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Original Scientific Paper

SYSTEMATIC AND TARGETED PROSTATE BIOPSY: A FIVE-YEAR EXPERIENCE IN A HIGH-VOLUME CENTER

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SUMMARY – Prostate biopsy is the gold standard diagnostic tool for prostate cancer. The number of targeted prostate biopsies based on multiparametric resonance imaging have increased in recent years, and this method is becoming increasingly utilized in patients in repeat biopsy settings, but also for biopsy-naive patients. The aim of this study was to analyze and present our results for the purpose of self-control and education. In the time period between January 2018 and December 2022, there were a total of 3385 prostate biopsies performed at the University Hospital Centre Zagreb. There were 2636 systematic (12 core) and 749 cognitive targeted biopsies, with an increasing trend in favor of targeted biopsy. The positivity of systematic biopsy was 45%, whereas positivity for targeted biopsies was 53.3%. The positivity of PI-RADS 3 lesions for targeted biopsies was 35%, 61% for PI-RADS 4, and 86% for PI-RADS 5. The median number of positive systematic cores was 3, and 4 cores for targeted biopsies, while the median cancer core involvements were 30% for systematic and 60% for targeted cores. In targeted cores, there was a higher percentage of ISUP grade 2 and 3 cancers when compared with systematic cores. Targeted biopsy is a valuable addition to the standard systematic biopsy in patients with suspicious lesions described on mpMRI.

Key words: *prostate cancer; prostate biopsy; targeted prostate biopsy; mpMRI*

Introduction

Prostate biopsy is the most crucial defining step in the diagnostic algorithm for prostate cancer (PCa) in order to obtain histopathological confirmation of the diagnosis. The decision to perform prostate biopsy is usually made based on PSA level and/or a suspicious digital rectal exam. There are also other important determinants such as age, comorbidities, and therapeutic considerations. Today, transrectal ultrasound (TRUS) is routinely used for prostate biopsy and is the standard of care. The biopsies can be obtained transrectally or transperineally, with no difference in cancer detection rates between the two approaches[1]. The recommended minimum number of cores obtained during systematic biopsy is 12, sampled from the peripheral zone of the prostate[2]. Image characteristics of the standard TRUS alone are not sensitive enough to detect suspicious lesion in prostatic tissue[3]. With the development of new technology, there are now new sonographic systems using high-frequency probes, with promising capabilities in identifying suspicious areas inside the prostatic tissue and showing promising results[4,5]. The positivity of systematic biopsy depends on prostate volume and cancer location and dimension, meaning that patients with prostate cancer can remain underdiagnosed after such bi-

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opsy. On the other hand, multiparametric magnetic resonance imaging (mpMRI) of the prostate shows good sensitivity for detection of clinically significant prostate cancer (ISUP grade 2 and higher)[6]. Currently, the use of mpMRI is strongly recommended prior to biopsy, even in biopsy-naive patients[7]. Studies have shown that targeted biopsy based on mpMRI significantly outperforms systematic biopsy in the detection of clinically significant PCa, especially in repeat biopsy settings[8,9]. However, it is still strongly recommended to perform systematic biopsy in addition to targeted, even in the case of evident suspicious lesions on mpMRI[7]. There is no clear superiority of PCa detection rates when comparing cognitive, software, and in-bore fusion mpMRI-guided biopsies[10]. In addition to the standard 12 cores, the recommended minimum number of targeted cores is 3-5, partially to compensate for targeting imprecision[11].

Materials and methods

The information system of the University Hospital Center Zagreb was searched for prostate biopsies performed from January 2018 to December 2022. All prostate biopsies were considered, both systematic and targeted. Targeted biopsies were performed if lesion ≥PIRADS 3 was described on mpMRI. Systematic biopsies included standard 12 core biopsy, and targeted biopsies included standard 12 core biopsy plus additional 6 cognitive targeted cores distributed among up to 3 leading regions based on the described PI-RADS lesions observed on mpMRI. Analyzed data included date of biopsy, PSA value, the multiparametric magnetic resonance (mpMRI) report, the histopathological report, and positivity and cancer core involvement in the targeted biopsy. Data are reported as median and IQR range. Data were collected using Microsoft Office Excel and SPSS, which were also used for charts and tables.

