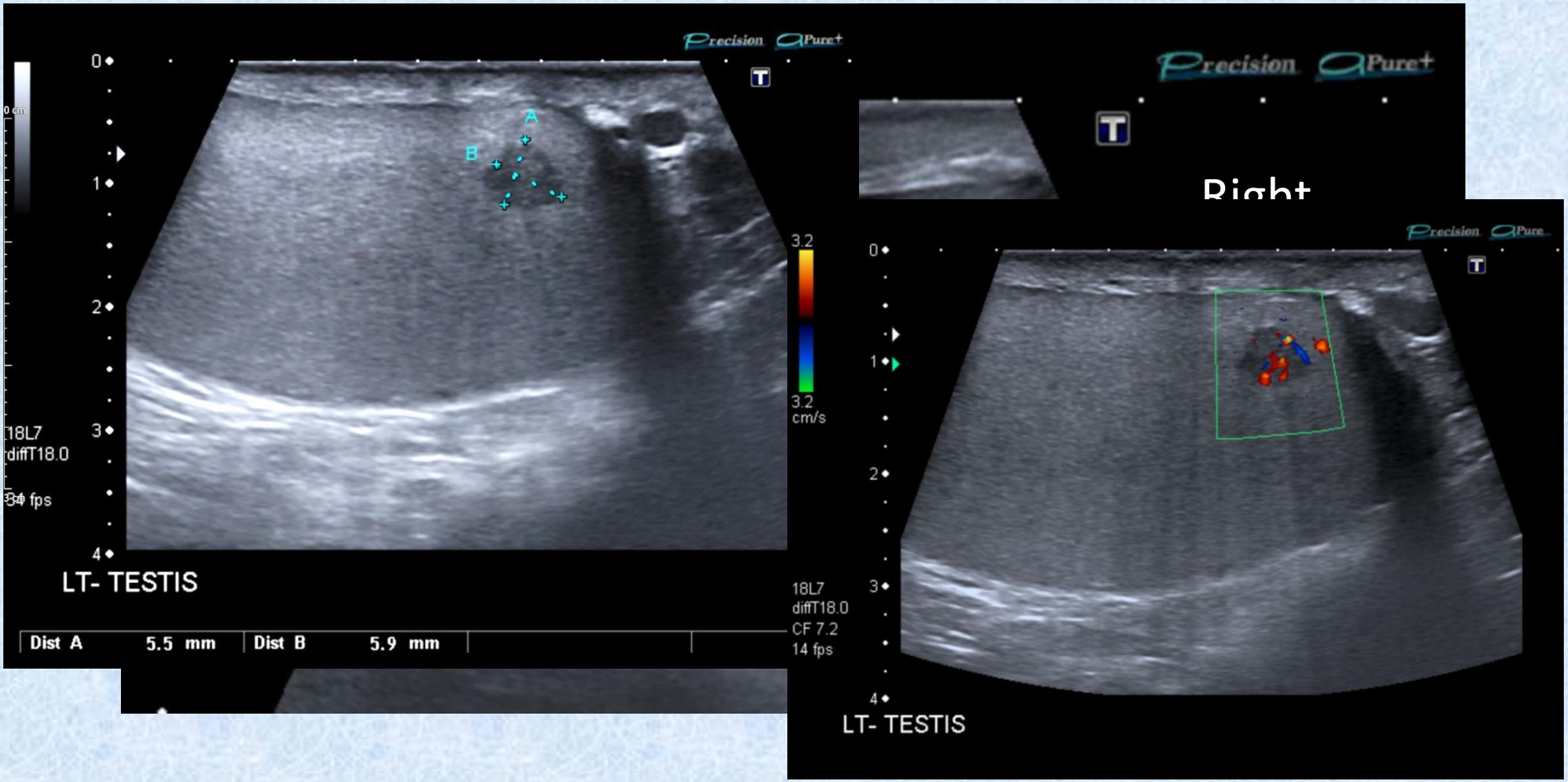
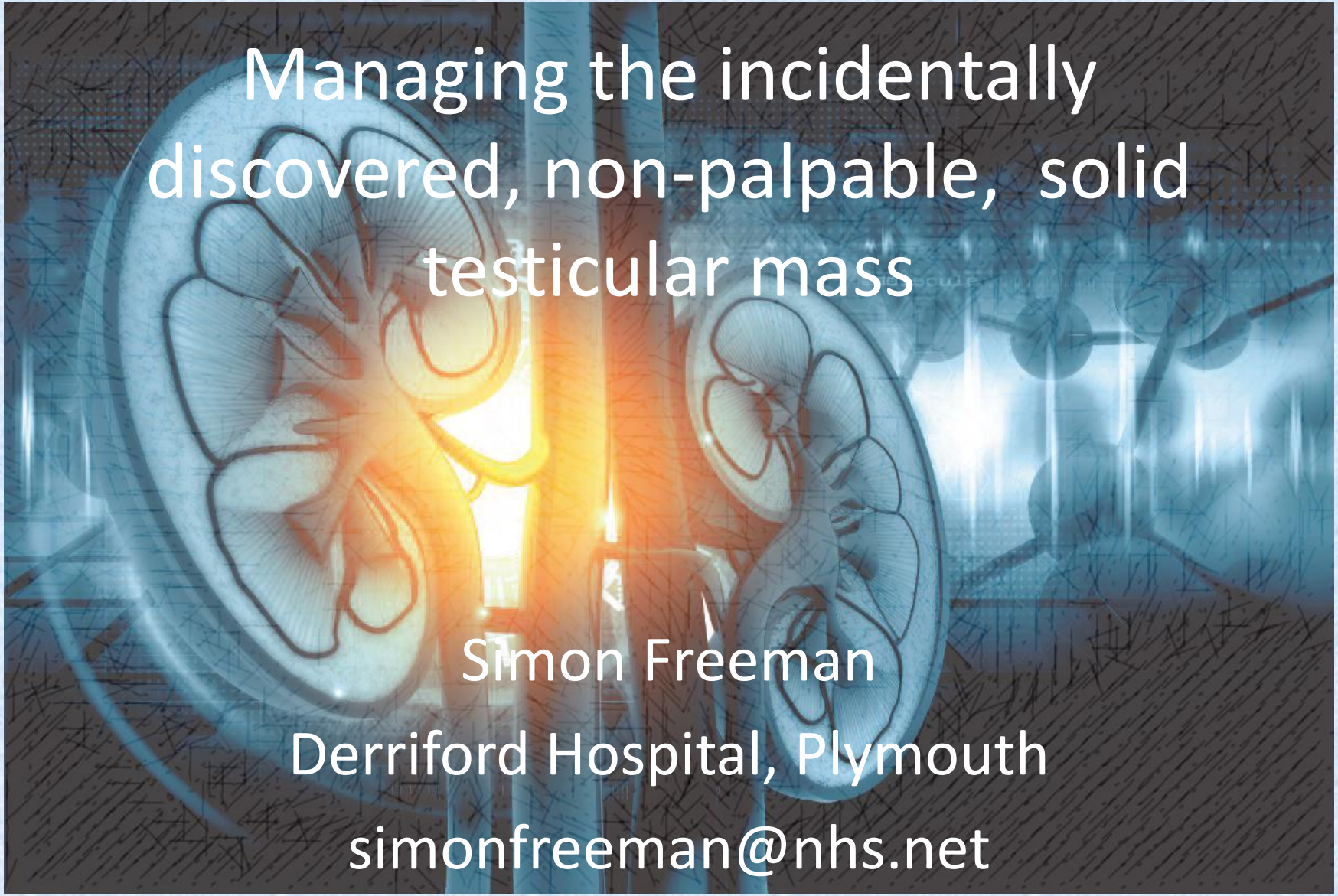


45 year old man. GP US referral.
Clinical details: Right scrotal discomfort for 6/12.
Normal scrotal examination.



Managing the incidentally discovered, non-palpable, solid testicular mass

Simon Freeman

Derriford Hospital, Plymouth

simonfreeman@nhs.net

WHO histological classification of testis tumours

Germ cell tumours	
Intratubular germ cell neoplasia, unclassified	9064/2[1]
Other types	
Tumours of one histological type (pure forms)	
Seminoma	9061/3
Seminoma with syncytiotrophoblastic cells	
Spermatocytic seminoma	9063/3
Spermatocytic seminoma with sarcoma	
Embryonal carcinoma	9070/3
Yolk sac tumour	9071/3
Trophoblastic tumours	
Choriocarcinoma	9100/3
Trophoblastic neoplasms other than choriocarcinoma	
Monophasic choriocarcinoma	
Placental site trophoblastic tumour	9104/1
Teratoma	9080/3
Dermoid cyst	9084/0
Monodermal teratoma	
Teratoma with somatic type malignancies	9084/3
Tumours of more than one histological type (mixed forms)	
Mixed embryonal carcinoma and teratoma	9081/3
Mixed teratoma and seminoma	9085/3
Choriocarcinoma and teratoma/embryonal carcinoma	9101/3
Others	
Sex cord/gonadal stromal tumours	
Pure forms	
Leydig cell tumour	8650/1
Malignant Leydig cell tumour	8650/3
Sertoli cell tumour	8640/1
Sertoli cell tumour lipid rich variant	8641/0
Sclerosing Sertoli cell tumour	
Large cell calcifying Sertoli cell tumour	8642/1
Malignant Sertoli cell tumour	8640/3
Granulosa cell tumour	8620/1
Adult type granulosa cell tumour	8620/1
Juvenile type granulosa cell tumour	8622/1
Tumours of the thecoma/fibroma group	
Thecoma	8600/0
Fibroma	8810/0
Sex cord/gonadal stromal tumour:	
Incompletely differentiated	8591/1
Sex cord/gonadal stromal tumours, mixed forms	8592/1
Malignant sex cord/gonadal stromal tumours	8590/3
Tumours containing both germ cell and sex cord/gonadal stromal elements	
Gonadoblastoma	9073/1
Germ cell-sex cord/gonadal stromal tumour, unclassified	
Miscellaneous tumours of the testis	
Carcinoid tumour	8240/3
Tumours of ovarian epithelial types	
Serous tumour of borderline malignancy	8442/1
Serous carcinoma	8441/3
Well differentiated endometrioid carcinoma	8380/3
Mucinous cystadenoma	8470/0
Mucinous cystadenocarcinoma	8470/3
Brenner tumour	9000/0
Nephroblastoma	8960/3
Paraganglioma	8680/1
Haematopoietic tumours	
Tumours of collecting ducts and rete	
Adenoma	8140/0
Carcinoma	8140/3
Tumours of paratesticular structures	
Adenomatoid tumour	9054/0
Malignant mesothelioma	9050/3
Benign mesothelioma	
Well differentiated papillary mesothelioma	9052/0
Cystic mesothelioma	9055/0
Adenocarcinoma of the epididymis	8140/3
Papillary cystadenoma of the epididymis	8450/0
Melanotic neuroectodermal tumour	9363/0
Desmoplastic small round cell tumour	8806/3
Mesenchymal tumours of the spermatic cord and testicular adnexae	
Secondary tumours of the testis	

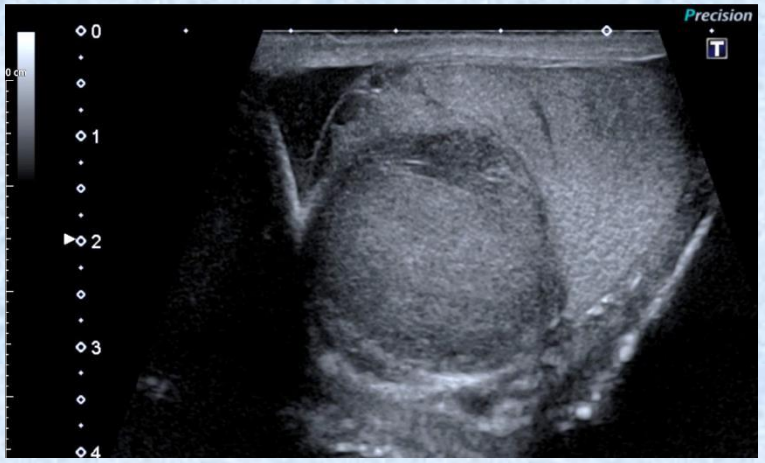
[1] Morphology code of the International Classification of Diseases for Oncology (ICD-O) [808] and the Systematized Nomenclature of Medicine (http://snomed.org). Behaviour is coded /0 for benign tumours, /2 for in situ carcinomas and grade III intraepithelial neoplasia, /3 for malignant tumours, and /1 for borderline or uncertain behaviour.

