Elastography of Focal Testicular Lesion: Current concepts and utility

**Short title:** Elastography of Focal Testicular Lesion

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Abstract

Newer sonographic technique, tissue elastography has been developed as a qualitative and potentially quantitative adjunctive tool to provide additional information on tissue stiffness, aiming to further improve diagnostic confidence of benign versus malignant focal testicular lesions. The purpose of this review is to provide an overview of the elastography techniques in assessing focal testicular lesions and their typical appearance on tissue elastography.
Introduction

Traditional assessment of the testis with B-mode and colour Doppler ultrasonography (US) has been the main workhorse for identifying and characterising focal testicular lesions owing to its superb spatial resolution of anatomical details and the superficial location of the testis. B-mode US accurately identifies the lesion size, shape, location (intra- or extra testicular) and its pattern of echogenicity. Colour Doppler US assesses the presence and the pattern lesion vascularity to increase the diagnostic confidence of a malignant lesion if disorganised vascularity is present or a benign lesion when the lesion is avascular / iso-vascular compared to the background testicular tissue. Newer sonographic techniques such as tissue elastography have been developed as a qualitative and potentially quantitative adjunctive tool to provide additional information on tissue stiffness, aiming to further improve diagnostic confidence of benign versus malignant lesions under the assumption that the malignant lesions are “harder” than benign lesions. The purpose of this review is to provide an overview of the elastography techniques in assessing focal testicular lesions and their typical appearance on tissue elastography.

Elastography techniques

Strain elastography

There are two types of elastography techniques, commonly referred to as strain and shear wave elastography. Strain elastography measures tissue strain response when a compression force is applied to the tissue. The strain elastography technique was first used in clinical practice, using a propriety technique known as Real-Time Elastography (RTE, Hitachi Medical Corporation, Tokyo, Japan). RTE evaluates the relative strain response of the tissue from the region of interest
and the adjacent tissue to mechanical stress by analysing echo signals before and when a light compression is applied by the transducer. The strain response of the tissue is converted into an elastic nodulus image known as an elastogram and displayed as a colour coded map, superimposed on to the conventional B-mode image. The colour spectrum ranges from red to blue representing soft to hard tissue stiffness. Visual elasticity score (VES) which grades the elastographic appearance into 5 or 6-point scales, adapted from breast elastography (1), has been used to categorize stiffness of a testicular abnormality (2–4), Table 1. A VES cut-off of 3 may be used to classify testicular lesion stiffness into “hard” (VES >3) or “soft” (VES ≤ 3). Besides the visual map, a strain ratio (SR) between the abnormal testicular tissue and adjacent normal testicular parenchyma can be calculated as a semi-quantitative numerical index. It is only a semi-quantitative method as it allows assessment of relative tissue elasticity between the region of interest and background tissue rather than the absolute tissue elasticity.

Shearwave elastography

Shearwave elastography differs from strain elastography, as it is a quantitative method of assessing tissue elasticity by measuring the speed of acoustic radiation force impulse induced shearwave travelling in the tissue of interest (5). Shearwave is a type of mechanical wave whose propagation speed within the soft tissue can be measured. The shearwave velocities are measured by the scanner in m/s and they can be converted to Young’s modulus of elasticity (kPa) using the simple equation \(E=3\rho c^2\) (E: Young’s modulus, \(\rho\) = tissue density, \(c\)=shearwave speed). Today, almost all commercial scanners will provide values both in m/s and KPa. However, value in m/s is preferred reporting method because it is the quantity directly measured by the machine and the
above simple conversion to Young’s modulus E is accurate only if several premade assumptions are true (6).

