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Apparent diffusion coefficient values and dynamic contrast enhancement patterns in differentiating seminomas from nonseminomatous testicular neoplasms

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ABSTRACT

Introduction: The aim of this study is to investigate the role of apparent diffusion coefficient (ADC) values and dynamic contrast enhancement (DCE) patterns in differentiating seminomas from nonseminomatous germ cell tumors (NSGCTs).
Materials and methods: The MRI examinations of the scrotum of 26 men with histologically proven testicular GCTs were reviewed. DWI was performed in all patients, using a single shot, multi-slice spin-echo planar diffusion pulse sequence and *b*-values of 0 and 900 s/mm^2. Subtraction DCE-MRI was performed in 20 cases using a 3D fast-field echo sequence after gadolinium administration. Time-signal intensity curves were created and semi-quantitative parameters (peak enhancement, time to peak, wash-in and wash-out rate) were calculated. The Student's *t*-test was used to compare the mean values of ADC, peak enhancement, time to peak, wash-in and wash-out rate between seminomas and NSGCTs. ROC analysis was also performed.
Results: Histopathology disclosed the presence of 15 seminomas and 11 NSGCTs. The mean ± s.d. of ADC values ($\times 10^{-3}$ mm^2/s) of seminomas (0.59 ± 0.009) were significantly lower than those of NSGCTs (0.90 ± 0.33) ($P = 0.01$). The optimal ADC cut-off value was 0.68 $\times 10^{-3}$ mm^2/s. No differences between the two groups were observed for peak enhancement ($P = 0.18$), time to peak ($P = 0.63$) wash-in rate ($P = 0.32$) and wash-out rate ($P = 0.18$).
Conclusions: ADC values may be used to preoperatively differentiate seminomas from NSGCTs.

1. Introduction

Testicular carcinoma represents between 1–1.5% of male tumors and 5% of urologic malignancies [1]. The estimated number of new cases of testicular cancer in the USA during 2014 was 8,820 and deaths related to testicular malignancies were estimated to occur in 380 patients [2]. The majority (95%) of testicular carcinomas are germ cell tumors (TGCTs), arising from the germinal epithelium of the seminiferous tubules [3–5]. The most important distinction of TGCTs is in two broad categories: seminomas and nonseminomatous germ cell tumors (NSGCTs), determining both prognosis and treatment planning. The gross morphology and histologic characteristics of these two types of neoplasms are different [3–5]. These pathologic differences are often correlated with imaging features [6–9].

Radical orchiectomy provides the definite histologic diagnosis in these patients and should be carried out before any further treatment, unless clinical indications require immediate chemotherapy [1]. In these cases, the preoperative knowledge of the histopathologic characteristics of testicular malignancy is extremely helpful.

Significant advancements in imaging evaluation of the scrotum have occurred during the last few years [10–16]. MRI of the scrotum has been proposed as a valuable supplemental imaging technique in the investigation of scrotal pathology [10–14]. Conventional MRI features of testicular germ cell tumors (TGCTs) have been found closely to correlate with histopathologic characteristics [8,9].

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Table 1
Clinical characteristics of the study population.

Clinical symptoms	Number ($n = 28$)
Palpable mass and/or painless scrotal enlargement	23
Pain	3
Incidentally discovered intratesticular mass lesion on sonography	1
Supraclavicular lymphadenopathy	1

Functional MRI techniques, including diffusion-weighted imaging (DWI) and dynamic contrast-enhanced (DCE) MRI provide useful additional diagnostic information in the interpretation of scrotal diseases [10,17–23]. Recently published reports have addressed on the role of DWI with measurements of apparent diffusion coefficient (ADC) values in the evaluation of various scrotal pathologies, including the diagnosis of testicular torsion, the detection and localization of impalpable testes and the differentiation between normal, benign and malignant scrotal contents [17–19]. DCE MRI has been reported useful in the diagnosis of testicular torsion and in the detection of testicular hemorrhagic necrosis [23]. DCE MRI may also be used to differentiate benign from malignant intratesticular mass lesions [20–22].

As to our knowledge, there are no reports in the English-language literature correlating the functional MRI findings of TGCNs with their histopathologic characteristics. The purpose of this retrospective study was to investigate the potential role of apparent diffusion coefficient values and dynamic contrast enhancement patterns in differentiating seminomas from non-seminomatous germ cell tumors.

2. Materials and methods

This study was a retrospective review of the MRI examinations of the scrotum of 28 men (mean age, 34 years; age range, 19–58 years) with histologically proven TGCTs, performed at our institution between July 2008 and March 2013. The clinical indications are presented in Table 1. The time interval between MRI and radical orchiectomy was less than two weeks in all patients.

Due to the retrospective nature of the study, the institutional review board did not require approval or patient's informed consent for the review of medical histories and MRI data.

