depending on GS grade ($F=2.25$; $p=0.14$) (Figure 6). The number of positive core biopsies strongly correlates with %VcaP and VPCa ($\rho=0.4$, $p=0.0004$; $\rho=0.29$, $p<.01$).

Analyzing the spatial distribution of the tumor, 49/75 (65%) patients had postoperative finding of apex involvement, of whom 17/49 (35%) patients also had simultaneous CZ involvement, and 9/17 (53%) patients had extracapsular extension. Of the 19 (23.5%) patients isolate with the largest dominant volume located within the CZ, as many as 89% of them had apex involvement, while 9/17 (59% of total EPE) of them had extracapsular extension (Figure 7). depict spatial distribution of specific site cancer involvement.

Observing the main differences between the above-mentioned groups, significant difference was proven only in the total VPCa and %VPCa, with the highest %VPCa in patients with dominant CZ invasion CZ (Table 3). Comparison of the differences among independent samples, by Mann-Whitney test, showed that patients with CZ invasion also had a higher PSA-t (median 8.9 versus 5.9; $p=0.002$) and PSA-d (median 0.26 versus 0.17; $p=0.0002$), contrary to the patients with no CZ involvement. Such differences are not shown in patients with or without apex involvement. Patients with primary central zone invasion, with or without apex involvement, differed in terms of mean %VPCa by only 3.4%; conversely, patients with apex involvement and CZ invasion had a higher % of tumor volume (13.2% and 31%, respectively; $p=0.007$) (Figure 8).

ROC analysis was performed according to the best %VPCa correlation variable, and it was shown that preoperative bilobar positive finding of needle biopsy generates AUC of 0.76 ($p<.001$), sensitivity and specificity of 84% and 70%, respectively; (+LR 2,8; PPV of 74%; NPV of 82%), with cut off $>10,4$ %VPCa (mean %VPCa for total group is 16%) (Figure 9). This means that in 3 out of 4 patients with bilateral preoperative positive needle biopsy finding a %VPCa higher than 10% of total prostate volume (PTP=74.7%) can be expected. Comparison of independent ROC curves with grouping variable of uni/bilateral positive findings, including classification variable of

more than 3 core positive biopsy findings, would not increase the discriminant power of uni/bil preoperative positive findings (Figure 10).

Stepwise logistic regression showed that the main independent variable of influence on %VPCa (higher or lower than 10%) is the bilateral preoperative finding of the needle biopsy (OR 1.3, $R^2=0.38$, $p=.0001$), followed by PSA-t, while VP, PSA-d, age and number of positive biopsies were excluded from model (results were not shown).

5. DISCUSSION

The use of Pixel Prostate Software showed group mean VP of 40.5 (median 31.8) cm³; the results are very similar to those from the literature, where median prostate volume was 36.6 cm³ (7), while group mean volume of PCa 5.99 (range 0.18-29.7) with median of 4.51 cm³ was higher compared with some reports, where median cancer volume was 3.92 cm³ (though in range 0.03-45.7 cm³) (3). However, 31% and 34.8% of patients from the study of Eminaga et al. had mean VPCa between 3-6 and >6 cm³ (5). Furthermore, the same study showed that 33.6% of the patients had %VPCa $<10\%$. In our study, mean %VPCa was 16% (0.1-67.2%), while 37.4% of the patients had %VPCa <10 . This suggests that %VPCa variable may be more significant than the total VPCa, since it depends on a large range of prostate volumes.

The calculated percentage share of GS grade shows that 25% of the specimens had Gleason score 3+3, then GS 3+4 with 51%, 4+3 with 15%, and 4+4 (+5) with 9% shares. Ishizaki et al. obtained somewhat different data, where 38.7% of needle biopsy specimens had GS 6, 32.3% of them had GS 7, while 29% of needle biopsy specimens had GS 8 (3). In the cohort study ($n=169$), a group of researchers from the UK obtained the following data: GS ≤ 6 was present in 30% of needle biopsy specimens, GS 7 in 40%, and GS ≥ 8 in even 30% of needle biopsy specimens (8).

Our study showed that almost 71% of postoperative specimens belonged to T2 stage, while 29% of them belonged to T3 stage. Some reports present somewhat different data, where cancer in T2 stage was diagnosed in 13% of the patients, while 87% of the patients were diagnosed in T3 stage (50% in T3a, and 37% in T3b), namely 55% for T1-T2, and 38% for T3-T4 tumor stages, according to UK researchers (8, 9).

