**Title** Role of Diffusion-Weighted Imaging (DWI) using Dynamic Contrast Enhancement (DCE) for the assessment of prostate cancer (PCa) aggressiveness in the peripheral zone.

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**Introduction and objective:** To develop the prediction of tumor grading prior to treatment, this study was aimed to investigate the efficacy of diffusion-weighted imaging (DWI) with the utility of dynamic contrast enhancement (DCE) for evaluation of tumor aggressiveness in peripheral zone prostate cancer (PCa).

**Specific aims:** To validate the role of DCE in the Prostate Imaging Reporting and Data System version 2 (PI-RADSv2) by using DWI for tumor upgrading in PZ lesions based on biopsy.

**Rationale and background:** PI-RADSv2 propose main pulse sequence in each zone of the prostate. The main sequence in Peripheral zone (PZ) lesions have suggested being DWI. DCE was determined to advance PI-RADSv2 overall score 3 lesions with DWI score 3 essentially, to PI-RADSv2 score 4 for DCE positivity. (1)

**Methods and materials:** Methods This IRB approved HIPAA compliant retrospective study included 237 patients with 291 lesions, who underwent 3-T multiparametric-MRI (mp-MRI) within 6 months before Robotic-assisted radical prostatectomy (RALP). The radiologists determined the regions of interest (ROIs) on the MR images. In a joint match meeting, the ROIs were compared to corresponding lesions on whole-mount histopathology (WMHP) slides. True positive peripheral zone lesions were included for evaluation of tumor grading (Low-grade GS=6 vs. high-grade GS=7). DWI PIRADSv2 score 3, with (overall PIRADSv2 score 4) and without (overall PIRADSv2 score 3) the upgrading with positive DCE MRI (Focal and early enhancement), as well as DWI PIRADSv2 score 4 (overall PIRADSv2 score 4) were compared for prediction of PCa lesion aggressiveness. The analysis was conducted in Stata version 15.

**Results:** Of the total 291 lesions, 69 (24%) were low-grade, and 222 (76%) were high-grade. Using PIRADSv2 (PV2) 139/291 (45%) were DWI score 3, and 152/291 (55%) of the lesions were DWI score 4. 61/139 (44%) of DWI 3 lesions had negative DCE with final PV2 score 3, and 78/139 (56%) of DWI 3 lesions had positive DCE with final PV2 score 4. High-grade PCa lesions were observed in 38/61 (62%) of DWI 3 with negative DCE, 63/78 (81%) of DWI 3 with positive DCE and, 121/152 (80%) of DWI 4 PCa lesions. DWI score 4 (PIRADSv2 score 4) showed significantly higher performance for PCa tumor grading ($p=0.01$) compared to DWI 3 with negative DCE (PV2 score 3). The DWI 3 with positive DCE achieved a significantly higher proportion of high-grade PCa lesions as compared to DWI 3 with negative DCE ($p=0.021$).

**Discussion and conclusion:** Recently, studies have reported the usefulness of DCE-MRI on detection, risk stratifying, and aggressiveness of PCa and suggest to develop DCE to other PI-RADS scores. (2-4) Several studies have evaluated the aggressiveness and classification of

lesions base on quantitative and qualitative parameters or curve type analysis of DCE. (3, 5-10) The current data validate the PI-RADS 3 + 1 by using positive DCE to improve a PI-RADS category. Our study evaluates the use of DCE in the prediction of PCa in the PZ in PI-RADSv2 category 3 lesions.

The results of this study suggest the ability of DCE for better discrimination of high-grade PCa lesions in the peripheral zone in PI-RADSv2 category 3 lesions. Future studies of other categories and evaluation of the whole prostate gland with other relevant dominant sequences will be required for clinical implications.

**References**


1. Weinreb JC, Barentsz JO, Choyke PL, Cornud F, Haider MA, Macura KJ, Margolis D, Schnall MD, Shtern F, Tempany CM, Thoeny HC, Verma S. PI-RADS Prostate Imaging - Reporting and Data System: 2015, Version 2. Eur Urol 2016;69(1):16-40. doi: 10.1016/j.eururo.2015.08.052
2. Greer MD, Shih JH, Lay N, Barrett T, Kayat Bittencourt L, Borofsky S, Kabakus IM, Law YM, Marko J, Shebel H, Mertan FV, Merino MJ, Wood BJ, Pinto PA, Summers RM, Choyke PL, Turkbey B. Validation of the Dominant Sequence Paradigm and Role of Dynamic Contrast-enhanced Imaging in PI-RADS Version 2. Radiology 2017;285(3):859-869. doi: 10.1148/radiol.2017161316
3. Vos EK, Litjens GJ, Kobus T, Hambrock T, Hulsbergen-van de Kaa CA, Barentsz JO, Huisman HJ, Scheenen TW. Assessment of prostate cancer aggressiveness using dynamic contrast-enhanced magnetic resonance imaging at 3 T. Eur Urol 2013;64(3):448-455. doi: 10.1016/j.eururo.2013.05.045
4. Hara N, Okuizumi M, Koike H, Kawaguchi M, Bilim V. Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is a useful modality for the precise detection and staging of early prostate cancer. Prostate 2005;62(2):140-147. doi: 10.1002/pros.20124
5. Hotker AM, Mazaheri Y, Aras O, Zheng J, Moskowitz CS, Gondo T, Matsumoto K, Hricak H, Akin O. Assessment of Prostate Cancer Aggressiveness by Use of the Combination of Quantitative DWI and Dynamic Contrast-Enhanced MRI. AJR Am J Roentgenol 2016;206(4):756-763. doi: 10.2214/ajr.15.14912
6. Choi YJ, Lee IS, Song YS, Kim JI, Choi KU, Song JW. Diagnostic performance of diffusion-weighted (DWI) and dynamic contrast-enhanced (DCE) MRI for the differentiation of benign from malignant soft-tissue tumors. J Magn Reson Imaging 2019. doi: 10.1002/jmri.26607
7. Cristel G, Esposito A, Briganti A, Damascelli A, Brembilla G, Freschi M, Ambrosi A, Montorsi F, Del Maschio A, De Cobelli F. MpMRI of the prostate: is there a role for semi-quantitative analysis of DCE-MRI and late gadolinium enhancement in the characterisation of prostate cancer? Clin Radiol 2019;74(4):259-267. doi: 10.1016/j.crad.2018.08.017
8. Schlemmer HP, Merkle J, Grobholz R, Jaeger T, Michel MS, Werner A, Rabe J, van Kaick G. Can pre-operative contrast-enhanced dynamic MR imaging for prostate cancer predict microvessel density in prostatectomy specimens? Eur Radiol 2004;14(2):309-317. doi: 10.1007/s00330-003-2025-2
9. Oto A, Yang C, Kayhan A, Tretiakova M, Antic T, Schmid-Tannwald C, Eggener S, Karczmar GS, Stadler WM. Diffusion-weighted and dynamic contrast-enhanced MRI of prostate cancer: correlation of quantitative MR parameters with Gleason score and tumor angiogenesis. AJR Am J Roentgenol 2011;197(6):1382-1390. doi: 10.2214/ajr.11.6861
10. Verma S, Turkbey B, Muradyan N, Rajesh A, Cornud F, Haider MA, Choyke PL, Harisinghani M. Overview of dynamic contrast-enhanced MRI in prostate cancer diagnosis and management. AJR Am J Roentgenol 2012;198(6):1277-1288. doi: 10.2214/ajr.12.8510