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**PREDICTIVE VALUE OF DIFFUSION PARAMETERS USING MACHINE
LEARNING IN LOW-AND INTERMEDIATE-RISK PROSTATE CANCER
PATIENTS TREATED WITH STEREOTACTIC ABLATIVE RADIOTHERAPY**

**NATIONAL SCIENTIFIC STUDENTS' ASSOCIATIONS CONFERENCE
APPLICATION WORK**

BIOMEDICAL ENGINEER MSC.

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Abstract

Aim: To investigate the predictive value of the pre-treatment diffusion parameters of diffusion weighted MRI using artificial intelligence (AI) for PSA response in patients with low- and intermediate-risk prostate cancer (PCa) treated with stereotactic ablative radiotherapy (SABR).

Materials and methods: Retrospective evaluation was performed using pretreatment multiparametric MR image datasets of 40 PCa patients between 2017 and 2021. MR-based mean- and minimum apparent diffusion coefficients (ADC_{mean} , ADC_{min}) were calculated for the intraprostatic dominant lesion where it was visible. Therapeutic response was assessed using prostate-specific antigen (PSA) levels. Two patient groups were created, divided by the median of the 1-year-PSA measurements. Three different prediction models, decision tree (DT), random forest (RF), and support vector machine (SVM) classifiers were established. Predictive performance was assessed by the receiver operating characteristic (ROC) analysis. For further statistical analysis, Spearman's correlation and Wilcoxon's signed-rank test were used, with a significance level of $p \leq 0.05$.

Results: No biochemical relapse was detected after a median follow-up of twenty-three months (range: 3–50), with a median PSA of 0.01 ng / ml (range: 0.006–2.8) at the time of the last examination. PSA nadir has not yet been achieved in 45% of patients. Moderate negative correlations were found between ADC_{mean} , ADC_{min} and PSA nadir values ($r = -0.5678$, $p < 0.0001$ and $r = -0.5633$, $p < 0.0001$). Furthermore, significant differences were observed between the pretreatment ADC_{mean} , ADC_{min} parameters, and the group averages of patients with low and high PSA nadir measurements ($p < 0.0001$, $p < 0.0001$). In prediction, the RF model outperformed the DT and SVM model, yielding area under the curves (AUC), with 0.722, 0.685, and 0.5, respectively.

Conclusion: Our findings suggest that pretreatment MR diffusion data may predict therapeutic response using novel approach of machine learning in PCa patients treated with SABR.

Abbreviations: *androgen deprivation therapy (ADT) *artificial Intelligence (AI) *apparent diffusion coefficient (ADC) * biochemical failure (BF) * centers of gravity of the seeds (COG) *clinical target volume (CTV) *deviation limit (DL) *decision tree (DT) *diffusion-weighted imaging (DWI) *diffusion-weighted magnetic resonance imaging (DW-MRI) *ISUP International Society of Urological Pathology *focal-cryoablation (FC) *Gleason score (GS score) *intrafractional organ motion review (IMR) *intermediate risk (IR) *low risk (LR) * machine learning (ML) *National Comprehensive Cancer Network criteria (NCCN) *prostate cancer (PCa) *prostate specific antigen (PSA) * planning target volume (PTV)* radiation technologists (RTT) *prostate stereotaxic ablative radiotherapy (SABR) *quality of life (QOL) *random forest (RF) *region of interest (ROI) *seminal vesicles (VS) *support vector machine (SVM) *real-time triggered kV images (TkVI) *Serum total prostate-specific antigen (tPSA) *transurethral resection of the prostate (TURP) * turbo spin echo (TSE) *volume of prostate gland (Volume)

Introduction

Prostate cancer is still the most prevalent and second-deadliest disease among males in the United States, with an incidence of 117 cases per 100,000 men and 19 deaths per 100,000 men, both age-standardized to the U.S. standard population of 2000 [1].

The final treatment options for prostate cancer are determined by a patient's risk, which is determined by prostate-specific antigen (PSA) level, clinical T-stage, Gleason pattern, and the number of cores positive, according to risk stratification [2-4].

The technical development of radiation therapy has enabled extra-cranial, prostate stereotaxic ablative radiotherapy (SABR), which delivers high doses with high precision, in a low (≤ 10) fraction number, with targeted inhomogeneity to target volumes outside the skull [5,6].

As a result, the number and indication of SABR treatments constantly expand worldwide [4,7,8].

In patients with prostate cancer (PCa), the use of SABR has been connected to improved progression-free survival and overall survival [7-11], might yield less local failure than multifraction [12], costs less [2,3], and appeared to result in a satisfactory quality of life (QOL) [13-15]. Furthermore, compared to focal-cryoablation (FC), SABR is associated with equivalent oncologic and functional results [16]. These findings highlight the value of SABR in treating PCa with low- to intermediate-risk.

For the detection and characterization of PCa, diffusion-weighted magnetic resonance imaging (DW-MRI) appears to be a viable imaging biomarker [17,18]. Additionally, it has been demonstrated that the use of DW imaging (DWI) and its measurement using the apparent diffusion coefficient (ADC) increases the sensitivity of PCa detection [19,20]. However, it is still unknown whether pre-treatment ADC can be used to predict outcomes following SABR in PCa.

The complexity and non-linearity of biological systems are inherent [21]. Thus, artificial intelligence (AI) based non-linear predictions in patients treated with various indications [22-24] and in PCa [19,25,26] are widely used among researchers.

AI includes a branch called machine learning (ML) in which computers are programmed to recognize patterns in data. The learning process is based on a set of mathematical guidelines and statistical presumptions. In addition, the medical industry has quickly developed and

applied it, particularly when creating predictive models [27]. As a result, it would be practical and promising to develop PCa prediction models using machine learning.

The use of tree models [28] and random forests - which are computationally quick - are frequently used as effective and efficient feature selection solutions in the evaluation of the presurgical status and further diagnose PCa [29], predicting lymph node involvement [30], or even for drunk driving recognition [31]. Additionally, alternative prediction techniques, such as the support vector machine (SVM), could work effectively on a sample with fewer elements [32].

