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► To cite this version:

Louis Lenfant, Clément Beitone, Jocelyne Troccaz, Aurélien Beaugerie, Morgan Rouprêt, et al.. 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. *European Urology Oncology*, 2023, 7 (3), pp.430-437. 10.1016/j.euo.2023.07.016 . hal-04195723

HAL Id: hal-04195723

<https://hal.science/hal-04195723v1>

Submitted on 4 Sep 2023

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

4
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29
30 Word Count: Abstract (307); Manuscript (3008)

31 References (32) Tables (1) Figures (2)

32 **Conflict of Interest:** Pierre Mozer and Jocelyne Troccaz are co-inventors in the
33 patents for the targeted biopsy device and have been involved in the license of the
34 Koelis UroStation system. All other authors have nothing to disclose

35 **Funding:** None

1 **Keywords (Mesh):** *Prostatic Neoplasms* / diagnostic imaging; Image-Guided*
2 *Biopsy*; Magnetic Resonance Imaging*; Imaging, Three-Dimensional* / methods;*
3 *volume difference; Ultrasonography / methods*; Prostate* / diagnostic imaging ; Biopsy*
4 */ methods**
5

1 **ABSTRACT**

2

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

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

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

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

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

19 **Results:** Overall, 1721 patients underwent targeted biopsy resulting in a total of 5593
20 targeted cores. The median relative SVD was significantly lower in patients diagnosed
21 with clinically significant prostate cancer compared to those with ISUP 0-1: (6.7%[IQR-
22 2.7,13.6] vs.8.0%[IQR3.3,16.4],p<0.01, respectively). Multivariate regression analysis
23 showed that a relative SVD of more than 10% of the MRI volume was associated with
24 a lower detection rate of clinically significant prostate cancer (OR=0.74[95CI:0.55-
25 0.98];p=0.038).

1 **Conclusion:** A relative segmentation volume difference of more than 10% of the MRI
2 segmented volume was associated with a lower detection rate of clinically significant
3 prostate cancer on targeted biopsy cores. The relative segmentation volume difference
4 can be used as a per-procedure quality indicator of 3D-TRUS segmentation.

5 **Patient summary:** A discrepancy of 10% or more between segmented MRI and TRUS
6 volume is associated with a reduced ability to detect significant prostate cancer on
7 targeted biopsy cores.

8

1 Introduction

2

3 In the past few years, the prostate cancer diagnosis pathway has improved, particularly
4 with the use of prostate magnetic resonance imaging (MRI) prior to biopsies to target
5 index lesions. Indeed, the MRI-first study reported that the combination of systematic
6 (SB) and MRI-targeted biopsies (MRI-TB) improved the detection of clinically
7 significant prostate cancers (csPCa; i.e., \geq ISUP 2)[1]. Similarly, the PRECISION study
8 showed that patients who underwent MRI-TB only had a higher detection rate of csPCa
9 and a lower detection rate of non-significant cancers (i.e., ISUP 1) compared to those
10 who underwent SB without prior MRI[2]. Thus, the EAU now recommends performing
11 MRI prior to biopsies, which can be targeted to the identified suspicious lesions in
12 addition to random systematic sextant biopsies[3]. The 2023 AUA guidelines also
13 evolved favoring the optional use of magnetic resonance imaging (MRI) prior to initial
14 biopsy to increase the detection of ISUP 2+ prostate cancer[4].

15 To this end, image fusion systems that register the segmented MRI and ultrasound
16 images have been developed to accurately localize the MRI-visible lesions to be
17 biopsied under transrectal ultrasound (TRUS) guidance.

18 TRUS image segmentation is challenging, with high intra- and inter-observer
19 variability[5], and the clinician often lacks a reliable and easy-to-use indicator to assess
20 its accuracy during the procedure. Conversely, Montagne et al. showed that whole
21 gland MRI segmentation has a low inter-reader variability with a mean Dice Score
22 (DSC) of 0.92 (\pm SD=0.02)[6], indicating that MRI segmentation seems more accessible
23 than TRUS image segmentation. We hypothesized that a difference in volume between
24 the segmentation of the two imaging modalities has a direct impact on the quality of
25 the registration and therefore, on the ability to accurately reach a target which would
26 be reflected in the cancer detection rate. This study aimed to assess the effect of the

1 relative volume difference between MRI and TRUS segmentation on the outcome of
2 MRI-TB biopsy.