Testicular Tumour Classification

- Germ cell tumours (malignant)
  - Seminoma, Non-seminoma, Mixed
- Sex cord/gonadal stromal (10% malignant)
  - Leydig cell, Sertoli cell, Granulosa cell thecoma/fibroma, mixed GCT/stromal
- Miscellaneous
  - Carcinoid, epithelial, nephroblastoma, paraganglioma
- Tumours of collecting duct/rete testis
- Haemopoietic
- Secondary tumours
  - Lymphoma, other tumours rare

It used to be so easy!

- Patients referred for scrotal US usually had a palpable mass
- The most common palpable intra-testicular lesion aged 15-34 is a malignant GCT[1]
- “There are no reliable sonographic features that can distinguish a malignant from a focally benign lesion”[2]
- “Radical orchidectomy remains the definitive procedure for pathological diagnosis…”[3]
- “When in doubt cut it out” (properly!)



1. Woodward PJ. Radiogr Rev Publ Radiol Soc N Am Inc 2002;22:189. 2. Strauss. Eur Radiol 2000 3. Campbell’s Urology 8th Edition

Now it is much more difficult!

- Most patients don't have a palpable (testicular) mass
- Indications for scrotal US have increased[1]
  - Evaluation of acute scrotal symptoms
  - Evaluation of scrotal asymmetry or enlargement
  - Evaluation of scrotal masses
  - Evaluation of varicocoele
  - Evaluation of infertility
  - Evaluation of testicular ischaemia or torsion
  - Evaluation of suspected infections or inflammatory scrotal disease
  - Detection of occult primary tumours in individuals with metastatic germ cell tumours

1. Anthem Clinical UM Guideline 05.05.2016

Incidental testicular masses

- Incidental, asymptomatic and non-palpable testicular masses are now regularly encountered on US (0.8-7.4%)[1]
- US is highly accurate in differentiating testicular from non-testicular masses
- Conventional US has low accuracy in differentiating benign from malignant masses[2]

1. Rocher L. Eur Radiol 2015 1-11 2. Coret A. Br J Urol 1995;76:216 2006;98:1001

Non-palpable lesions are different

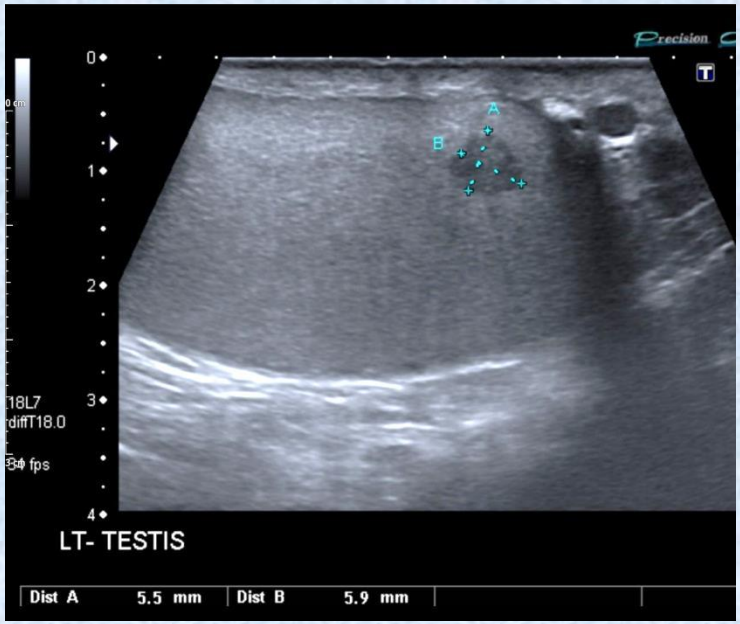
- Systematic review of the literature in 2010: 111 patients with non-palpable masses: 81 benign (73%)[1]
- Leydig cell tumours most common (45%)[2]
- Many radical orchidectomies performed for benign disease. Implications for fertility, endocrine function, preservation of body image

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

1. Giannarini G. European urology 2010;57
2. Brunocilla E Anticancer Res 33:5205

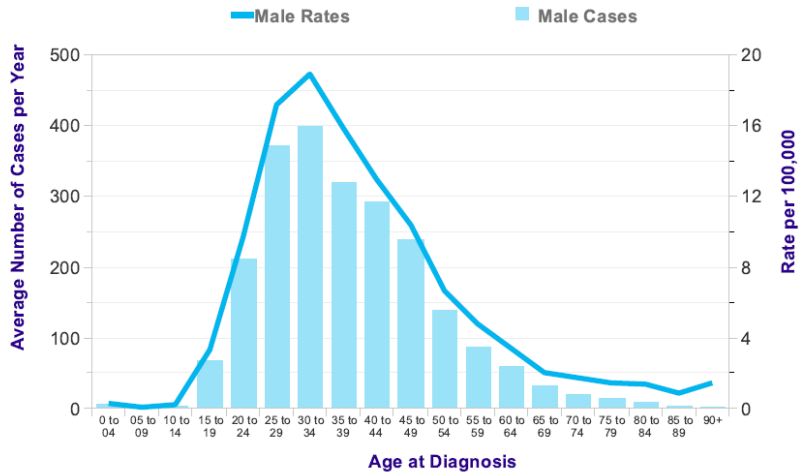
Reducing the number of (unnecessary) radical orchidectomies

- Pre-test probability
- Clinical history
- Greyscale features
- Multiparametric approach
  - CEUS
  - Elastography
- US surveillance
- Testis preserving surgery



Pre-test probability

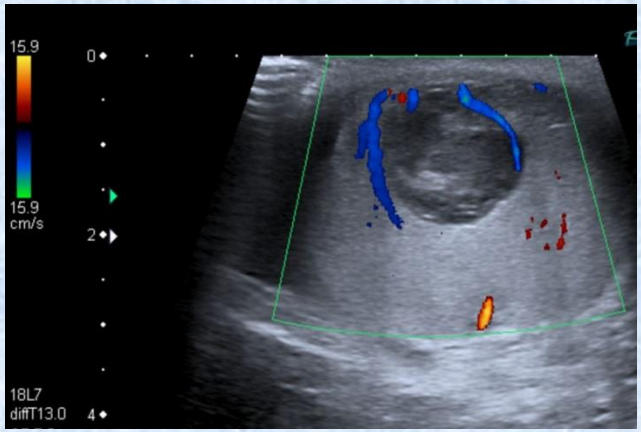
- Risk factors for TGCT
  - Age
  - Cryptorchidism (risk↑ x4 - 8)
  - Contralateral tumour (risk↑ x12.4 - 27.5)
  - Family history – first degree relative (risk↑ x4 - 8)
- Risk for Leydig cell hyperplasia
  - Kleinfelter's syndrome.
  - Consider karyotyping if small testis and infertility



Rustom P. BJUI 2009;104:1329

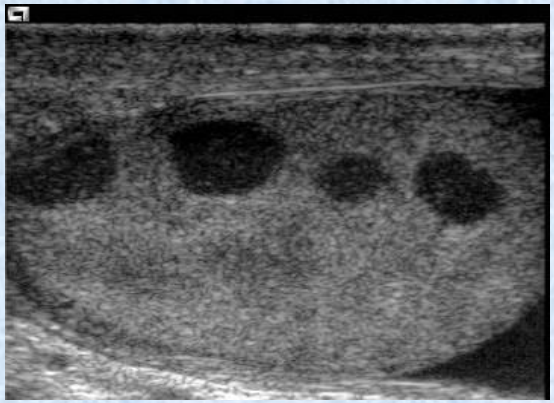
Clinical History

- Trauma
- Infection (focal orchitis or abscess)
- Granulomatous disease (Sarcoid/TB)
- Malignancy (esp. lymphoma)
- Endocrine disease (CAH)
- Features of hormone secretion (Gynaecomastia)

