Multiparametric Ultrasound of the Non-palpable Solid Testicular Mass

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45 year old man. GP US referral.
Clinical details: Right scrotal discomfort for 6/12.
Normal scrotal examination.
Reducing the number of unnecessary radical orchidectomies

Recommendation #4:
Non-palpable, testicular, solid, single, sporadic nodules without any microliths are often benign. In such cases, the report should avoid advice leading to the removal of the entire testis.

Rocher L. European Radiology 2016:26:2268-2278
What I was taught 20 years ago!

• The most common palpable intra-testicular lesion aged 15-34 is a malignant GCT\(^1\)

• Conventional US has low accuracy in differentiating benign from malignant masses: “when an intra-testicular lesion is detected on US, even when there is no clinical suspicion of neoplasm, exploration of the scrotum is indicated.”\(^2\)

2. Coret A. Br J Urol 1995;76:216
Non-palpable lesions are different

- The majority of palpable solid testicular masses are malignant.¹
- The majority of incidentally discovered non-palpable masses are benign (73%)²
- Leydig cell tumours most common (45%)³
- Many radical orchidectomies performed for benign disease. Implications for fertility, endocrine function, preservation of body image

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Patient (n)</th>
<th>Benign (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buckspan</td>
<td>1989</td>
<td>4</td>
<td>100</td>
</tr>
<tr>
<td>Hopps</td>
<td>2002</td>
<td>4</td>
<td>50</td>
</tr>
<tr>
<td>Carmignani</td>
<td>2003</td>
<td>10</td>
<td>80</td>
</tr>
<tr>
<td>Leroy</td>
<td>2003</td>
<td>15</td>
<td>73</td>
</tr>
<tr>
<td>Sheynkin</td>
<td>2004</td>
<td>9</td>
<td>67</td>
</tr>
<tr>
<td>Carmignani</td>
<td>2004</td>
<td>3</td>
<td>100</td>
</tr>
<tr>
<td>Colpi</td>
<td>2005</td>
<td>5</td>
<td>80</td>
</tr>
<tr>
<td>Rolle</td>
<td>2006</td>
<td>7</td>
<td>86</td>
</tr>
<tr>
<td>Assaf</td>
<td>2006</td>
<td>6</td>
<td>50</td>
</tr>
<tr>
<td>Muller</td>
<td>2006</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td>Powell</td>
<td>2006</td>
<td>4</td>
<td>50</td>
</tr>
<tr>
<td>Eifler</td>
<td>2008</td>
<td>19</td>
<td>100</td>
</tr>
<tr>
<td>Hallak</td>
<td>2009</td>
<td>5</td>
<td>80</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td><strong>111</strong></td>
<td><strong>81</strong></td>
</tr>
</tbody>
</table>

1. Isidori AM. Radiology 2014:273; 606-618.  
2. Giannarini G. European Urology 2010;57:780-790  
3. Brunocilla E. Anticancer Res 2013:33;5205-5210
Managing incidentally discovered testicular masses is now a problem for us all

- Incidental, asymptomatic and non-palpable solid testicular masses are now regularly encountered on US (0.8-7.4%).

- Should all these patients be offered a radical orchidectomy?

1. Rocher L. Eur Radiol 2016:26:2268-2278
Safely reducing the number of (unnecessary) radical orchidectomies

- Pre-test probability
  - Age, cryptorchidism, FHx, Hx contralateral tumour, Kleinfelter’s
- Clinical history
  - Trauma, infection, granulomatous/endocrine disease
- Tumour markers
- Ultrasound examination:
  - Greyscale + CD features
  - Microlithiasis
  - Multiparametric approach
- Alternatives to radical orchidectomy
  - US surveillance
  - Testis preserving surgery
Multiparametric ultrasound

1. Grey scale
2. Doppler (CD, PD, SMI)
3. Tissue elastography
4. CEUS
Tumour markers

<table>
<thead>
<tr>
<th>Marker</th>
<th>AFP</th>
<th>B-hCG</th>
<th>LDH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal level</td>
<td>&lt; 40 μg/l</td>
<td>&lt; 5 iU/l</td>
<td>1.5-3.2 ukat/l</td>
</tr>
<tr>
<td>Elevated in</td>
<td>&gt; 60% NSGCT</td>
<td>Seminoma Choriocarcinoma Embryonal</td>
<td>40-60% GCT Any</td>
</tr>
<tr>
<td>Half life</td>
<td>5-7 days</td>
<td>24-36 hours</td>
<td>Varies</td>
</tr>
<tr>
<td>Expected return to normal post surgery</td>
<td>20-28 days</td>
<td>4-6 days</td>
<td>Varies</td>
</tr>
</tbody>
</table>

All tumour markers lack sensitivity and specificity
Other markers: Placental alkaline phosphatase (seminoma), Neuron-specific enolase (seminoma), TRA-1-60 (NSGCT), Lectin reactive AFP (NSGCT), Cell-free circulating DNA (GCT)

What is the significance of TML?