Results

From January 2018 to December 2022, there were a total of 3385 prostate biopsies performed at the University Hospital Centre Zagreb. There were 2636 systematic (12 core) and 749 targeted biopsies. The number of performed biopsies is shown in **Figure 1**. The median age of patients was 66 years (39-84). The median PSA in the targeted group was 8.4 ng/mL (0.5-1000). In the systematic biopsy group, prostate cancer was diagnosed in 45% of the patients, HG-PIN in 8.6%, and ASAP in 4.6%. There were 41.8% negative biopsies. 36.3% of patients had ISUP grade I, 28.3% had ISUP grade II, 13.5% had ISUP grade III, and 21.9% of patients had ISUP grade IV and higher. In the targeted biopsy group, there were 53.3% positive biopsies and 38.4% negative biopsies. HG-PIN was diagnosed in 4.7%, and ASAP in 3.6%. The ISUP grades for the systematic vs. targeted biopsy groups are shown in **Figure 2**. In the targeted biopsy group, there were 353 PI-RADS 3, 256 PI-RADS 4, and 132 PI-RADS 5 lesions. The positivity of the targeted biopsy in correlation to PI-RADS is shown in **Figure 3**. The median number of positive systematic

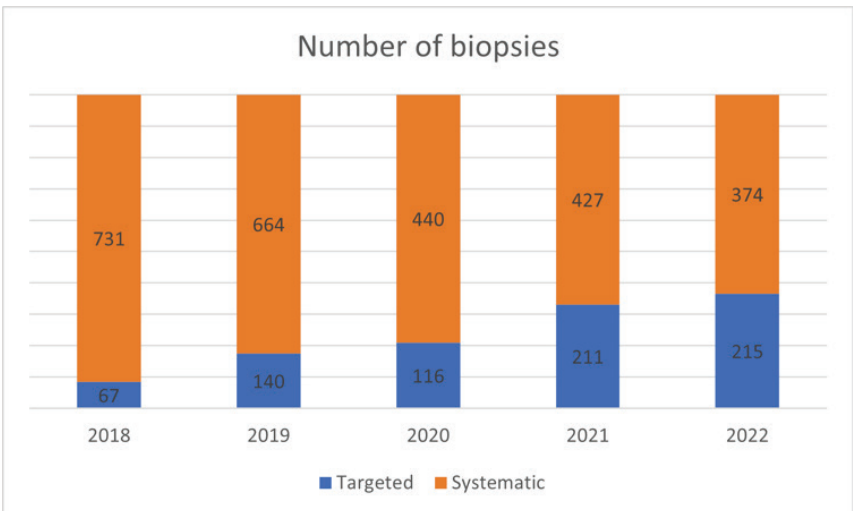

Figure 1. Number and distribution of targeted and systematic biopsies during the five-year period.

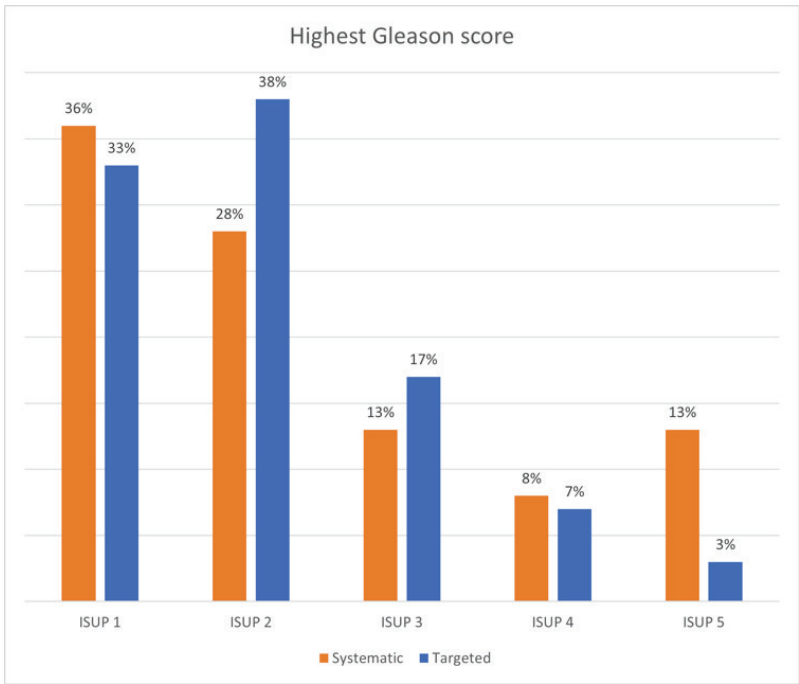

Figure 2. Highest Gleason score, systematic vs. targeted biopsy (ISUP – International Society of Urological Pathology grade).

