






RESEARCH ARTICLE

Impact of qualitative, semi-quantitative, and quantitative analyses of dynamic contrast-enhanced magnet resonance imaging on prostate cancer detection

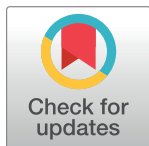
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Abstract

Dynamic contrast enhanced imaging (DCE) as an integral part of multiparametric prostate magnet resonance imaging (mpMRI) can be evaluated using qualitative, semi-quantitative, or quantitative assessment methods. Aim of this study is to analyze the clinical benefits of these evaluations of DCE regarding clinically significant prostate cancer (csPCa) detection and grading. 209 DCE data sets of 103 consecutive patients with mpMRI (T2, DWI, and DCE) and subsequent MRI-(in-bore)-biopsy were retrospectively analyzed. Qualitative DCE evaluation according to PI-RADS v2.1, semi-quantitative (curve type; DCE score according to PI-RADS v1), and quantitative Tofts analyses (K^{trans} , k_{ep} , and v_e) as well as PI-RADS v1 and v2.1 overall classification of 209 lesions (92 PCa, 117 benign lesions) were performed. Of each DCE assessment method, cancer detection, discrimination of csPCa, and localization were assessed and compared to histopathology findings. All DCE analyses ($p < 0.01$ – 0.05), except v_e ($p = 0.02$), showed significantly different results for PCa and benign lesions in the peripheral zone (PZ) with area under the curve (AUC) values of up to 0.92 for PI-RADS v2.1 overall classification. In the transition zone (TZ) only the qualitative DCE evaluation within PI-RADS (v1 and v2.1) could distinguish between PCa and benign lesions ($p < 0.01$; AUC = 0.95). None of the DCE parameters could differentiate csPCa from non-significant (ns) PCa ($p \geq 0.1$). Qualitative analysis of DCE within mpMRI according to PI-RADS version 2.1 showed excellent results regarding (cs)PCa detection. Semi-quantitative and quantitative parameters provided no additional improvements. DCE alone wasn't able to discriminate csPCa from nsPCa.

Introduction

Prostate cancer (PCa) shows increased perfusion compared to normal tissue due to higher micro-vessel density, arteriovenous shunts, and higher vascular permeability. Therefore,

dynamic contrast enhanced MRI (DCE) represents an additional tool for the detection of PCa, especially in the peripheral zone (PZ) [1]. Since the 2015 updated Prostate Imaging Reporting and Data System (PI-RADS) version (version 2), focal early or contemporaneous enhancement in DCE of a suspicious lesion (in T2/DWI) can upgrade lesions from PI-RADS overall assessment category 3 to 4 unless it demonstrates features of benign prostatic hyperplasia (BPH) on T2-weighted images [2]. The benefit of a qualitative DCE analysis is its relatively simple and timesaving usage. However, this approach represents a subjective judgment of the reader and the gathered information of the exact perfusion is limited [3,4].

A semi-quantitative approach as implemented in the first version of PI-RADS requires analysis of the concentration time-curve assigned to three different types with distinct likelihoods of the presence of PCa [5]. The curve type provides information about the in- and out-flow of contrast media (CM) into the tissue over time.

Based on pharmacokinetic models, such as the extended two-compartment model by Tofts et al., analysis of perfusion parameters (K^{trans} , k_{ep} , and v_e) allows the exact quantification of the CM flowrate into the tissue and back to the intravascular compartment after assessment of the arterial input function. The transfer constants K^{trans} and k_{ep} characterize the transfer rate of CM between the intravascular and the extravascular extracellular space whereas v_e represent the fractional extravascular extracellular space volume. As a quantitative method with absolute values, this approach permits a direct comparison of perfusion parameters (K^{trans} , k_{ep} , and v_e) in tumor, physiological peripheral (PZ) or transition zone (TZ) tissue [6]. This method requires specific software assistance, additional time, and expertise. Although the quantitative and semi-quantitative analyses are of great interest in scientific investigation, the additional benefit in clinical routine is still controversial. As far as we know, there was no intra-individual comparison of all three DCE assessment methods available in the literature at the time of this study.

To avoid overdiagnosis and overtreatment, there is a need to identify clinically significant (cs) PCa, mostly defined as International Society of Urological Pathology (ISUP) Grade Group ≥ 2 (Gleason score of $\geq 3+4 = 7$), since significant tumors require timely treatment while low-grade tumors can be monitored within active surveillance [7,8]. Post therapeutic complications and complaints after treatment of insignificant disease represent a major problem [9]. Therefore, it is not only of scientific but also of clinical interest to investigate if DCE is able to distinguish between csPCa and non-significant (ns) PCa.