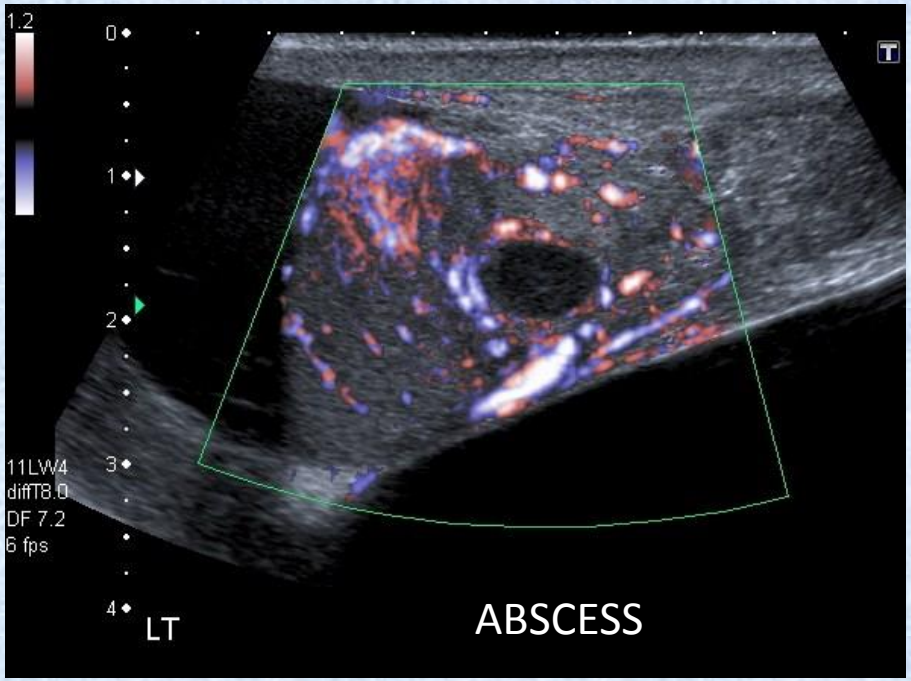


Trauma

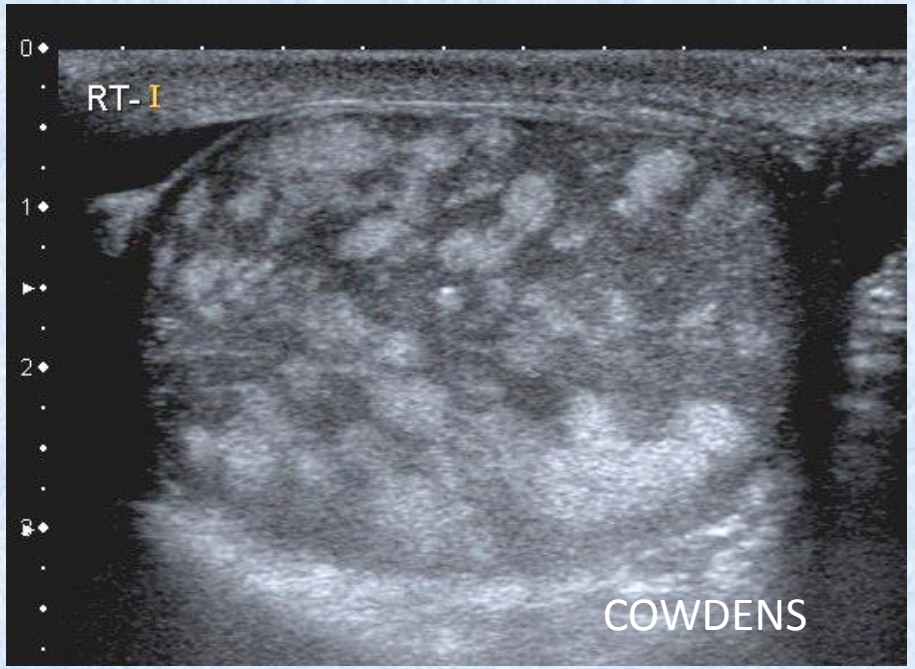
Sarcoidosis



CAH



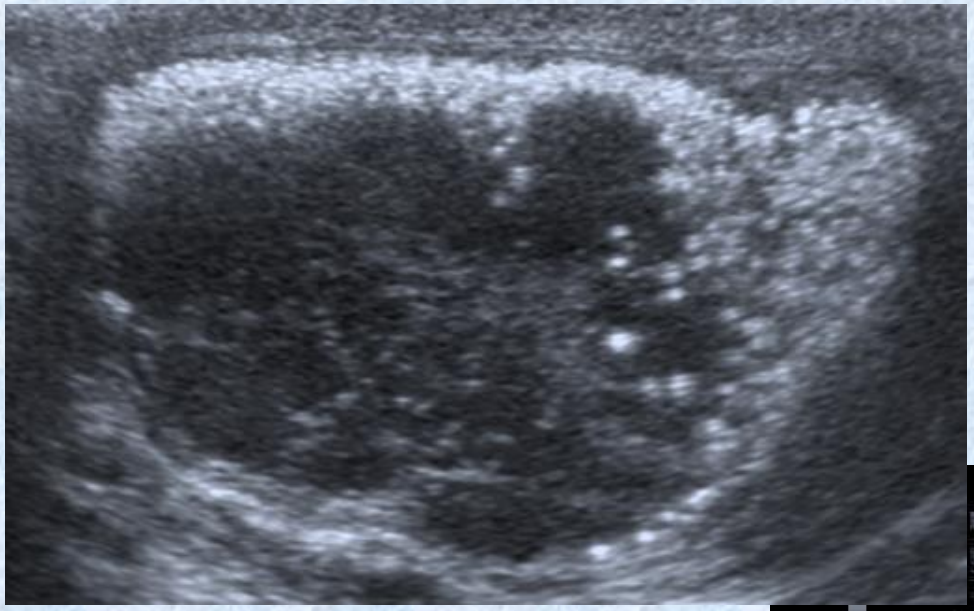
ABSCESS

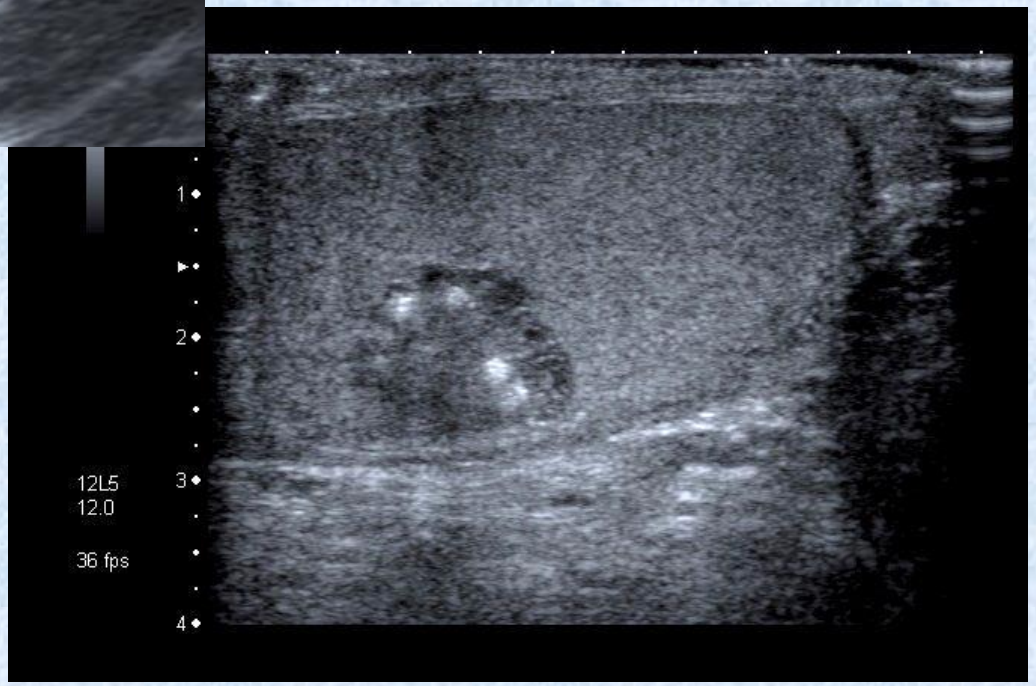


COWDENS


SEX CORD STROMAL TUMOUR

Additional findings

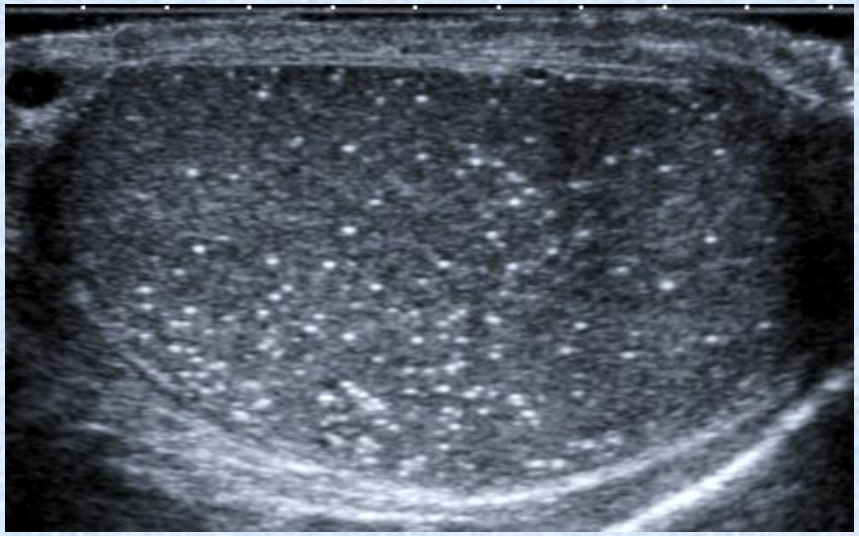




- TML
- Intra-tumoural macrocalcifications

What is the significance of TML?

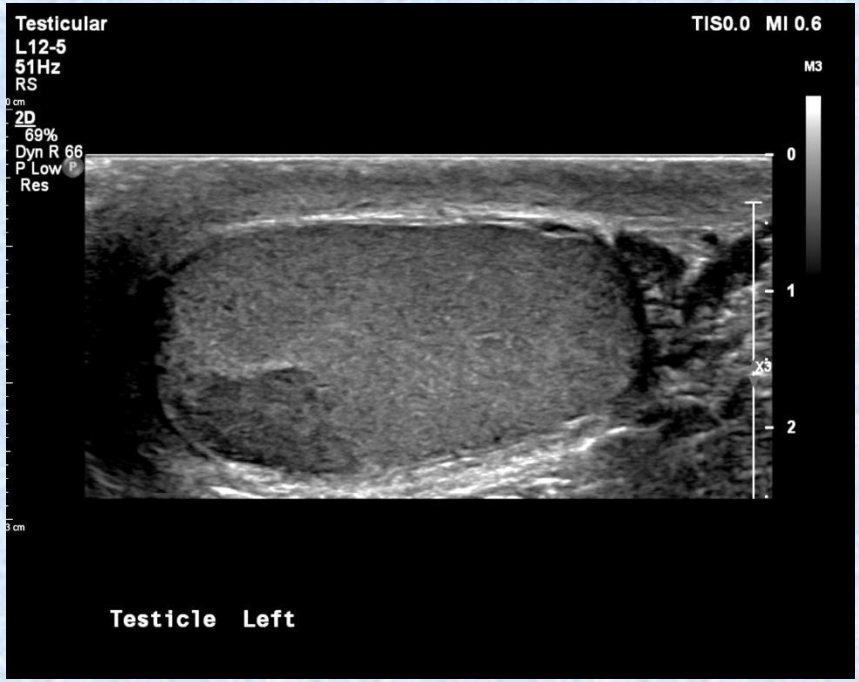
- Prevalence 2.7% in adult males[1]
- Association with GCT does not prove cause
- Risk in patients without a second risk factor for TGCT is low[2,3]
- However: TML in association with an hypoechogenic nodule suggests GCT (esp. seminoma)[4]



1. Mullooly C. Int J STD AIDS 2012;23:620 2. Richenberg J Eur Radiol 2012;22:2540 3. Tan MH. Nature Reviews Urology 2011;8:153 4. Rocher L. Eur Radiol. 2015;1-11

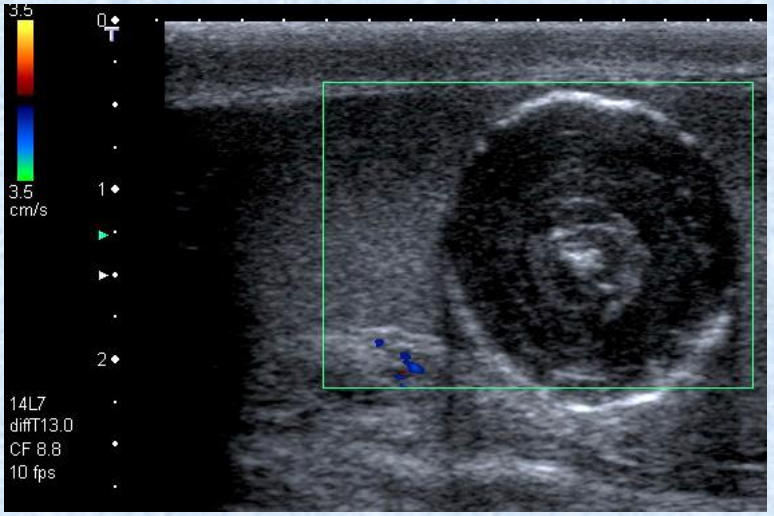
US: Greyscale features

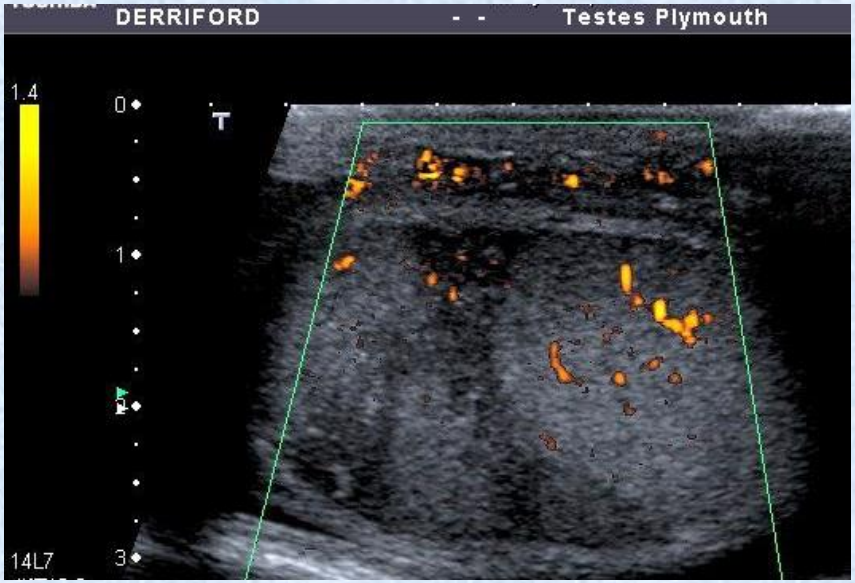
Benign patterns	Malignant patterns
< 0.5 cm	> 1cm
Well defined	Irregular margins/ill-defined
Simple cyst	Heterogeneous
Onion skin pattern	Hypoechoic areas
Normal parenchyma	TML
Hyperechogenic	Macrocalcifications