- Prevalence 2.7% in adult males\(^1\)
- Association with GCT does not prove cause
- Risk in patients without a second risk factor for TGCT is low\(^2,3\)
- However: TML in association with a hypoechoic nodule suggests GCT (esp. seminoma)\(^4\)

1. Mullooly C. Int J STD AIDS 2012;23:620  
# US: Greyscale features

<table>
<thead>
<tr>
<th>Benign patterns</th>
<th>Malignant patterns</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non palpable</td>
<td>Palpable</td>
</tr>
<tr>
<td>Well defined</td>
<td>Irregular margins/ill-defined</td>
</tr>
<tr>
<td>Simple cyst</td>
<td>Solid or mixed</td>
</tr>
<tr>
<td>Uniformly hyperechoic</td>
<td>Echopoor or Hypoechoic areas</td>
</tr>
<tr>
<td>Normal parenchyma</td>
<td>TML</td>
</tr>
<tr>
<td>Onion skin pattern</td>
<td>Macrocalcifications</td>
</tr>
<tr>
<td>Geographic/‘wedge shaped’</td>
<td>Round or irregular</td>
</tr>
</tbody>
</table>
Grey scale features: benign patterns
Colour Doppler

- Lack of blood flow increases the probability of a benign aetiology\(^1\)
- Blood flow can be difficult to demonstrate in small lesions (< 16mm) with conventional colour/power Doppler\(^2\)

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28 yr. old man  Hx: Malignant teratoma

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New Doppler techniques may help

- SMI™ Superb Microvascular Imaging
- Can demonstrate very low velocity flow (normally removed by filters)
Best of all: CEUS

- Virtually all tumours show some vascularity with CEUS\(^1\)
- No enhancement suggests a benign aetiology\(^2\)
- CEUS not ideal for testis due to bubble size
  - Use 4.8 mls SonoVue
  - Lower transducer frequency

1. Huang DY. BJR 2012:85;S41-53
Minor Trauma
29 yrs. old
Epidermoid cysts

Features of Testicular Epidermoid Cysts on Contrast-Enhanced Sonography and Real-time Tissue Elastography

Kriti Patel, FRCR, Maria E. Sellar, MBBS, FRCR, Jane L. Clarke, MSc, Paul S. Sidhu, BSc, MRCP, FRCR

Patel K. J Ultrasound Med 2012;31

- Four grey scale patterns recognised.¹ Always avascular on Colour Doppler
- CEUS increases confidence – no internal vascularity, rim enhancement in some cases²

Can CEUS differentiate benign from malignant?

- 197 patients with at least one solid lesion
- 82 palpable lesions – 96% malignant
- 115 non palpable lesions (54% scans for infertility)
  - 38% malignant tumours, 37% benign tumours, 25% non-neoplastic
- Combined grey-scale US features with CEUS
- Overall sensitivity 82%, specificity 91% for differentiation of benign vs. malignant

TGCT vs Sex cord stromal tumours

- Rapid wash in and washout is a malignant feature
- Prolonged washout more suggestive of sex cord stromal tumour
- Insufficient data to recommend in isolation

Sertoli cell tumour

Seminoma
Sonoelastography

- Strain elastography (SE) and Shear wave elastography (SWE)
- Limited data in testis
- Harder lesions more likely to be malignant\(^1\) (but remember that cysts are often stiff – including epidermoid)
  
  - Aigner:\(^2\) 50 lesions sensitivity 100%, specificity 81% NPV 100%
  
  - Goddi:\(^3\) 144 lesions: sensitivity 87.5%, specificity 98.2% accuracy 95.8%
  
  - Two further studies suggest elastography useful for small lesions:\(^4,5\)