The primary objective of this study was to compare qualitative, semi-quantitative, and quantitative DCE assessment methods in order to evaluate the significance for detection of csPCa.

Materials and methods

Study design

This retrospective cohort study was conducted in the Department of Diagnostic and Interventional Radiology and the Department of Urology at the University Hospital Düsseldorf (Medical Faculty, Heinrich-Heine-University, Düsseldorf, Germany) from August 2015 to May 2020. All data were fully anonymized before been accessed. The study has been approved by the local institutional review board (Ethical Review Committee, Medical Faculty, Heinrich-Heine-University Düsseldorf; study number 3612). All patients signed a written informed consent for their medical records/images to be used in research. Refusal to take part in the study did not influence patients care.

Consecutive patients with standard-of-care mpMRI prostate examinations with suspected PCa and subsequent MR-(in-bore)-biopsy plus systematic 12-core TRUS-guided biopsy

between January and December 2012 were retrospectively included. All patients had elevated PSA-levels >4 ng/ml, no known prostate tumor, and no contraindications to MRI or prostate biopsy. All patients with a PI-RADS v1 overall classification of 4 or 5 had received a targeted MR-(in-bore)-biopsy of every described lesion in the MRI report (independent of the PI-RADS v1 lesion score). The majority of patients were previously enrolled in prospective randomized trials comparing MR-(in-bore)-biopsy to MRI-ultrasound fusion or systematic transrectal ultrasound guided prostate biopsy either in patients after initial biopsy or in biopsy-naïve men (ClinicalTrials.gov identifier: NCT02220517, NCT01553838). Diagnostic performance of mpMRI and MRI-guided biopsy has been reported earlier [10,11] and is not part of this study.

Different DCE methods of all histologically confirmed lesions were retrospectively analyzed in consensus by two experienced urologists with more than 10 years of experience in reading prostate MRI (LS and MQ).

The distinct DCE methods were compared in matter of their differentiation between PCa and benign lesions and between csPCa with an ISUP Grade Group ≥ 2 (Gleason score $\geq 3 + 4 = 7$) and nsPCa with an ISUP Grade Group 1. Patient's age, PSA values, biopsy history, PI-RADS scoring, ADC values, biopsy results including localization, quantity of lesions, and Gleason scoring were assessed. Lesion size was measured in three diameters in the Picture Archiving and Communicating System (PACS; Sectra Imtec AB, IDS7, Sweden). Measurements were performed on the sequence that shows the lesion best, usually T2-weighted images or ADC (especially for peripheral lesions).

Image acquisition

Images were acquired with a 3 Tesla (T) MRI scanner (Magnetom TIM Trio Systems, Siemens Healthcare GmbH, Germany) using a six-channel phased-array body combined with 32-channel spine coil. The mp-MRI protocol included T2 (axial, sagittal, and coronal), T1, DWI, and DCE (S1 Table): axial T2-weighted turbo spin-echo sequences (TR 10,630 ms, TE 117 ms, field of view (FOV) 12.8 cm, slice thickness 3.0 mm), axial T1-weighted turbo spin-echo images (TR 650 ms, TE 13 ms, FOV 30 cm, slice thickness 5.0 mm), and axial diffusion weighted imaging with a singleshot spin-echo echo-planar sequence (TR 4,600 ms, TE 90 ms, FOV 20.4 cm, slice thickness 3.0 mm) using five b-values (0, 250, 500, 750, 1000 s/mm^2). The T1 volumetric interpolated breath-hold examination (VIBE) DCE sequence (TR 5.26 ms, TE 1.76 ms, flip angle 12°) was conducted with a field of view (FoV) of 192x192 mm, a resolution of 128x128 pixels, and a temporal resolution of 9.8s. Voxel size was 3 mm with no gap. In total 31 dynamic scans were acquired. Acquisition time was 5:05 minutes. Gadolinium based contrast agent Gd-DOTA (Dotarem R, Guerbet, France) was injected after the initial native measurements with a flow of 3 ml/s and a dosage of 0.1 mmol/Kg body weight followed by a 50 ml flush of NaCl. Patients received butylscopolamine (20 mg Buscopan[®], Boehringer Ingelheim Pharma, Ingelheim, Germany) to suppress bowel peristalsis. No additional rectal preparation was performed.

