Multiparametric MRI (mp-MRI) of the scrotum—A Helpful Tool in differentiating sex-cord stromal tumours from non-stromal malignant testicular neoplasms

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Authors: A. M. Abualruz, M. Mafraji, K. Al-Rumaihi, I. Al-Bozom, S. Yadav, M. Khanna; Doha/QA
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Aims and objectives

Background:

Testicular cancer is the most common tumor encountered in young men aged 15-35 years (1-4).

Among this age group, about 95% of primary testicular cancers are germ cell tumors (GCT). Sex cord stromal tumors (ST) represent the remaining 5% of primary testicular tumors (5).

Seminomas comprise 50% of GCTs; the other half is non-seminomatous (NS-GCTs) subtype such as yolk sac, embryonal carcinomas, teratomas, choriocarcinomas and mixed germ cell tumors.

Stromal tumors (ST) originate from the testicular interstitium that is derived from mesenchymal cells. They are mostly benign; malignancy in ST is reported in about 10% of cases (1). ST subtypes include leydig cell tumors, sertoli cell tumors, granulosa cell tumors, and thecomas (6).

In older men, lymphoma is the most common testicular malignancy. Testicular metastases are rare (1, 7).

Imaging plays an essential role in the diagnosis and workup of testicular neoplasms. Ultrasound is the key initial imaging modality with a sensitivity reaching up to 100% when combined with the physical examination (8). However, the differentiation between benign and malignant tumors remains a challenge especially in equivocal cases (1).

Magnetic resonance (MR) imaging is superior to ultrasound in local staging of testicular tumors and in retroperitoneal nodal assessment (8-10). Recent studies showed that MR imaging is a helpful tool in evaluation and characterization of benign and malignant features of testicular tumors with sensitivity and specificity of nearly 100% and 88%, respectively (1, 8). The availability, long scanning time and costs involved are the main limiting factors for its wide use in practice (1).

Differentiation between benign ST and NSMT is important from the management point of view, as radical inguinal orchiectomy is the standard of care for suspected testicular cancer. On the other hand, consideration can be given to partial orchiectomy in cases
of benign ST as only about 10% of ST turn malignant with size > 5 cm being one of the predictive factors (11).

**Purpose:**

To evaluate the potential role of Multiparametric MRI (mp-MRI) in differentiating testicular sex-cord stromal tumors (ST) from non-stromal malignant testicular neoplasms (NSMT).
Methods and materials

Study type & Patients:

A retrospective pre-operative scrotal mp-MRI evaluation of 16 patients (age range: 18-67; mean - 35 years) referred to the radiology department for clinical and sonographically detected testicular mass, between April 2011 and September 2016, was performed.

All patients had histopathologic confirmation post radical orchiectomy.

MRI technique:

All MR studies were performed on a 1.5 and 3-Tesla magnet systems (MAGNETOM Avanto and/or Skyra, Siemens Healthcare), using the circular surface coil. All patients were examined in a supine position with the penis dorsiflexed and tapped into the anterior pelvic wall to prevent motion.

Multi-sequence image acquisition was done in axial, coronal and sagittal planes before and after intravenous contrast administration.

Table 1: Magnetic Resonance Imaging Parameters used in this study on a 1.5 Tesla clinical scanner.

<table>
<thead>
<tr>
<th>MR Sequence</th>
<th>Imaging plane</th>
<th>Field of view (mm)</th>
<th>Matrix size (mm)</th>
<th>Slice thickness / gap (mm)</th>
<th>TR/TE (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spin-echo T1-weighted images</td>
<td>Axial</td>
<td>210 X 300</td>
<td>180 X 256</td>
<td>2-3/0.5 mm</td>
<td>500-650/13-15</td>
</tr>
<tr>
<td>T2-weighted fast spin-echo images</td>
<td>Axial / Sagittal</td>
<td>210 X 300</td>
<td>180 X 256</td>
<td>2-3/0.5 mm</td>
<td>4000/100-120</td>
</tr>
<tr>
<td>DWI (b 50, 400, 800)</td>
<td>Axial</td>
<td>210 X 300</td>
<td>128 × 128</td>
<td>2-3/0.5 mm</td>
<td>3300/80</td>
</tr>
<tr>
<td>T1 3D VIBE pre and delayed</td>
<td>Axial</td>
<td>210 X 300</td>
<td>180 X 256</td>
<td>2-3/0.5 mm</td>
<td>4.75 / 2.39</td>
</tr>
</tbody>
</table>
**Semi-quantitative analysis:**

Two radiologists, blinded to histopathology results, performed the multiparametric (mp) MR imaging assessment at GE RIS-PACS system (version RIS-i 4.2 plus).