Further analysis found perineural invasion in 76% of the patients, extraprostatic extension in 23% of the patients, lymphovascular invasion in 12% of the patients – data that present a significant discrepancy compared with the data from the literature, according to which EPE was found in 86%, and LVI in 64% of the patients (9).

The detection of prostate cancer using needle biopsy, though a gold standard, is limited both by excessive detection of indolent cancers and failure to detect clinically relevant cases. Research shows a high overgrading rate (25-40%) on final RPES specimens, which suggests that biopsy often fails to detect high-grade lesions (10). In the present study, the results showed that 27 patients (36%) had preoperative undergrading. Similar data are shown in reports, with significant undergrading of preoperative GS ranging between 19-57%; this has significant repercussions on the choice of treatment. According to some authors, this discrepancy between GS of pros-

tate needle biopsy and postoperative GS reaches the level of 76% (11).

The characteristic multifocality of prostate cancer was reflected in the results of this study and it was proven that there is a significant difference in the actual spatial distribution of prostate cancer. Needle biopsy specimens showed bilateral cancer localization in 51% of the cases, while the final postoperative findings showed bilateral Casp read in 87% of the cases. This proved that needle biopsy failed to detect as much as 36% of bilateral localized cancers. Postoperative mean %VPCa in bilateral finding was 17.3%, while in unilateral finding it was 6.5%. Similar data were obtained in other studies as well, in which it was shown that 66% of needle biopsy specimens assessed as unilateral localized cancer, were actually bilateral (1).

In addition to uni/bilateral cancer localization, PP software provided a more detailed spatial orientation of the cancer. Thus, results were obtained showing central zone involvement in 23.5% of the cases, and apex involvement in 65% of the cases. It was shown that in 89% of the cases, patients with CZ invasion also had apex invasion. Naturally, these were high-volume tumors, thus cancers spread from the peripheral zone of the prostate probably invaded apex, while rarely isolated CZ involvement had a smaller volume, as proven by significant differences between VPCa and %VPCa in patients with CZ and apex involvement (Table 3 and Figure 8). Prestiatal. concluded that it was necessary to perform the so-called "midline" biopsy (central and transition zone biopsy) in order to achieve prostate cancer detection rate of 44%. In the previous study, the results of 12-core needle biopsy were classified in several groups, and the following cancer distribution results were obtained: peripheral zone (54%), prostate apex (50%), central zone (48%). This indicates that central zone biopsies, as well as apex biopsies, significantly contribute to the detection of prostate cancer and should be always included in basic biopsy schemes (12).

It was shown that VPCa and %VPCa correlate well with postoperative GS, PSA-t, and PSA-d ($p < .001$). According to reports, PSA-d represents a strong parameter for assessing the prostate cancer volume in the so-called "grey zone" (patients with serum PSA value < 10 ng/ml) (13). Furthermore, according to Carvalhal et al., the value of preoperative PSA-t has a strong statistical correlation with cancer volume (14).

Good correlation was also shown with bilateral core biopsy findings, and multiple positive core biopsy findings. A group of Korean researchers suggested that the number of positive needle biopsies has the highest predictive power for cancer volume, as well as pathological stage (4).

One of the aims of this study was to examine which preoperative diagnostic parameter has the strongest correlation with VPCa and %VPCa, calculated by Pixel Prostate software. Stepwise logistic regression model that was performed showed that preoperative bilateral needle biopsy findings had the greatest influence on %VPCa, followed by the value of PSA-t. ROC curve also showed AUC of 0.76 ($p < .0001$) in the prediction of %VPCa $> 10\%$ in positive biopsy bilateral findings (PTP = 75%). This finding has very important implications for planning and postoperative follow-up of patients, since it was shown that %VPCa $> 20\%$ has significant impact on PSA recurrence and tumor aggressiveness (2). May et al. also found that %VPCa $> 25\%$ was predictive of PSA recurrence, and that VPCa was not

(15).

6. CONCLUSION

The possibility of precise orientation of prostate cancer using PP software is important not only for the determination of PCa volume, but also for a better insight into the present multilocularity of tumor foci, extraprostatic extension, apex invasion, and CZ, as important prognostic determinants of cancer progression and aggressiveness. Simultaneously, with time, they offer better insight to a clinician for the planning of future prostate biopsies, being an important factor in clinical decision making.

- **Author's contribution:** D.A. and B.K. gave substantial contribution to the conception or design of the work and in the acquisition, analysis and interpretation of data for the work. S.R. and N.B. analysed each postprostatectomy specimen, than depicted it in the PP Software. Each author had role in drafting the work and revising it critically for important intellectual content. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- **Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms
- **Conflicts of interest:** There are no conflicts of interest.
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