MR-guided biopsy

MRI-(in-bore)-biopsy was performed transrectally with the same MRI system in prone position by experienced urologists (LS and MQ) [12]. Images for biopsy planning were obtained using sagittal and transverse T2-haste sequences (TR 2000 ms; TE 76 ms; FOV 28 cm; slice thickness 3.0 mm). Image data was transferred to a workstation (DynaCAD, Invivo, Philips Healthcare, USA) for biopsy planning. A needle-in control scan was performed in two different planes to ensure correct needle placement. At least two samples per lesion were

gathered with an MR compatible 18-gauge biopsy-gun (Invivo). Afterwards, an additional systematic 12-core transrectal ultrasound-guided biopsy was performed by an experienced urologist blinded to the MRI report with an 18-gauge biopsy gun (Bard Medical, Karlsruhe, Germany).

Qualitative DCE analysis

Qualitative analysis was conducted retrospectively according to the PI-RADS v2.1 criteria [3]. The focal early or contemporaneous enhancement of a suspicious lesion in T2W and/or DWI was considered as positive DCE PI-RADS v2.1 single score. Additionally, a PI-RADS v2.1 overall lesion classification using all mpMRI information with respect to the dominant sequence correlated to the lesion localization (peripheral or transition zone) was determined retrospectively.

Semiquantitative DCE analysis

Mean signal intensities (SI) of all pixels within a region of interest (ROI) were integrated in a SI-curve. The curve was converted into a CM-time-curve (CTC) using DynaCAD[®]. The CTC was afterwards assigned to one of three different curve types (progressive curve type, plateau curve type, and wash-in/wash-out curve type) as implemented in PI-RADS v1. In addition to the curve-typing, DCE PI-RADS v1 single score and PI-RADS v1 overall lesion classification were also determined [5].

Quantitative DCE analysis

Perfusion maps for K^{trans} , k_{ep} , and v_e were generated by the commercially available software DynaCAD[®] using the customized DCE sequence parameters (magnet strength, flip angle, repetition time, number of phases, CM arrival delay, CM dose, injection duration, enhancement threshold, and fit coefficient). DynaCAD[®] uses a population-based arterial input function (AIF) [13]. Quantitative perfusion parameters K^{trans} and k_{ep} for all lesions were determined in the corresponding perfusion map by ROI based measurements (in min^{-1}). v_e was calculated as quotient of K^{trans} and k_{ep} .

Histopathology

All biopsy samples were evaluated by an experienced pathologist following the recommendations of the International Society of Urological Pathology (ISUP) [14]. For this study an ISUP Grade Group ≥ 2 (Gleason score $\geq 3+4 = 7$) was considered as csPCa. Reference standard for pathology was the targeted MR-(in-bore)-biopsy of each lesion.

Statistics

Statistical analysis was performed with SPSS 21 (IBM, Armonk, New York, USA). Results are presented with mean value and standard deviation (SD) or median and interquartile range (IQR). Mann-Whitney-U-test was employed for unpaired samples. A two-tail p-value ≤ 0.05 was considered significant. Receiver operating characteristic (ROC) analysis was conducted. AUC values were classified excellent (0.90–1), good (0.80–0.90), fair (0.70–0.80), poor (0.60–0.70), and/or fail (0.50–0.60).

Results

Study population

One hundred three patients were included in this study. PCa was verified by biopsy in 92 lesions of 53 patients. ISUP grades were as follows: ISUP 1: 18 lesions of 8 patients, ISUP 2: 54 lesions of 30 patients, ISUP 3: 13 lesions of 11 patients, ISUP 4: 3 lesions of 2 patients, and ISUP 5: 4 lesions of 2 patients. 119 lesions were located in TZ, 75 in PZ, 15 in the AFS/CZ (anterior fibromuscular struma or central zone). 117 lesions and 50 patients showed negative biopsy results. Age, PSA-values, prostate volume, and PSA-density with corresponding p-values are shown in Table 1.

Qualitative, semi-quantitative, and quantitative DCE analysis

All lesions. PI-RADS single score for DCE (v1 and v2.1) and PI-RADS overall classification (v1 and v2.1) per lesion were able to differentiate PCa (n = 92) from benign (n = 117) lesions with $p < 0.01$, whereas curve type and quantitative DCE analysis did not provide statistically significant results. In ROC analysis PI-RADS v2.1 overall classification demonstrated the highest area under the curve (AUC = 0.94), whereas among the other DCE analysis AUC of DCE v2.1 was highest (AUC = 0.91).

Peripheral zone (PZ) lesions. All parameters (qualitative, semiquantitative, and quantitative DCE analysis including multiparametric analysis with PIRADS overall classification v1 and v2.1), except v_e were statistically different between PCa and benign lesions in PZ with highest AUC in ROC for PI-RADS v2.1 (AUC = 0.92), followed by DCE v1 (AUC = 0.91) and DCE v2.1 (AUC = 0.90) (Table 2, Figs 1 and 2).