3

4 **Materials and Methods**

5 *Study design*

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

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

22

23 *MRI protocol*

24 Overall, 1033 (60%) MRI scans were performed at our institution prior to the biopsy by
25 an expert radiologist who had access to the clinical data. Images acquisition and

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

12

13 *Prostate biopsy protocol*

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

23 Both MRI and TRUS images were segmented by the operator at the time of the biopsy
24 procedure. The MRI and the TRUS images were segmented using a probabilistic atlas
25 and a spatially constrained deformable model [13]. After manually positioning three

1 reference points (Apex, bladder neck, and posterior median point), the algorithm
2 adjusted the atlas to build a 3D model of the prostate that could be further manually
3 adjusted for MRI and TRUS images. Final 3D models of the prostate were used to
4 calculate the prostate volume for each imaging modality.

5 Once the 3D contours were defined on the MRI and the TRUS images, the fusion of
6 the acquired data was performed according to the elastic image fusion algorithm [14].
7 Transrectal prostate biopsies were performed by physicians (N=31) with different
8 levels of experience, ranging from no experience to expert. Novice practitioners
9 performed the first 15 procedures under the supervision of the same expert physician
10 and operators were qualified as “experienced” after 50 procedures.

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

21

22 *Definition of terms*

23 Clinically significant PCa (csPCa) was defined as any PCa with an ISUP ≥ 2 , based on
24 the ISUP classification[19]. Each biopsy sample was referred to as a core and a

1 positive core was defined by the presence of prostate cancer on histopathology
2 findings.

3 The segmentation volume difference (SVD) referred to the volume difference between
4 the 3D MRI and TRUS models obtained after segmentation ($SVD = MRI \text{ volume} -$
5 $TRUS \text{ volume}$). The relative SVD was defined as $SVD/MRI \text{ volume}$ to account for the
6 prostate volume in the estimation of volume difference.

7

8

9 *Study outcomes*

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

15

16

17 *Statistical analysis*

18 Descriptive statistics were obtained reporting median and interquartile range (IQR) for
19 continuous variables, and frequencies and proportions for categorical variables, as
20 appropriate. Continuous variables were analyzed with the Wilcoxon test. Differences
21 between categorical variables were assessed using the Chi 2 and Fisher exact tests,
22 when appropriate. Binomial regression models were developed to assess the influence
23 of key variables on the detection rate of csPCa on targeted biopsy cores. The effects
24 of age, PSA density, relative SVD, Likert score, operator experience, target size (max
25 diameter in mm) to the square root of prostate volume (cc) ratio (target to prostate size

1 ratio = target size / $\sqrt{(\text{prostate volume})}$, and the number of targeted biopsy cores on
2 the dependent variable were explored. Violin plots were created to illustrate variations
3 in the relative SVD according to the biopsy result, stratified by operator experience,
4 prostate volume, and Likert score.

5 Retrospective statistical analyses of the prospectively collected data were performed
6 using the open-source R statistical software v.3.4.0 (R Foundation for Statistical
7 Computing, Vienna, Austria). All tests were two-sided with a significance set at $p <$
8 0.05.

9

10

11

1 **Results**

2 *Study population*

3 Overall, 1721 patients underwent MRI-TB with a median number of 3 (IQR 2.4) cores
4 per procedure, resulting in a total of 5593 targeted cores. Among the included patients,
5 695 (40%) and 357(20%) were diagnosed with csPCa and non-clinically significant
6 prostate cancer (i.e., ISUP 1) on the targeted cores, respectively. Most of the men
7 enrolled (76%) had not undergone a previous biopsy (Table 1).

8

9

10 *Clinically significant prostate cancer PCa detection*

11 Median relative SVD was significantly lower in patients diagnosed with csPCa on MRI-
12 TB compared to those with ISUP 1 or negative MRI-TB: (6.5 % [IQR-2.6, 12.6], vs.
13 7.7% [IQR 3.3, 15.0], $p < 0.01$, respectively). Specifically, analysis of the relative SVD
14 distribution showed that in the case of ISUP 0-1 MRI-TB, relative SVD values were
15 more spread out with more outliers between 20 and 40% (Figure 1A).