This study aimed to determine the best predictors for the treatment outcome of patients diagnosed with MR-DWI using supervised machine learning methods. Additionally, this study sought to assess the relationship between the potential variables that turned out to be the most accurate predictors of the outcome of PCa.

Materials and Methods

Patients

Between January 2017 and December 2021, 40 low- and intermediate-risk PCa (National Comprehensive Cancer Network criteria [NCCN], [IRPCa]) patients were treated with SABR in “Moritz Kaposi” Teaching Hospital, Dr. József Baka Diagnostic, Radiation Oncology, Research and Teaching Center, Kaposvár, Hungary and enrolled to our study.

Patient characteristics are summarized in **Table 1**. Almost half of the patients (45%) received androgen deprivation therapy (ADT). Serum total prostate-specific antigen (tPSA) >4 ng/ml, abnormal digital rectal exam, or imaging findings suggestive of suspected prostate cancer were all reasons for prostate biopsy. The histopathology review consisted of 10–12 cores of systematic biopsy performed on all patients for staging. The following conditions were required for exclusion: (1) contraindications to epidural anesthesia or MRI, transurethral resection of the prostate (TURP) within six months, (2) significant TURP defect, a high (>18) International Prostate Symptom Score (IPSS), (3) a maximum uroflow rate of fewer than ten milliliters per second, (4) a prostate volume greater than sixty cubic centimeters, (5) the presence of pubic arch interference.

Treatment

Prostate SABR was introduced after national ethical committee approvals (OGYEI: 5838/2017, 66793/2018, 69293/2017). Consequently, a total of forty low-risk (LR) and selected intermediate-risk (IR) patients were treated with VMAT-based SABR monotherapy. The chosen treatment schedule was 36.25 Gy in five fractions (fx).

For each patient prior to treatment, three gold seeds (1mm x 3 mm, [CP Medical, Portland, USA]) were implanted into the prostate. Efforts were made to insert marker(s) in the close vicinity of the intraprostatic dominant lesion if present on multi-parametric MRI. The centers of gravity of the seeds (COG) in the planning CT were defined as markers/references for the deviation limit (DL). DL was equal to the posterior planning target volume (PTV) margin. In intrafractional organ motion review (IMR), a circular overlay was centered at the marker position and was projected onto each triggered image. The radius of this circle

corresponds to the DL, and color-based coding was used to indicate whether the seed is in (green) or outside (red) the DL or not detectable (orange). Furthermore, contours for each marker with a 3 mm margin around the center of the seeds were also defined and used as overlay structures during real-time triggered kV images (TkVI).

All patients were prepared according to our institutional bladder and rectal filling protocol: requesting a full bladder (500 ml water intake 30-40 min after voiding) and an empty rectum (dietary advice, laxatives, rectal suppositories), both for planning and daily treatments. Target definition was based on co-registered planning CT and MRI series in identical patient positions. The clinical target volume (CTV) included the prostate plus proximal seminal vesicles (VS) in patients with IR disease. In contrast, for patients with LR disease and boost cases, the CTV was represented by the prostate only. The PTV was defined isotropically, expanding the CTV by 5 mm as standard, reduced to 3 mm in the posterior direction in the case of conflict with rectal dose constraints. For boost cases, the posterior margin was consequently 3 mm. Treatment plans were designed and optimized according to two 6 MV full volumetric modulated (VMAT) arcs and were delivered on a TrueBeam LINAC using flattening filter-free photon beams. Before each radiation fraction delivery, CBCT (pre-CBCT) and two 2-dimensional orthogonal kV images were acquired to verify the correct marker position and rotational error (≤ 3 mm) with the OARs conditions (full bladder, empty rectum) requested. In the case of rectal filling, which considerably differed from baseline, patients were removed from the table, and rectal suppositories, a wind-pipe, or both were applied. In case of empty bladder, patients were asked to continue drinking. Re-setup was also performed in case of exceeded rotational error.

After repositioning, the image verification procedure was repeated. During treatment, beam delivery triggered kV imaging at an interval of 3 seconds was acquired. After marker-based matching (COG) and couch adjustment, the treatment started with an oblique TkVI, allowing control on both vertical and longitudinal seed displacement after couch repositioning. If one or more seeds exceeded the DL dose, delivery was manually paused while the acquisition of TkVI continued. If deviation persisted on the next TkVIs or deviation involved, two out of three markers beam were also interrupted, and a 2D/3D match was performed. Adjustments were made if there was a tendency for marker shifting toward DL (“zero” correction). If a sizeable systematic displacement occurred with the appearance of a rectal gas bubble, the beam was also interrupted, and a second CBCT (viol-CBCT) was acquired. At the same time, the actions mentioned above were applied (wind-pipe $\pm$ rectal suppositories or forced drinking).

Beam interruption was always executed manually. After the two VMAT beams, a second CBCT (post-CBCT) was acquired to evaluate volume changes of OARs and residual errors. The same procedure was applied in our Institute and was more fully explained in a prior paper^[33].

Imaging

Examinations were performed using a hybrid PET/MR scanner (Biograph mMR, Siemens Healthcare GmbH., Erlangen, Germany). After proper patient preparation (removal of metal implants, hearing aids, and metal objects in the region), images were obtained of the pelvic position using dedicated coils. Thus, only 3.0 T MRI parameters were included in the research.

After a localizer, native MRI sequences were T2-weighted turbo spin echo (TSE) sagittal (TR/TE/FA 4200/133 ms/120°, FOV: 240 mm, slice thickness: 3 mm, 256 × 256) and T2-weighted TSE transversal (TR/TE/FA 6500/106 ms/149°, FOV: 240 mm, slice thickness: 3 mm, 320 × 320) images. In addition, T2-weighted TSE coronal (TR/TE/FA 3700/133 ms/120°, FOV: 240 mm, slice thickness: 3 mm, 256 × 256) and T1 TSE transversal (TR/TE/FA 700/9.3 ms/110°, FOV: 200 mm, slice thickness: 3 mm, 256 × 256) pictures were also recorded.

