Effect of 3D Modeling of S-fusion software on Positive surgical Margins in Patients who Underwent Radical Retropubic Prostatectomy: A Randomized Prospective Study

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Purpose: To investigate the effect of using three-dimensional (3D) modeling before the surgery on positive surgical margins (PSM) in patients who underwent radical retropubic prostatectomy (RRP).

Materials and Methods: A prospective data analysis of 81 patients who underwent RRP between April 2021 and December 2023 was performed. Patients were randomized into 2 groups. In "3D group" (n:41), patients were evaluated by the surgeon and radiologist by using a 3D modeling of the mpMRI images which were done by two experienced radiologists just before the surgery. In "non-3D group" (n:40), the surgeon evaluated the mpMRI scans and reports by himself without a 3D modeling of the mpMRI before the operation. Finally, positive surgical margins of two groups were compared.

Results: The mean age of the patients was 66.7 ± 5.2 and 65.3±4.9 years in 3D group and non-3D group, respectively. (p = .65) Preoperative PSA value, prostate volume, preoperative PIRADS 4 and PIRADS 5 scores, postoperative ISUP grades and T stages were statistically similar in both groups. (p > .05) The PSM rate was 24 (29.6%) in the overall patient population. PSM was detected in 6 (14.6%) and 18 (45%) of the patients in 3D group and non-3D group, respectively. (p = .005)

Conclusion: Using a 3D modeling of the mpMRI images before the surgery decreased the PSM rates after radical retropubic prostatectomy. The present study also reveals the importance of collaboration between radiologists and urologists in the accurate preoperative evaluation of prostate cancer.

Keywords: radical retropubic prostatectomy; 3D modeling; positive surgical margin

INTRODUCTION

Prostate cancer (PCa) is the second most commonly diagnosed solid tumor in men worldwide.[1,2] The treatment modalities of PCa have been improving according to the clinical stage of the disease over the years. Radical prostatectomy (RP) is the main surgical treatment modality which can be performed in all stages of the disease recently.[3] The main aim of RP is the eradication of cancer and preserving pelvic organ functions in local and locally advanced disease.[4] However, biochemical recurrence occurs in up to 69% of patients at 8 years after surgery.[5] Because patients with positive surgical margin (PSM) after RP have a high risk of progression, various methods have been investigated to reduce surgical margin positivity.[6-8]

Preoperative 3D virtual models have been used to improve oncologic results of robot assisted laparoscopic radical prostatectomy (RARP), recently.[6-8] However there is no data about the effect of 3D reconstruction technology on surgeon's 3D perception for oncologic results of radical retropubic prostatectomy (RRP) which is an open surgical approach.

The present study aimed to investigate the impact of a 3D virtual model by reconstructing the MRI images on the PSM after RRP, prospectively.

MATERIALS AND METHODS

Study population

The study was approved by the Ethics Committee of our university (KAEK-02, 01.04.2021). A prospective data analysis of 81 patients who underwent RRP consecutively between April 2021 and December 2023 was performed. Patients were randomized into 2 groups by using a simple randomization. In "3D-group" (n:41), the surgeon evaluated the anatomy of prostate and tumors with two radiologists by using a 3D modeling of the multiparametric magnetic resonance imaging (mpMRI) just before the surgery. In "non-3D-group" (n:40), surgeon evaluated the mpMRI scans and reports by himself without a 3D reconstruction of the mpMRI before the operation.

Inclusion and exclusion criteria

Eighty-one consecutive patients who underwent RRP and who were imaged using a suitable mpMRI protocol described below were included in the study. Patients who were not suitable for mpMRI or patients with inappropriate MRI were excluded. Patients who underwent a laparoscopic RP were also excluded due to the effect of the learning curve (n:6). All patients included under-

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Received April 2024 & Accepted December 2024