Table 1. Baseline characteristics.

	all	PCa	no PCa	p-value
Patients	103	53	50	-
MRI lesions	209	92	117	-
Age (mean \pm SD)	67 \pm 7.5	68 \pm 7.7	66 \pm 7.2	0.1
PSA (median—IQR)	7.7 (5.8–10)	8.1 (6–11)	7.1 (5.6–10)	0.3
PV (median—IQR)	47 (36–71)	45 (33–62)	58 (40–84)	0.01
PSAD (median—IQR)	0.15 (0.11–0.22)	0.17 (0.12–0.32)	0.13 (0.10–0.18)	<0.01

PV = Prostate volume; PSAD = PSA density; IQR = interquartile range; SD = standard deviation; p-values ≤ 0.05 are considered to be significant and are given in bold.

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Table 2. Peripheral zone (PZ): Comparative analyses of qualitative (DCE v2.1), semiquantitative (DCE v1 and curve type), and quantitative (K^{trans} , k_{ep} , v_e) DCE parameters and multiparametric PI-RADS v2.1 and PI-RADS v1 in PZ lesions with and without prostate carcinoma (PCa).

PZ	PCa (n = 48)	benign (n = 27)	p-value
PI-RADS _{v2.1} (median—IQR)	4 (4–5)	3 (3–3)	<0.01
DCE _{v2.1} (median—IQR)	1 (1–1)	0 (0–0)	<0.01
PI-RADS _{v1} (median—IQR)	5 (4–5)	3 (3–4)	<0.01
DCE _{v1} (median—IQR)	4 (3–4)	2 (2–3)	<0.01
Curve type (median—IQR)	2 (2–2)	2 (1–2)	<0.01
K^{trans} (min^{-1}) (mean \pm SD)	0.15 \pm 0.10	0.9 \pm 0.08	0.001
k_{ep} (min^{-1}) (mean \pm SD)	2.5 \pm 1.5	2.0 \pm 1.7	0.05
v_e (mean \pm SD)	0.06 \pm 0.02	0.05 \pm 0.02	0.2

IQR = interquartile range; SD = standard deviation; p-values ≤ 0.05 are considered to be significant and are given in bold.