DW measurement was done as part of a routine examination. In this case, a 2D spin-echo DWI echo-planar (EP) sequence (FOV: 315 mm, TR: 5000 ms, TE minimum: 72 ms, TI 200 ms, FA: 90°, slice thickness: 3 mm) was used. First, the implemented software automatically generated an ADC map from the DWI pictures. Then, the restricted diffusion rate was quantified by calculating the apparent diffusion coefficient. A 100 s/mm² “b” value was used as the first measurement (the other b values were 800 s/mm², 1500 s/mm², and 2000 s/mm²) to reduce the perfusion effect on the ADC calculation.

Furthermore, a T1-weighted TSE axial sequence (TR/TE/FA 700/9.3 ms/85°, FOV: 200 mm, slice thickness: 3 mm, 256 × 256) and a T1-weighted TSE StarVIBE FS transversal sequence (TR/TE/FA 3.83/1.75 ms/9°, FOV: 200 mm, slice thickness: 3 mm, 320 × 320, with an isotropic resolution of 1 mm³) were conducted after 0.1 mmol per kg of bodyweight contrast material (Gadovist© Bayer Healthcare, Leverkusen, Germany) was injected into the patient.

Using the eRAD PACS Desktop Viewer 8.0 program, the location of lesions was evaluated on the ADC map. We selected the tumor's prominent and most homogeneous part as a benchmark for all entities in this investigation, which used the single-slice measuring approach [34]. The Region of Interest (ROI) was manually placed on the most solid part of the tumor, which has the highest signal intensity on DWI pictures (hyperintense) and the lowest signal intensity on the ADC map [35,36] (**Figure 1**). Consequently, the researchers took precautions during the ADC measurement, such as removing regions with gross necrosis from the sample (ROI) while constructing an elliptic ROI [37]. ADCmean and ADCmin were used as standard measurement units to reduce the impact of tumor heterogeneity in all lesions. These were also the standard units to be used as a reliable parameter because they reflected the tumor heterogeneity in the given slice and allowed the researcher to distinguish the various entities in the same image [36,38].

Clinical evaluation

We aimed to evaluate the therapeutic tumor responses based on 1-year measured PSA information. Therefore, the ratio of the normalized PSA level of the 1-year measured PSA value to the baseline PSA, which shows the rate of the decline, was normalized and divided into two patient groups based on the median value. Accordingly, a “low PSA nadir” and a “high PSA nadir” group were established as a result.

Model development

Python scripts and in-house machine learning models (decision tree [DT], random forest [RF], and SVM) based on the Python software environment for statistical computing (version 3.8; Python Software Foundation, Beaverton, OR) were used following the guidelines of numpy, scipy, seaborn, and sci-kit-learn software packages for all statistical analyses carried out.

In all of our models, scaling (via “StandardScaler”) and cross-validation (via “cross_val_score”) were done for the raw data. Because of using binary outputs, DT and RF classifier methods have been chosen (“DecisionTreeClassifier” and “RandomTreeClassifier,” respectively). “sklearn.tree” has been split and utilized for training for the DT model. The RF model was trained and separated using the “sklearn.ensemble” function. SVM model performed

via “sklearn.svm”. Model filtered by radial basis function (RBF), setting the two hyperparameters, cost (C) and gamma, to 1 and 0.1, respectively. Models have been developed to determine the relative importance of each predictor candidate in the therapy response classification as measured by the Gini index.

Data analysis

A receiver operating characteristic (ROC) curve was made for the primary tumor ADC values to assess the predictive value of recurrence at any time with the maximum sensitivity and specificity. During the ROC curve analysis, the area under the curve (AUC) was calculated. The AUC must be equal to or greater than 0.5 to be considered clinically accurate.

To determine if the measured ADC_{min} , ADC_{mean} , Age, volume of the prostate gland (Volume), initial PSA (iPSA), and PSA nadir values were average ($p < 0.0001$), the Shapiro-Wilks test [27] was utilized. The Wilcoxon rank-sum test was used to compare groups because these tests revealed non-normality distributions of the ADC_{min} , ADC_{mean} , Age, iPSA, Volume, and PSA nadir ($p < 0.0001$, $p < 0.0001$, $p = 0.0001$, $p < 0.0001$, $p < 0.0001$, $p < 0.0001$, respectively) in the population. Spearman’s correlation coefficient was used to describe the strength of the correlation between the data pairs. Statistical significance was defined as p values less than 0.05.

Results

A total of 40 patients were enrolled in this study. The patients' characteristics are summarized in **Table 1**. Well-visualized primary lesions were defined in all patients with the initial 3T MR, except patients with a collection of potentially incorrect images (n=10). Such patients are not included in the end. The mean ADC_{mean} (+standard deviation [SD]) and ADC_{min} values were $781.34 \pm 56.15 \text{ } 10^{-6} \text{ mm}^2/\text{s}$ (range, 605.66–905.85), and $771.33 \pm 45.15 \text{ } 10^{-6} \text{ mm}^2/\text{s}$ (range, 602.82–898.41), respectively.

Correlation analysis

Significant correlations occurred between ADC_{mean} and iPSA, ADC_{min} and iPSA, as well as ADC_{min} and Volume ($p = 0.0212$, $p = 0.0423$, $p=0.0213$, respectively) otherwise, no further significant connections between Age, iPSA, Volume, ADC_{min} and the ADC_{mean} for the patients treated with SABR was noted. The results of the correlation analysis are summarized in **Figure 2**.

With a median PSA of 0.01 ng/ml (range: 0.006-2.8) at the time of the last examination and a median follow-up of twenty-three months (range: 3-50), no biochemical relapse was seen. Although, 45% of patients have not yet reached their PSA nadir. The median time to PSA nadir was 17.6 months (range: 2-34).