Table 1. Characteristics of the groups

	3D group n=41	Non-3D group n=40	p
Age (year)	66.7±5.2	65.3±4.9	.65[a]
Preopeoperatif PSA (ng/ml)	8.1 (5.19)	7.45 (7.58)	.55[b]
Prostate volume (gr)	55 (28.5)	48 (29.25)	.07[b]
PIRADS 4 lesion existence n (%)	25 (61%)	24 (60%)	1.00[c]
PIRADS 5 lesion existence n (%)	16 (39%)	12 (30%)	.59[c]
Nerve sparing surgery n (%)	6 (14.6%)	4 (10%)	.48[d]
Erythrocyte transfusion n (%)	8 (19.5%)	7 (17.5%)	.86[c]
Preop. organ-confined possibility %	72.5 (11-92)	61 (11-90)	.42[b]
ISUP grade of RRP n (%)			
ISUP 1	14 (34.2%)	16 (40%)	
ISUP 2	10 (24.4%)	11 (27.5%)	.19[b]
ISUP 3	7 (17.1%)	7 (17.5%)	
ISUP 4	5 (12.2%)	4 (10%)	
ISUP 5	5 (12.2%)	1 (2.5%)	
pT stage n (%)			
T2	26 (63.4%)	31 (77.5%)	.13[b]
T3	15 (36.6%)	9 (22.5%)	
ePLND n (%)	15 (36.6%)	18 (45%)	.06[c]
PSM n (%)	6 (14.6%)	18 (45%)	.005[c]

[a]Student *t* test
[b]Mann-Whitney *U*
[c]Chi Square Continuity Correction (Minimum expected count (MEC); 5<MEC<25)
[d]Fisher's Exact Test Correction (MEC<5)
Abbreviations: PSA, Prostate specific antigen; PIRADS, Prostate Imaging Reporting and Data System; RRP, Radical retropubic prostatectomy; ISUP, International Society of Urological Pathology; ePLND, extended pelvic lymph node dissection; PSM, positive surgical margin

went a mpMRI of prostate before the prostate biopsy. Patients underwent a RRP procedure at least 6 weeks after the biopsy. A 3D virtual model by reconstructing the mpMRI images was created for all patients in 3D-group. (**Figure 1**)
Operations were all performed by two high-volume oncourologists. mpMRI scans were all evaluated by two experienced radiologists. Then, a 3D modeling for each patient in 3D-group was created by the same experienced interventional radiologist.

Procedures
All procedures were performed in a supine position under general anesthesia. About 8 to 10 cm lower midline incision is made between the umbilicus and pubic symphysis. The incision is deepened through all layers of the abdominal wall. The retropubic space is developed bluntly and the peritoneal contents are swept in a cephalad direction. A good exposure of puboprostatic ligaments, dorsal vein and pelvic fascia was achieved after careful dissection of the fibroadipose tissue covering the prostate. The dorsal vein complex was ligated following the incision of the endopelvic fascia. Apical and posterior dissections were performed carefully considering 3D images and/or mpMRI images. Preservation or wide excision of the neurovascular bundle (NVB) was planned before the operation according to the appropriate images in both groups. After the division of the bladder neck and excision of the seminal vesicles, vesicourethral anastomosis was performed with the help of foley catheter via six 4-0 absorbable sutures.
An extended pelvic lymph node dissection (ePLND) was performed in patients with high risk for lymph node metastasis or with a suspicious lymph node involvement in imaging methods.

Evaluations
The materials of radical prostatectomy were identified in a 10% buffered formaldehyde solution. Following identification, the right lobe of the prostate was stained black, the left lobe was stained green, and the midline was marked with a red surgical margin dye. The seminal vesicles, vasa deferentia, and three dimensions of the prostate were measured. The seminal vesicles and vasa deferentia were separated, and the transition zones with the prostate were blocked entirely, both on the right and left sides. The weight of the prostate was recorded. Surgical boundaries of the apex and bladder neck were separated and blocked. Subsequently, the entire prostate was numbered at 4mm intervals from the apex to the bladder neck, sliced, and sections were arranged on paper in an additional cross-sectional manner: right anterior, right posterior, left anterior, left posterior, passing through the urethra, numbered, and photographed. Macroscopic examination was conducted and recorded for all sections. Then, all pieces were placed in recorded direction-specific blocks. Prepared tissue samples were put into routine follow-up (Thermo Scientific Excelsion ES). Following tissue tracking, paraffin blocks were prepared by placing each section surface down. Sections of 5 micrometers thickness were taken from paraffin blocks using a microtome (Leica RM 2125, Tokyo, Japan) and stained with Hematoxylin and Eosin (H&E) for histopathological examination. Examination was performed using a light microscope (Nikon Eclips Ci). (**Figure 2**)
The photomicrographs, revealing the histopathologic diagnoses, were taken by an experienced uropathologist, blinded to the previous images.