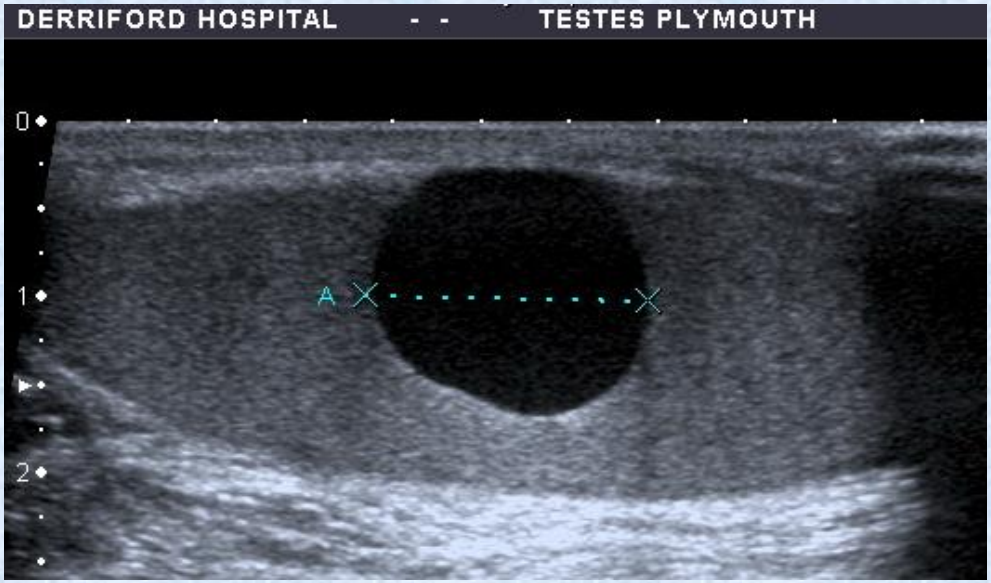


Adapted from Rocher L. Eur Radiol 2015

Grey scale features: benign patterns

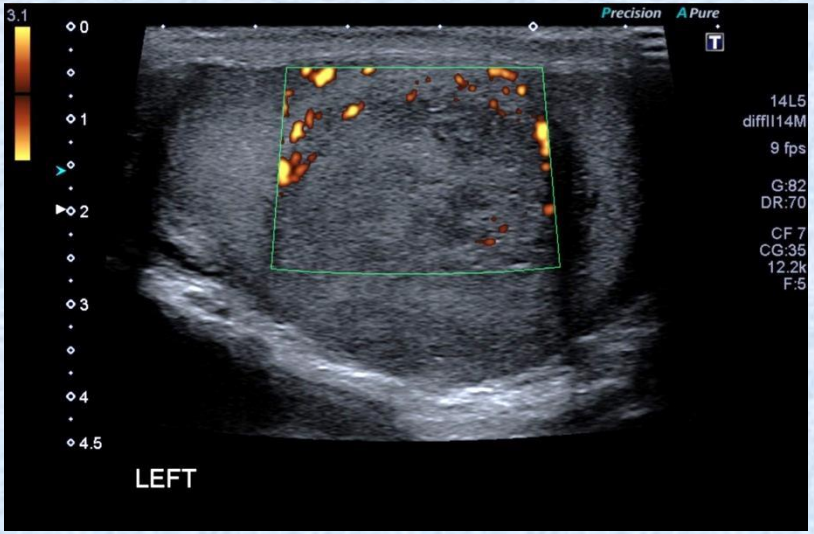






Colour Doppler

- 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]

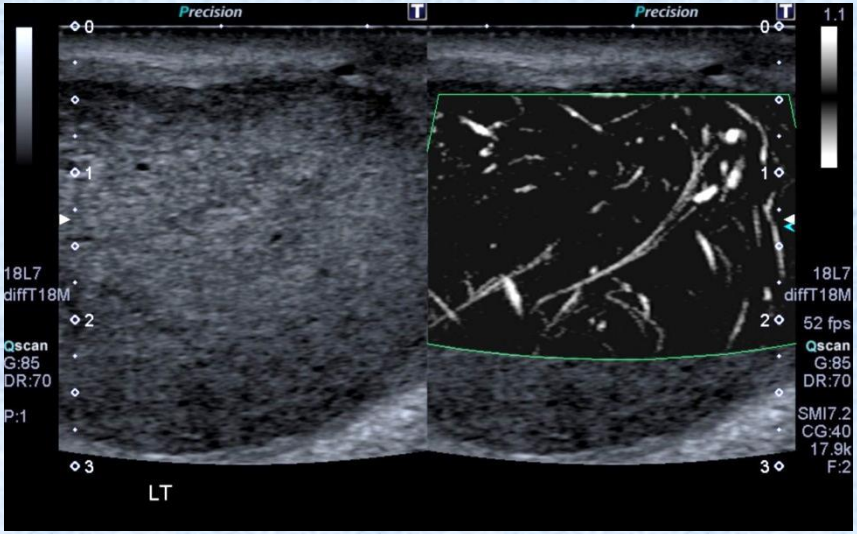


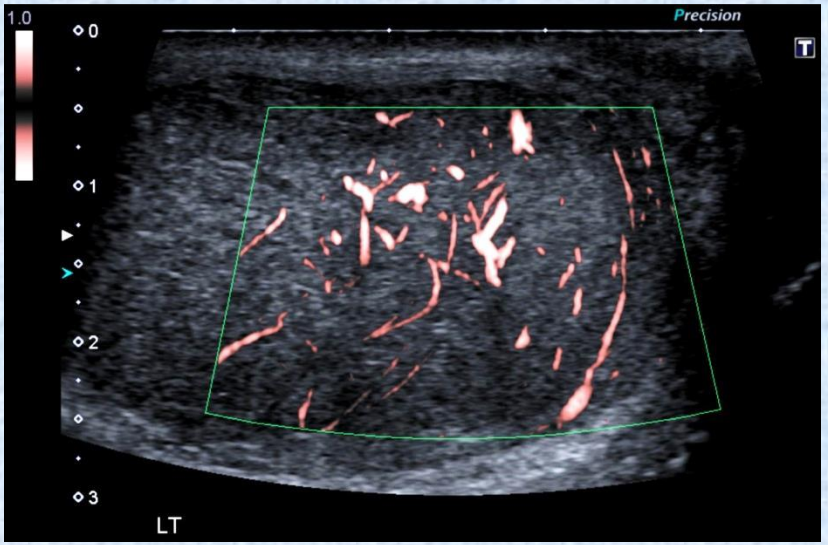
28 yr. old man Hx: Malignant teratoma

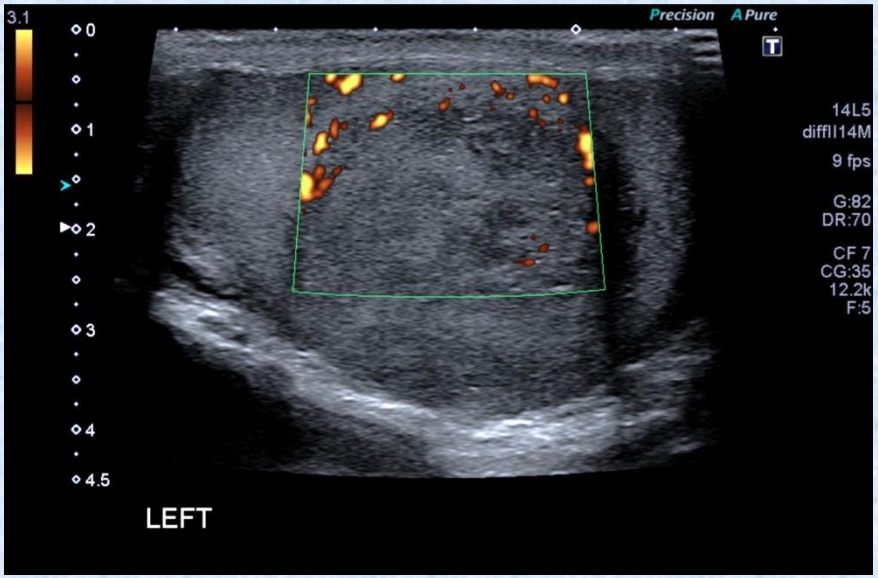
1. Shah A. Clin Radiol 2010;65:496 2. Horstman WG. Radiology 1992;185:733

New Doppler techniques may help

- SMI™ Superb Microvascular Imaging
- Can demonstrate very low velocity flow (normally removed by filters)