Moreover, there were weak negative associations ($r = -0.5678$, $p < 0.0001$ and $r = -0.5633$, $p < 0.0001$) between ADC_{mean}, ADC_{min}, and PSA nadir values. The pre-treatment ADC_{mean}, ADC_{min},

Volume and group averages of subjects with low and high PSA nadir values also showed statistically significant differences ($p < 0.0001$ and $p < 0.0001$, $p < 0.0001$, respectively) (**Figure 3**) (**Supplementary figure 1**).

Measured parameters, machine learning, and response

Due to the relatively low number of patients, the ML data of PC patients were classified into a training (30%) and a validation set (70%). As a result, the developed random forest model outperformed the decision tree and the support vector machine model in terms of prediction, with corresponding areas under the curves (AUC) of 0.722, 0.685, and 0.5, respectively (**Figure 4**). **Table 2** shows the performance of the RF model. The relative importance ranks of the features are in **Figure 5**, whereas ADC_{min} ranked third. The process visualized in **Figure 6**.

Discussion

Overall, this study mainly focused on DWI imaging parameters' combined role in predicting tumor response to therapy in PCa patients. After a 2-year median follow-up, no biochemical relapse was detected in our study, in accordance with the literature.

Risk stratification is essential for selecting the best PCa treatment plan and forecasting patient outcomes. The most crucial prognostic markers for predicting the success of the therapy (e.g., biochemical failure [BF]) in patients after radical prostatectomy are pre-treatment PSA levels, clinical stage, and GS [39]. However, additional elements like RT dose, irradiation fields, and ADT were discovered to be connected to BF in patients who undergo definitive RT [40,41]. Thus, a detailed evaluation of the entire prostate is necessary before performing definitive RT, in which the staging is based on clinical and radiologic findings, and the histological evaluation is based primarily on prostate biopsy results. Therefore, non-invasive techniques may be a good alternative for assessing the whole prostate and tumor biology before RT. These were areas where DWI-MRI shows promise since it allows for examination of the entire prostate gland, significantly lowering the chance of sampling error during a biopsy.

The quantification of tumors is made possible by DW-MRI calculations generated from ADC. The presence of more cells, larger nuclei, more macromolecular proteins, and less extracellular space in malignant tumors may result in lower ADC readings[42]. In PCa patients, earlier research showed a negative correlation between ADC values and tumor aggressiveness [43,44], which was also confirmed in our study. In addition, Chatterjee et al. discovered a negative correlation between GS and ADC values and lower ADC values in patients with high-risk characteristics such as a high serum PSA level, stage, or tumor grade, implying that ADC values could be used to predict prognosis [45]. In agreement with earlier research, we noticed a negative correlation between tumor ADC values and increased blood iPSA levels in our patient group receiving SABR; however, this correlation was not statistically significant in our instance. Onal et al. noted that patients who progressed had a lower mean ADC value than those who did not, with a considerably larger patient population (n=503) [19]. We identified a similar pattern in this single-institute study when predicting the therapeutic outcome during the shorter follow-up of our IRPCa patients.

The ROC analysis in our study proved the clinical utility of the RF model, which outperforms the DT and SVM models. Nevertheless, researchers are still divided over which model performs better. Chen et al. found that predicting SVM models was the best, followed

by RT and DT. Regarding prediction, the researchers discovered that SVM models performed the best, with RT and DT following [46]. Even though SVM may perform better with smaller samples, the low number of elements in our analysis may cause this mismatch.

A few constraints must be acknowledged. First, the limited number of cases, along with the retrospective nature across the cohort and the number of patients, represents our paper's main restriction. For some machine learning techniques, the sample size might not be sufficient. Second, the training and test datasets came from the same hospital, necessitating further external validation at different institutions to support the results. Third, several crucial possible predictors or variables were left out of our models. For instance, positron emission tomography-based uptake values (e.g., metabolic tumor volume [MTV], total lesion glycolysis [TLG]) and their ratios with ADC values might have been included, altogether the dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) derived volume transfer constant (K^{trans}). The first assessment examining a homogeneous group of patients (low-intermediate risk patients treated with SABR) while using DWI was carried out in this study. In addition, as mentioned earlier, the predictive value of the group using machine learning is also being investigated for the first time in this study.

Conclusion

Using our developed, validated, and compared machine learning methods, pre-treatment MRI-DWI values could predict therapeutic response in PCa patients treated successfully (without biochemical relapse) with SABR.

The strength of this study is the use of an MRI-DWI parameter, which includes diffusion evaluations. Moreover, ADC_{min} and ADC_{mean} values significantly predicted the clinical outcome; thus, their inclusion in risk stratification may be of additional value for predicting patient treatment outcomes.

Conflict of Interest/Disclosure

The author declares no conflict of interest. This study is under publication in the American Journal called Frontiers of Oncology (Q1, IF₂₀₂₀: 6.13).

Key points

Short Title: ML based prediction of MRI-DWI in PCa

Question: How can MRI-DWI values predict the outcome of prostate cancer treated with SABR using machine learning?

Pertinent findings: The retrospective study reveals correlations between baseline MR DWI-based parameters (ADC_{min}, ADC_{mean}) and cancer-specific features (iPSA, Volume) and highlights their impact on the therapeutic response (low PSA nadir, high PSA nadir).

Implications for patient care: Clinicians should measure and integrate the suggested parameters (ADC_{min}, ADC_{mean}) to provide the most accurate therapy for the patient.