16

17 *Logistic regression*

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

24

25

1 *Analysis of SVD variation*

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

12

13 *Analysis by core*

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

21

22

1 Discussion

2

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

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

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

24

25 The main finding of the present study is that a segmentation volume difference
26 between MRI and TRUS higher than 10% relative to the MRI volume is associated with

1 a lower detection of csPCa on MRI-TB and each MRI-TB core. Therefore, this relative
2 SVD could be a useful tool for the physician during the procedure by being used as a
3 safeguard to measure the quality of the 3D TRUS segmentation and refine the contours
4 in case of discrepancy between the volume of both imaging modalities.

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

9 Among all prostate imaging modalities, both MRI and 3D TRUS have been shown to
10 correlate well with the surgical specimen weight[25, 26]. In a study evaluating the
11 reproducibility and modality differences of prostate contouring between various
12 imaging modalities, MRI and 3D TRUS volumes displayed the closest correspondence
13 between modalities with an MRI-3D TRUS inter-modality volume standard error of
14 measurement (SEM) of 5.6 cc[27]. Another study comparing prostate volume variability
15 between MRI and 3D TRUS contoured images reported a strong similarity in volume
16 determination between modalities with a US/MR prostate volume ratio of 0.99 +/-
17 0.08[28]. Therefore, the results of these two studies tend to confirm our findings. There
18 seems to exist a small systematic volume difference between both modalities possibly
19 related to the physical process of creating 3D TRUS and 3D MRI volume. However, a
20 relative SVD of more than 10% should be considered inappropriate as it reflects a
21 suboptimal segmentation. Indeed, a registration based on a suboptimal 3D TRUS
22 segmentation would result in a mapping of the target in a less accurate location in the
23 prostate. However, most of the studies evaluating the correlation between MRI and
24 TRUS volume have been performed in patients treated with brachytherapy and
25 therefore with small prostate volumes. Although these correlation studies could not be

1 fully extrapolated to all prostate volumes, our study used an SVD normalized to MRI
2 volume, which allows us to use it regardless of prostate volume.

3

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

16

17 Operator expertise also played a role in segmentation quality. Thus, the variability of
18 the relative SVD was greater for less experienced operators (Figure 1C), indicating
19 that segmentation may be more difficult for novices and may be one factor impeding
20 the broad adoption of targeted fusion biopsy. Operator expertise was also predictive of
21 a SVD $> 10\%$ in a multivariate analysis (Figure S3; supplementary materials). Learning
22 curve analysis of MRI-TB has been evaluated but without any specific data on skills
23 acquired in image-based planning[30, 31]. Segmentation learning analysis is a crucial
24 topic for MRI-TB learning and should be the subject of dedicated study in the future.

25

1 Our study is not devoid of limitations. First, the data are from a tertiary center that
2 pioneered computer-assisted fusion for MRI-TB. Despite a large number of operators
3 with different levels of experience that could minimize this potential limitation, the
4 expert center effect probably tends to improve the overall diagnostic performance in
5 this study. However, if this is the case, a lower detection of cs-PCa TB increases the
6 difficulty of finding significant predictive factors for this group. Therefore, we believe
7 that the safeguard of a less than 10 % difference between MRI and 3D TRUS
8 segmentation remains applicable regardless of center experience. Second, all MRI-TB
9 were performed with Koelis™ platform. Thus, our results may not be directly applicable
10 to other fusion systems. Third, this study was unable to comprehensively identify all
11 the factors affecting the quality of segmentation. Data on image quality, echogenicity,
12 and prostate architecture are lacking and may be useful in predicting more difficult
13 segmentation of TRUS images. A future study should attempt to identify these potential
14 predictive factors. Additionally, with the rapid growth of transperineal biopsy, there
15 might arise a valid concern regarding the ongoing relevance of our findings. Despite
16 the potential reduction in the human factor through the use of a stationary probe in
17 transperineal biopsy, it is important to note that the core principles of segmentation and
18 registration remain unchanged. Consequently, the quality of segmentation continues
19 to play a crucial role in determining the accuracy of registration, thereby directly
20 impacting the overall precision of the biopsy. Nevertheless, it would be interesting to
21 validate these data on a cohort of patients biopsied using the transperineal approach.
22 Finally, apart from the quality of the segmentation reflected by the SVD, there are other
23 human factors influencing the accuracy of the biopsy procedure reflected by the csPCa
24 diagnostic rate. The precise localization of the target on the MRI and the dexterity of

1 the operator to reach the target are among them but are unfortunately difficult to
2 quantify in this type of study.