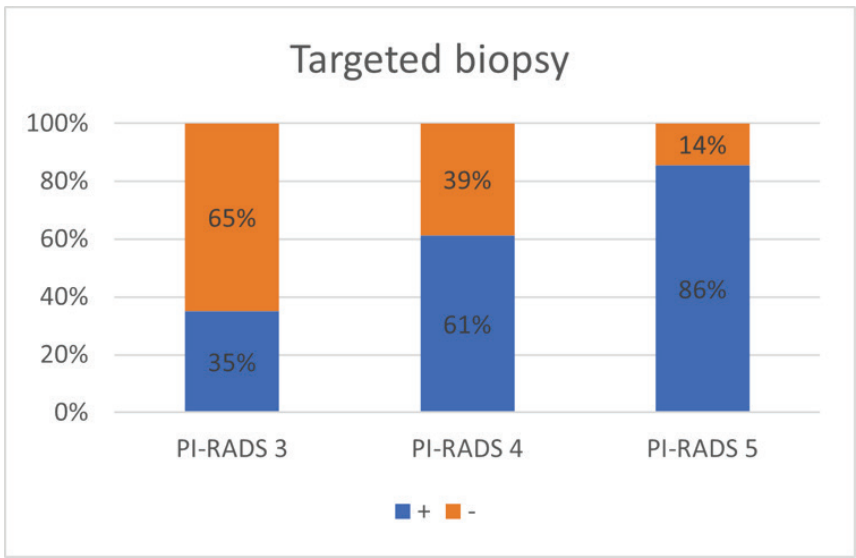

Figure 3. The positivity of targeted biopsy regarding PI-RADS (PI-RADS – Prostate Imaging Reporting and Data System).

cores was 3, and 4 cores for targeted biopsies, while the median cancer core involvement was 30% (0%-95%) for systematic and 60% (0%-95%) for targeted cores. **Table 1** shows the relationship in positivity between the systematic and targeted biopsies obtained from the same patients. The distribution of positivity between systematic and targeted cores in correlation with PI-RADS is presented in **Figure 4**. The distribution of the highest GS in correlation with PI-RADS is shown in **Figure 5**.

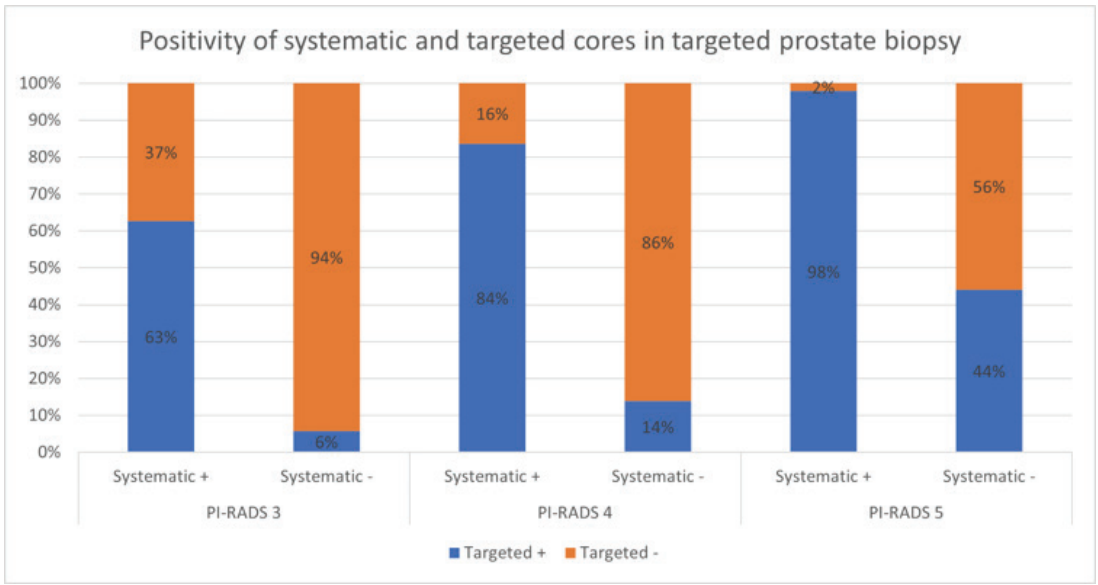

Figure 4. Crosstabulation of systematic and targeted cores obtained during a targeted biopsy in correlation with PI-RADS (PI-RADS - Prostate Imaging Reporting and Data System)