Acknowledgement

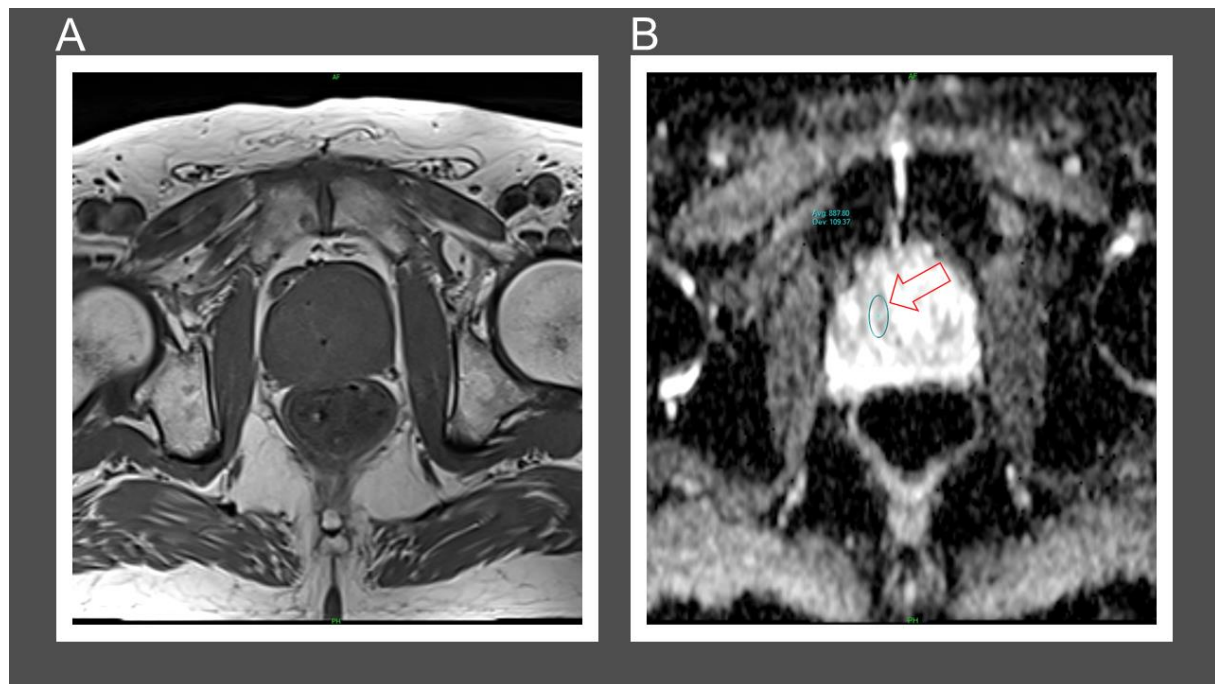
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Figures



*Figure 1. Axial T1-weighted TSE sequence (A) was used as an anatomical map. On the corresponding ADC map (B), the area of low signal intensity is shown and measured by the ellipsoid ROI (blue ellipse). The tumor is located in the right posterior transitional zone of the prostate on the left side. The 10 mm, elongated proliferation with irregular borders (red arrow) shows rapid uptake, washing out of contrast material, and diffusion restriction (ADCmean: $887.8 \pm 109.37 \times 10^{-6} \text{ s/mm}^2$). *region of interest (ROI) * turbo spin echo (TSE) * apparent diffusion coefficient (ADC)*