3

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

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

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1 **Data availability Statement**

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

4

5

6 **Figure Legend**

7

8 Figure 1. Distribution of the relative SVD between MRI and TRUS segmentation
9 according to the positivity of targeted biopsies.

10 1A. Distribution analysis in the overall population

11 1B. Distribution analysis stratified by Likert score.

12 1C. Distribution analysis stratified by operator experience.

13 1D. Distribution analysis stratified by prostate volume.

14 SVD: Segmentation Volume Difference

15

16

17 Figure 2. Binomial logistic regression for clinically significant prostate cancer
18 positiveness

19 PSA: Prostate-Specific Antigen; SVD: Segmentation Volume Difference (MRI-TRUS),

20 OR: Odds Ratio

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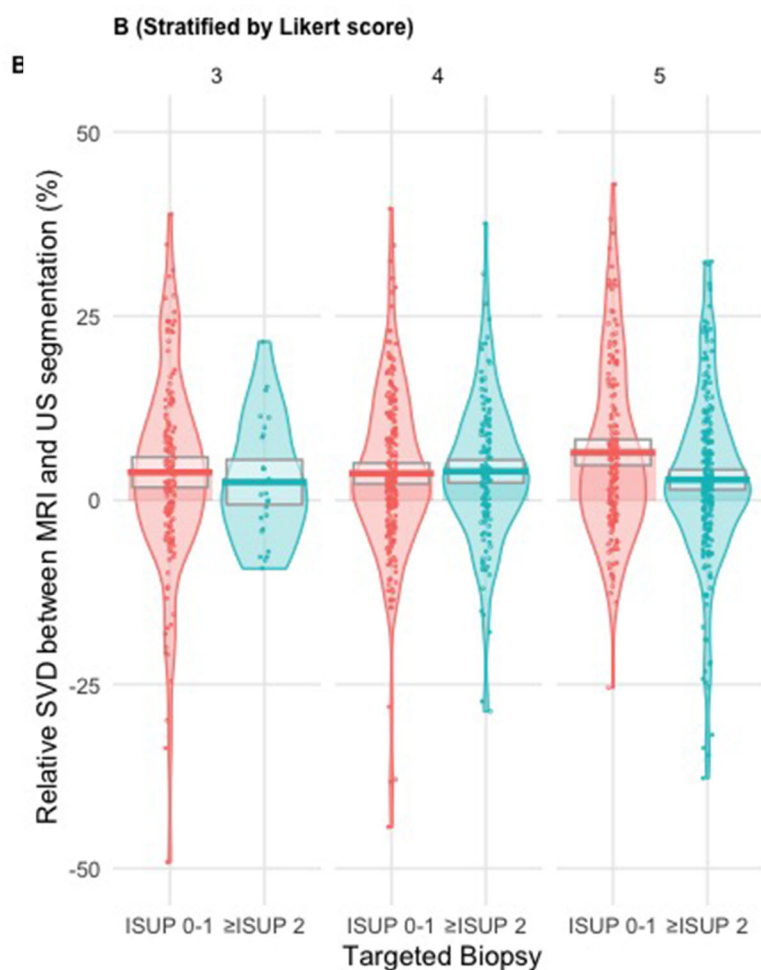
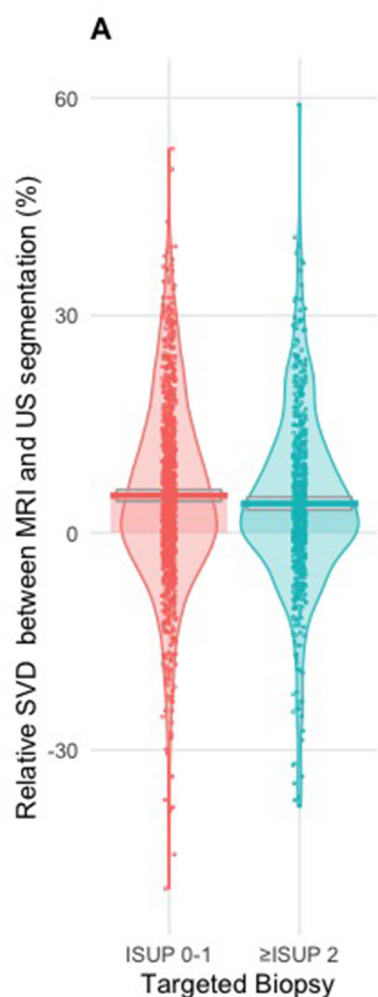
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Table 1. Baseline Characteristics of the study population

