ISUP Recommendations on Macroscopy and Prognostic Factors in Testicular Tumours Boston March 2015

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Handling and Reporting of Orchidectomy Specimens with Testicular Cancer: Areas of Consensus and Variation among 25 Experts and 225 European Pathologists

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Short Running Title: Reporting of Orchidectomy specimens

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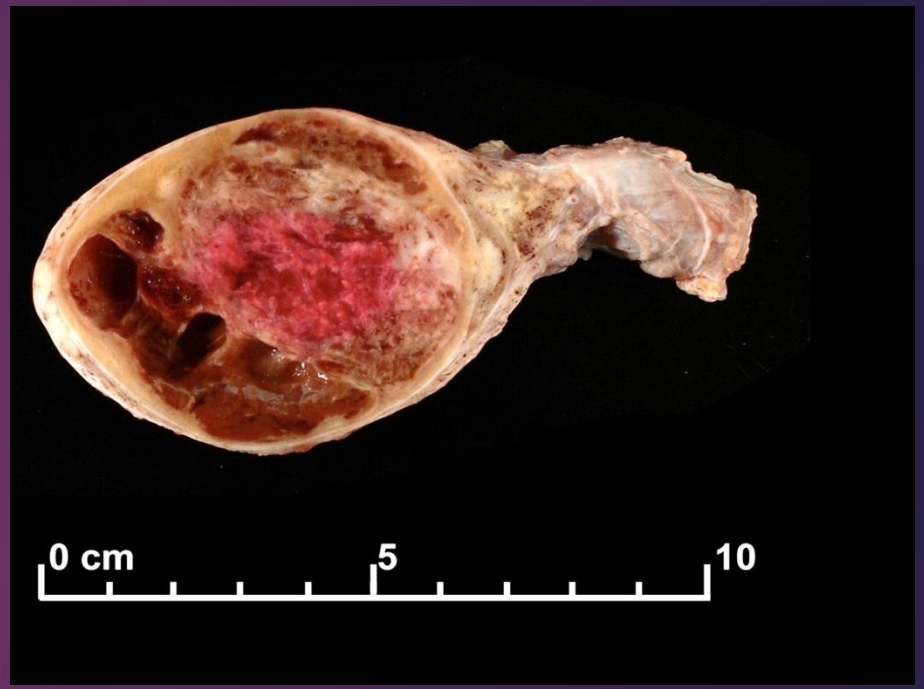
Macroscopic handling of testicular tumours



TESTIS AND RLPND

J PERRY-KEENE; P HUMPHREY; M ZHOU; A LOPEZ BELTRAN; J SRIGLEY.

Specimen receipt - recommendations

- If received fresh, deal with the specimen as appropriate for your institution and fix promptly
- If received in formalin, deal with the specimen as appropriate for your institution and fix promptly
- Think of ink in selected situations (if tunica vaginalis stuck down or if spermatic cord palpably involved)
- Bivalve the specimen:
  - Incise tunica vaginalis at the lateral aspect
  - Slice through the lateral border cutting towards the hilum and epididymis

RECOMMENDATIONS… Orchidectomy for tumour

- Spermatic cord margin: Optimal to take prior to incision but be practical depending on your laboratory
- Macroscopic description:
  - Dimensions of specimen
    - length of cord
    - testis in 3 dimensions
  - Dimensions of tumour
  - Macroscopic description of cut surface
  - Extent of tumour to be noted including relationship to tunica vaginalis, rete, hilar soft tissue, epididymis & invasion of spermatic cord

RECOMMENDATIONS… Orchidectomy for tumour

- Blocking:
  - Extensive sampling to include all grossly different areas of the tumour and relationship to tunica albuginea, tunica vaginalis (visceral and parietal), rete and hilum, epididymis and spermatic cord
  - Spermatic cord sections: at least margin and base of spermatic cord, others if indicated/desired
- Block in total up to 10 blocks
  - 1 block per cm in larger tumours
  - Consider total submission for testis-confined tumours
- Sample uninvolved testis (if present)

Base of spermatic cord

- Unfortunately there is no established histologically defined anatomical landmark present between paratesticular soft tissues and spermatic cord.
- Best assessed macroscopically as the point where the tunica vaginalis reflects over the head of the epididymis

Retroperitoneal Lymph node dissections – residual mass post treatment

- Document anatomic site of LNs
- Measure nodal mass in 3 dimensions
- Inking for margins **is** recommended – in order to give minimal distance to margin
- Block all residual viable tumour
- Comprehensive sampling especially at the interface between viable and necrotic material
- Include some areas of necrosis
  - In rare cases, you may wish to embed the entire specimen if the specimen is necrotic or non-viable to exclude a small focus of viable tumour

MICROSCOPIC REPORTING OF TESTICULAR GERM CELL TUMORS
USCAP
Boston 2015

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TNM 7th ed

- pT1 Tumour limited to testis and epididymis without vascular/lymphatic invasion; tumour may invade tunica albuginea but not tunica vaginalis.
- pT2 Tumour limited to testis and epididymis with vascular/lymphatic invasion, or tumour extending through tunica albuginea with involvement of tunica vaginalis.
- pT3 Tumour invade spermatic cord with or without vascular/lymphatic invasion.
- pT4 Tumour invade scrotum with or without vascular/lymphatic invasion.