Imaging protocol and interpretation
mpMRI images of prostate segmented using a Samsung RS 85 ultrasound device by using S-fusion software. 3D Modeling of S-fusion software allows safe navigation and precise targeting during prostate biopsies based on 3D models created from MRI data sets, and also provides a function to report biopsy location. We used 3D modeling feature of this system for preoperative assessment. (**Figure 2**) All prostate segmentations and lesion identifications on 3D modeling of prostate

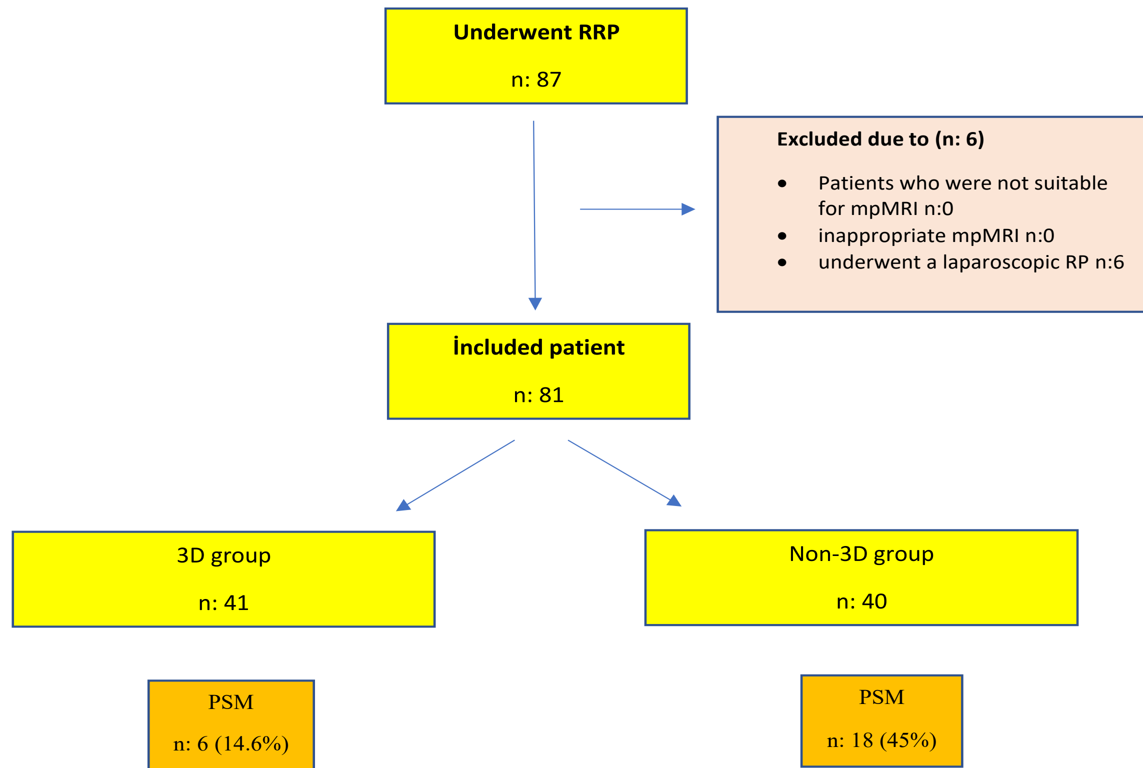

Figure 1. Study flow chart
Abbreviations: RRP, radical retropubic prostatectomy; mpMRI, multiparametric MRI; PSM, Positive surgical margin

images performed by an interventional radiologist experienced with prostate TRUS-mpMRI fusion biopsy procedure. After segmentation and 3D modeling, all 3D images evaluated by surgeon and radiologists together using X-Y-Z axis directions to cooperate better preoperative surgical margins.

Statistical Analysis

Statistical analyses were performed with SPSS software, version 25 (IBM Corporation, Armonk, NY, USA). In the power analysis performed at the beginning of the study, 80% power was targeted and the sample size was found to be 41 for both groups (3d-Non 3D) as given in Supplementary Tables. As a result of the power analysis performed for the chi-square test between the surgical margin positive and 3D group categorical variables, it is seen in Supplementary Tables that the power of the test is 0.87. Since the other hypotheses were not rejected, power analysis was not needed. Normality tests and Q-Q plots for quantitative variables were used to determine whether the quantitative variables were normally distributed before starting the analyses. The test of normality results of quantitative variables is given in **Supplementary Tables** and the Q-Q plots for quantitative variables were given in Supplementary Figure. The normality of data was assessed using the Kolmogorov–Smirnov test. Normally distributed quantitative data were presented as mean ± standard deviations (SD) and compared using Student's t-test. Non-normally distributed variables were compared using Mann-Whitney U test and were presented as median and inter quartile range (IQR). Descriptive analyses were presented using medians for the non-normally distributed and ordinal variables. Categorical variables between the independent groups were compared by Fisher's Exact test and Chi-Square Continuity Correction. The application of Fisher's Exact test and Chi-Square Continuity Correction tests depends on the Minimum expected count value. If the MEC value is between 5 and 25, the test to be used is Continuity Correction, and if the MEC value is less than 5, Fisher's Exact Test is used.
A *p*-value of less than 0.01 was consider to show a statistically significant result.