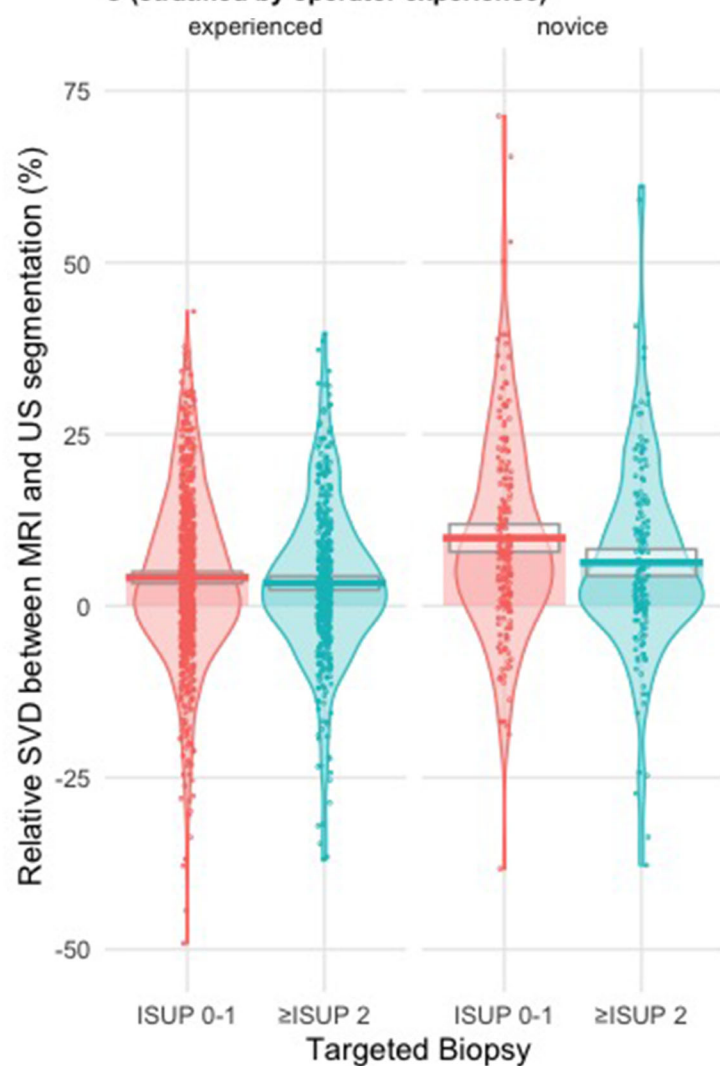
Characteristics	Overall, N = 1,721	ISUP 0-1, N = 1,026	ISUP ≥ 2 , N = 695	p-value
Age — years	66.0 (61, 72)	65.0 (60, 70)		<0.001
Prostate Volume on MRI segmentation — cc (IQR)	47.2 (34.5, 65.7)	53.1 (37.8, 71.2)	40.6 (31, 54.2)	<0.001
PSA — ng/ml (IQR)	7.0 (5, 10)	6.0 (5, 9)	8.0 (5, 12)	<0.001
MRI done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

