Impact of Relative Volume Difference Between Magnetic Resonance Imaging and Three-dimensional Transrectal Ultrasound Segmentation on Clinically Significant Prostate Cancer Detection in Fusion Magnetic Resonance Imaging–targeted Biopsy

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Impact of Relative Volume Difference between MRI and 3D-TRUS Segmentation on Clinically Significant Prostate Cancer Detection in Fusion MRI-Targeted Biopsy

Louis Lenfant, MD\textsuperscript{1,2,3*},
Clément Beitone, PhD\textsuperscript{2},
Jocelyne Troccaz, PhD\textsuperscript{2},
Aurélien Beaugerie, MD\textsuperscript{1},
Morgan Rouprêt, MD PhD\textsuperscript{1},
Thomas Seisen, MD PhD\textsuperscript{1},
Raphaëlle Renard-Penna, MD PhD\textsuperscript{4},
Sandrine Voros, PhD\textsuperscript{2},
Pierre C. Mozer, MD PhD\textsuperscript{1,3}

\textsuperscript{1} Sorbonne Université, GRC n°5, Predictive Onco-Urology, AP-HP, Hôpital Pitié-Salpêtrière, Urologie, F-75013 Paris, France
\textsuperscript{2} Univ. Grenoble Alpes, CNRS, INSERM, Grenoble INP, TIMC, Grenoble, France.
\textsuperscript{3} Sorbonne Université, CNRS UMR 7222, INSERM U1150, Institut des Systèmes Intelligents et Robotique (ISIR), 75005, Paris, France
\textsuperscript{4} Academic Department of Radiology, Hôpital Pitié-Salpêtrière, Assistance Publique des Hôpitaux de Paris, Paris, France

*Corresponding author:
Louis Lenfant, MD,
Department of Urology, Pitié Salpêtrière Academic Hospital,
47-83 Boulevard de l’Hôpital, 75651 Paris Cedex 13, France.
Tel: +33 (0) 1 42 17 71 41; Fax: +33 (0) 1 42 17 65 94;
E-mail: louis.lenfant@aphp.fr

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**ABSTRACT**

**Background:** The segmentation of 3D transrectal ultrasound (TRUS) images is known to be challenging and the clinician often lacks a reliable and easy-to-use indicator to assess its accuracy during the fusion MRI-targeted prostate biopsy procedure.

**Objective:** To assess the effect of the relative volume difference between 3D-TRUS and MRI segmentation on the outcome of targeted biopsy.

**Design, Setting, and Participants:** All adult males who underwent MRI-targeted prostate biopsy for clinically suspected prostate cancer between February 2012 and July 2021 were consecutively included.

**Intervention:** All patients underwent fusion MRI-targeted prostate biopsy with a Koelis™ device.

**Outcome Measurements and Statistical Analysis:** 3D-TRUS and MRI prostate volumes were calculated using 3D prostate models issued from the segmentations. The primary outcome was the relative Segmentation Volume Difference (SVD) between transrectal ultrasound and MRI divided by the MRI volume (SVD = MRI volume - TRUS volume / MRI volume) and its correlation to clinically significant prostate cancer (e.g., ISUP≥ 2) positiveness on targeted biopsy cores.

**Results:** Overall, 1721 patients underwent targeted biopsy resulting in a total of 5593 targeted cores. The median relative SVD was significantly lower in patients diagnosed with clinically significant prostate cancer compared to those with ISUP 0-1: (6.7%[IQR-2.7,13.6] vs.8.0%[IQR3.3,16.4],p<0.01, respectively). Multivariate regression analysis showed that a relative SVD of more than 10% of the MRI volume was associated with a lower detection rate of clinically significant prostate cancer (OR=0.74[95CI:0.55-0.98];p=0.038).
Conclusion: A relative segmentation volume difference of more than 10% of the MRI segmented volume was associated with a lower detection rate of clinically significant prostate cancer on targeted biopsy cores. The relative segmentation volume difference can be used as a per-procedure quality indicator of 3D-TRUS segmentation.