RESULTS

The mean age of the patients was 66.7±5.2 and 65.3±4.9 years in 3D group and non-3D group, respectively. (p = .65) Median- IQR preoperative PSA values were 8.1 (5.19) ng/mL and 7.45 (7.58) ng/mL in 3D group and non-3D group, respectively. (p = .55) Median-IQR prostate volume of the patients was 55 (28.5) gr and 48 (29.25) gr in 3D group and non-3D group, respectively. (p = .07). Distribution of preoperative PIRADS 4 (p = 1.00) and PIRADS 5 (p = .59) scores in mpMRI were

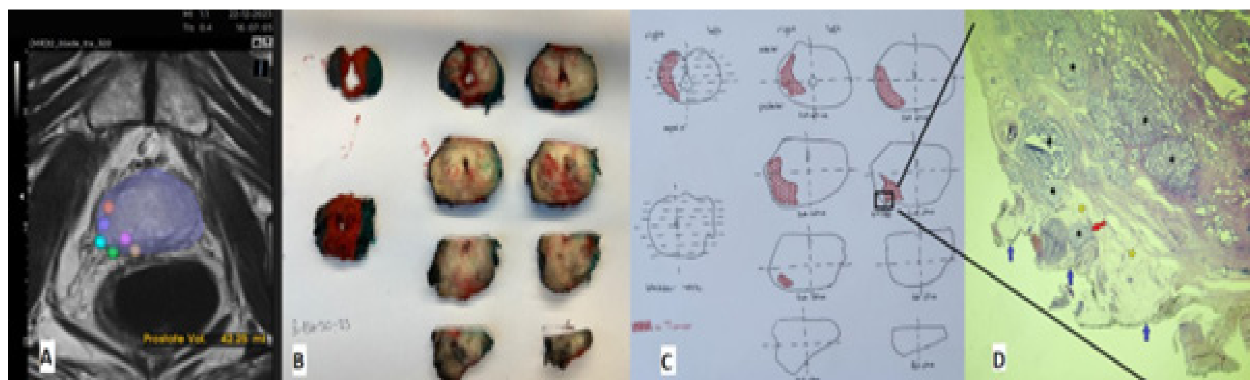

Figure 2A: mpMRI image of prostate segmented using a Samsung RS 85 ultrasound device by using S-fusion software **2B:** Macroscopic view of the prostate slices **2C:** Diagram of tumor localizations in prostate slices **2D:** Microscopic view of the surgical margine. black stars shows tumor, red arrow represents extraprostatic extension, blue arrows indicate surgical margin paint , yellow stars show periprostatic fat tissue (1XHE)

also similar in both groups. Postoperative ISUP grades (p = .19) and pT stages (p = .13) were statistically similar in both groups. It was detected that 36.6% of the patients in 3D group had stage pT3 tumor which means extracapsular extension or seminal vesical invasion. In non-3D group, the rate of stage pT3 tumor was 22.5%. (**Table 1**)

Nerve-sparing surgery (NSS) (p = .48) was performed for 6 (14.6%) and 4 (10%) of the patients in 3D group and non-3D group, respectively. Postoperative erythrocyte transfusion (p = .86) was necessary for 8 (19.5%) patients in 3D group and for 7 (17.5%) patients in non-3D group.

The median rate of organ-confined prostate cancer (p = .42) according to Partin Nomogram before the surgery was 72.5% (11%-92%) in 3D group and 61% (11%-90%) in non-3D group. An extended PLND (p = .44) was performed for 15 (36.6%) and 18 (45%) patients in 3D group and non-3D group, respectively. Finally, pathologic lymph node invasion was detected in one patient from each group.