3.1
Precision
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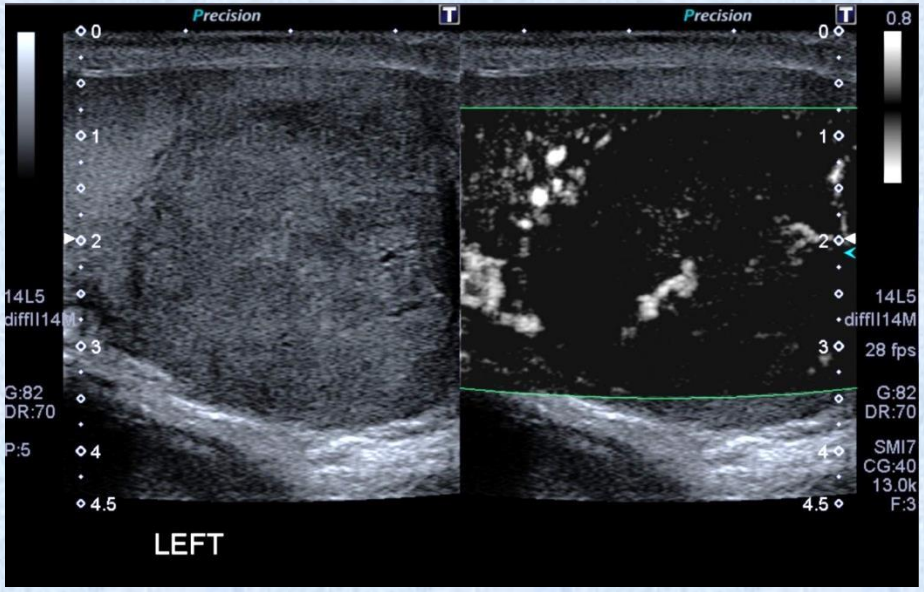
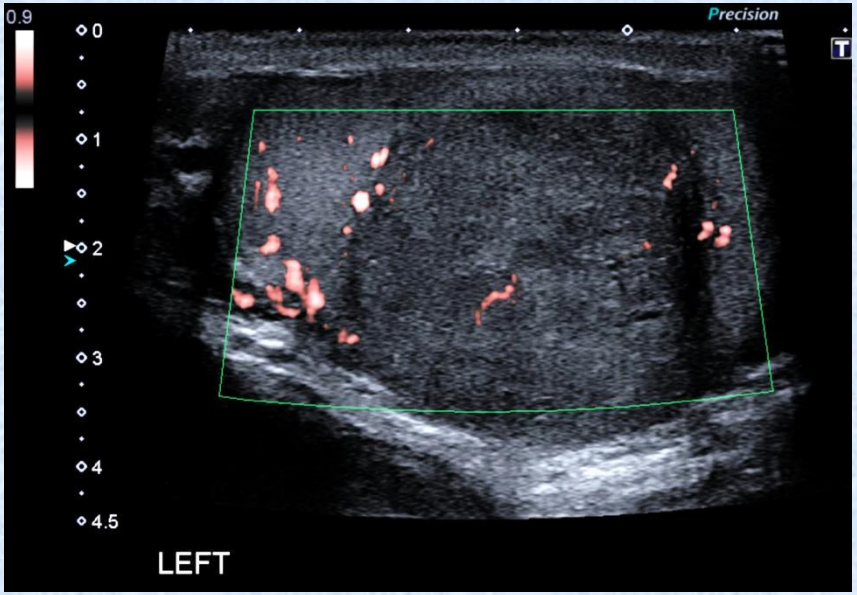
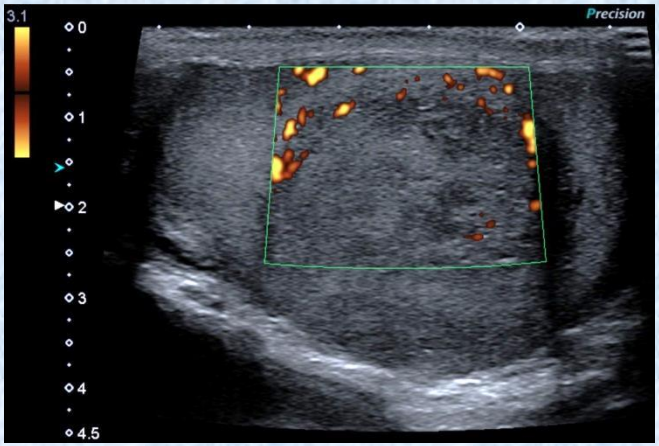
diffII14M
9 fps
G:82
DR:70
CF 7
CG:35
12.2k
F:5
LEFT

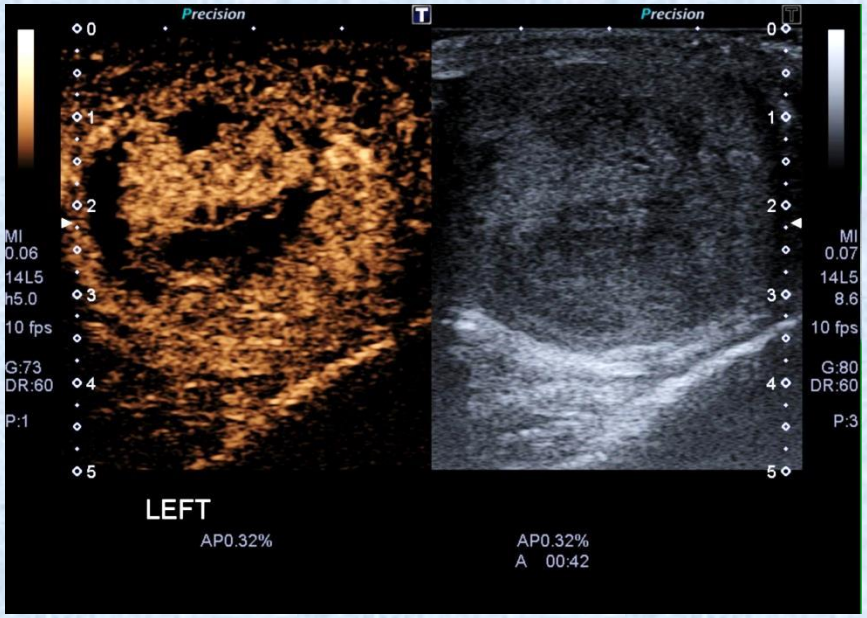

Precision
Precision
0.8
14L5
diffII14M
28 fps
G:82
DR:70
SMI7
CG:40
13.0k
F:3
LEFT


0.9
Precision
LEFT

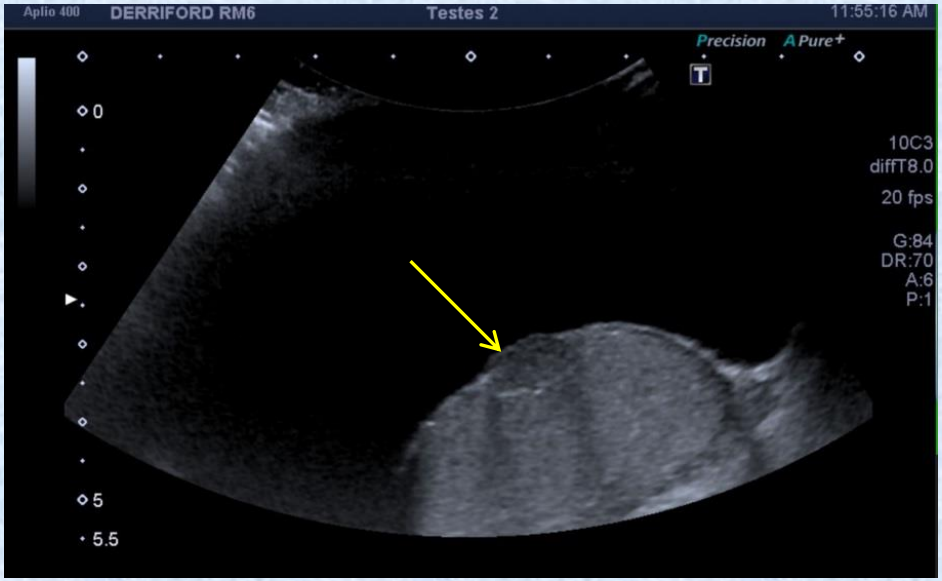
Best of all: CEUS

- 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. Lock G. Urology 2011;77 2. Piscaglia F. Ultraschall in Med 2011


Aplio 400
DERRIFORD RM6
Testes 2
11:55:16 AM
Precision
A Pure+
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20 fps
G:84
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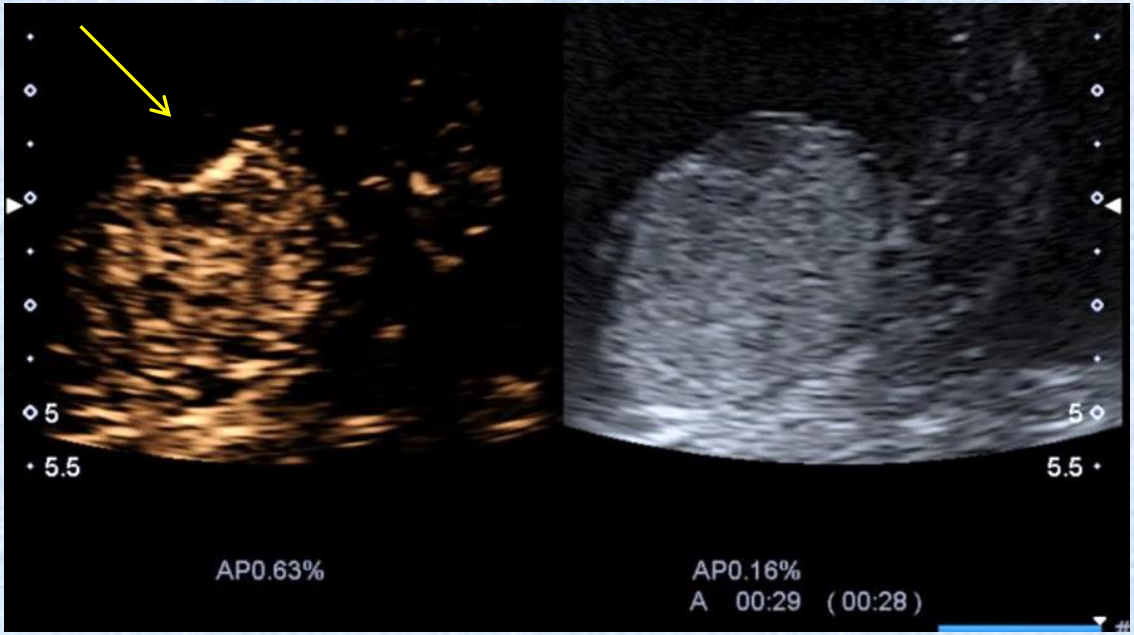

5
5.5
5
5.5
AP0.63%
AP0.16%
A 00:29 (00:28)

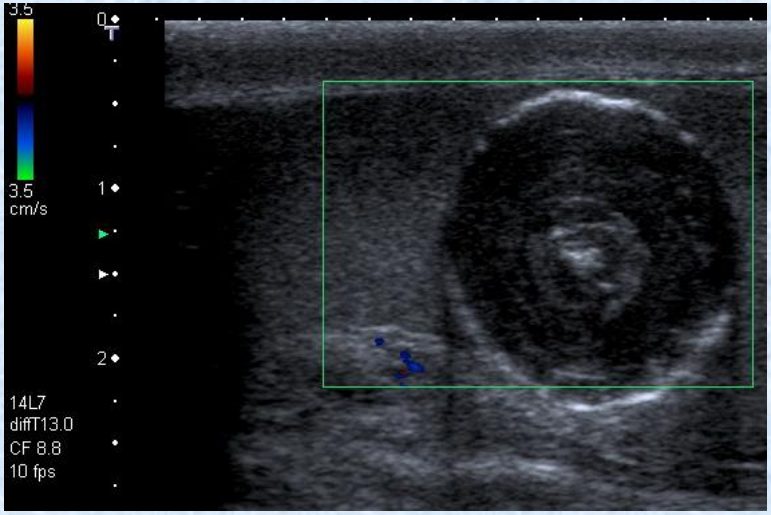
Epidermoid cysts


CASE SERIES

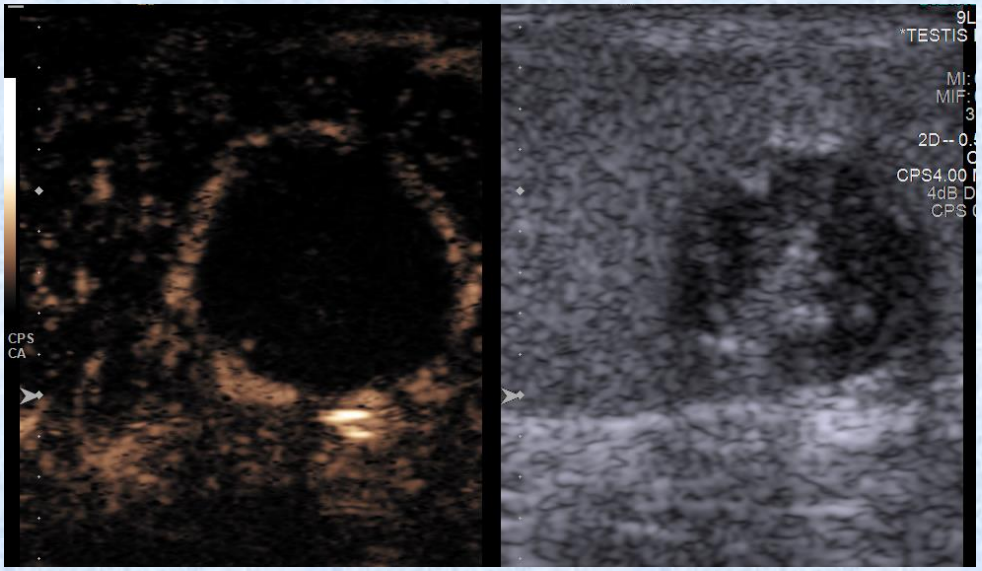
Features of Testicular Epidermoid Cysts on Contrast-Enhanced Sonography and Real-time Tissue Elastography