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

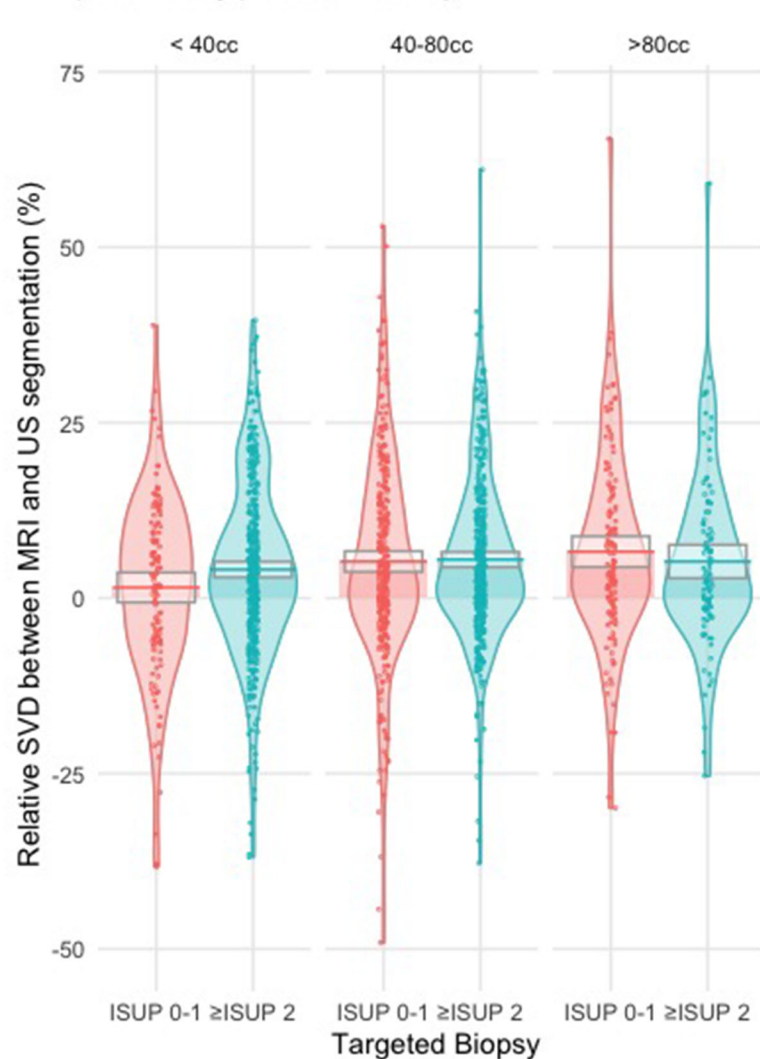
* Experienced operator: > 50 procedures; Novice: < 50 procedures



C (stratified by operator experience)



D (stratified by prostate volume)