Patient summary: A discrepancy of 10% or more between segmented MRI and TRUS volume is associated with a reduced ability to detect significant prostate cancer on targeted biopsy cores.
In the past few years, the prostate cancer diagnosis pathway has improved, particularly with the use of prostate magnetic resonance imaging (MRI) prior to biopsies to target index lesions. Indeed, the MRI-first study reported that the combination of systematic (SB) and MRI-targeted biopsies (MRI-TB) improved the detection of clinically significant prostate cancers (csPCa; i.e., $\geq$ ISUP 2)[1]. Similarly, the PRECISION study showed that patients who underwent MRI-TB only had a higher detection rate of csPCa and a lower detection rate of non-significant cancers (i.e., ISUP 1) compared to those who underwent SB without prior MRI[2]. Thus, the EAU now recommends performing MRI prior to biopsies, which can be targeted to the identified suspicious lesions in addition to random systematic sextant biopsies[3]. The 2023 AUA guidelines also evolved favoring the optional use of magnetic resonance imaging (MRI) prior to initial biopsy to increase the detection of ISUP 2+ prostate cancer[4]. To this end, image fusion systems that register the segmented MRI and ultrasound images have been developed to accurately localize the MRI-visible lesions to be biopsied under transrectal ultrasound (TRUS) guidance. TRUS image segmentation is challenging, with high intra- and inter-observer variability[5], and the clinician often lacks a reliable and easy-to-use indicator to assess its accuracy during the procedure. Conversely, Montagne et al. showed that whole gland MRI segmentation has a low inter-reader variability with a mean Dice Score (DSC) of 0.92 ($\pm$SD=0.02)[6], indicating that MRI segmentation seems more accessible than TRUS image segmentation. We hypothesized that a difference in volume between the segmentation of the two imaging modalities has a direct impact on the quality of the registration and therefore, on the ability to accurately reach a target which would be reflected in the cancer detection rate. This study aimed to assess the effect of the
relative volume difference between MRI and TRUS segmentation on the outcome of MRI-TB biopsy.

Materials and Methods

Study design

Patients who had an elevated PSA (i.e., ≥4ng/mL) or an abnormal digital rectal examination (DRE) were advised to undergo a prostate MRI. Patients were eligible for MRI-TB upon a lesion with a Prostate Imaging Reporting and Data System (PIRADS) or Likert score of 3 or higher. All adult males (≥18 years old) who underwent fusion MRI-targeted prostate biopsy for clinically suspected prostate cancer between February 2012 and July 2021 were consecutively included in our study. Patients who did not have an MRI before the biopsy and those who underwent systematic biopsies only were excluded. The study was approved by the local IRB and ethics committee (Comité de Protection des Personnes, decision 30062004).

The study clinical data were prospectively collected into a secure anonymized database, approved by the Commission Nationale de l'Informatique et des Libertés (CNIL), by a data manager who was not involved in patient care. Anonymization was done at the time of biopsy by allocating a computerized random number for each patient. Segmentation data were prospectively stored as mesh data in the fusion biopsy system, and the volumes of segmented data were calculated using the VTK library (VTK mass properties class)[7].

MRI protocol

Overall, 1033 (60%) MRI scans were performed at our institution prior to the biopsy by an expert radiologist who had access to the clinical data. Images acquisition and
interpretation were done according to international guidelines[8]. The MRI system used was a 1.5T or 3T clinical system (Siemens Healthcare) with a 32-channel phased-array torso coil. T2-weighted, contrast-enhanced, and diffusion-weighted series were obtained, as described previously[9, 10]. Before 2015, suspicious prostatic lesions were graded according to the ESUR score and a 5-point Likert scoring system[11] to assess the likelihood of clinically significant PCa. After 2015, lesions were scored according to the PIRADS V2 and V2.1 score [8, 12]. The remaining MRI scans were performed outside our center according to a routine imaging protocol with a standardized report but no standardized review. The quality and interpretation of the multiparametric MRI were reviewed by the operator before the biopsy procedure and in case of any uncertainty, a review of the MRI was performed by our expert radiologist.

Prostate biopsy protocol

Patients who had a positive MRI (i.e. PIRADS or Likert score ≥ 3) underwent MRI-TB under real-time ultrasonographic guidance at our institution with a Koelis™ device (Meylan, France) as described previously[10]. Between February 2012 and April 2014, Urostation V2 was used for the computer-assisted fusion of labeled T2-weighted MRI images over real-time prostate ultrasound scans, followed by UroStation Touch until August 2015, and finally, the Trinity™ system until July 2021. Each of these systems incorporated identical segmentation and registration algorithms, as well as a motorized end-fire ultrasound probe. The subsequent innovations were primarily aimed at enhancing usability.