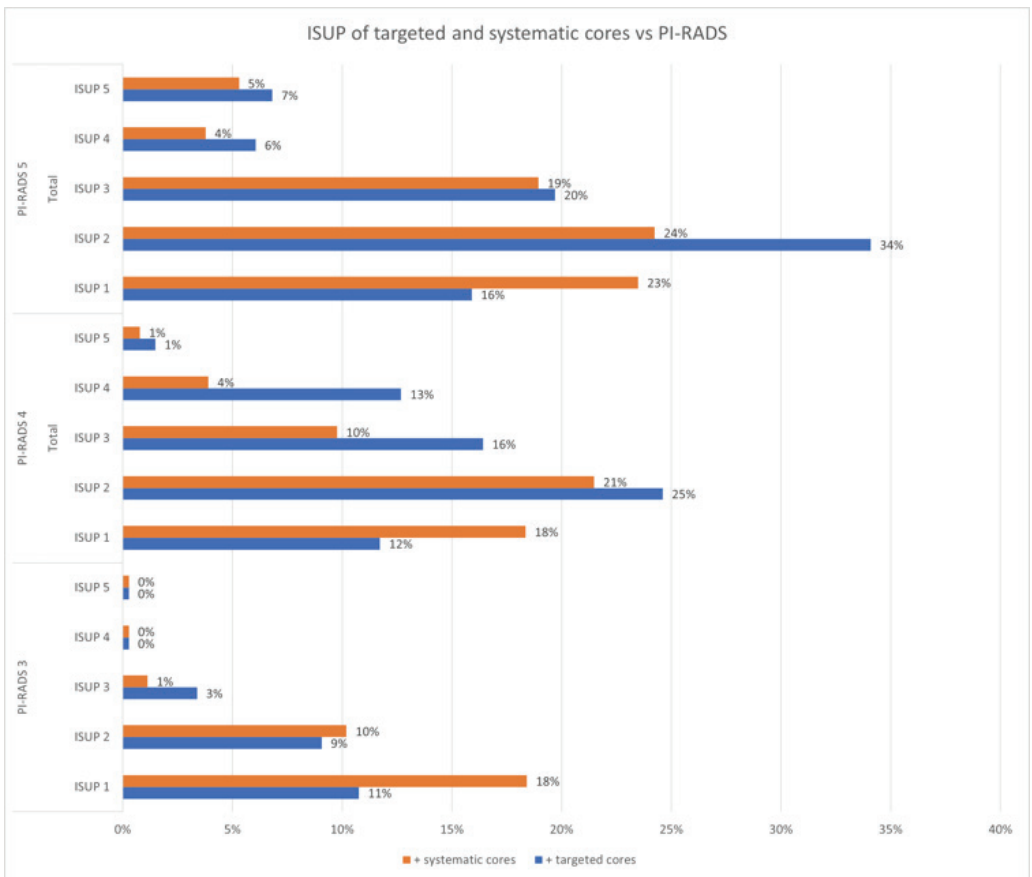

Figure 5. Correlation between PI-RADS classification and positivity of targeted and systematic cores (ISUP – International Society of Urological Pathology grade, PI-RADS – Prostate Imaging Reporting and Data System).

Table 1. Crosstabulation of positivity of targeted and systematic cores in targeted biopsy

	Targeted +	Targeted -	Total
Systematic +	38.19 %	8.91 %	47.00 %
Systematic -	6.07 %	46.83 %	52.90 %
Total	44.26 %	55.74 %	100.00 %