MR imaging variables included: lesion size, signal intensity in T1 and T2 weighted images, diffusion-weighted images (DWI) with apparent diffusion coefficient (ADC) maps, dynamic contrast enhancement (DCE) pattern and characteristics.

Tumor signal intensity was categorized low, iso-, high or heterogeneous in comparison to the normal background of the ipsilateral testis or contralateral testis if the tumor was replacing the whole testis.

ADC region of interest (ROI) plotted at areas of restricted diffusion in each testicular lesion avoiding areas of hemorrhage or necrosis.

Tumors enhancement type was classified as none, homogenous, heterogeneous and peripheral enhancement patterns.

The radiologists defined a circular region of interest (ROI) covering # 50% of the lesion size, excluding areas of necrosis or hemorrhage. The measurement was done in pre-contrast, arterial, venous and delayed phases.

DCE-time intensity curves were generated and defined as type 1 (progressive continuous enhancement), type 2 (plateau) and type 3 (wash-in and wash-out).
**Fig. 1:** Schematic diagram of the DCE MR Time intensity curve types: type 1 (progressive), type 2 (plateau), and type 3 (wash-in and washout) (13).


MRI findings were then retrospectively correlated with the histopathologic findings, which were the standard of reference. The specimens were reviewed by a staff pathologist having more than 20 years of experience in the urogenital system.

The inter-observer agreement on MRI interpretation between the two radiologists was quantified by using weighted kappa statistics.
Results

Post radical orchiectomy histopathology results revealed the presence of 16 testicular neoplasms.

Seven cases (44%) were found to be GCTs including classic seminoma \( (n = 4) \); embryonal carcinoma \( (n = 1) \); immature teratoma \( (n = 1) \), mixed germ cell tumor \( (n = 1) \).

One case (6%) of testicular lymphoma \( (n = 1) \) and another case (6%) was labeled as carcinoma of unknown origin \( (n = 1) \).

Seven cases (44%), proved histologically to be benign stromal tumors (ST) including calcifying Sertoli cell tumor \( (n = 1) \), Granulosa cell tumor \( (n = 1) \) and Leydig cell tumor \( (n = 5) \).

In our series, statistically significant difference was noted between the sizes of ST and NSMT \( (\text{mean} \pm \text{SD}: 1.27 \pm 0.56 \text{ cm vs. } 5.38 \pm 2.36 \text{ cm; } p=0.001) \).

Although no significant differences were noted in the ADC values between the ST and NSMT \( (ST = 960 \pm 259 \times 10^{-3} \text{ mm}^2/\text{s vs. NSMT}=787 \pm 197 \times 10^{-3} \text{ mm}^2/\text{s; } p=0.17) \), however NSMT demonstrated significant diffusion restriction than ST on visual analysis \( (p=0.005) \), (Figure-2).

ST demonstrated a homogenous and intense enhancement unlike NSMT, which showed a heterogeneous pattern of enhancement \( (p=0.01) \), (Figure-3).

The degree of enhancement for ST was significantly more marked when compared to NSMT \( (p=0.04) \) and also to the background normal testis (T) \( (\text{mean difference of ST-T: } 139.2; p=0.039 \text{ vs. NSMT-T: } 38.9; p=0.99) \). This difference was most apparent in the delayed phase \( (p=0.039) \), (Figure-4).

Semi-quantitative DCE assessment showed no significant differences in the enhancement curves between ST and NSMT, (Figure-4).

Overall inter-observer agreement for all the MRI variables was good \( (k = 0.898 -1) \).
Table 2. Subjective imaging findings and semi-quantitative assessment of testicular lesions at multi-parametric MRI.