Both MRI and TRUS images were segmented by the operator at the time of the biopsy procedure. The MRI and the TRUS images were segmented using a probabilistic atlas and a spatially constrained deformable model [13]. After manually positioning three
reference points (Apex, bladder neck, and posterior median point), the algorithm
adjusted the atlas to build a 3D model of the prostate that could be further manually
adjusted for MRI and TRUS images. Final 3D models of the prostate were used to
calculate the prostate volume for each imaging modality.

Once the 3D contours were defined on the MRI and the TRUS images, the fusion of
the acquired data was performed according to the elastic image fusion algorithm [14].

Transrectal prostate biopsies were performed by physicians (N=31) with different
levels of experience, ranging from no experience to expert. Novice practitioners
performed the first 15 procedures under the supervision of the same expert physician
and operators were qualified as “experienced” after 50 procedures.

A virtual biopsy was performed before the insertion of the real needle for each core to
ensure the proper positioning of the probe to adequately reach the target. Mapping of
virtual and real biopsy cores to the reference TRUS volume was performed using
organ-based tracking iconic fusion algorithm [15]. All biopsy specimens were analyzed
by a senior genitourinary pathologist with more than 10 years of experience, who
graded the biopsy according to the ISUP classification using grades from 1 to 5,
reflecting the increasing severity of the disease. Tumor differentiation was determined
using the Gleason score and the highest Gleason score for each biopsy was recoded
to ISUP grade[16, 17]. All results are presented according to START (Standards of
Reporting for MRI-TB Studies) recommendations[18].

Definition of terms

Clinically significant PCa (csPCa) was defined as any PCa with an ISUP ≥2, based on
the ISUP classification[19]. Each biopsy sample was referred to as a core and a
positive core was defined by the presence of prostate cancer on histopathology findings.

The segmentation volume difference (SVD) referred to the volume difference between the 3D MRI and TRUS models obtained after segmentation \((SVD = MRI \text{ volume} - TRUS \text{ volume})\). The relative SVD was defined as \(SVD/\text{MRI volume}\) to account for the prostate volume in the estimation of volume difference.

**Study outcomes**

The primary outcome was the relative SVD and its influence over csPCa detection on targeted biopsy cores in the overall patient population. Secondary outcomes were the variability in relative SVD according to biopsy results stratified by operator experience, prostate volume, and Likert score. Secondary outcomes also included the variability in relative SVD according to the detection of csPCa across all targeted biopsy cores.

**Statistical analysis**

Descriptive statistics were obtained reporting median and interquartile range (IQR) for continuous variables, and frequencies and proportions for categorical variables, as appropriate. Continuous variables were analyzed with the Wilcoxon test. Differences between categorical variables were assessed using the Chi 2 and Fisher exact tests, when appropriate. Binomial regression models were developed to assess the influence of key variables on the detection rate of csPCa on targeted biopsy cores. The effects of age, PSA density, relative SVD, Likert score, operator experience, target size (max diameter in mm) to the square root of prostate volume (cc) ratio (target to prostate size
ratio = target size / √(prostate volume), and the number of targeted biopsy cores on the dependent variable were explored. Violin plots were created to illustrate variations in the relative SVD according to the biopsy result, stratified by operator experience, prostate volume, and Likert score.

Retrospective statistical analyses of the prospectively collected data were performed using the open-source R statistical software v.3.4.0 (R Foundation for Statistical Computing, Vienna, Austria). All tests were two-sided with a significance set at p < 0.05.
Results

Study population
Overall, 1721 patients underwent MRI-TB with a median number of 3 (IQR 2.4) cores per procedure, resulting in a total of 5593 targeted cores. Among the included patients, 695 (40%) and 357(20%) were diagnosed with csPCa and non-clinically significant prostate cancer (i.e., ISUP 1) on the targeted cores, respectively. Most of the men enrolled (76%) had not undergone a previous biopsy (Table 1).