The PSM rate was 24 (29.6%) in the overall patient population. PSM was detected in 6 (14.6%) and 18 (45%) of the patients in 3D group and non-3D group, respectively. (p = .005) (**Table 1**)

The risk (odds ratio = 0.317) of having a PSM with 3-dimensional drawing is 31.7% compared to the case without 3-dimensional drawing. In other words, the use of 3-dimensional drawing reduces the risk of a PSM approximately 3-fold compared to surgery without 3-dimensional drawing. With 95% confidence, this risk can vary between approximately 2 and 7 times. For multivariate modelling, binary logistic regression was applied to reveal the effect of other variables on the PSM variable. According to the results of the logistic regression analysis, the only variable with a significant effect on PSM was found to be 3D group.

DISCUSSION

Prostate cancer is one of the most commonly diagnosed tumors in men all around the world.[1,2] Radical prostatectomy is still the main surgical treatment modality of the disease and has been used for local, locally advanced and also metastatic disease. This procedure involves removing the entire prostate with its capsule intact and seminal vesicles. After the description of a detailed anatomy by Walsh in 1982, open retropubic approach became more popular. In the early 2000s, robot assisted laparoscopic radical prostatectomy was introduced using da Vinci Surgical System® by Binder et al.[9,10]

With the improving technology and experience, outcomes of the procedure have also become better. For improving the oncologic outcomes, 3D images of the prostate have been transferred to Da Vinci surgical system to guide surgeon.[6] However, the impact of the improvement of 3D perception of the surgeon before the open surgery has not been investigated, yet.

We evaluated the effect of tumor mapping by a 3D imaging before the RRP on the PSM in the present study. According to our results, the risk of PSM decreased 3–fold (odds ratio=0.317) by using a 3D imaging for tumor mapping just before the surgery (14.6% vs. 45%). The main aim of RP is the eradication of cancer in local and locally advanced disease.[4] However, despite the definitive therapy with RP, many patients will go on to develop biochemical recurrence range up to 69%.[5] It is well known that PSM is an important predictor for biochemical recurrence and the disease progression such as ISUP grade, T-category and PSA level.[11,12] Among these prognostic factors surgical margin status is the only one which can be influenced by surgical technique and success. Thus, urologists tried to decrease the PSM rates by using various approaches with the help of other branches of medical sciences. Schlomm et al. described the “neuroSAFE” which offers a frozen-section examination during RP in 2012. With the NeuroSAFE technic, they showed an increased nerve-sparing frequency and reduced positive surgical margins in both open and robot-assisted laparoscopic radical prostatectomy.[13] von Bodman et al. reduced the PSM to 3% by using intraoperative frozen section of the prostate.[14] Numerous following studies also indicated the efficacy of intraoperative frozen section to reduce PSM rates after RP.[15]

Another approach to reduce PSM rates and improve oncologic outcomes was using a 3D image reconstruction of the prostate during the RARP. Canda et al. described this approach in five cases in 2020.[6] Porpiglia et al. assessed the use of hyper-accuracy 3D reconstruction based on mpMRI during RALP. They evaluated 30 patients and concluded that hyper-accuracy 3D reconstruction allowed performance of RALP.[7] Schiavina et al. evaluated the impact of a 3D model with augmented reality on surgical planning to guide nerve sparing during RARP. They included 26 consecutive patients with PCa to their study. According to their results, PSM rate

was 15.4% in the overall patient population. It was also detected that augmented reality-3D technology changed the nerve-sparing surgical plan in 38.5% of patients.[8] There are numerous papers reported on the use of 3D reconstructed models of which some reported on virtual reality technique, and some reported on augmented reality technique for surgical guidance in RARP.[16] However, there is no study about the effect of 3D reconstructed models on the outcomes of open RP techniques in literature.

Simpfendörfer et al. and Lanchon C described the augmented reality visualization by using transurethral ultrasound during laparoscopic radical prostatectomy (LRP). However, they did not evaluate the effect of this approach on oncologic results of LRP.[17,18]

It was demonstrated that careful attention to surgical details with experience improves the outcomes of the RP surgeries by reducing PSM rates and that is why high-volume surgeons have lower PSM rates.[19,20] According to our results using a 3D imaging of the prostate and tumors by the surgeon increased the attention to surgical details and decreased the PSM.

CONCLUSIONS

With the present study, it was demonstrated that mapping the tumor by using a 3D modeling technology of images and being aware of the characteristics of cancer during open RP, increased the attention of urologists to surgical details. Thus, collaboration between the urologist and radiologist improved oncologic outcomes of the open RP.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

APPENDIX

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