<https://doi.org/10.1371/journal.pone.0249532.t002>

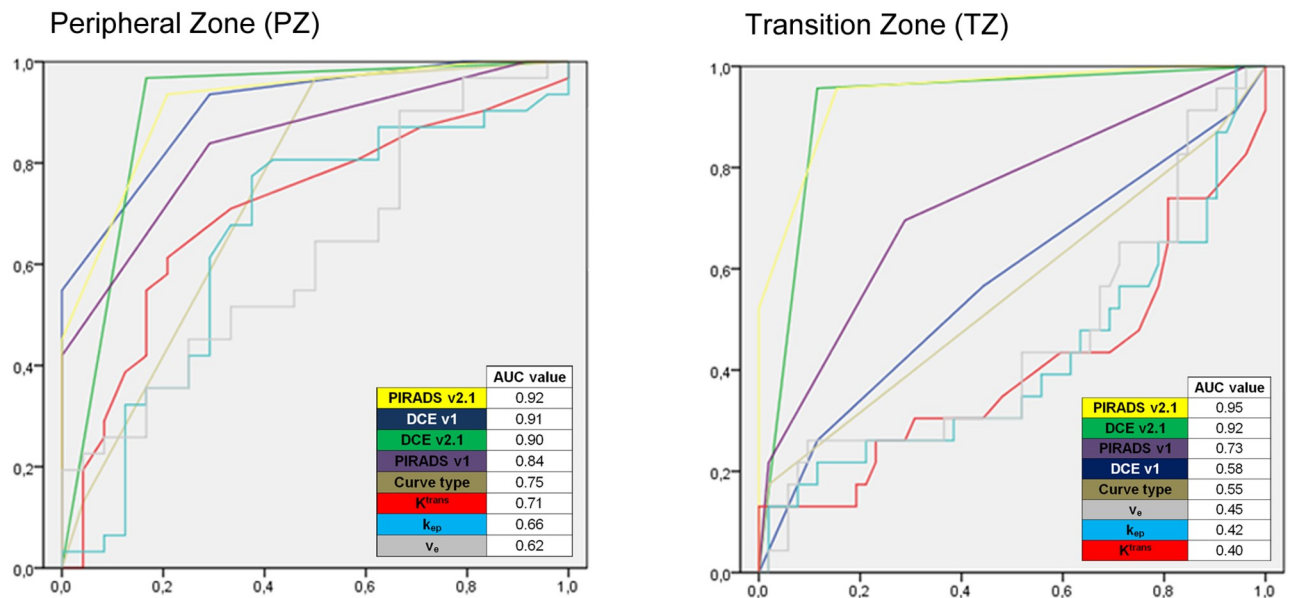


Fig 1. PI-RADS v2.1 shows excellent performance in assessing DCE. ROC-analysis of qualitative (DCE v2.1), semiquantitative (DCE v1 and curve type), and quantitative (K^{trans} , k_{ep} , v_e) DCE parameters and multiparametric PI-RADS v1 and PI-RADS v2.1 for differentiation of prostate cancer and benign lesions in the peripheral zone (PZ, right) and transition zone (TZ, left). Areas under the curve (AUC) values are given in the bottom of each plot.

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Transition zone (TZ) lesions. When comparing PCa and benign lesions in TZ, only values for PI-RADS overall classification (v1 and v2.1) and DCE score (v2.1) were statistically significant with highest AUC in ROC for PI-RADS v2.1 (AUC = 0.95), followed by DCE v2.1 (0.92) and PI-RADS v1 (AUC = 0.73). None of the other DCE methods demonstrated significant results (Table 3, Fig 1).

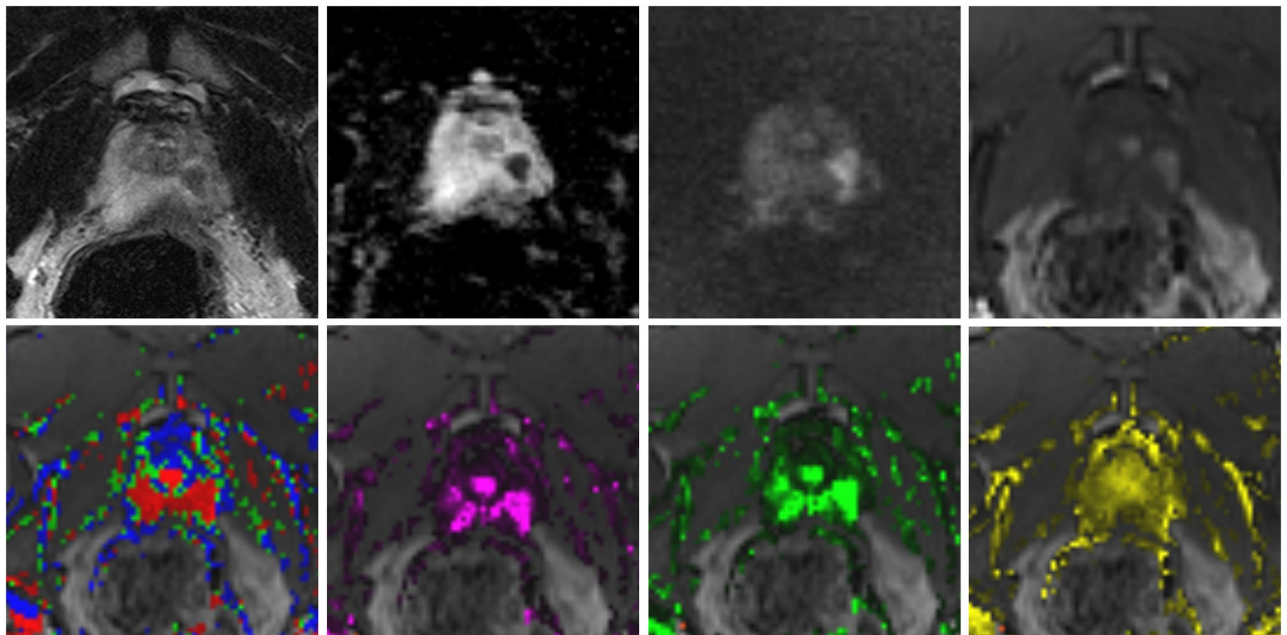


Fig 2. Peripheral PCa lesion is declivable in most of the perfusion maps. Example of a peripheral PCa lesion. Upper row: multiparametric MRI (from left to right with T2, DWI, ADC, and DCE showing a left peripheral carcinoma with gleason score 4+3 = 7 in a 48 year old patient. Lower row: corresponding perfusion maps (from left to right) colour-coded, K^{trans} , k_{ep} , and v_e .

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Table 3. Transition zone (TZ): Comparative analyses of qualitative (DCE v2.1), semiquantitative (DCE v1 and curve type), and quantitative (K^{trans} , k_{ep} , v_e) DCE parameters and multiparametric PI-RADS v2.1 and PI-RADS v1 in TZ lesions with and without prostate carcinoma (PCa).