Clinically significant prostate cancer PCa detection
Median relative SVD was significantly lower in patients diagnosed with csPCa on MRI-TB compared to those with ISUP 1 or negative MRI-TB: (6.5 % [IQR-2.6, 12.6], vs. 7.7% [IQR 3.3, 15.0], p<0.01, respectively). Specifically, analysis of the relative SVD distribution showed that in the case of ISUP 0-1 MRI-TB, relative SVD values were more spread out with more outliers between 20 and 40% (Figure 1A).

Logistic regression
The binomial multivariate logistic regression model for csPCa positivity showed that patients who had a relative SVD higher than 10% were less likely to have csPCa on MRI-TB (OR=0.74[95 CI: 0.55-0.98]; P=0.038)., Likert 3 targets and a previous prostate biopsy were also predictive of lower detection of csPCa. On the opposite, age, PSA density, target-to-prostate size ratio, and the use of targeted biopsy only were associated with a higher risk of csPCa diagnosis (Figure 2).
Analysis of SVD variation

Distribution analysis showed that relative SVD was higher for patients with negative MRI-TB in the overall population (Figure 1A) but also in the subgroups of novice operators (<50 cases)(Figure 1C), and Likert 5 lesions (Figure 1B). Interestingly, for experienced operators, the distributions of relative SVD were tightly clustered around the median, with fewer outliers regardless of the biopsy result. In contrast, for prostates larger than 80 cm3, SVD values were more spread out, with a higher median relative SVD in patients with ISUP 0-1 targeted biopsy results. In a multivariate analysis including age, PSA density, Likert score, operator experience, and target size ratio, the only predictors of SVD > 10% were operator experience and target size ratio (supplementary materials; Figure S3).

Analysis by core

Median relative SVD was higher for ISUP 0-1 (N= 3,957) cores compared to csPCa positive cores (N= 1,636) (6.7% [IQR 2.9,13.2] vs 6.0% [IQR 2.6,11.3], p<0.001). Binomial multivariate logistic regression showed that relative SVD > 10%, anterior lesion, as well as small target-to-prostate size ratio were predictive of lower detection of csPCa. Distribution analysis illustrated by violin plots highlighted that relative SVD was significantly higher and more widely distributed when the cores are negative for csPCa (Supplementary materials).
Discussion

Although targeted prostate biopsy is recommended by most scientific associations, the adoption of computer-assisted fusion MRI-TB is not predominantly widespread among urologists[20, 21], perhaps due to the complexity of the various process steps, which may vary according to the type of technology incorporated by the different platforms available.

There is conflicting evidence when comparing the accuracy of elastic and rigid fusion systems. Although one meta-analysis showed no differences between rigid and elastic fusion[22], recent studies have shown that systems that incorporate elastic fusion were more accurate than those performing rigid point-matching fusion in ex-vivo[23] and in-vivo[24] comparison studies. Yet, this precision comes at the cost of a more complex procedure as it requires segmentation of the prostate on MRI and TRUS. Indeed, TRUS segmentation is one of the most challenging steps in the image-planning MRI-TB as reflected by its high intra- and inter-observer variability, even among experts. However, our study shows that the use of elastic fusion and segmentation allows for quality control of the planning by measuring the difference in volume between MRI and TRUS segmentation. This indicator should be useful to refine the TRUS segmentation if necessary and help the physician improve his daily practice.

The main strengths of the present study are the large number of patients included, the analysis of standardized volume calculated from segmented data directly extracted from the biopsy platform, the inclusion of several operators with different levels of experience, and finally, the patient-based and core-based data analysis.

The main finding of the present study is that a segmentation volume difference between MRI and TRUS higher than 10% relative to the MRI volume is associated with
a lower detection of csPCa on MRI-TB and each MRI-TB core. Therefore, this relative
SVD could be a useful tool for the physician during the procedure by being used as a
safeguard to measure the quality of the 3D TRUS segmentation and refine the contours
in case of discrepancy between the volume of both imaging modalities.

The difference in prostate volume between different imaging modalities has been
extensively studied, especially in the case of BPH and brachytherapy. The volume
calculation method, the prostate volume itself, and the imaging modality influence the
relative difference measured between the different modalities.