Normal testes

The colour map of the strain elastogram from a normal testicle demonstrates a testicular central parenchymal green colour with blue edges which is surrounded by red bands (Figure 1). This is known as a 3-ring structure (7). Mean shearwave velocities of 0.76 m/s (95% CI: 0.75-0.78) from 130 normal testicles and 1.07 m/s from 20 patients have been reported by Pederson MR et al (8) and Macro J et al (9) respectively, both using VTIQ (Siemens Medical Solution, Mountain View, CA, USA). It has also been reported that the centre of the testis shows significantly lower shearwave velocity than the measurement obtained from the inferior and superior portion of the testis, through results obtained from 60 healthy testes using SuperSonic Imaging (Aixplorer, Paris, France) by Tottmann M et al (10). Therefore, one may want to consider using different normal values as reference when comparing the results of pathological testicular tissue or focal lesions in different areas. In addition to intra-testicular shearwave velocity variability, a study has demonstrated significant differences in shearwave velocities measured on different machines (11). Trottmann M et al showed that values obtained using SuperSonic Imaging were significantly higher than values measured using VTIQ in 58 healthy testes (12) which suggests shearwave velocity value are not interchangeable across different commercial systems, a similar limitation with the shear wave assessment of liver fibrosis.

Testicular neoplastic lesions
*Strain elastography*

Intra-testicular lesions can be subdivided into neoplasm malignant, neoplasm benign and non-neoplastic benign lesions. Testicular germ cell tumour account for over 95% of primary malignant testicular tumours and they can be further divided into non-seminomatous or seminoma germ cell tumours contributing to 60% and 40% of germ cell tumours respectively. Testicular seminomas are typically well defined, homogenously hypoechoic lesions with no features of local invasion of the tunica albuginea on B-mode US. On strain elastograms, a seminoma displays a uniformly stiff nature (Figure 2). The non-seminomatous germ cell tumours include embryonal cell carcinoma, teratoma, choriocarcinoma and mixed tumours containing more than one histological cell types (Figure 3). These tumours also display “hard” tissue stiffness but may have a less homogenous elastogram map due to the heterogenous cellular structures. Sertoli and Leydig cell tumours belong to gonadal stromal tumours which represent approximately 5% of all testicular neoplasms. The majority of Leydig cell tumours are benign neoplasms, only 10% of them have been reported to have a malignant potential on histological analysis (13). Gonadal stromal cell tumours are often small well-defined focal testicular lesions with reduced reflectivity and often show increased peripheral vascularity on colour Doppler imaging. Their tissue stiffness can vary from “mildly hard” to “hard” on strain elastography (14,15) (Figure 4). However, the vascularity pattern has been reported to differ from germ cell tumours showing significant shorter filling time than germ cell tumours (14) and persisting longer than the normal testicular parenchymal enhancement (16). Primary lymphoma of the testis is rare with reported incidence of 0.09 per 100,000, but lymphoma represents the most common testicular malignancy in older men (age>60 years) (17). In a cohort of 6 patients with
histological confirmation of primary testicular lymphoma, all lesions appear “hard”; 5/6 and 1/6, and showed an elasticity visual score of 5 and 4 respectively (Figure 5).

Testicular epidermoid and dermoid cysts are the most common benign neoplastic lesions and demonstrate “hard” elastographic properties (15,19,20). They are often uniformly “hard” on strain elastography with SR often exceeding 40. However, it is the often typical B-mode sonographic feature of an “onion ring” configuration of alternating hypo- and hyperechoic rings and the avascular nature on colour Doppler US that will differentiate the epidermoid cyst from malignant lesions (Figure 6). Testicular haemangioma is a benign rare testicular neoplasm, however seen in the same age group (2nd – 4th decades) where primary germ cell tumour predominates (Figure 7). Bernardo et al reported a case of capillary haemangioma which demonstrated relatively “soft” tissue stiffness on strain elastography with an elasticity visual score of 3 and strain ratio of 2.3 (21).