All MR examinations were performed on a 1.5-T scanner (Philips Medical Systems, Cleveland, OH, USA), with the use of a one-element circular surface coil. Patients were examined in supine position, with the testes placed at a similar distance from the coil, by means of a towel placed beneath them, and the penis draped on the lower abdominal wall. Transverse spin-echo T1-weighted sequences (TR/TE, 500–650/13–15 ms) and axial, sagittal and coronal fast spin-echo T2-weighted images (TR/TE, 4000/100–120 ms) were used for data analysis. Images were of 3–4 mm section thickness, with a 0.5 mm intersection gap. The image matrix was 180×256 mm and the field of view was 240×270 mm.

DWI (TR/TE, 3900/115) was performed along the transverse plane during quiet breathing, with the following parameters: matrix, 180×256 mm; field of view (FOV), 240×270 mm; number of signals averaged, 1; motion-probing gradient (MPG), 3; spectral fat saturation; and water excitation with b-values of 0 and 900 s mm^{-2}. An average of 24 slices, with a total acquisition time of 29 s was obtained to cover the scrotal area. The orientation and location of these slices were identical to the conventional transverse images. Full echo information was obtained with a bandwidth of 1, 5774 kHz/pixel, a slice thickness of 3–4 mm and an intersection gap of 0.5 mm. No parallel imaging was used. DW sequences were obtained in all patients ($n = 28$).

Dynamic contrast-enhanced subtraction MR imaging was performed using a three-dimensional (3D) fast field-echo (FFE) sequence (TR/TE, 9/4.1; flip angle: 35°) in 20 cases. Other imaging parameters of the 3D FFE sequence were as follows: 4 mm section thickness, no intersection gap, 12 slices acquired, 219×219 mm FOV, 256×256 mm matrix and 60 s per sequence. Peripheral intravenous tubing with a 22-ga catheter was placed in a subcutaneous vein of the antecubital fossa. Coronal images were obtained before and after a rapid injection of 0.2 mmol of gadopentetic acid (Magnevist; Bayer Healthcare, Berlin, Germany) per kilogram of body weight, performed manually and followed by a flush of 20 mL of physiologic saline solution. Seven consecutive imaging sets were acquired immediately after the start of contrast injection, with no interval between sets.

The data set obtained before administration of gadopentetic acid was used as a mask for subsequent image subtraction. Each of the seven data sets obtained after contrast administration was subtracted section by section, using commercially available software (Philips Medical Systems, Cleveland, OH, USA).

MRI data were interpreted by two radiologists in consensus, both of whom were experienced in the field of urogenital imaging (a senior radiologist, with 9 years of experience and a junior radiologist, with 1 year of experience, respectively). Both reviewers were unware of the histopathologic data. Two cases were excluded from data analysis, due to unsatisfactory image quality of DW sequences. Therefore, the MRI data of 26 TGCNs were analyzed.

DW images were read in conjunction with the transverse T2-weighted images and the signal intensity of intratesticular malignancy, compared to that of normal testis was recorded. Subsequently, ADC maps were created on a workstation using the formula $S = S_0 \times \exp(-b \times \mathrm{ADC})$, where S is the measured signal. For the quantitative analysis, a single radiologist defined a circular region of interest (ROI) to be as large as possible within testicular tumor. The presence of carcinoma on the ADC maps was suggested when areas of low signal intensity were noted. For heterogeneous neoplasms, special attention was paid not to involve areas of hemorrhage and/or necrosis, with the aid of the corresponding transverse T1 and T2-weighted images. Three measurements were made and averaged.

The patterns of enhancement of testicular neoplasms were evaluated on the image that was maximally enhanced and were classified as heterogeneous or homogeneous. Signal intensity mean values of circular regions of interest (ROIs), as large as possible were placed on parts of maximal tumor enhancement, with care not to include areas of hemorrhage and/or necrosis, and the aid of corresponding T1 and T2-weighted images. Special care was also taken to avoid partial-volume effects and subtraction artifacts.

The time-signal intensity (TSI) plots of the measured MR signal in arbitrary units (a.u.) versus time in seconds (s) were assembled for each ROI. The measured signal intensities S_i ($i = 0,1,\ldots,7$) were normalized using the precontrast measurement So according to the formula $(S_i - S_0)/S_0$. The following parameters were calculated using the normalized measurements:

(a) the peak enhancement PE, defined as the maximum S_i, the time to peak TTP, equal to the time t_i of maximum S_i, the wash-in rate WIR, defined as the maximum slope of tumor enhancement before TTP and given by the formula [24] $\mathrm{WIR} = \max \frac{S_i - S_{i-1}}{t_i - t_{i-1}}$
(b) the wash-out rate WOR defined as PE-S_7, i.e., the difference between the maximum signal and the signal at the last time point.

The Kolmogorov–Smirnov test was used to assess normality of the data. The Student's t-test was used to compare the mean values of ADC, PE, TTP, WIR and WOR rate between seminomatous and nonseminomatous germ cell tumors. Receiver operating

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