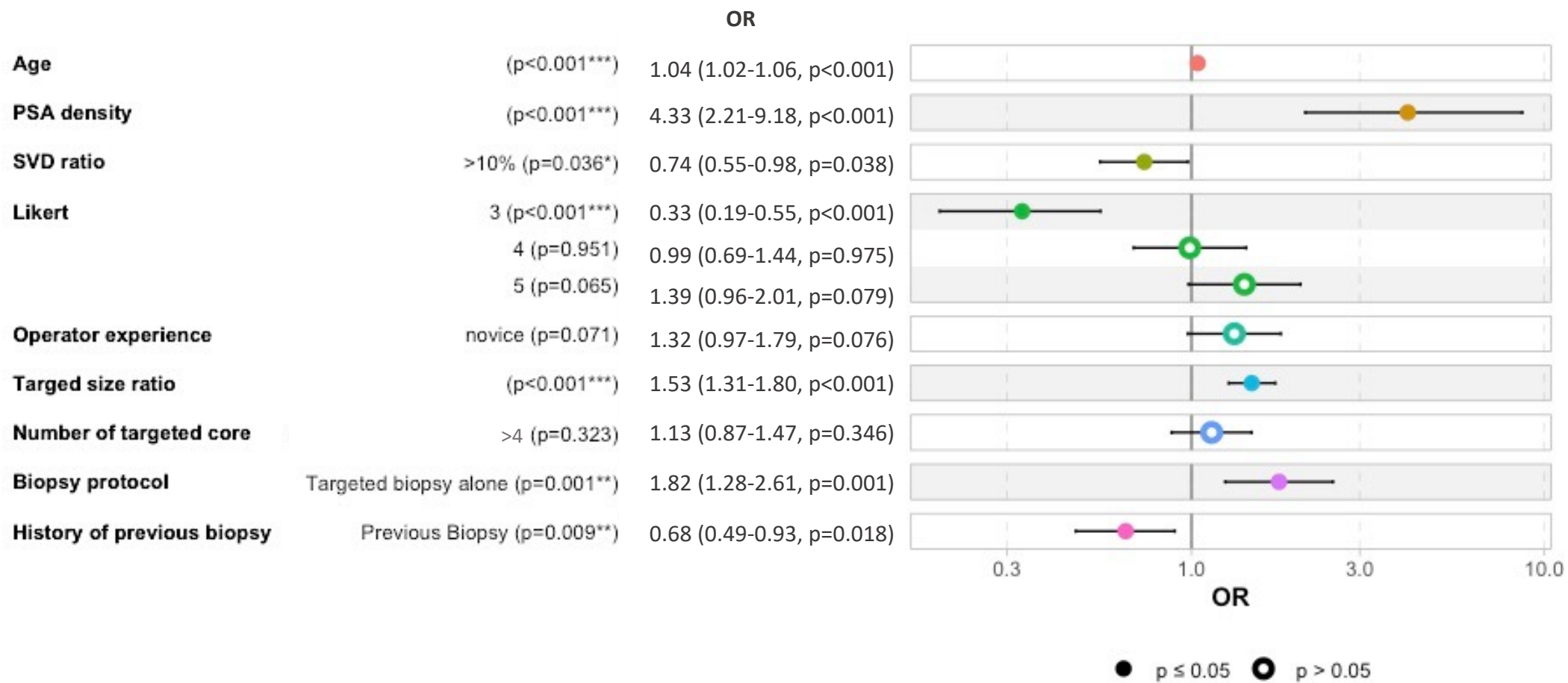


Figure. Secondary regression analysis by core positivity

core_positive: OR (95% CI, p-value)			
SVD ratio	>10		0.76 (0.63-0.92, p=0.004)
Likert	<3		-
	3		0.24 (0.16-0.35, p<0.001)
	4		0.75 (0.58-0.96, p=0.022)
	5		1.28 (1.02-1.61, p=0.037)
Operator experience	novice		1.33 (1.09-1.63, p=0.005)
nb_targeted_biopsy_bin	>6		-
	1-3		0.78 (0.55-1.12, p=0.174)
	4-6		0.87 (0.64-1.18, p=0.370)
Biopsy protocol	Targeted biopsy alone		1.21 (0.97-1.50, p=0.086)
History of previous biopsy	Previous Biopsy		0.80 (0.66-0.97, p=0.026)
core_localisation_anterior	posterior		1.71 (1.41-2.09, p<0.001)

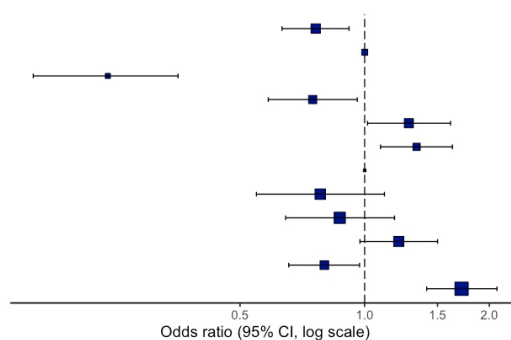


Figure S1. Multivariate analysis of predictors associated with individual core positivity.