A handful of studies have investigated the ability of strain elastography to differentiate malignant neoplasms from benign neoplasms using VES and SR. Whilst “hard” elastograms, defined as VES of >3 demonstrates a high sensitivity of between 81.1% to 100% in differentiating malignant testicular neoplasm versus benign lesions, the specificity varies considerably among studies (25% to 98.2%) (2,4,15,19,22). In a cohort containing 30 testicular neoplasms, Pastore et al showed that SR provided adjunctive information of tumour characteristics to B-mode and colour Doppler, which aided the diagnosis of neoplasm origin of testicular abnormality (23). Pozza et al showed that higher SR values are found in malignant lesions versus benign lesions...
and neoplastic lesions versus non-neoplastic lesions in a cohort comprising 144 testicular lesions (4). However, there is limited diagnostic ability of SR alone in differentiating malignant from benign testicular with reported sensitivity of 59.4% and specificity of 66.6% using a cut-off value for SR of >1.41 for malignant lesions (4). The elasticity score derived from visual elastogram assessment has higher diagnostic accuracy (AUC: 0.804) compared to SR (AUC: 0.631) (4). However, conflicting results were reported by Konstantatou where SR was a significantly better assessment than elasticity visual score in diagnosing malignant lesions (15). In their cohort of 86 patients, a SR cut-off value of 3.21 was identified to differentiate benign from malignant lesions with associated AUROC of 0.722 (15). Currently, the role of SR in characterising testicular lesions is limited. The cut-off value for SR is system-specific and the value is dependent on the prevalence of aetiology of the testicular lesion in the study cohort. Whilst there is evidence supporting the role of strain elastography in differentiating benign versus malignant testicular lesion, strain elastography cannot differentiate benign neoplastic and malignant neoplastic lesions. Konstantatou showed that 14/17 benign neoplasms and 25/31 malignant neoplasms have a VES of 4 to 6 (15).

Shear Wave Elastography

In distinction to strain elastography which is a qualitative assessment of tissue stiffness, shear wave elastography provides a quantitative assessment by measuring the shear wave velocity. A preliminary study involving 15 testicular germ cell tumours showed significantly higher shear wave velocities in seminomas (mean 10.6 kPa, 4.5 kPa – 15.8 kPa) compared to non-seminomatous germ cell tumours (mean 47.0 kPa, range 29.0 – 65.5 kPa) (24). The authors postulated that the difference in shear wave velocities may be due to difference in histologic
features between the seminoma and non-seminoma; non-seminoma tumours consist of undifferentiated cells with prominent stromal component and some of which may contain cartilage or bony components (24). A cohort study by Rocher et al described multiparametric testicular ultrasound features of a 10 burnt out testicular tumours, where much higher tissue stiffness was demonstrated compared to the surrounding tissue (13 kPa versus 2kPa) using shear wave elastography (Supersonic Imaging, Aix-en-Provence, France) (25). The increased tissue stiffness could not distinguish burnt out tumour from residual tumour. The diagnosis of burnt out tumour may be suspected in the presence no or very poor enhancement of the tissue on contrast enhanced ultrasound. Currently there is only one study that have investigated the value of shear wave velocities in characterising neoplastic testicular lesions (24).

**Testicular non-neoplastic lesions**

*Strain elastography*

There are a variety of non-neoplastic intratesticular abnormalities which may present as focal intra-testicular abnormalities and cause a diagnostic conundrum. These indeterminate tumour like lesions may include a focal abscess, prominent rete testis, haematoma (3), segmental testicular infarction (26,27) venous infarction (28), focal orchitis, sarcoidosis (16). The majority of non-neoplastic testicular lesions should not require surgical management unlike the majority of neoplastic lesions where orchidectomy or testicular sparing surgery is essential. Therefore, the ability to differentiate these benign lesions from the malignant lesion on imaging is of paramount importance if orchidectomy is to be avoided.
Several cohort studies have tried to compare the tissue elasticity of non-neoplastic lesions with neoplastic lesions. In general, non-neoplastic lesions appear softer than neoplastic lesions. Konstantatou et al showed the median SR for non-neoplastic lesions was 1.95 compared to 4.64 and 3.78 for neoplastic malignant and neoplastic benign lesions (15). Aigner et al showed that 100% of orchitis (n=6), 75% of cysts (n=4) and 80% of partial testicular infarction (n=5) were “soft” (29). Several case reports and case series have reported strain elastography findings in non-neoplastic lesions such as segmental testicular infarction, testicular haematoma (3), abscess, atypical rete testis and cyst. Intra-testicular hematoma is often a consequence of trauma, although at presentation patients often have no recollection of injury (Figure 8). Yusuf et al evaluated a cohort of 16 hematomas with strain elastography and the strain ratio showed that 13/16 had an elasticity visual map score of 3 and the reported mean strain ratio was 1.19 (range 0.41 – 2.36) (3). Intra-testicular hematoma are often “soft” lesions and are in a sub-capsular position. Segmental testicular infarction is a rare cause of testicular pain and discomfort. The B-mode US and tissue elastography features depend on the timing of sonographic examination after the trauma. The area of abnormality may initially show “soft” characteristics due to the presence of swelling and increased water content. As it evolves, the area may demonstrate “hard” features on elastography colour map (Figure 9). Focal orchitis may also present with an indeterminate testicular lump. On B-mode US, it appears as an ill-defined abnormality with reduced echogenicity. There may be the ancillary findings such as hydrocele or epididymitis. The area of abnormality is often hypervascular on colour Doppler. On strain elastography, the abnormality initially appears as a “hard” lesion but as it evolves it becomes “softer” (Figure 10). Testicular torsion leads to an ischaemic insult to the testes if presenting acutely is a surgical emergency and sonographic investigation should not be attempted particularly if it causes delay in surgical
exploration. However, ultrasound has a role in differentiating delayed presentation of testicular torsion from other pathologies. By comparing the pathological evaluation of surgical specimen with pre-op testicular torsion at different time points and different degree of torsion, Herek et al showed that the testicular tissue stiffness gradually increased from 360 degree and 720-degree torsion and becoming softer at 1080 degree where necrosis occurs and damage to the testes becoming irreversible. They have also showed that the contralateral testis was also affected with increased tissue stiffness. Therefore, in cases of partial torsion where testicular viability and salvageability of the testis is in question, strain elastography of the testis may add additional benefit to the colour Doppler US examination (30). The non-neoplastic testicular lesion tends to be “softer” than their neoplastic counterparts. However, in a study by Konstantaou et al, 16/38 lesions have an elasticity visual score of 4 (n=4), 5 (n=7) and 6 (n=5) respectively, indicating there is significant overlap between the tissue stiffness of neoplastic and non-neoplastic lesions (15).

