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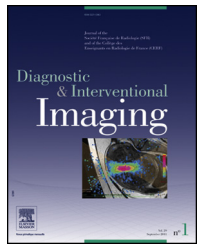

ORIGINAL ARTICLE /*Genito-urinary imaging*

Characteristics of undetected prostate cancer on diffusion-weighted MR Imaging at 3-Tesla with a b-value of 2000 s/mm^2: Imaging-pathologic correlation

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KEYWORDS
Diffusion-weighted MR imaging;
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Prostate cancer

Abstract
Objective: To assess the accuracy of Diffusion-Weighted MR Imaging (DW-MRI) at 3-Teslas (3 T) with a b-value of 2000 s/mm^2 (b-2000 DW-MRI) to detect prostate cancer (PCa) and to describe the histological features of missed tumors.
Methods: Prior to radical prostatectomy, 35 patients with a mean age of 64 ± 6.2 years old [51—77 years old] had a b-2000 DW-MRI at 3-T, without rectal coil (acquisition time: 2 min, 15 s), and were analysed on an eight-sector basis by two independent readers blinded to the rest of the multiparametric-MRI protocol. Pathological tumor foci were matched with high intensity focal areas on MRI and correlated for Gleason score, sector location and largest axial diameter.
Results: Of the 280 sectors analysed, histology showed PCa in 113 (113/280, 40%). Overall DW-MRI sensitivity, specificity and accuracy for tumor detection were 79—81%, 99—95% and 92—82%

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for readers 1 and 2, respectively (kappa test: 0.78). Of all, 28 (28/113, 25%) and 22 (22/113, 20%) tumor foci were not detected by reader 1 and 2 respectively. These undetected tumor foci had a mean pathological axial axis of 5 mm (range: 3—15 mm) and a Gleason score of 6, 7 (3 + 4), 7 (4 + 3) and > 7 in 15/28 (54%), 9/28 (32%), 3/28 (10%) and 1/28 (4%) of cases for reader 1, and in 11 (50%), 5 (23%), 5 (23%) and 1 (4%) of cases for reader 2.
Conclusion: A normal b-2000 DW-MRI at 3-T may miss small tumors without or with a minor Gleason 4 component.

It is now established that up to 30% of prostate cancers (PCa) detected by sextant transrectal ultrasound (TRUS)-guided biopsies have a small volume, are well differentiated, and may not be considered for radical treatment [1]. Some researchers suggested that over-diagnosis of potentially indolent tumors may lead to radical over-treatment [2]. Conversely, fear of missing and/or underestimating tumor aggressiveness [3] often leads to repeated biopsies and saturation biopsies [4], which induce a substantial increase in morbidity, mainly represented by haemorrhage and prostatitis, particularly in patients with no cancer [5]. Therefore, it becomes legitimate to identify men with clinical significant PCa and avoid detection of indolent tumors by unnecessary biopsies.

Patients with suspected PCa can benefit of power Doppler ultrasound, elastography and dynamic contrast-enhanced magnetic resonance imaging (MRI) [6—10]. Recently, diffusion-weighted MR imaging (DW-MRI) has emerged as an accurate tool that significantly improved PCa detection and characterization of multiparametric-MRI (mp-MRI) [11,12]. Recently, the use of ultra-high b-values DW-MRI ($\geq 1500\,s/mm^2$), by increasing the weighting of the diffusion sequence, has demonstrated a higher accuracy for PCa detection than b-value of $1000\,s/mm^2$ [13—16]. On the other hand, some researchers suggested that tumor aggressiveness was inversely correlated to the value of the apparent diffusion coefficient (ADC) [17]. Indeed, impeded diffusion increases with cellular density, which induces a proportional decrease in the ADC. Assuming that high Gleason grade tumors have higher cellular density, the ADC of these foci should be expected to be lower [13,17]. However, no cut-off value has been clearly defined to predict the presence of high Gleason score tumors, first because of a large overlap of ADC between low and high-grade tumors (reflecting tumors histologic heterogeneity) [18], and second because the ADC is highly dependent on the DW-MRI protocol [19]. As a result, ADC cannot yet be consistently used to distinguish low-grade from high-grade tumors.

We hypothesized that the qualitative assessment of DW-MR images obtained with a single b-value of $2000\,s/mm^2$ (b-2000 DW-MRI) at 3-Tesla (3 T) could increase the conspicuity of areas with the highest cellular density and differentiate benign from malignant tissue. We further hypothesized that a normal examination at ultra-high b-value (i.e. the absence of hyperintense foci), would only miss small volume and/or low-grade tumors, and could thus be confidently used to avoid overlooking aggressive tumors, and to avoid over-diagnosis of indolent tumors.

To assess the accuracy of DW-MRI at 3 T with a b-value of $2000\,s/mm^2$ to detect PCa and to describe the histological features of missed tumors.

Materials and methods

This retrospective, single-centre study was approved by our institutional review board and informed consent was waived. The MR imaging database of our department was queried to identify all patients with clinically localized PCa referred for prostate mp-MRI at 3-Tesla, including an acquisition with a ultra-high b-value ($b = 2000\,s/mm^2$) and subsequently treated by radical prostatectomy. From May 2011 through September 2012 inclusively, 35 patients with a mean age of 64 ± 6.2 years old were ultimately eligible for the study. Interval between DW-MRI and surgical resection was less than 3 months in all patients and no patient received hormonal deprivation before surgery.

MR imaging Protocol

All patients underwent a prostate mp-MRI using a 3-T system (Magnetom Skyra®, Siemens Healthcare, Erlangen, Germany) with an 8 channels anterior phased-array surface coil and an 18-channel phased-array posterior spine coil. Patients were imaged in supine position after rectal preparation to eliminate gas and faeces (sodium biphosphate and sodium phosphate enema). An antispasmodic agent (Phloroglucinol, 80 mg) was injected intravenously. Diffusion-weighted MR images were performed in the axial plane and included first a sequence with three diffusion gradient factors (b-values = 50, 400, $800\,s/mm^2$) for measurement of the ADC value and second, a separate acquisition with a single ultra-high b-value of $2000\,s/mm^2$. Diffusion-weighted MR images were acquired after the T2-weighted (T2-W) MRI and prior to gadolinium intravenous injection. Ultra-high b-value ($b = 2000\,s/mm^2$) DW-MRI images were acquired with a Fast Spin-Echo Echo-planar imaging sequence with the following parameters: spectral adiabatic fat saturation; TR/TE: 5200 ms/70 ms; slice thickness: 1.6 mm, no gap; field of view: 240×160; matrix size: 75×100; number of excitations: 12; voxel size: $1.6 \times 1.6 \times 3$ mm; acquisition time: 2 min 15 s.

Image analysis

MR images were analyzed using a commercially available workstation (Siemens Healthcare, Forsheim, Germany) by