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Research article

# Magnetic resonance diffusion tensor imaging of the testis: Preliminary observations

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ABSTRACT

*Introduction:* To evaluate the feasibility of testis diffusion tensor imaging (DTI), to determine normative apparent diffusion coefficient (ADC) and fractional anisotropy (FA) values and to assess the efficacy of DTI in characterizing testicular pathology.

*Materials and methods:* Fifty-six men underwent MRI of the scrotum, including DTI. Parametric and non-parametric statistical tests were used to compare the ADC and FA between the cranial, middle and lower thirds of normal testis and between the bilateral testicular thirds. Comparison between the ADC and FA of normal testis, malignant and benign testicular lesions was performed.

*Results:* No significant differences of the ADC and FA in normal testis between the cranial, middle and lower thirds and between the bilateral testicular thirds were found. ADC was significantly lower in malignancies compared to normal testis ($P = 0.006$) and benign testicular lesions ($P = 0.006$). FA was significantly higher both in malignancies ($P = 0.001$) and benign lesions ($P < 0.001$) compared to normal testis. FA in malignancies did not differ from FA in benign lesions ($P = 0.221$)

*Conclusions:* This study shows the feasibility of testis DTI. Both ADC and FA significantly differ between testicular lesions and normal testis, although FA did not show an incremental diagnostic value compared to ADC in lesion differentiation.

## 1. Introduction

Diffusion-weighted imaging (DWI) is a functional imaging technique used to assess the displacement distribution of the water molecules in living tissues, providing information for the structure and geometric organization [1,2]. Recent work addressing on the role of DWI in the interpretation of testicular pathology includes various applications, such as the detection and localization of impalpable testes, the early diagnosis of testicular torsion, the detection of testicular fibrosis in men with varicocele and the characterization of testicular mass lesions [3–10].

As diffusion is in fact a three-dimensional process, molecular mobility in tissues may occur with different probabilities in various directions that means in an anisotropic manner, especially in tissues with a specifically oriented organization. Diffusion tensor imaging (DTI) was developed on the basis of DWI to demonstrate the direction and speed of water molecule diffusion [11,12]. DTI can provide both apparent diffusion coefficient (ADC) and fractional anisotropy (FA) values, which may reflect physiological characteristics and pathologic alterations at microscopic level [11,12].

Significant advances in the characterization of tissue microstructure and pathophysiology by means of DTI, originally in neuroimaging and musculoskeletal imaging have been reported [11–14]. DTI also has been applied in the evaluation of myocardium after infarction, in normal prostate and detection of prostatic carcinoma, in normal breast and differentiation of breast lesions, in normal and pathologic kidneys, in normal and pathologic liver, in normal pancreas and detection of pancreatic carcinoma, in anal canal, in normal uterus and in the evaluation of the female pelvic floor [11–23].

As to our knowledge, the anisotropy of the normal testis and the possible diagnostic value of DTI for differential diagnosis of testicular pathology have not been investigated. The purpose of this prospective study was to evaluate the feasibility of testis DTI, to determine normative ADC and FA values and to assess the efficacy of the technique in

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the characterization of various testicular diseases.

## 2. Materials and methods

### 2.1. Patient population

From June 2013 until January 2017, 56 men (age range, 17–76 years; mean age, 41 years) were referred for scrotal MRI with various clinical indications: vague scrotal pain and/or painless scrotal enlargement (n = 37); signs of acute epididymitis/epididymoorchitis (n = 10); painless, palpable mass (n = 7); recent penile trauma (n = 1), and recent penile enlargement (n = 1). The standard of reference included clinical and imaging follow-up, surgical and pathologic results. In cases of testicular malignancies, the time interval between MRI and radical orchiectomy was less than two weeks.

The institution's Review Board approved the study. All participants were informed about the study and written consent was obtained from all of them.

### 2.2. MR protocol

All MR examinations were performed on a 1.5-T scanner (Philips Medical Systems, Cleveland, OH, USA), with the use of a circular surface coil. Patients were examined in the supine position, with the testes placed at a similar distance from the coil, by placing a towel beneath them, and the penis draped on the lower anterior abdominal wall. Conventional sequences used for data analysis included transverse spin-echo T1-weighted (T1WI) (TR/TE, 500–650/13–15 ms) and axial, sagittal and coronal fast spin-echo T2-weighted (T2WI) (TR/TE, 4000/100–120 ms). These 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 (FOV) was 240 × 270 mm.

DTI (TR/TE, 3756/131 ms) was performed along the coronal plane, during quiet breathing, using fat-saturated single-shot spin-echo planar imaging sequence and the following parameters: ACQ Matrix (M × P), 128 × 87; FOV, 250 × 227 $mm^2$; slice thickness, 3,0 mm; intersection gap, 0 mm; number of signals averaged (NSA), 2; water excitation with *b*-values of 0 and 700 $s/mm^{-2}$ and six diffusion directions. The total acquisition time was 2,07 min.