Table S1 . Baseline characteristics by cores positivity

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

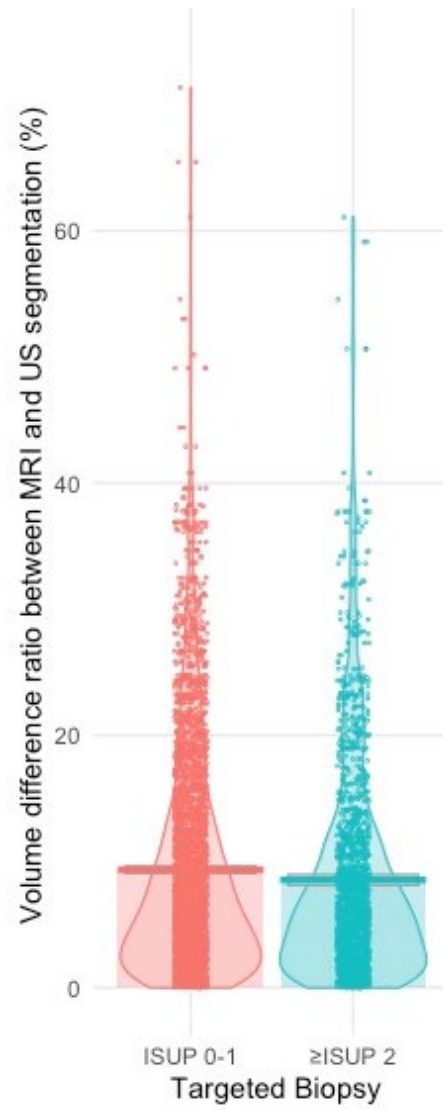


Figure S2. Distribution of absolute relative SVD between MRI and US segmentation according to the positivity of the targeted cores

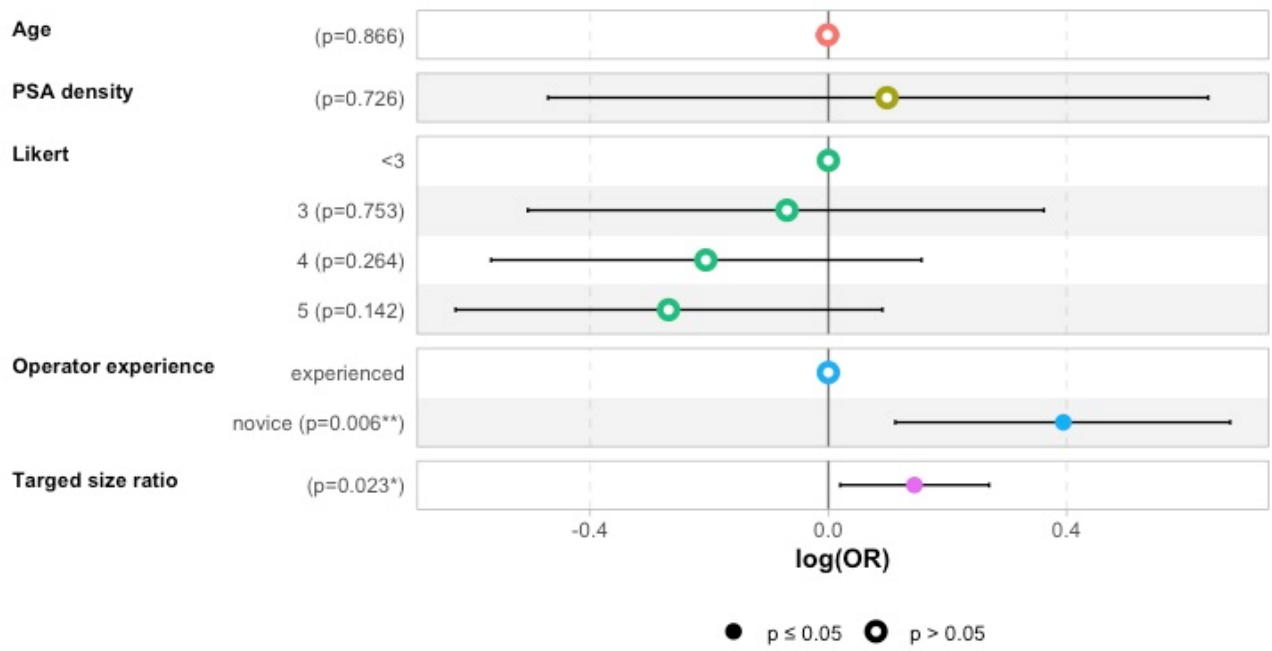


Figure S3. Multivariate analysis : Predictors associated with SVD > 10%