Ketul Patel, FRCR, Maria E. Sellars, MBBS, FRCR, Jane L. Clarke, MSc, Paul S. Sidhu, BSC, MRCP, FRCR

Patel K. J Ultrasound Med 2012;31



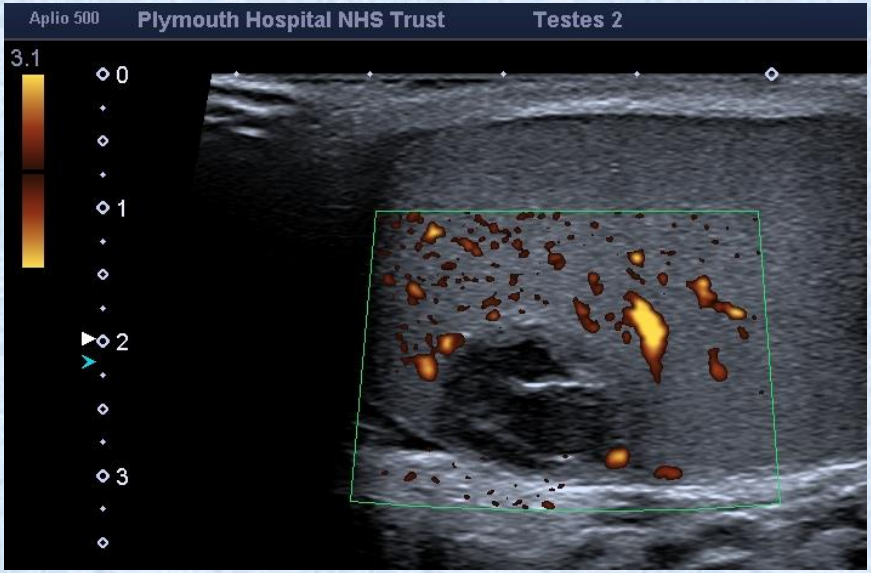
- Four grey scale patterns recognised.[1] Always avascular on Colour Doppler
- CEUS increases confidence – no internal vascularity, rim enhancement in some cases[2]

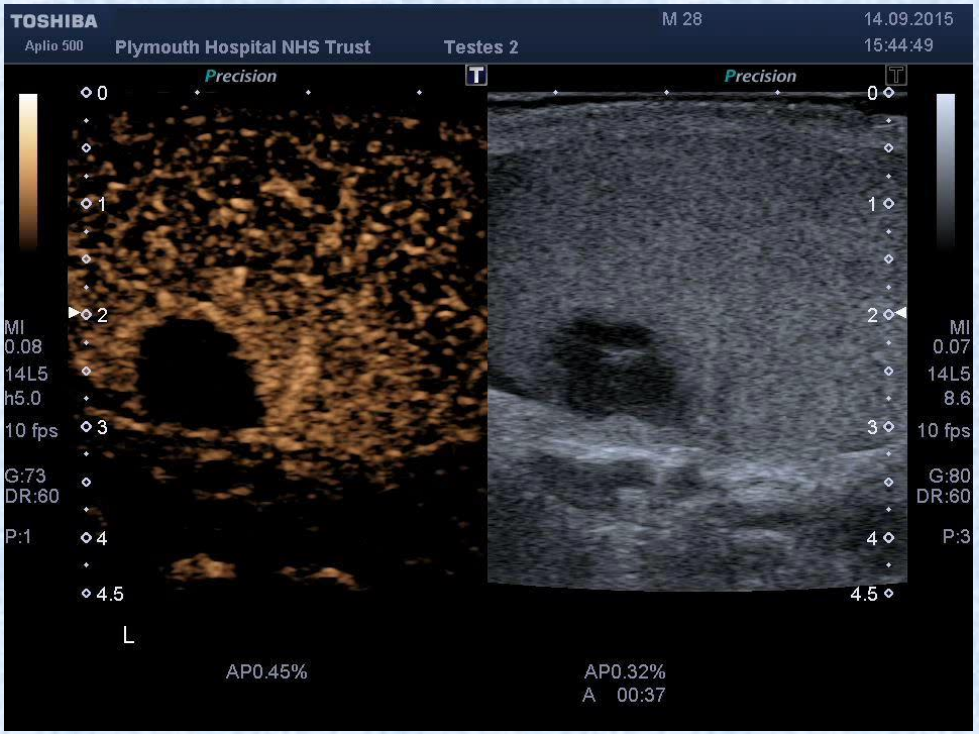


Courtesy Prof P Sidhu.

1. Atchley JTM Clinical Radiology 2000;22 2. Patel K. J Ultrasound Med 2012;31

Minor Trauma
29 yrs. old





Can CEUS differentiate benign from malignant?

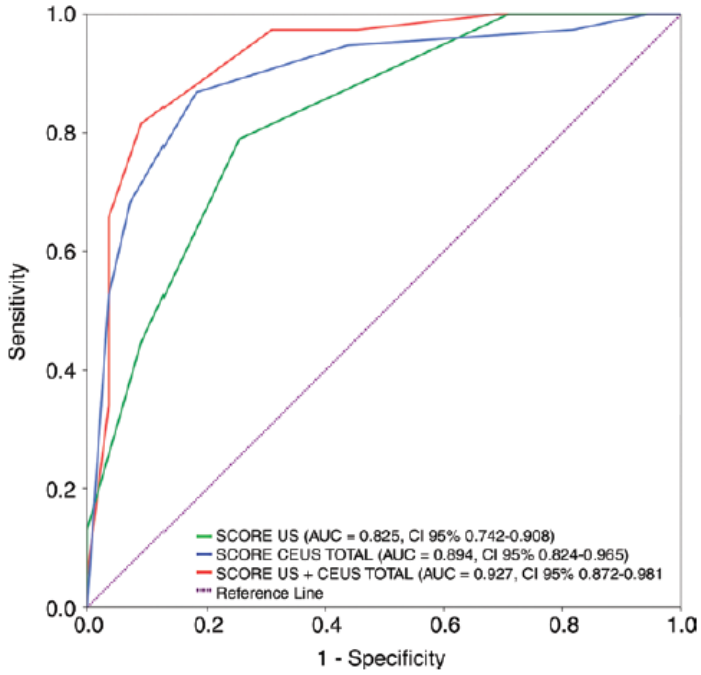


Figure 5: Diagnostic accuracy in identification of malignant tumors. ROC curves of US score (green), total contrast-enhanced US *(CEUS)* score (qualitative and quantitative, blue), and their combination (red). Combination of US and qualitative and quantitative contrast-enhanced US (time to washout and time to peak) scores showed best performance (A_z = 0.927; 95% CI = 0.872, 0.981; $P < .001$).

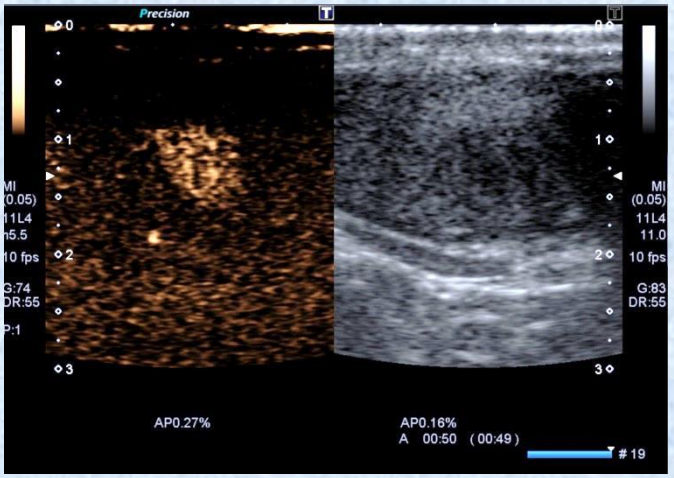
Isidori, Radiology 2014

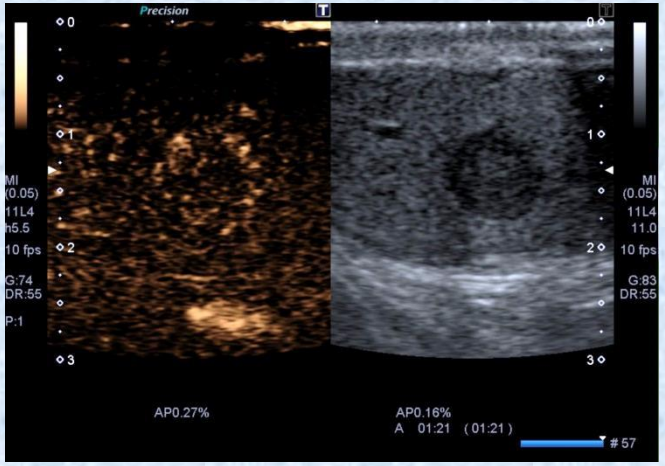
- 115 non palpable lesions
  - 38% malignant tumours
  - 37% benign tumours
  - 25% non-neoplastic
- Combined grey-scale US features with CEUS
- Overall sensitivity 82%, specificity 91% for differentiation of benign vs. malignant (area under ROC curve 0.927)

Isidori AM. et al. *Radiology* 273.2 (2014): 606-618.