TZ	PCa (n = 33)	benign (n = 86)	p-value
PI-RADS _{v2.1} (median—IQR)	5 (4–5)	3 (3–3)	<0.01
DCE _{v2.1} (median—IQR)	1 (1–1)	0 (0–0)	<0.01
PI-RADS _{v1} (median—IQR)	4 (3–5)	3 (3–4)	<0.01
DCE _{v1} (median—IQR)	3 (2–4)	3 (2–3)	0.8
Curve type (median—IQR)	2 (2–3)	2 (2–2)	0.3
K^{trans} (min ⁻¹) (mean ± SD)	0.13 ± 0.22	0.19 ± 0.12	0.4
k_{ep} (min ⁻¹) (mean ± SD)	2.0 ± 2.1	3.5 ± 3.8	0.3
v_e (mean ± SD)	0.05 ± 0.03	0.06 ± 0.03	0.6

IQR = interquartile range; SD = standard deviation; p-values ≤ 0.05 are considered to be significant and are given in bold.

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PCa grading. None of the applied methods was able to distinguish csPCa (ISUP Grade Group ≥ 2) from nsPCa (ISUP Grade Group 1) (Table 4). ROC analysis (csPCa vs. nsPCa) showed poor AUC values (highest AUC for PI-RADS (v1) with 0.63) (Fig 3).

Discussion

Multiparametric MRI analysis according to PI-RADS v2.1 including qualitative DCE evaluation offered excellent diagnostic accuracy for PCa detection. Quantitative and semi-quantitative perfusion parameters were inferior compared to the PI-RADS. No analyzed DCE assessment method was able to significantly differentiate tumor-aggressiveness.

Tan et al. demonstrated that qualitative and semi-quantitative analyses of DCE perform similarly in PCa detection [15]. Chesnais et al. tested eight different semi-quantitative and quantitative DCE parameters for PCa detection in TZ. None of the parameters seemed to demonstrate additional information [16]. Hansford et al. assigned a poor performance of curve type for the differentiation of PCa and benign lesions in PZ [17]. In our study, semi-quantitative perfusion parameters did not show significant differences between PCa and benign lesions in TZ whereas in PZ results were statistically significant, but with lower, fair AUC values in ROC analysis in comparison to qualitative DCE analyses. The fact that both, Type-2 and -3 curves go along with a fast “wash-in” corresponding to a visible early enhancement as

Table 4. Comparative analyses of qualitative (DCE v2.1), semiquantitative (DCE v1 and curve type), and quantitative (K^{trans} , k_{ep} , v_e) DCE parameters and multiparametric PI-RADS v2.1 and PI-RADS v1 in all lesions with prostate carcinoma (PCa) vs. benign (left) and all lesions with clinically significant carcinoma (csPCa) with Gleason Score ≥ 7 (ISUP Grade Group ≥ 2) vs. non-significant carcinoma (nsPCa) with Gleason Score 6 (ISUP Grade Group 1) (right).

	csPCa (n = 72)	nsPCa (n = 20)	p-value
PI-RADS _{v2.1} (median—IQR)	5 (4–5)	4 (4–5)	0.1
DCE _{v2.1} (median—IQR)	1 (1–1)	1 (1–1)	0.9
PI-RADS _{v1} (median—IQR)	4 (3–5)	4 (4–5)	0.2
DCE _{v1} (median—IQR)	4 (3–4)	3 (3–4)	0.8
Curve type (median—IQR)	2 (2–2)	2 (2–2)	0.5
K^{trans} (min ⁻¹) (mean ± SD)	0.19 ± 0.18	0.14 ± 0.1	0.4
k_{ep} (min ⁻¹) (mean ± SD)	2.9 ± 2.1	2.9 ± 2.2	0.9
v_e (mean ± SD)	0.06 ± 0.02	0.05 ± 0.02	0.2

IQR = interquartile range; SD = standard deviation; p-values ≤ 0.05 are considered to be significant and are given in bold.