<table>
<thead>
<tr>
<th>Imaging Finding</th>
<th>ST (n= 7)</th>
<th>NSMT (n= 9)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Reader 1</td>
<td>Reader 2</td>
<td>Reader 1</td>
</tr>
<tr>
<td><strong>DWI diffusion restriction</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present:</td>
<td>1/7 (15%)</td>
<td>1/7 (15%)</td>
<td>Present:</td>
</tr>
<tr>
<td>Absent:</td>
<td>5/7 (70%)</td>
<td>5/7 (70%)</td>
<td>Absent:</td>
</tr>
<tr>
<td>Not available:</td>
<td>1/7 (15%)</td>
<td>1/7 (15%)</td>
<td>Not available:</td>
</tr>
<tr>
<td><strong>Post-contrast enhancement pattern</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Homogenous:</td>
<td>4/7 (57%)</td>
<td>5/7 (70%)</td>
<td>Heterogenous:</td>
</tr>
<tr>
<td>No enhancement:</td>
<td>2/7 (38%)</td>
<td>2/7 (30%)</td>
<td>Homogenous:</td>
</tr>
<tr>
<td>Peripheral:</td>
<td>1/7 (15%)</td>
<td>1/9 (10%)</td>
<td>Peripheral:</td>
</tr>
<tr>
<td><strong>DCE-Time intensity curve type</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type-1:</td>
<td>5/7 (70%)</td>
<td>5/7 (70%)</td>
<td>Type-1:</td>
</tr>
<tr>
<td>Type-3:</td>
<td>0/7 (0%)</td>
<td>0/7 (0%)</td>
<td>Type-3:</td>
</tr>
</tbody>
</table>

p-value = 0.01
<table>
<thead>
<tr>
<th></th>
<th>Not available: 2/7 (30%)</th>
<th>Not available: 2/7 (30%)</th>
<th></th>
<th></th>
</tr>
</thead>
</table>

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Fig. 1: Schematic diagram of the DCE MR Time intensity curve types: type 1 (progressive), type 2 (plateau), and type 3 (wash-in and washout) (13).

Conclusion

Discussion:

The distinction of benign ST from NSMT is crucial as testicular carcinoma typically affects young men aged 15-35 years (1). It is also necessary to find reliable imaging tool as part of the pre-operative evaluation to avoid unnecessary orchiectomy (11).

Serra et al reported an overall accuracy of 91% for MR imaging in differentiating benign from malignant testicular lesions in a study of 29 testicular masses, following inconclusive clinical and sonographic evaluation [8, 14].

Dynamic contrast-enhanced (DCE) MR imaging features of malignant testicular lesions typically demonstrate rapid enhancement followed by contrast washout (Type-3 curve) (12). On the other hand, benign lesions typically demonstrate continuous increasing enhancement or increasing enhancement that plateaus (Type-1 or 2) (12).

Our study demonstrated that in the presence of continuous progressive enhancement of a testicular mass (Type-1 curve), homogenous intense enhancement pattern (ST / NSMT = 60-70-% vs. 10%; p=0.01) along with absent restricted diffusion (ST / NSMT = 70-% vs 0%; p=0.01) are both sensitive and specific imaging findings differentiating benign ST from NSMT (k = 0.898 -1).

A variety of other subjective parametric data obtained using a multi-parametric MR technique, namely ADC values derived from DWI and semi-quantitative curve analysis of DCE did not differ between ST and malignant NSMT (p>0.05).

Conclusion:

1. Mp-MRI can provide satisfactory pre-operative differentiation between sex-cord stromal tumors (ST) and malignant non- stromal testicular neoplasms (NSMT).
2. In an incidentally detected small (< 2cm), testicular lesion by ultrasound, MRI can be performed to differentiate the two pathologies.
3. Marked progressive enhancement strongly indicates the stromal nature of the lesion rather than non-stromal origin (GCT or lymphoma).
Fig. 2: DW image and corresponding apparent diffusion coefficient (ADC) maps. (A): Absent diffusion restriction in a Leydig-cell tumor of the right testis. (B): Left testicular Germ cell tumor with diffusion restriction.

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Fig. 3: Axial T1-weighted MR images pre and post IV contrast administration. (A): Leydig-cell tumor in a 30 years-old patient, showing small homogeneously enhancing right testis tumor. (B): Germ cell tumor in a 29 years-old patient demonstrates a large heterogeneously enhancing mass replacing the left testis.

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Fig. 4: DCE-time intensity curves of the ST, NSMT and background normal testis during the pre-contrast, arterial, venous and delayed phases post IV contrast injection. Note that both ST and NSMT show type-1 curve, however, ST show more intense enhancement especially during the delayed phase (p=0.039).

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**Personal information**

1. Abdulrahman Abualruz MD., Diagnostic radiology resident  
   E-mail: abdulrahman.abualruz@hotmail.com

2. Mustafa Mafraji MBBS., Diagnostic radiology resident  
   E-mail: mmafraji@hamad.qa

3. Maneesh Khanna MD., Consultant Radiology

Hamad General Hospital  
Doha, Qatar  
P.O.BOX:3050
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