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1. Pallwein L. Eur Uro Suppl 2006;5:96
2. Aigner F. Radiology 2012;263:584
5. Pastore AL. Cancer Imaging 2014;14:29
• 106 patients with non-palpable lesions (all < 15mm), all surgically removed for histology
  – 34.7% malignant, 35.9% benign, 29.2% non-neoplastic
• Strain elastography, three point scale (ES 1 – 3)
• SE 81.8% sensitive 79.1% specific in identifying malignancy
• Strain ratio measurement did not improve accuracy
• SE can not be used alone but is a valuable in supporting conventional US when findings are equivocal
Five point and three point elastography scales

• SWE may be able to differentiate seminomas from non-seminomatous GCT
• Small study (15 patients: 7 seminoma, 8 NSGCT)
• NSGCT stiffer than seminoma (10.6 kPa vs. 47.0 kPa)
• 68 testicular lesions (palpable and non-palpable)
• 79.4% neoplastic (87% malignant 13% benign)
• CEUS performs best. Strain elastography cannot be recommended alone due to low specificity

<table>
<thead>
<tr>
<th>Modality</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B mode</td>
<td>100</td>
<td>43</td>
<td>87</td>
<td>100</td>
<td>88</td>
</tr>
<tr>
<td>Colour</td>
<td>81</td>
<td>86</td>
<td>96</td>
<td>55</td>
<td>82</td>
</tr>
<tr>
<td>CEUS</td>
<td>93</td>
<td>85</td>
<td>96</td>
<td>73</td>
<td>91</td>
</tr>
<tr>
<td>ES score</td>
<td>98</td>
<td>25</td>
<td>85</td>
<td>75</td>
<td>85</td>
</tr>
<tr>
<td>Strain Ratio</td>
<td>90</td>
<td>45</td>
<td>86</td>
<td>56</td>
<td>81</td>
</tr>
</tbody>
</table>
Alternatives to radical orchidectomy for non-palpable masses

- Testis-sparing surgery
- Ultrasound Surveillance
Testis sparing surgery (TSS)

• EUA guidelines 2011
  – Synchronous bilateral tumours
  – Metachronous contra-lateral tumour
  – Lesion in a solitary testis (volume <30% of testis)
• Indications expanding
  – Can be the best management for non-palpable masses <2cm
  – US needle localisation may be needed
  – Frozen section after enucleation – testicular repair or orchidectomy depending on the result
• Intermediate and long-term follow up shows no significant risk for local or distant recurrence and better aesthetic and functional outcomes
• No prospective studies on radical orchidectomy vs. TSS

1. Brunocilla E. Anticancer Research 2013;33:5205
US Surveillance for small masses?

- Limited evidence
- If mp US suggests a benign lesion <10mm\(^1\)
- All lesions < 5mm? \(^2\)
- Must be tumour marker negative
- ?? Should have CT abdomen (+ CXR or CT thorax)
- US every 3/12 for 1 year then annual (for how long - ? 3 years)

Classical seminoma – no change in size over 1 year

1. Connolly SS. BJU International 2006;98:1005  
Retrospective study of STMs (<10mm)

1. 101 patients – Overall 14.9% malignant, 29.4% hypoechoic lesions malignant (Leydig cell counted as malignant)
2. 16.8% immediate surgery (US features of concern for TGCT – hypoechoic, vascular, TML), 7.9% surgery after US follow up, 75.3% US only – surgery avoided
3. For hypoechoic lesions size (> 4.5mm) was the only independent US predictor of malignancy (not vascularity, number, location or TML)
4. US follow up was 6-84 months (median 13)
5. Recommendations: 3 month interval, minimum of 6 months surveillance

Li Q. Infertility 2016;7:6-9
Multi-parametric MRI

• Mp MRI (T2, DWI and DCE) emerging as an accurate tool for scrotal imaging

• Potentially useful for:
  – Lesion characterisation
  – Differentiation between GCT and stromal tumours
  – Characterisation of histological subtype of GCT
  – Local staging
  – Operative planning for TSS
Impalpable STM (not simple cyst)

Tumour markers negative

Risk Factors
Clinical History
Other US findings (TML)

mp US

likely benign

Patient preference
TSS or surveillance

likely malignant

< 10 - 20 mm
Patient preference

>20 mm
Radical orchidectomy

TSS

Still Indeterminate

Patient preference

Consider MRI

Tumour marker positive

Radical orchidectomy
Which is the imposter?
Origin: Tavistock 11th Century