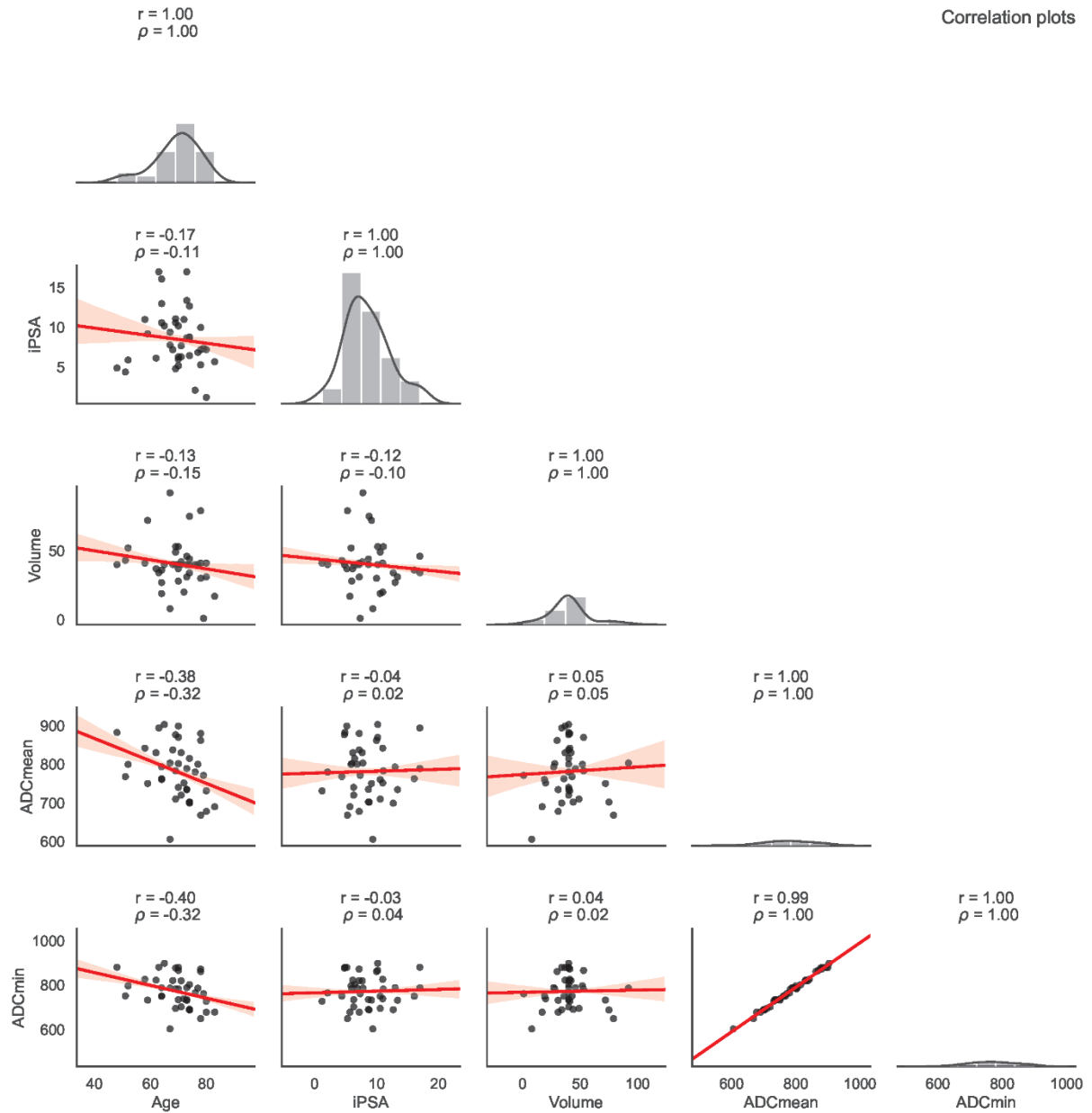


Figure 2. Correlation plots (lower triangle) with Spearman correlation coefficients and histograms (diagonal) are shown in the plot matrix of pre-treatment. *Minimum Apparent Diffusion Coefficient (ADC_{min}) *Pre-treatment/Initial Prostate Specific Antigen (iPSA) *Mean Apparent Diffusion Coefficient (ADC_{mean}). *prostate-specific antigen (PSA)

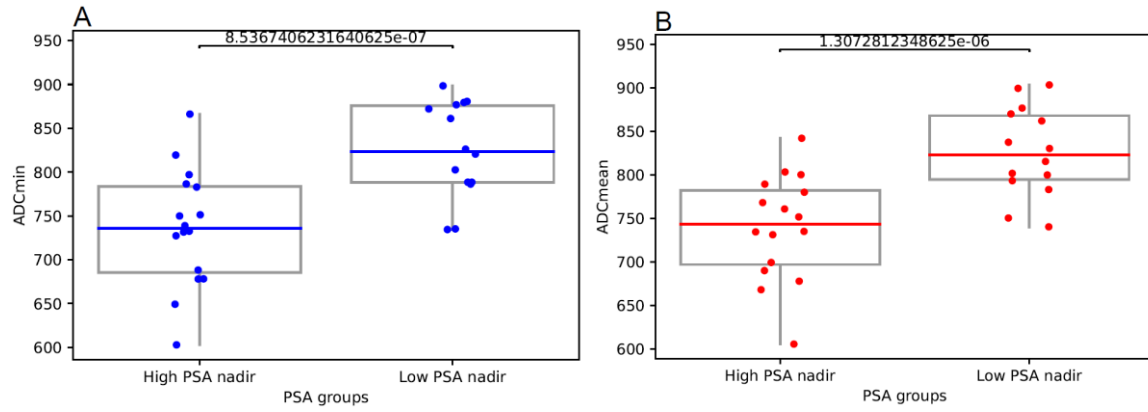


