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Variability induced by the MR imager in dynamic contrast-enhanced imaging of the prostate

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Abstract
Purpose: To evaluate the variability induced by the imager in discriminating high-grade (Gleason ≥ 7) prostate cancers (HGC) using dynamic contrast-enhanced MRI.
Material and methods: We retrospectively selected 3T MRIs with temporal resolution < 10 seconds and comprising T1 mapping from a prospective radiologic—pathologic database of patients treated by prostatectomy. Ktrans, Kep, Ve and Vp were calculated for each lesion seen on MRI using the Weinmann arterial input function (AIF) and three patient-specific AIFs measured in the right and left iliac arteries in pixels in the center of the lumen (psAIF-ST) or manually selected by two independent readers (psAIF-R1 and psAIF-R2).

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Results: A total of 43 patients (mean age, 63.6 ± 4.9 [SD]; range: 48—72 years) with 100 lesions on MRI (55 HGC) were selected. MRIs were performed on imager A (22 patients, 49 lesions) or B (21 patients, 51 lesions) from two different manufacturers. Using the Weinmann AIF, Kep ($P = 0.005$), Ve ($P = 0.04$) and Vp ($P = 0.01$) significantly discriminated HCG. After adjusting on tissue classes, the imager significantly influenced the values of Kep ($P = 0.049$) and Ve ($P = 0.007$). Using patient-specific AIFs, Vp with psAIF-ST ($P = 0.008$) and psAIF-R2 ($P = 0.04$), and Kep with psAIF-R1 ($P = 0.03$) significantly discriminated HGC. After adjusting on tissue classes, types of patient-specific AIF and side of measurement, the imager significantly influenced the values of Ktrans ($P = 0.0002$), Ve ($P = 0.0072$) and Vp ($P = 0.0003$). For all AIFs, the diagnostic value of pharmacokinetic parameters remained unchanged after adjustment on the imager, with stable odds ratios.

Conclusion: The imager induced variability in the absolute values of pharmacokinetic parameters but did not change their diagnostic performance.

Because recent literature indicates that many well-differentiated prostate cancers are unlikely to cause symptoms during the patient's lifetime [1—3], current research focuses on improving detection of potentially lethal aggressive cancers [4]. Prostate multiparametric magnetic resonance (MR) imaging has shown excellent results in detecting Gleason ≥ 7 prostate cancer [5—7], and is increasingly used before biopsy [8—11]. However, it lacks specificity due to large overlap of MR appearances between benign conditions, low-grade cancers and high-grade cancers [12]. Furthermore, it is limited by substantial inter-reader variability [13,14], even when the Prostate Imaging Reporting and Data System version 2 (PI-RADS v2) diagnostic criteria are used [15—17]. These PI-RADS v2 criteria rely only on visual assessment of MR images. Therefore, many research groups have developed computer-aided diagnosis (CAD) systems aimed at improving visual diagnosis by measuring quantitative MR parameters [18—20]. Unfortunately, there is substantial variability in quantitative measurement across MR imagers from different manufacturers. As a result, it may be difficult to define quantitative thresholds that could be applied to all imagers [21,22]. Of the many CAD systems published in recent literature, only a few have been proven robust enough to be used on imagers from different manufacturers [23,24].

There is currently no consensus on how quantification of dynamic contrast-enhanced (DCE) MR imaging data should be performed. A pharmacokinetic (PK) approach that allows the calculation of parameters related to the underlying vascular physiology seems particularly appealing. A large body of literature shows that PK parameters such as the rates of forward (Ktrans) and backward (Kep) leakage, the fractional volume of extracellular space (Ve) or the plasma volume fraction (Vp) can accurately distinguish cancers from normal prostate tissue [25—32], and even help assessing cancer aggressiveness [31,33,34]. However, current literature also points out issues that need to be addressed if PK parameters are to be used in CAD systems. First, the calculation of PK parameters is prone to many sources of variability including the choice of the arterial input function (AIF) and the analysis software program [27,35—38]. Second, to our knowledge, the variability of the measurements of PK parameters on imagers from different manufacturers has never been assessed. Third, PK parameters have been mostly compared in cancers and normal-looking prostate tissue. To be helpful for routine interpretation, these parameters must be able to distinguish aggressive cancers within lesions visually found suspicious by the radiologist.

Therefore, the purpose of this study was to evaluate the variability induced by the MR imager in discriminating, by pharmacokinetic modeling, high-grade (Gleason ≥ 7) cancers among prostate lesions seen at multiparametric MR imaging.

Materials and methods

Radiologic-pathologic database

Between September 2008 and May 2014, patients who underwent prostate multiparametric MR imaging and subsequent prostatectomy at our institution and who gave informed consent were included in a prospective institutional review board-approved radiologic-pathologic database. This database has been described in details elsewhere [5]. Briefly, all MR examinations included T2-weighted, diffusion-weighted and DCE imaging. They were interpreted by two independent radiologists who noted all lesions in the prostate with a Likert score ≥ 2. In the peripheral zone (PZ), suspicious lesions were defined as lesions with low signal intensity on T2-weighted images and/or apparent diffusion coefficient (ADC) maps and/or with early enhancement on DCE images. In the transition zone (TZ), they were defined as lesions with homogeneous low signal intensity on T2-weighted images, ill-defined margins, no capsule, and no cyst [39—42]. After side-by-side comparison of MR images and prostatectomy whole-mounts, the radiologists and a pathologist with more than 10 years of experience delineated by consensus on MR images the so-called 'ground truth' regions of interest (ROIs). First, they delineated histologic cancers that had been detected by at least one radiologist, paying attention to adjust the size and shape of the ROI as closely as possible to the size and shape of the actual histological cancer. These ROIs will be referred to

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