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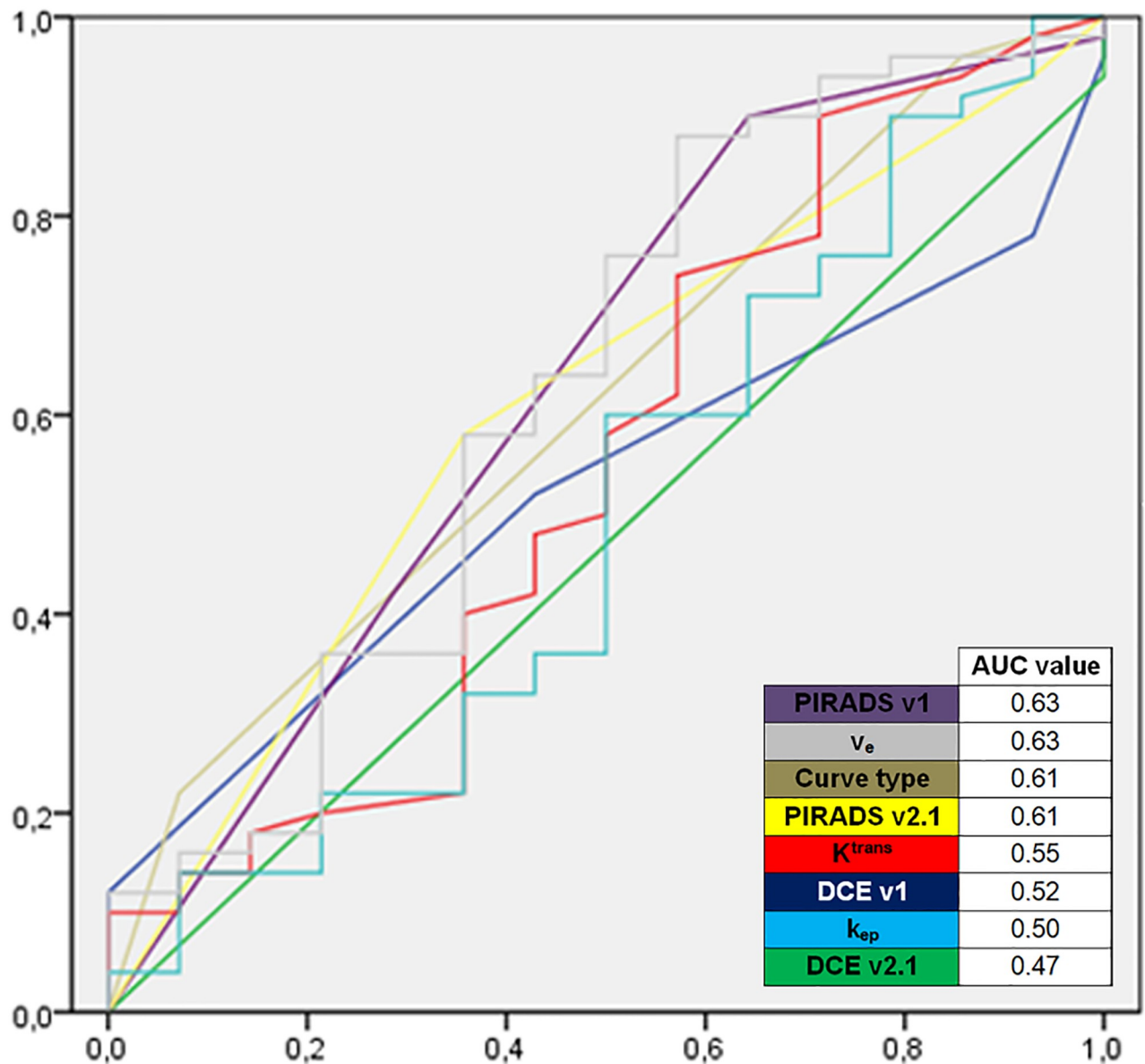


Fig 3. None of the other DCE methods can differentiate low grade tumor from clinically significant tumor alone. ROC-analysis of qualitative (DCE v2.1), semiquantitative (DCE v1 and curve type), and quantitative (K^{trans} , k_{ep} , v_e) DCE parameters and multiparametric PI-RADS v1 and PI-RADS v2.1 for differentiation of clinically significant carcinoma with Gleason score ≥ 7 vs. insignificant carcinoma with Gleason score < 7 . Areas under the curve (AUC) are given in the bottom right.

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implemented in DCE evaluation by PIRADS v2.1 may explain the results. Moreover, semi-quantitative analysis is independent from T2- and DWI whereas the evaluation of DCE in PI-RADS v2.1 requires a suspicious finding in one of the other sequences. Thus, it already includes mpMRI information which represents a major advantage and presumably improves PCa detection rate. This may explain the higher, excellent AUC in ROC analysis for the PI-RADS DCE score. Depending on the micro-vessel density and the leakiness of vessels in the examined tumors all three curve types may occur in PCa (although with different probability) reducing specificity of this method.