Among all prostate imaging modalities, both MRI and 3D TRUS have been shown to
correlate well with the surgical specimen weight[25, 26]. In a study evaluating the
reproducibility and modality differences of prostate contouring between various
imaging modalities, MRI and 3D TRUS volumes displayed the closest correspondence
between modalities with an MRI-3D TRUS inter-modality volume standard error of
measurement (SEM) of 5.6 cc[27]. Another study comparing prostate volume variability
between MRI and 3D TRUS contoured images reported a strong similarity in volume
determination between modalities with a US/MR prostate volume ratio of 0.99 +/-
0.08[28]. Therefore, the results of these two studies tend to confirm our findings. There
seems to exist a small systematic volume difference between both modalities possibly
related to the physical process of creating 3D TRUS and 3D MRI volume. However, a
relative SVD of more than 10% should be considered inappropriate as it reflects a
suboptimal segmentation. Indeed, a registration based on a suboptimal 3D TRUS
segmentation would result in a mapping of the target in a less accurate location in the
prostate. However, most of the studies evaluating the correlation between MRI and
TRUS volume have been performed in patients treated with brachytherapy and
therefore with small prostate volumes. Although these correlation studies could not be
fully extrapolated to all prostate volumes, our study used an SVD normalized to MRI volume, which allows us to use it regardless of prostate volume.

It is noteworthy that in the present study, the distribution of the relative SVD was comparable regardless of prostate volume. However, this result is not surprising since the relative SVD is calculated by adjusting for prostate volume to be used regardless of the prostate size. However, prostate volume is a significant factor influencing the biopsy result. Indeed, the low target-to-prostate size ratio was predictive of lower detection of csPCa (OR=1.53 [95 CI: 1.31-1.80], p< 0.001). Given that targeted biopsies have particularly demonstrated their added value in increasing the diagnostic yield of csPCa in prostates larger than 40cc [29], it seems essential to develop tools to aid operators in obtaining the most reliable segmentation possible, especially for large prostates, to guarantee maximum accuracy of the biopsy procedure. This further highlights the potential benefit of MRI-TB when we target a small lesion in a large prostate as well as the need for precise registration in this setting.

Operator expertise also played a role in segmentation quality. Thus, the variability of the relative SVD was greater for less experienced operators (Figure 1C), indicating that segmentation may be more difficult for novices and may be one factor impeding the broad adoption of targeted fusion biopsy. Operator expertise was also predictive of a SVD > 10% in a multivariate analysis (Figure S3; supplementary materials). Learning curve analysis of MRI-TB has been evaluated but without any specific data on skills acquired in image-based planning[30, 31]. Segmentation learning analysis is a crucial topic for MRI-TB learning and should be the subject of dedicated study in the future.
Our study is not devoid of limitations. First, the data are from a tertiary center that pioneered computer-assisted fusion for MRI-TB. Despite a large number of operators with different levels of experience that could minimize this potential limitation, the expert center effect probably tends to improve the overall diagnostic performance in this study. However, if this is the case, a lower detection of cs-PCa TB increases the difficulty of finding significant predictive factors for this group. Therefore, we believe that the safeguard of a less than 10% difference between MRI and 3D TRUS segmentation remains applicable regardless of center experience. Second, all MRI-TB were performed with Koelis™ platform. Thus, our results may not be directly applicable to other fusion systems. Third, this study was unable to comprehensively identify all the factors affecting the quality of segmentation. Data on image quality, echogenicity, and prostate architecture are lacking and may be useful in predicting more difficult segmentation of TRUS images. A future study should attempt to identify these potential predictive factors. Additionally, with the rapid growth of transperineal biopsy, there might arise a valid concern regarding the ongoing relevance of our findings. Despite the potential reduction in the human factor through the use of a stationary probe in transperineal biopsy, it is important to note that the core principles of segmentation and registration remain unchanged. Consequently, the quality of segmentation continues to play a crucial role in determining the accuracy of registration, thereby directly impacting the overall precision of the biopsy. Nevertheless, it would be interesting to validate these data on a cohort of patients biopsied using the transperineal approach. Finally, apart from the quality of the segmentation reflected by the SVD, there are other human factors influencing the accuracy of the biopsy procedure reflected by the csPCa diagnostic rate. The precise localization of the target on the MRI and the dexterity of
the operator to reach the target are among them but are unfortunately difficult to quantify in this type of study.