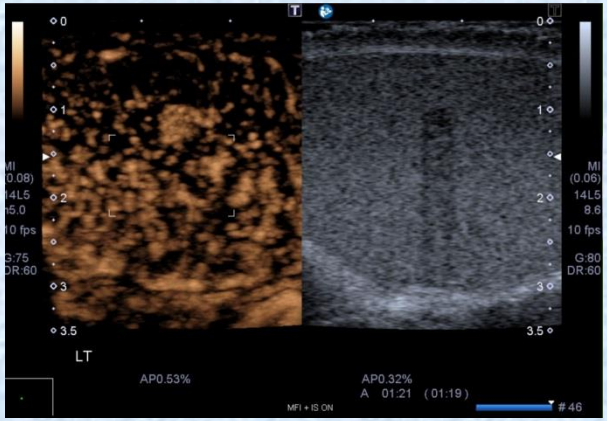
TGCT vs Sex cord stromal tumours

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





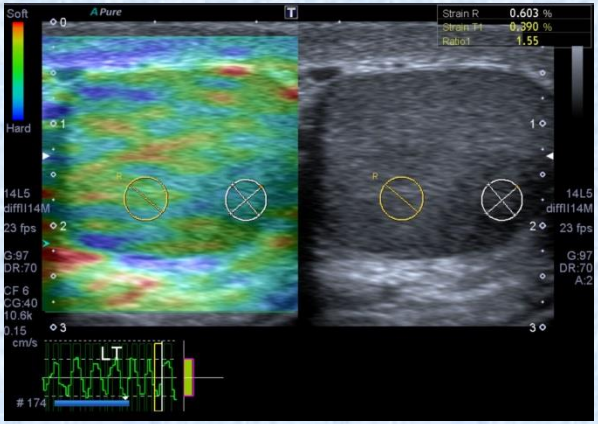
Seminoma



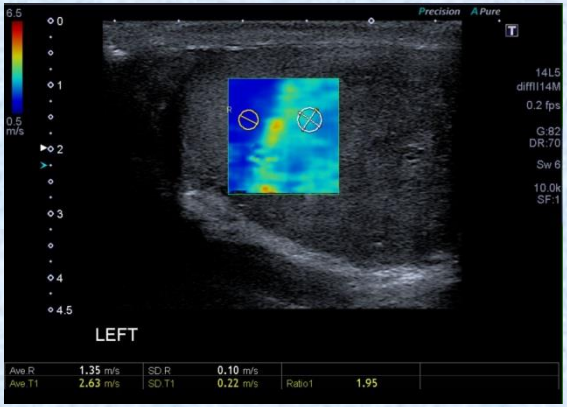
Sertoli cell tumour

Sonoelastography

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



SE - Seminoma

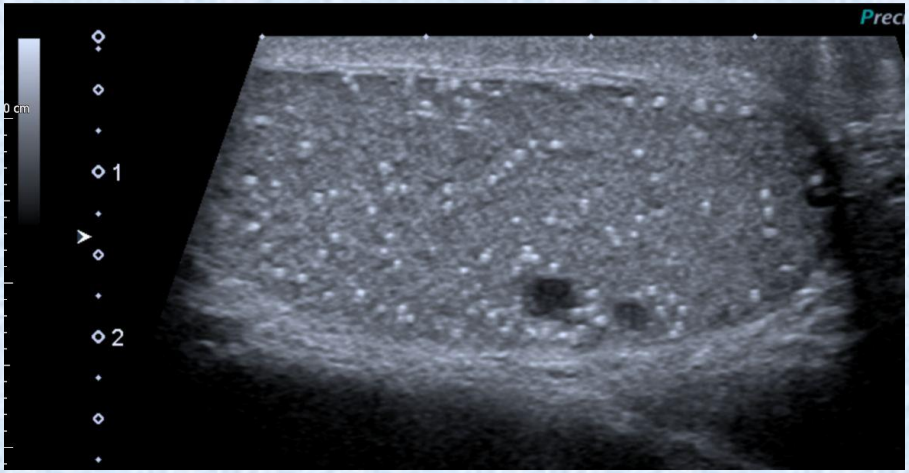


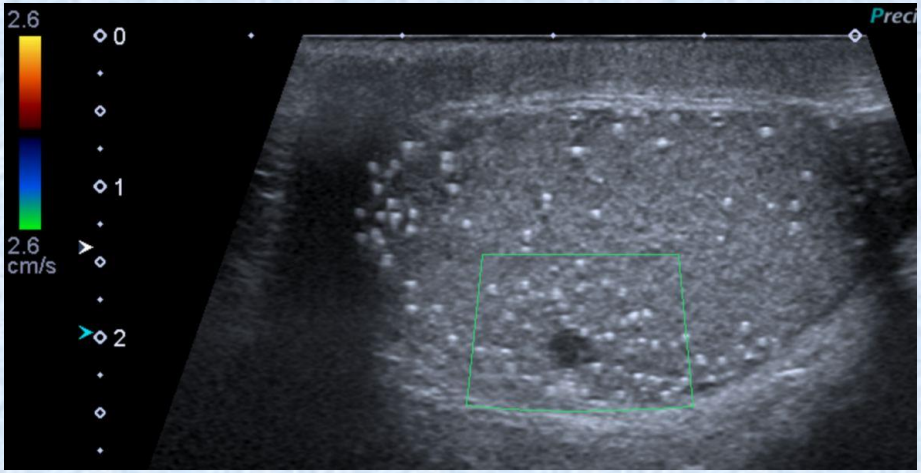
SWE – Malignant teratoma

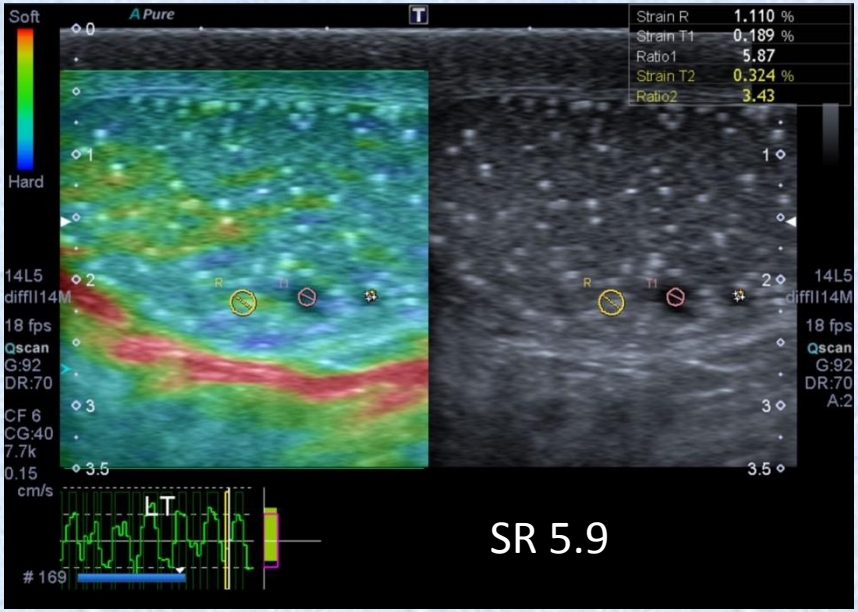
1. Aigner F. Radiology 2012;263:584 2. Goddi A. Eur Radiol 2012;22:721 3. Grasso M. Arch Int Urol Androl. 2010;82:160 4. Pastore AL. Cancer Imaging 2014;14:29

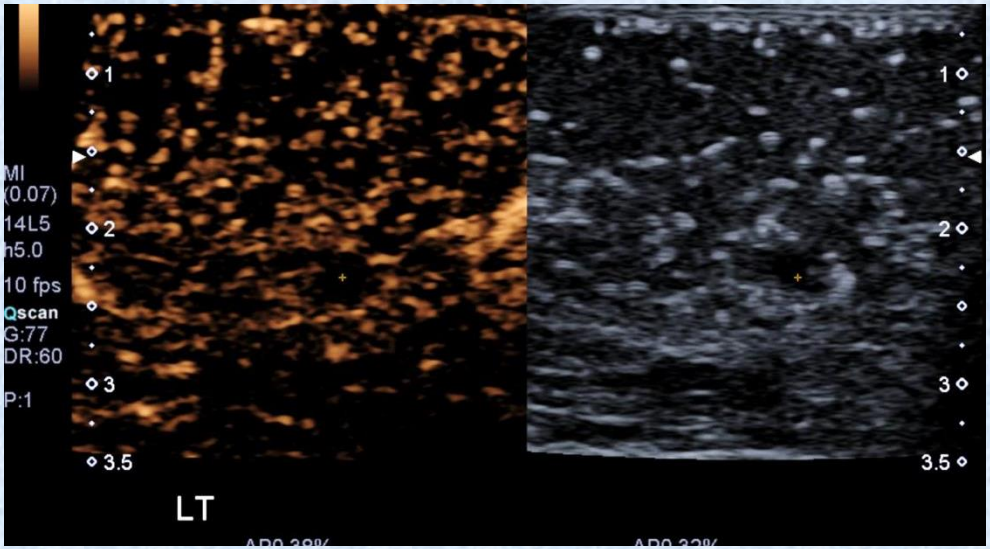
“Multiparametric ultrasound”

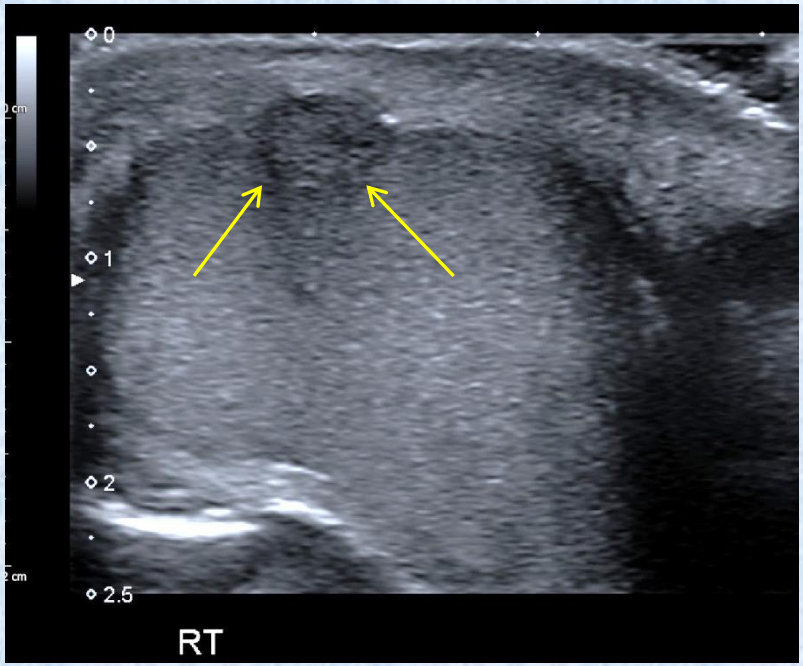
Grey-scale, Doppler, CEUS and elastography may be able to differentiate benign from malignant non-palpable testicular lesions with acceptable accuracy