Figure 3. Boxplots show the distributions of ADCmin (A) and ADCmean (B) parameters in the therapy response-based subgroups, patients who achieve low PSA nadir and high PSA nadir. The p-value of the Wilcoxon rank-sum test is shown in the upper part of the plot. *Minimum Apparent Diffusion Coefficient (ADC_{min}) *Mean Apparent Diffusion Coefficient (ADC_{mean}) Prostate Specific Antigen

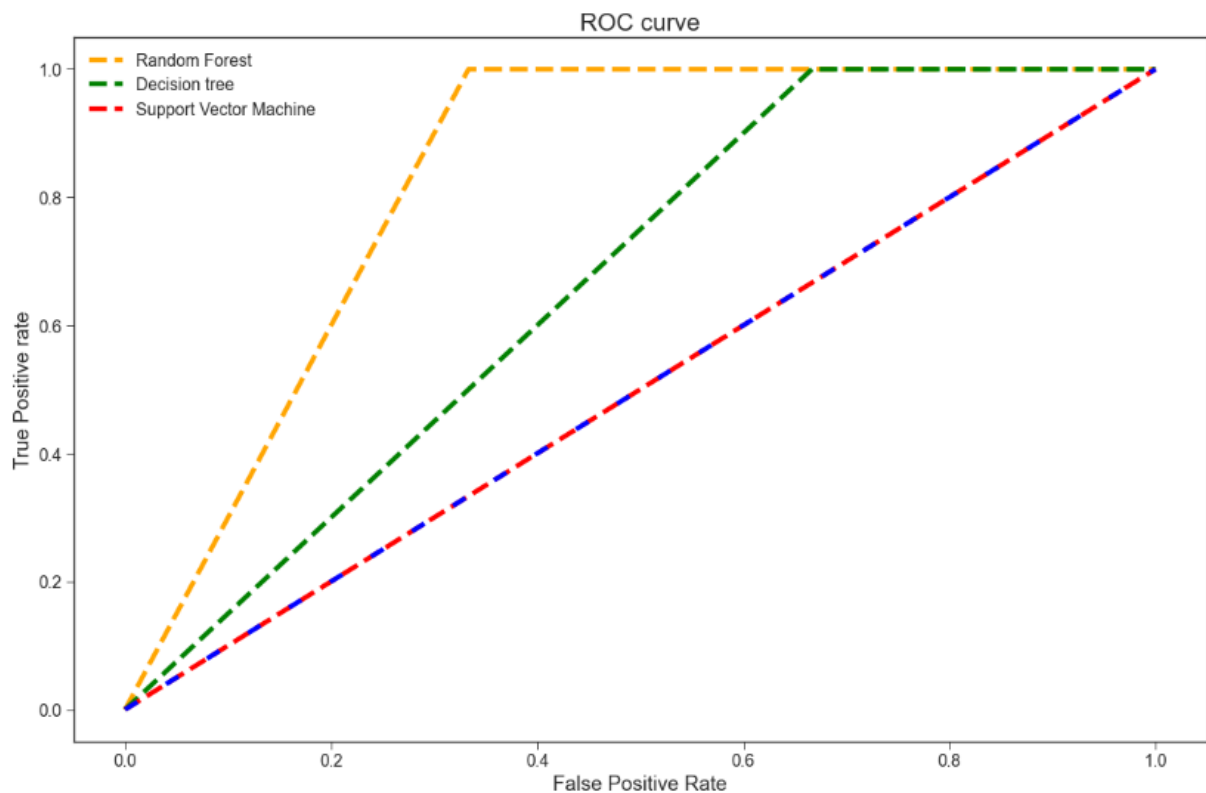
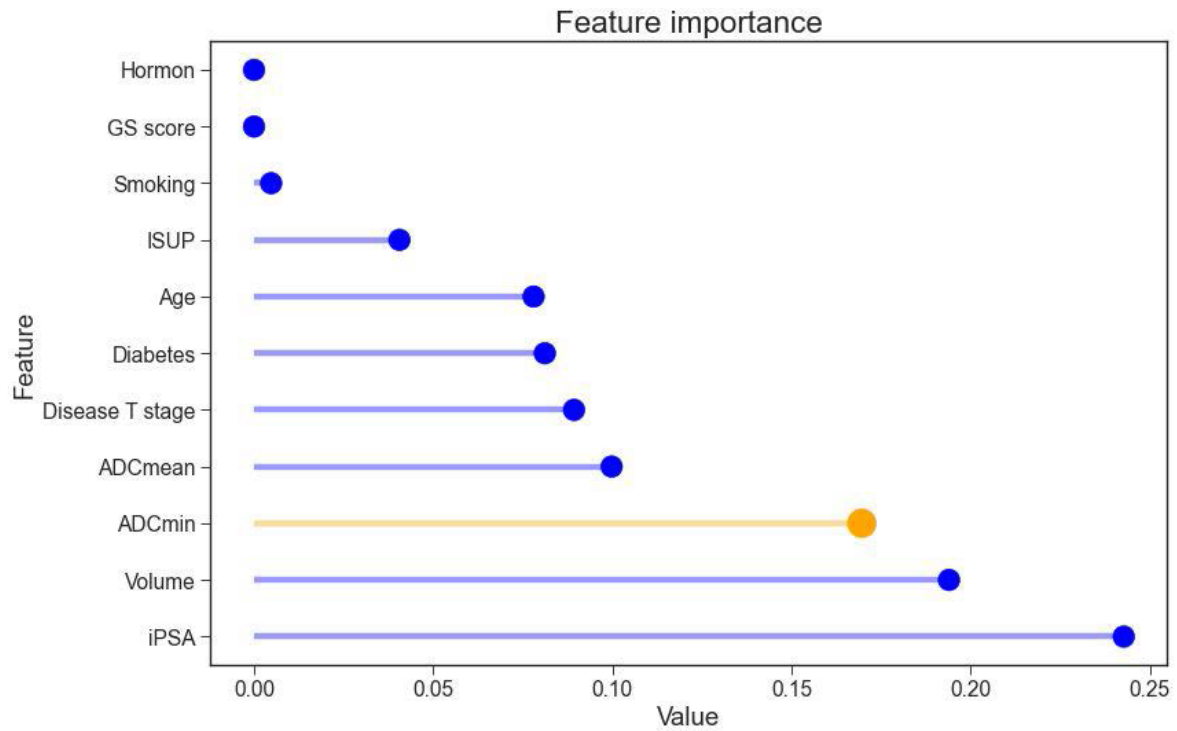