In conclusion, the difference in segmentation volume between MRI and TRUS can be used as a surrogate for high-quality segmentation. A relative SVD between MRI and TRUS of more than 10% of the segmented MRI volume is associated with lower detection of csPCa on targeted cores. By integrating SVD into the workflow, operators can effectively assess the quality of segmentation and make real-time adjustments, thus minimizing the likelihood of errors. This approach has the potential to improve consistency and accuracy across different operators, ultimately enhancing patient outcomes and the overall effectiveness of the procedure.

Looking toward the future, Artificial Intelligence (AI) will play a crucial role in assisting physicians during the segmentation process [32]. The development of AI algorithms will enable the integration of SVD as a safeguard, significantly enhancing the accuracy of segmentation. By incorporating SVD within the AI algorithms, we can ensure more precise and reliable segmentations. This exciting prospect of integrating AI and SVD as safeguards holds great promise for advancing medical imaging practices and improving the overall accuracy of segmentation.

References


Data availability Statement

The data sets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Figure Legend

Figure 1. Distribution of the relative SVD between MRI and TRUS segmentation according to the positivity of targeted biopsies.
1A. Distribution analysis in the overall population
1B. Distribution analysis stratified by Likert score.
1C. Distribution analysis stratified by operator experience.
1D. Distribution analysis stratified by prostate volume.
SVD: Segmentation Volume Difference

Figure 2. Binomial logistic regression for clinically significant prostate cancer positiveness
PSA: Prostate-Specific Antigen; SVD: Segmentation Volume Difference (MRI-TRUS), OR: Odds Ratio
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Overall, N = 1,721</th>
<th>ISUP 0-1, N = 1,026</th>
<th>ISUP ≥ 2 , N = 695</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age — years</strong></td>
<td>66.0 (61, 72)</td>
<td>65.0 (60, 70)</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prostate Volume on MRI segmentation — cc (IQR)</td>
<td>47.2 (34.5, 65.7)</td>
<td>53.1 (37.8, 71.2)</td>
<td>40.6 (31, 54.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PSA — ng/ml (IQR)</td>
<td>7.0 (5, 10)</td>
<td>6.0 (5, 9)</td>
<td>8.0 (5, 12)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MRI done at the host center (%)</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No</td>
<td>326 (24)</td>
<td>162 (20)</td>
<td>164 (29)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1,033 (76)</td>
<td>641 (80)</td>
<td>392 (71)</td>
<td></td>
</tr>
<tr>
<td>Likert Score — no. (%)</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>13 (1.1)</td>
<td>11 (1.7)</td>
<td>2 (0.4)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>198 (17)</td>
<td>171 (27)</td>
<td>27 (5.2)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>460 (40)</td>
<td>269 (42)</td>
<td>191 (37)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>492 (42)</td>
<td>192 (30)</td>
<td>30 (58)</td>
<td></td>
</tr>
<tr>
<td>No. of cores on MRI-targeted biopsy — no. (IQR)</td>
<td>3.0 (2, 4)</td>
<td>3.0 (2, 4)</td>
<td>4.0 (3, 5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SVD — cc (IQR)</td>
<td>1.6 (-1.1, 5.7)</td>
<td>2.0 (-1.2, 6.8)</td>
<td>1.2 (-0.9, 4.1)</td>
<td>0.005</td>
</tr>
<tr>
<td>Relative SVD — % (IQR)</td>
<td>7.1 (3.1, 14.2)</td>
<td>7.7 (3.3, 15.0)</td>
<td>6.5 (2.6, 12.6)</td>
<td>0.004</td>
</tr>
<tr>
<td>Operator experience — no. (%)</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Experienced*</td>
<td>1,325 (77)</td>
<td>819 (80)</td>
<td>506 (73)</td>
<td></td>
</tr>
<tr>
<td>Novice</td>
<td>396 (23)</td>
<td>207 (20)</td>
<td>189 (27)</td>
<td></td>
</tr>
<tr>
<td>Previous biopsy result — no. (%)</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Positive</td>
<td>151 (8.9)</td>
<td>108 (11)</td>
<td>43 (6.2)</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>262 (15)</td>
<td>168 (17)</td>
<td>94 (14)</td>
<td></td>
</tr>
<tr>
<td>No Previous biopsy</td>
<td>1,289 (76)</td>
<td>732 (73)</td>
<td>557 (80)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>19</td>
<td>18</td>
<td>1</td>
<td></td>
</tr>
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</table>