In quantitative DCE analysis, none of the three examined parameters demonstrated statistically significant differences between PCa and benign lesions in the TZ. In contrary, K^{trans} , and k_{ep} could significantly differentiate PCa in PZ. However, AUC values were only fair. Sanz-Requena et al. [18] and Ocak et al. [19] have also demonstrated the ability of K^{trans} and k_{ep} for the detection of PCa in PZ, while v_e failed. Mehrabian et al. confirmed that K^{trans} is appropriate to separate PCa in PZ [20]. Bonekamp et al. could show that DCE ameliorates sensitivity and specificity of cancer detection in PZ, but not in TZ [21]. The quoted literature is consistent with our data. While the additional effort of quantitative DCE analysis in comparison to qualitative evaluation cannot be justified by a better performance in PCa detection objective, absolute values may facilitate comparability and reproducibility of DCE results between facilities and may represent an attractive tool e.g. for therapy monitoring. In contrast, qualitative analyses depend on the reader's subjective impression and image interpretation.

PI-RADS v2.1 assessment demonstrated excellent results to identify PCa independently of the lesions' localization. Even though the diagnostic accuracy of prostate mpMRI for PCa detection has been validated in the literature [22,23], more and more authors abandon standard employment of DCE and emphasize a biparametric approach [24]. Although ROC analysis demonstrated a high AUC for the DCE PI-RADS v2.1 single score, the dichotomous nature of this parameter restricts its diagnostic value and the parameter is influenced by multiparametric information.

None of the DCE assessment methods alone was able to distinguish non-significant PCa (ISUP Grade group 1) from clinically significant PCa (ISUP Grade Group ≥ 2). However, mpMRI, as a combination of anatomic and functional imaging, is able to identify csPCa [7]. How far DCE information can contribute to the tumor grading and identifying ISUP Grade Group ≥ 2 cancers would be clinically relevant. Sun et al. found evidence that mpMRI in combination with texture analysis is able to stratify tumor aggressiveness in PCa [25]. Mirak et al. identified quantitative and semi-quantitative DCE parameters as possible contributors to assess tumor aggressiveness [26]. More aggressive PCa may be accompanied by greater probability of tumor-necrosis which may hinder DCE performance and explain our results since necrotic tissue has a low vascularization which reduces SI on DCE imaging for the assessed lesion.

This study has some limitations. First, DCE analyses were performed retrospectively only on lesions histologically confirmed using MRI-(in-bore)-biopsy. Therefore, sensitivity, specificity of the DCE, and the question of undetected PCa could not be assessed. Since the study analyzes 92 lesions, including benign and cancer lesions, selection bias is limited. Second, systematic biopsy results were not investigated; therefore the value in non MRI-detected lesions remains unclear. However, only precisely histologically confirmed lesions allowed us to test various DCE metrics on a lesion base analysis. Third, quantitative perfusion parameters were assessed by the DynaCAD software, thus the measured values depend on the software algorithm and the applied AIF. Moreover, there are numerous other semi-quantitative parameters that have not been evaluated in this study. It is possible that a different AIF method or other semi-quantitative parameters would have provided slightly different results. Finally, we did not assess the added value of the different DCE analyses to PI-RADS and special scenarios (e.g. PI-RADS 3).

In conclusion, quantitative and semi-quantitative perfusion analyses do not seem to offer a benefit for PCa detection compared to qualitative analysis. Since mpMRI with qualitative DCE analysis has provided excellent results in PZ and in TZ our data confirm current usage of PI-RADS v2.1 standard for PCa detection. Although none of the presented methods could predict tumor aggressiveness, further scientific efforts should be attempted to minimize overdiagnosis of low-grade tumors and associated complications.

Supporting information

S1 Table. MRI-Sequence parameters.
(XLS)

Author Contributions

Conceptualization: Dirk Blondin, Michael Quentin, Lars Schimmöller.

Data curation: Hannes Irmer, Michael Quentin, Lars Schimmöller.

Formal analysis: Farid Ziayee, Hannes Irmer.

Investigation: Tim Ullrich, Dirk Blondin, Hannes Irmer, Christian Arsov, Michael Quentin, Lars Schimmöller.

Methodology: Tim Ullrich, Dirk Blondin, Hannes Irmer, Gerald Antoch, Michael Quentin, Lars Schimmöller.

Project administration: Michael Quentin, Lars Schimmöller.

Resources: Christian Arsov, Gerald Antoch.

Software: Farid Ziayee, Hannes Irmer.

Supervision: Dirk Blondin, Gerald Antoch, Michael Quentin, Lars Schimmöller.

Validation: Tim Ullrich, Christian Arsov, Lars Schimmöller.

Visualization: Farid Ziayee, Lars Schimmöller.

Writing – original draft: Farid Ziayee.

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