Shearwave elastography

Shearwave elasticity value of 1.7 kPa using SuperSonic Imagine (Aixplorer Provence, Paris, France) has been described in a case report of a segmental testicular infarction compared to elasticity value of 2.6 KPa in adjacent normal testicular parenchyma (31). A study of 248 patients including 130 normal testicular tissue, 99 patients with microlithiasis and 19 patients with testicular cancer showed that the mean shearwave velocity from three measurements taken from centre, upper and lower pole of the testis or testicular lesion are significantly higher in patients with testicular cancer (mean velocity of 1.92 m/s) compared to normal testicular tissue (0.76 m/s) and testicular microlithiasis (0.79 m/s) (8).
CONCLUSION

Strain or shearwave elastography allows further characterisation of tissue stiffness on ultrasound. It has been shown that neoplastic lesions are “harder” than non-neoplastic lesions, and malignant neoplastic lesions are “harder” than neoplastic benign lesions. However, significant overlap exists. Assessment of the B-mode US appearance, lesion vasculature with colour Doppler US and contrast enhanced ultrasound in addition to tissue elastography as part of a multiparametric ultrasound examination (32), is indispensable to increase diagnostic accuracy and confidence when placing indeterminant lesions under surveillance or subjecting the patient to surgery (16).
REFERENCES


Table 1. Visual elasticity scores (adapted from (15))

<table>
<thead>
<tr>
<th>Visual Elasticity Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The lesion is almost completely green but with some red spots</td>
</tr>
<tr>
<td>2</td>
<td>The entire lesion is homogenously green</td>
</tr>
<tr>
<td>3</td>
<td>The lesion is almost completely green but with some small blue spots</td>
</tr>
<tr>
<td>4</td>
<td>The lesion is green at the periphery with central blue area</td>
</tr>
<tr>
<td>5</td>
<td>The lesion is almost completely blue with central small green or red areas</td>
</tr>
<tr>
<td>6</td>
<td>The lesion is completely blue</td>
</tr>
</tbody>
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Figure Legends

Figure 1. (A) and (B) show RTE appearances of two patients with normal testes. The blue rim on the outside of the normal testis is referred to as a ‘boundary’ effect (arrow). It is thought to arise because the soft tissue is more ‘tethered’ at the testicular margin and so suffers less deformation when stress is applied. This is demonstrated in an exaggerated fashion in a long-standing atrophied testis (A).