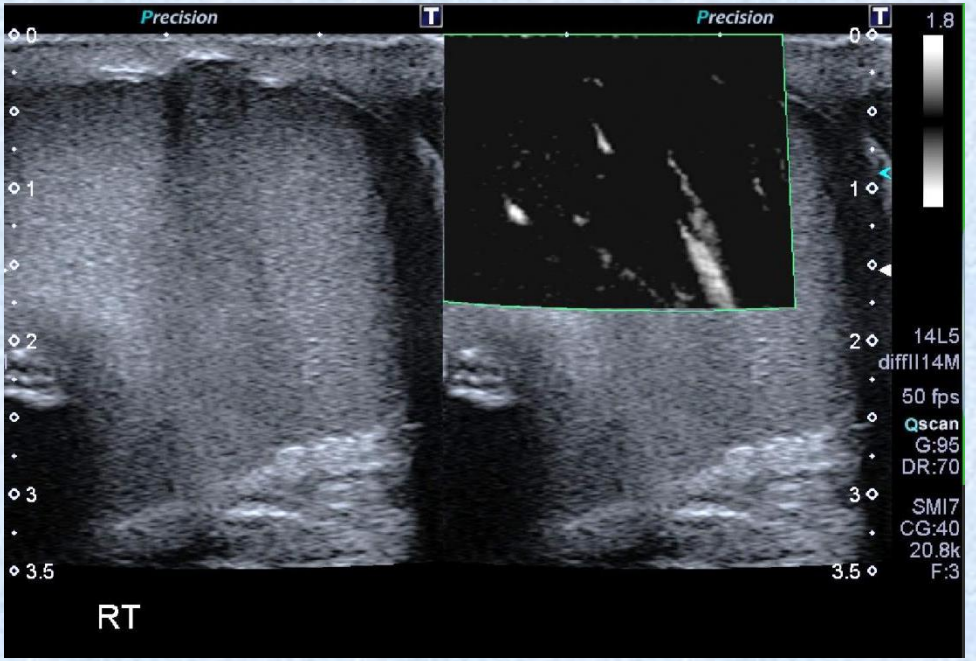


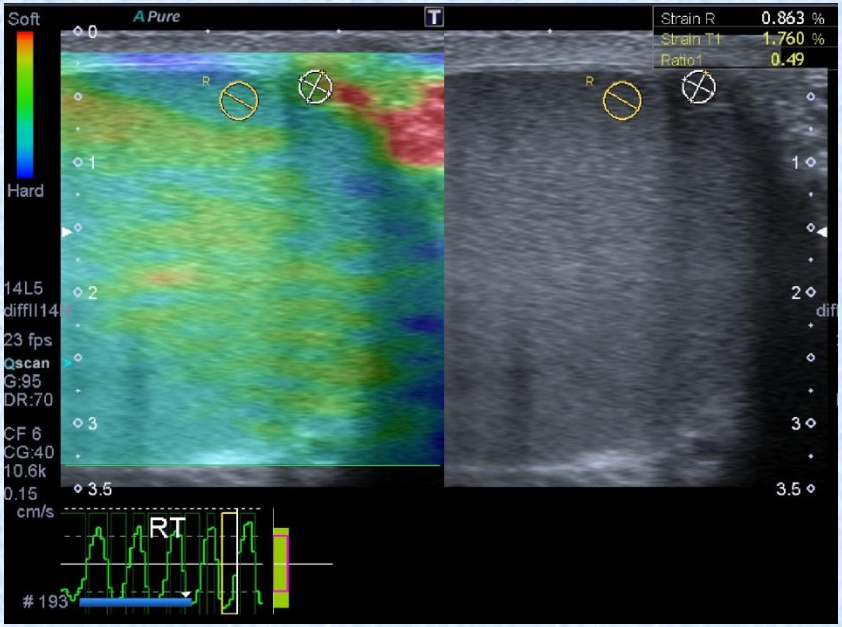


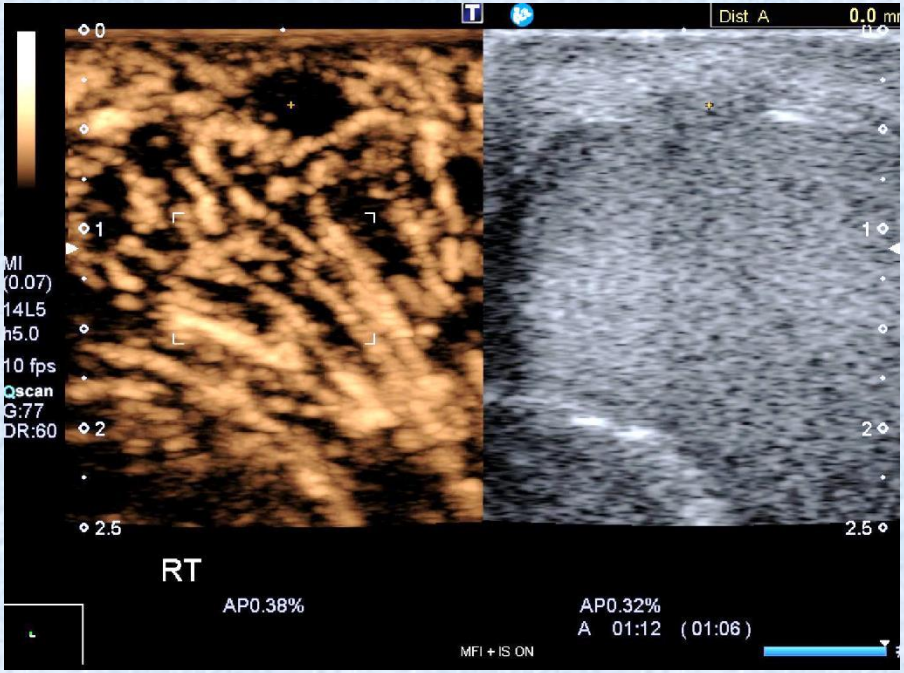

Soft
Hard
A Pure
Strain R 1.110 %
Strain T1 0,189 %
Ratio1 5.87
Strain T2 0.324 %
Ratio2 3.43
14L5
diffII14M
18 fps
Qscan
G:92
DR:70
CF 6
CG:40
7.7k
0.15
cm/s
LT
169
SR 5.9


MI
(0.07)
14L5
h5.0
10 fps
Qscan
G:77
DR:60
P:1
LT


RT


Precision
Precision
RT


Soft
Hard
A Pure
Strain R 0.863 %
Strain T1 1.760 %
Ratio1 0.49
RT


Dist A
RT
AP0.38%
AP0.32%
A 01:12 (01:06)
MFI + IS ON

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[1]
  - 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[1]
- No prospective studies on radical orchidectomy vs. TSS

1. Brunocilla E. Anticancer Research 2013;33:5205

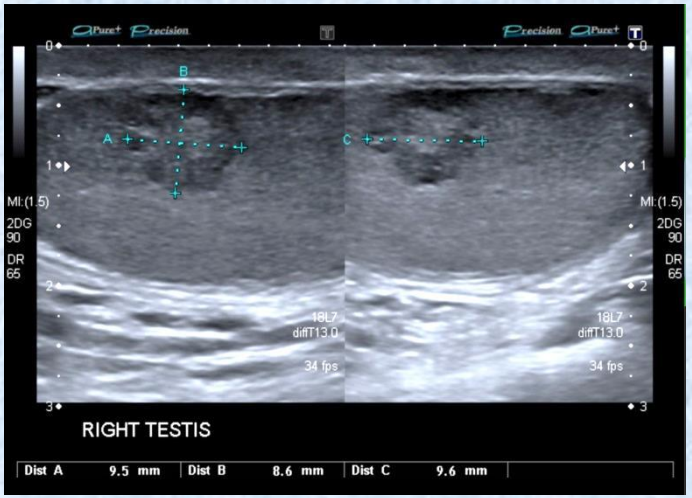
What if ultrasound is wrong!

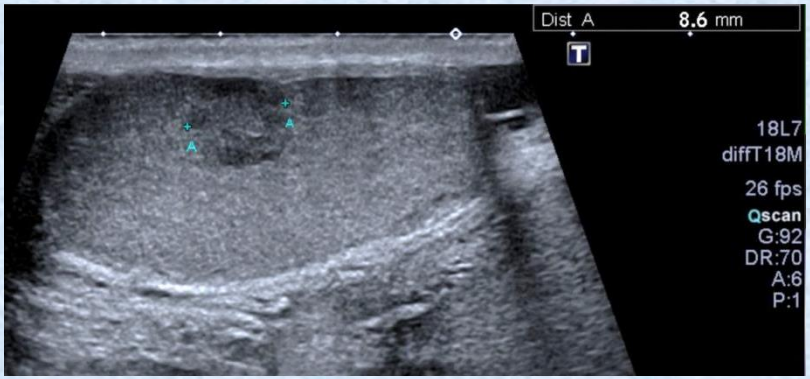
- It doesn't matter if TSS is performed (by mistake) for small TGCTs
  - TSS for malignant GCT
    - German testicular cancer study group:[1] 101 cases of GCT treated by TSS. Radiotherapy (18Gy) for all patients with TIN on biopsy.
    - Cancer specific survival 100/101. Local Recurrence 6/101 (4 refused radiotherapy)
  - "TSS is a safe option and should be considered for small GCTs"[2]

1. Heidenreich A. J Urol 2001;166:2161 2. Giannarini G Eur Urol 2010;57:780

US Surveillance for small masses?

- If mp US suggests a benign lesion <10mm[1]
- All lesions < 5mm? [2]
- Tumour marker negative
- US every 3/12 for 1 year then annual (for how long - ? 3 years)



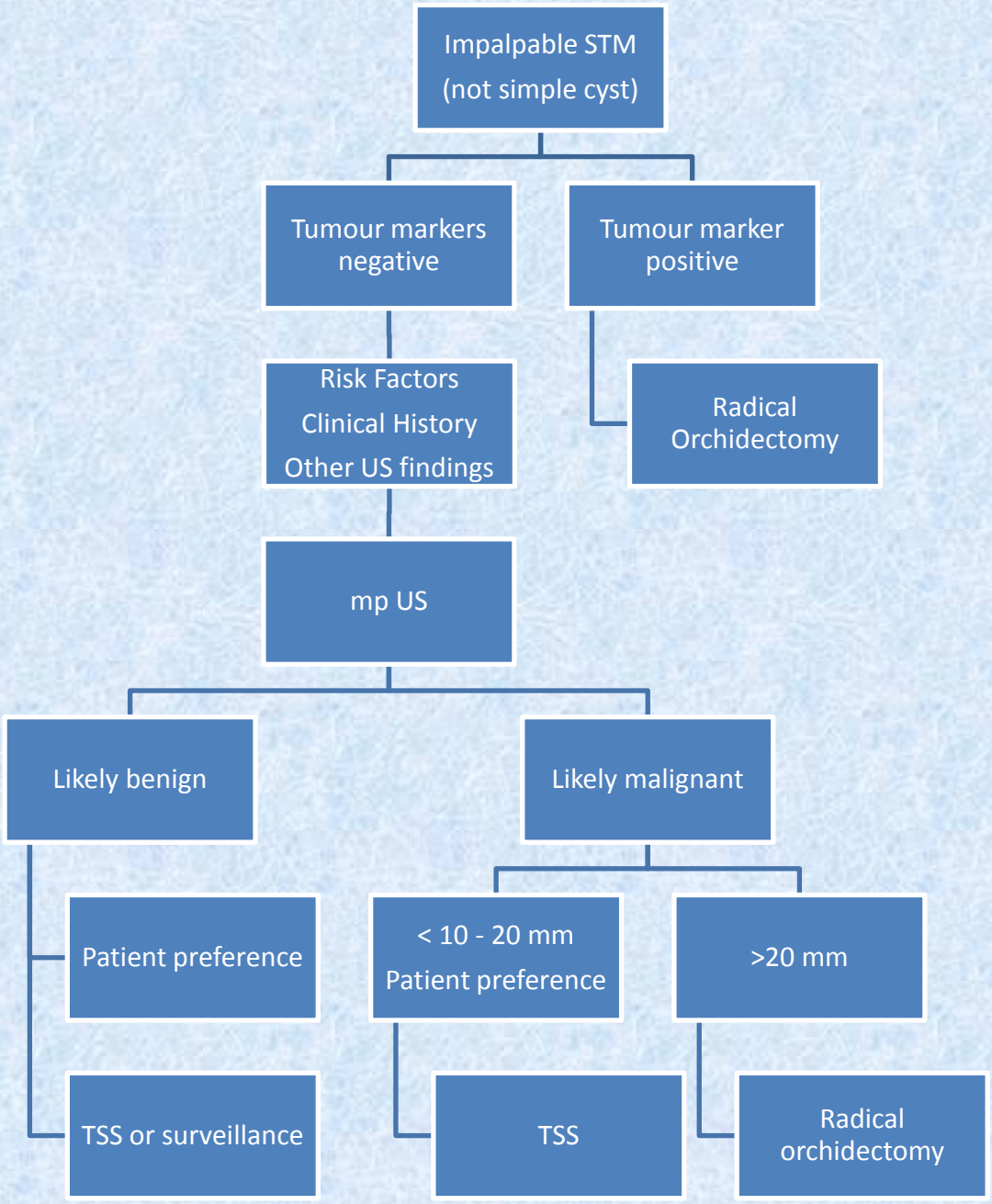


1. Connolly SS. BJU International 2006;98:1005
2. Eifler JB Jr. J Urol 2008;180:261

Classical seminoma – no change in size over 1 year

Conclusion

- Most non-palpable incidentally discovered testicular masses are benign
- Radical orchidectomy is performed too often in these patients
- Ultrasound (“multiparametric”) shows considerable promise in differentiating benign from malignant
- Active surveillance or TSS is appropriate for many patients


Impalpable STM
(not simple cyst)
Tumour markers negative
Tumour marker positive
Risk Factors
Clinical History
Other US findings
Radical Orchidectomy
mp US
Likely benign
Likely malignant
Patient preference
< 10 - 20 mm
Patient preference
>20 mm
TSS or surveillance
TSS
Radical orchidectomy