Figure 4. Predictive performance of models. ROC of DT, RF, and SVM models in the test set. *decision tree (DT) *random forest (RF)*region under the curve (ROC) support vector machine (SVM)



*Figure 5. Feature importance plot of all relevant parameters (relative importance). Classification using a random forest identification of the features that could have the most significant effect on differentiating the study groups ordered according to their Gini coefficient. *Minimum Apparent Diffusion Coefficient (ADC_{min}) *Mean Apparent Diffusion Coefficient (ADC_{mean}). *Gleason score (GS score), *Pre-treatment/Initial Prostate Specific Antigen (iPSA) *prostate-specific antigen (PSA)*

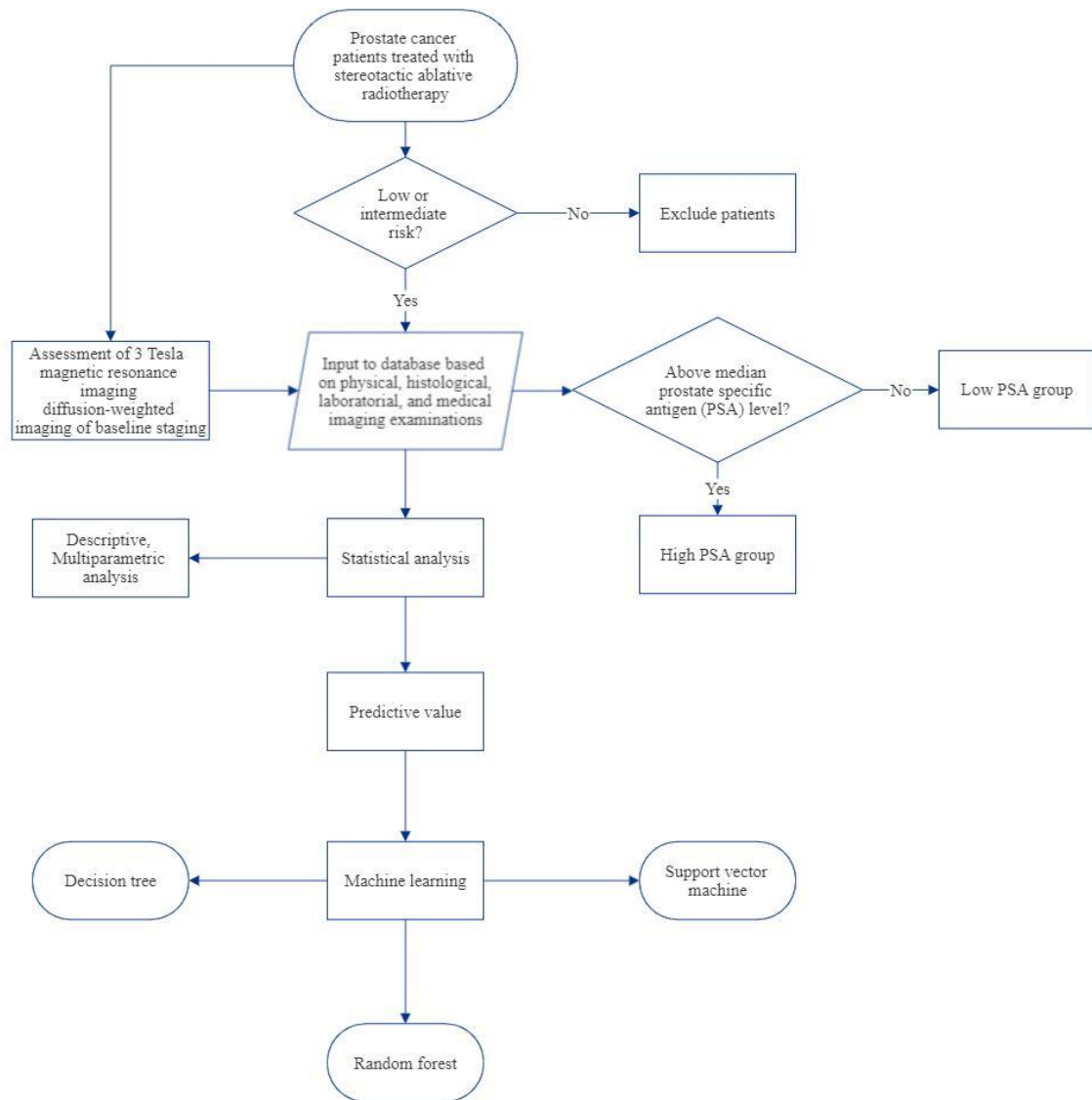


Figure 6. Flow chart of machine learning used for prediction. *prostate specific antigen (PSA)

Tables

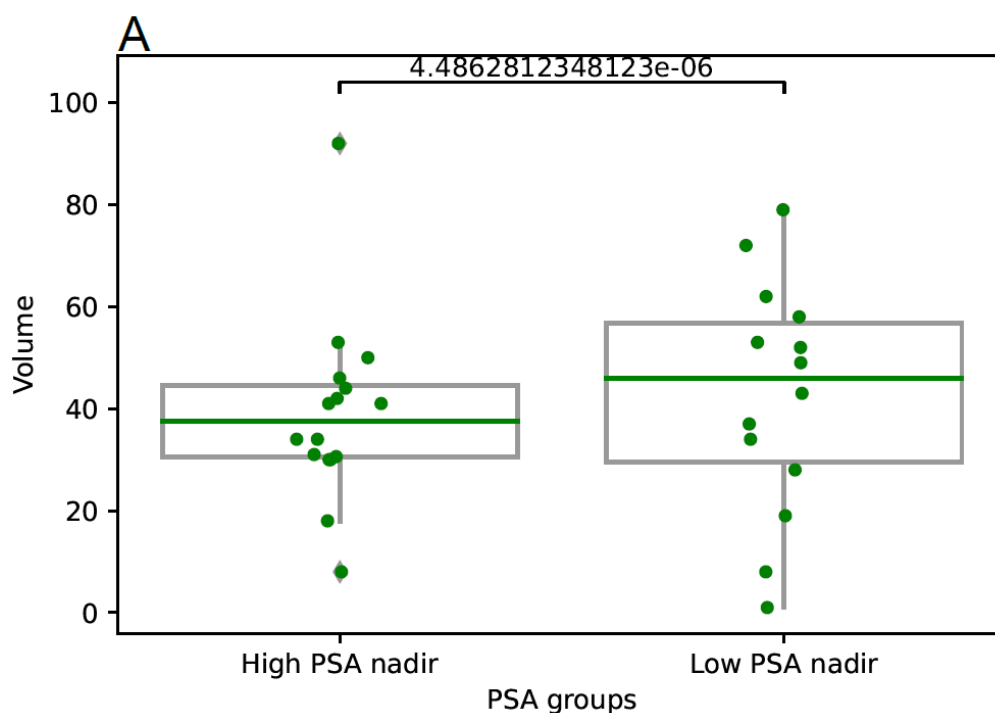
<i>Characteristics</i>	<i>Value (% / range)</i>
<i>Number of patients</i>	40 (100)
<i>Median age (year)</i>	69±7.9 (48-83)
<i>T stage [†], N</i>	
1c	25 (62.5)
2a	9 (22.5)
2b	6 (15)
<i>iPSA, ng/ml, mean</i>	8.52±3.57 (1.2-17)
<i>1-year-PSA, ng/ml, mean (num. of pts = 30)</i>	0.53±0.58 (<0.003-1.91)
<i>Gleason Score, mean</i>	6.35±0.53 (5-7)
<i>Mean gland volume (cm³)</i>	41.72±18.34 (8-92)
<i>Risk group</i>	
Low risk	17 (42.5%)
Intermediate risk	23 (57.5%)
<i>ISUP grade</i>	
1	23 (57.5%)
2	15 (37.5%)
3	2 (5%)
<i>Follow-up (month)</i>	23 (3-50)

Table 1 Patient and tumor characteristics. *initial prostate specific antigen (iPSA) * ISUP International Society of Urological Pathology [†] Based on clinical (American Joint Committee on Cancer Staging System, 8th edition) and pelvic MRI stage *pts patients

	<i>Precision</i>	<i>Recall</i>	<i>f1-score</i>	<i>Support</i>	<i>Number</i>
Test dataset	0.67	0.50	0.57	4	
Training dataset	0.60	0.75	0.67	4	
Accuracy	-	-	0.62	8	
Macro average	0.63	0.62	0.62	8	
Weighted average	0.63	0.62	0.62	8	
<i>Mislabeled in training set</i>					1
<i>Mislabeled in test set</i>					2

Table 2. Confusion matrix and classification report for random forest

Supplementary material



Supplementary figure 1 Boxplots show the distributions of Volume (cm³) and * parameters in the therapy response based groups, patients which achieve low PSA nadir and high PSA nadir. The p-value of the Wilcoxon rank-sum test is shown in the upper part of the plot. *volume of prostate gland (Volume)

Literature

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