Discussion

Targeted prostate biopsy based on mpMRI findings is becoming the most valuable tool in diagnosis of prostate cancer, even in biopsy-naive patients. At the UHC Zagreb, it is most commonly performed in the clinical settings of repeated biopsy. During the five year study period, a reduction in performed biopsies was observed and is shown in **Figure 1**. This is in correlation with a 20% decrease of prostate cancer incidence in 2020 compared with 2019, as reported by the Croatian National Cancer Registry[12]. This decrease is caused primarily by the decrease in the number of biopsies in our and other institutions during the COVID-19 pandemic. An increase in incidence of prostatic cancer is to be expected in the following years, while the effect on mortality will only become clear after a decade or more. Targeted prostate biopsy is a highly operator-dependent procedure, but also dependent on the radiologist and PI-RADS classification. The data shown in **Table 1** shows 6.1% of patients with positive targeted and negative systematic cores, while on the other hand had 8.9% positive systematic and negative targeted cores. One could misinterpret these findings by saying that 6.1% of patients would remain undiagnosed if systematic biopsy alone were performed, versus 8.9% who would remain undiagnosed if only targeted biopsy were performed. This unexpectedly high percentage of positive systematic cores has also been observed in other studies, and has been explained by operator bias[13]. When performing targeted biopsy, we always sample the targeted core first, and after that we perform systematic biopsy. During systematic biopsy, the operator, deliberately or not, directs systematic cores towards suspicious areas described on the mpMRI, in order to compensate for imprecision and to increase the chance for diagnosis. This theory is also supported by data, namely that the median number of positive cores in targeted biopsy was 4, while it was 3 for the systematic biopsies. Additionally, the median core cancer involvement for targeted cores was 60%, compared with the 30% for systematic cores. When analyzing the clinical significance of diagnosed cancer with targeted and systematic biopsies (Figure 2), a higher percentage of ISUP grade 2 and 3 and a lower percentage of ISUP grade 1 cancer was diagnosed in the targeted group. On the other hand, there was an expected higher percentage of ISUP grade 4 and 5 in the systematic biopsy group. An examination of **Figure 4**, which shows positivity of targeted and systematic cores in the same patients, depending on PI-RADS, allows us to draw many conclusions. In patients with PI-RADS 3 lesions, there was a relatively high number of cases with negative targeted and positive systematic cores, while there were only two cases in patients with PI-RADS 5 lesions. Additionally, there was a higher ratio of positive targeted vs. negative systematic cores, with higher PI-RADS. This low detection rate of targeted biopsies in PI-RADS 3 lesions was also reported in other studies[14]. This could be explained by the relatively small difference between PI-RADS 2 and PI-RADS 3 lesions in some cases, and the fact that radiologist interpretations of such findings are somewhat subjective. Today, the European Association of Urology (EAU) strongly recommends the use of PSA density in decision-making for patients with PI-RADS 3 lesions, especially in repeated biopsy settings[7]. In patients with PI-RADS 3 lesions and PSA density <0.10 ng/mL/cc, repeated biopsy is not recommended[7]. The distribution of the ISUP grades of targeted and systematic cores is also highly dependent on PI-RADS, as shown in **Figure 5**. A higher number of ISUP grade I cancer was diagnosed in systematic cores, regardless of PI-RADS. ISUP grade 2 and 3 cancers were diagnosed more frequently with targeted cores in patients with PI-RADS 4 and 5 lesions.

Cognitive-targeted prostate biopsy is an operator-dependent procedure. It is mandatory for the per-

forming urologist to be familiar with PI-RADS classification in order to interpret the images independently of the radiologist. Constant education and self-evaluation, as well as collaboration with pathologists and radiologists, is necessary to obtain the best results. Targeted prostate biopsy using mpMRI has become the standard of care in prostate cancer diagnosis, but we have shown that there were cases in which targeted cores were negative, while systematic biopsies were positive. For that reason, targeted biopsy is still only a valuable addition, but certainly not a replacement for systematic biopsy. New technologies, such as artificial intelligence and highly advanced ultrasound and robotic platforms, are expected to further increase the detection rates of targeted biopsies in the future.

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Sažetak

SHEMATSKE I CILJANE BIOPSIJE PROSTATE: PETOGODIŠNJE ISKUSTVO U CENTRU VELIKOG VOLUMENA

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Biopsija prostate je zlatni standard u dijagnostici karcinoma prostate. Broj ciljanih biopsija temeljenih na multiparametrijskoj magnetskoj rezonanciji se povećao zadnjih nekoliko godina te se sve češće upotrebljava kod pacijenata s prethodno negativnim biopsija, ali i kod onih kod kojih do sada nije učinjena biopsija prostate. Cilj ove studije je analiza i prikaz naših rezultat u svrhu samokontrole i edukacije. U vremenskom periodu od siječnja 2018. do prosinca 2022., u Kliničkom bolničkom centru Zagreb je učinjeno 3385 biopsija prostate, od čega 2636 shematskih i 749 ciljanih biopsija. Pozitivitet shematskih biopsija je bio 45%, a ciljanih, 53.3%. Kod ciljanih biopsija prostate, pozitivno je bilo 35% biopsija s PI-RADS 3, 61% s PI-RADS 4 i 86% s PI-RADS 5 lezijom. Medijan broja pozitivnih cilindara je bio 3 za shematske, a 4 za ciljane cilindre dok je medijan postotka pozitiveta cilindra bio 30% za shematske i 60% za ciljane. Kod ciljanih biopsija je bio viši postotak dokazanih ISUP 2 i 3 karcinoma, u usporedbi s shematskim. Ciljana biopsija je vrijedan dodatak standardnoj shematskoj biopsiji, kod pacijenata s sumnjivim lezijama opisanim pomoću multiparametrijske magnetske rezonancije.

Ključne riječi: *rak prostate, biopsija prostate, ciljana biopsija prostate, mpMRI*