Figure 2. (A) Incidental finding of a testicular seminoma in a 55-year old man. RTE and B-mode images demonstrate a small lesion with uniform low reflectivity and uniformly hard tissue stiffness as displayed by the monogenous “blue” colour within the lesion. (arrow) (B) A testicular seminoma in a 40-year-old man presented with left testicular pain. RTE and B-mode images demonstrate a large multiloculated mass with no evidence of tunica albuginea invasion (arrows). On strain elastography, the lesion demonstrates uniformly hard tissue stiffness.

Figure 3: A mixed non-seminomatous germ cell tumour in a 38-year-old man presented with two-week history of mild testicular discomfort. The B-mode US image demonstrates a large heterogenous mass with cystic areas (arrow). On the strain elastography image, the lesion demonstrates predominant hard tissue stiffness as shown in blue colour (arrow).

Figure 4: Three examples of Leydig cell tumours. (A) Incidental finding in a 65-year-old man. (B) 41-year old man presented with left testicular pain. (C) 37-year-old man was found to have a lump in his left testicle on physical examination. On B-mode US, all three Leydig cell tumours demonstrate typical appearances of small well-defined lesions with homogenous low reflectivity.
On tissue elastography (arrow), they can have variable appearance. They can be “hard” (A, strain ratio 10.48) or “mildly hard” (B and C).

**Figure 5:** A testicular lymphoma in an asymptomatic 30-year-old man. On the B-mode US, the lesion appears as a diffuse enlargement of the testis with decreased echogenicity of the entire testis. On tissue elastography, it appears as an almost uniformly hard lesion.

**Figure 6.** A testicular epidermoid in a 15-year-old boy with history of microlithiasis. On B-mode US, epidermoid has typical sonographic features of an “onion ring” configuration with alternating hyperechoic and hypoechoic rings (arrow). The strain elastography colour map shows that it is predominantly “hard”, with the blue colour distributed in over 80% of the abnormality.

**Figure 7.** A testicular capillary haemangioma in a 60-year-old man. The lesion appears relatively homogenous with slightly increased echogenicity (arrows). The tissue stiffness colour map suggests the lesion is a relatively “soft” lesion with a predominantly green colour mixed with some blue areas.

**Figure 8.** A testicular hematoma in a 30-year-old man presented with persistent right testicular pain. The lesion is oval shaped with low echogenicity located in the periphery of the testis (arrows). The strain elastography colour map shows a “soft” lesion as indicated by the green colour in over 80% of the lesion with scattered red colour.
**Figure 9.** Testicular segmental infarction in a 27-year-old man presented with 2-day history of testicular pain and discomfort. A) On the B-mode US, at presentation, the lesion appears as a peripheral wedge-shaped area with slightly reduced echogenicity (arrows). On tissue elastography colour map, the lesion appears has a “soft” lesion indicated by the predominant green colour (arrows). B) Two weeks later, the lesion has evolved, becoming “hard” shown as a predominant blue colour (arrows).

**Figure 10.** Focal orchitis in a 31-year-old man presented with a testicular lump. A) On the B-mode US, the lesion appears as an ill-defined area of reduced echogenicity (arrows) with associated features such as thickening of the epididymis and presence of a small hydrocele. On tissue elastography colour map, it appears initially as a “hard” lesion (arrows). B) Ten days later, the lesion is less obvious on the B-mode US (arrows) and becomes less “hard” (arrows) on follow-up imaging.
Figure 1A

(A) and (B) show RTE appearances of two patients with normal testes. The blue rim on the outside of the normal testis is referred to as a ‘boundary’ effect (arrow). It is thought to arise because the soft tissue is more ‘tethered’ at the testicular margin and so suffers less deformation when stress is applied. This is demonstrated in an exaggerated fashion in a long-standing atrophied testis (A).
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Figure 2A

(A) Incidental finding of a testicular seminoma in a 55-year-old man. RTE and B-mode images demonstrate a small lesion with uniform low reflectivity and uniformly hard tissue stiffness as displayed by the monogenous "blue" colour within the lesion.

(B) A testicular seminoma in a 40-year-old man presented with left testicular pain. RTE and B-mode images demonstrate a large multiloculated mass with no evidence of tunica albuginea invasion (arrows). On strain elastography, the lesion demonstrates uniformly hard tissue stiffness.
Figure 2B

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