PSA: Prostate-specific antigen; IQR: interquartile range; ISUP: Prostate cancer grade according to the International society of urological pathology; TRUS: transrectal ultrasound; SVD: segmentation volume difference

* Experienced operator: > 50 procedures; Novice: < 50 procedures
OR

- **Age**
  - (p<0.001***) 1.04 (1.02-1.06, p<0.001)

- **PSA density**
  - (p<0.001***) 4.33 (2.21-9.18, p<0.001)

- **SVD ratio**
  - >10% (p=0.036) 0.74 (0.55-0.98, p=0.038)

- **Likert**
  - 3 (p<0.001***) 0.33 (0.19-0.55, p<0.001)
  - 4 (p=0.951) 0.99 (0.69-1.44, p=0.975)
  - 5 (p=0.065) 1.39 (0.96-2.01, p=0.079)

- **Operator experience**
  - novice (p=0.071) 1.32 (0.97-1.79, p=0.076)

- **Targeted size ratio**
  - (p<0.001***) 1.53 (1.31-1.80, p<0.001)

- **Number of targeted core**
  - >4 (p=0.323) 1.13 (0.87-1.47, p=0.346)

- **Biopsy protocol**
  - Targeted biopsy alone (p=0.001***) 1.82 (1.28-2.61, p=0.001)

- **History of previous biopsy**
  - Previous Biopsy (p=0.009***) 0.68 (0.49-0.93, p=0.018)

**Note:**
- ● p ≤ 0.05
- ○ p > 0.05
Figure. Secondary regression analysis by core positivity

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall, N = 5,593</th>
<th>ISUP 0-1, N = 3,957</th>
<th>ISUP ≥2, N = 1,636</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age - years, (IQR)</td>
<td>66.0 (61.0, 72.0)</td>
<td>66.0 (61.0, 71.0)</td>
<td>69.0 (63.0, 73.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prostate Volume on MRI</td>
<td>47.0 (34.5, 66.0)</td>
<td>50.3 (36.0, 70.5)</td>
<td>40.6 (31.7, 53.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>segmentation - cc, (IQR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate-specific antigen — ng/ml, (IQR)</td>
<td>7.0 (5.0, 11.0)</td>
<td>7.0 (5.0, 10.0)</td>
<td>8.0 (6.0, 14.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Likert Score — no. (%)</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>36 (0.9)</td>
<td>32 (1.2)</td>
<td>4 (0.3)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>597 (15)</td>
<td>540 (20)</td>
<td>57 (4.4)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1,597 (40)</td>
<td>1,181 (43)</td>
<td>416 (32)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1,813 (45)</td>
<td>1,001 (36)</td>
<td>812 (63)</td>
<td></td>
</tr>
<tr>
<td>Relative SVD, no. (%)</td>
<td>6.4 (2.8, 12.5)</td>
<td>6.7 (2.9, 13.2)</td>
<td>6.0 (2.6, 11.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Operator experience — no. (%)</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Experienced</td>
<td>4,323 (77)</td>
<td>3,142 (72)</td>
<td>1,181 (27)</td>
<td></td>
</tr>
<tr>
<td>Novice</td>
<td>1,270 (29)</td>
<td>815 (64)</td>
<td>475 (37)</td>
<td></td>
</tr>
<tr>
<td>Target localisation— no. (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.3</td>
</tr>
<tr>
<td>Anterior</td>
<td>1,402 (25)</td>
<td>1,007 (25)</td>
<td>395 (24)</td>
<td></td>
</tr>
<tr>
<td>Posterior</td>
<td>4,191 (75)</td>
<td>2,950 (75)</td>
<td>1,241 (76)</td>
<td></td>
</tr>
</tbody>
</table>

Figure S1. Multivariate analysis of predictors associated with individual core positivity.
Figure S2. Distribution of absolute relative SVD between MRI and US segmentation according to the positivity of the targeted cores.
Figure S3. Multivariate analysis: Predictors associated with SVD > 10%