Coronal subtracted dynamic contrast-enhanced (DCE) images, using a three-dimensional fast field-echo sequence (TR/TE, 9/4.1 ms) also were used for data interpretation (flip angle: 35°; section thickness, 4 mm; no intersection gap; matrix, 256 × 256 mm; FOV, 219 × 219 mm; and 60 s per sequence). Peripheral intravenous tubing with a 22-gauge catheter placed in a subcutaneous vein of the antecubital fossa was performed. Seven consecutive sets were acquired immediately after the rapid injection of 0.2 mmol of gadolinium chelate compounds per kilogram of bodyweight, performed manually and followed by a flush of 20 mL of physiologic saline solution, with no interval between them. Each of the seven data sets obtained after contrast medium administration was subtracted section by section, using the unenhanced data as a mask and commercially available software.

### 2.3. Image analysis

Two radiologists in consensus (ACT and AN, with 13 and four years of experience, each in scrotal MRI), blinded to the final diagnosis, analyzed the MRI data. The DW trace image, ADC map, and FA map were automatically generated using the DTI processing software on the Philips workstation and sent to the hospital picture archiving and communication system (PACS). Using coronal T2WI as guidance, coronal ADC and FA maps at the level of the mediastinum testis were selected for measurements. Three identical circular regions of interest (ROIs) were drawn in the cranial, middle and caudal thirds of the bilateral testes, to obtain the average ADC and FA values of normal testis (Fig. 1). ROIs were as large as possible to include the majority of normal testis, with care not to overlap each other. The ROIs also were manually drawn to be as large as possible on areas of testicular lesions. Three different ROIs were placed on each testicular lesion and the measurements were averaged. Care was taken to exclude artifacts and areas of hemorrhage and/or necrosis, with the aid of the corresponding T1WI, T2WI and subtracted DCE T1WI.

### 2.4. Statistical analyses

Statistical analysis was performed using IBM SPSS version 20.0 (IBM, Inc., Armonk, NY, USA). The normality of distribution of parameters was assessed by a Kolmogorov-Smirnov test. The cranial, middle and caudal thirds of each testis were compared and analyzed by a one-way repeated-measures analysis of variance (ANOVA) test, when the data revealed a normal distribution. Comparisons between the bilateral testicular thirds were made using a paired samples *t*-test. Non-parametric tests, including the Kruskall-Wallis one-way analysis of variance and the Mann-Whitney *U* test were used to compare differences among measurements, if data did not assume a normal distribution. Two different control subgroups were selected in order to age-match the malignant and benign groups. Parametric and non-parametric statistical tests were used to compare the ADC and FA of normal testis to that of malignant and benign testicular lesions. Statistical significance was set at P-value's of $< 0.05$.

## 3. Results

Thirty eight out of one hundred and twelve testes were excluded from measurements due to the following: significant hydrocele (n = 4), testis malposition (n = 2), signal heterogeneity of the testis (n = 2), presence of very small, intratesticular tumor, difficult to measure, proved to correspond to benign Leydig cell tumor on pathology (n = 1), contralateral testes in men with testicular malignancies (n = 7), bilateral testes in men with varicocele (n = 20), contralateral testis in a patient with left varicocele and segmental testicular infarction (n = 1) and testicular implant (n = 1). Therefore, a total number of 74 testes were measured, including measurements in 56 normal testes and 18 testicular lesions, seven of which were malignant and 11 benign.

Fifty six testes from 36 men (age range: 17–76 years; mean age: 44 years) were characterized as 'normal' based on the signal intensity on conventional sequences and/or the absence of abnormal testicular lesions found during subsequent clinical and/or sonographic follow-up studies.

ADC followed a normal distribution as evaluated using the Kolmogorov-Smirnov test. The mean ADC ± std ( × $10^{-3}$ $mm^2/s$) in the cranial, middle and lower testicular thirds was 1.14 ± 0.16, 1.16 ± 0.17, and 1.15 ± 0.16, respectively. ANOVA analysis showed no differences between the three groups (F = 0.183, degrees of freedom = 2, P = 0.833, Table 1). The ADC in the bilateral testicular thirds in 20 participants was included in the analysis. No significant differences were found (Table 2).

Non-parametric tests were used for FA comparisons. The median FA in the cranial, middle and lower testicular thirds was 0.11, 0.11, and 0.11, respectively. No differences between the three groups were found (degrees of freedom = 2; P = 0.963, Table 3). FA was not different in the bilateral testicular thirds (Table 4).

All tumors (n = 7) proved to represent testicular germ cell neoplasms (TGCNs) on pathology, four of which were seminomas and three nonseminomatous neoplasms (embryonal carcinoma, n = 1; embryonal carcinoma, teratoma, yolk sac tumor, n = 2). The age of patients with testicular malignancies ranged from 20 to 42 years, with a mean age of 32 years. The mean ± s.d. of ADC ( × $10^{-3}$ $mm^2/s$) and the median of FA in TGCNs were 0.82 ± 0.31 and 0.26 (range: 0.18-0.42), respectively (Figs. 2 and 3). Benign testicular lesions included 10 cases of acute orchitis and one case of segmental testicular infarction. The age of patients with benign testicular pathologies ranged from 24 to 75 years,