Lymphovascular Invasion (LVI)

- Do you always report whether vascular invasion is present or absent ?
  - 99.6% yes (pre-meeting survey)
- Do you distinguish between lymphatic and blood vessel invasion ?
  - 24% Yes, 77% No (pre-meeting survey)
- Most studies do not discriminate between lymphatic and venous/arterial invasion

- Recommendations:
  - Routinely report LVI
  - Do not distinguish between LI or VI

LVI: Seminoma vs NSGCT

- Most studies show LVI prognostic for NSGCT but in the few studies looking at seminomas the data is not as clear.
- LVI more common in NSGCT than seminoma.
- *Recommendation: There is not enough data to alter the TNM staging system at present to have a split seminoma/NSGCT system.*
  - *Continue to report LVI in all GCT.*
- No recommendation reached over whether to report the subtype of tumour showing LVI

Reproducibility of LVI assessments

- *Using IHC markers as an adjunct is an option in selected cases where it may be useful but is not mandatory*
- Often the problem is not whether tumour is in a vessel or not, but whether it is artefact or genuine
  - Histiocytes in cord vessels – pitfall
  - Best to look at periphery of tumour and in tunica albuginea.
  - Tends to be over diagnosed in seminoma

Morphological Features of True LVI

- Tumour occupies a lymphovascular structure lined by flattened endothelial cells.
- The cluster may not conform to the exact shape of the vascular lumina.
- Associated fibrinous thrombosis and or mural attachment and re-endothelialization.

Morphological Features of True LVI

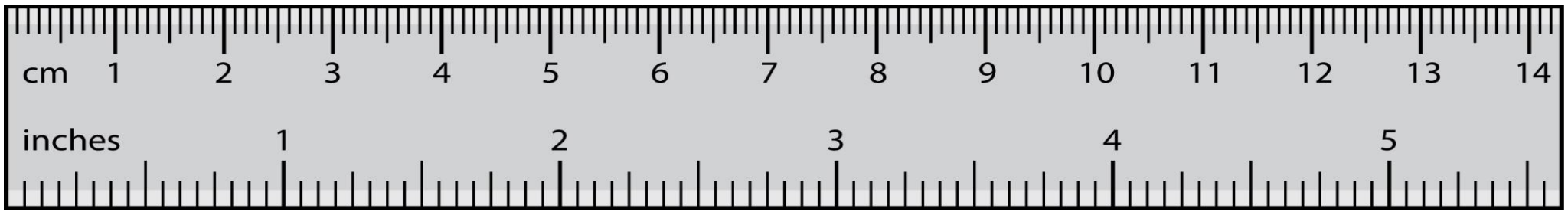
- Lack of obvious background artefactual deposition of germ cell tumour cells on the tunica surface.
- Cluster is more cohesive and has a rounded smooth edge.
- Cluster looks markedly different in its architecture from surrounding tumor.
- The LVI may be peripheral, intratumoural or in the cord, all count as T2
- *If equivocal – don't call it LVI*

MEASUREMENTS OF THE TUMOUR – primary tumour

- Robust risk factor for classical seminoma for disease progression, across the literature in cohort studies.
- Some literature is based on it as a continuous variable, some with a specific cut off eg 4cm, 3cm, 6cm.
  - We do not know where to draw the line
- Size is not a predictive factor in non-seminomatous germ cell tumour
- Multifocality has no effect on staging and no effect on prognosis

Measurements of the tumour – classical seminoma

- If size is a robust risk factor for disease progression, why is it not in the TNM ?
- No definite data about where the actual cut off for significance is and no clear justification for a split seminoma/NSGCT system
- Size: Seminomas
  - >4cm have a 2 x increased risk of recurrence.
  - Size (>4cm) and rete testis stroma invasion 3.4 x increased risk of recurrence than if neither present
  - *(Pooled analysis of data from 4 large cohort studies)*


cm 1 2 3 4 5 6 7 8 9 10 11 12 13 14
inches 1 2 3 4 5

Q27 Do you always report the percentages of different tumour types of a germ cell tumour ?

- ISUP pre-meeting survey
  - Yes 94%
  - No 4.%
  - Only percentage of embryonal carcinoma 0.4%
  - Other 1.%

- Recommendation:
  - *Percentages of different elements are reported*

- Problem of different cut-offs according to the studies
  - 35-90% EC reported to be predictive across the literature

Immaturity in Teratoma

- Not necessary in WHO 2004
- No prognostic implications
- But many pathologists are still reporting it
- Q28 For teratoma do you report the degree of immaturity?
  - 48% yes
  - 52% no

Reporting of different tumour type

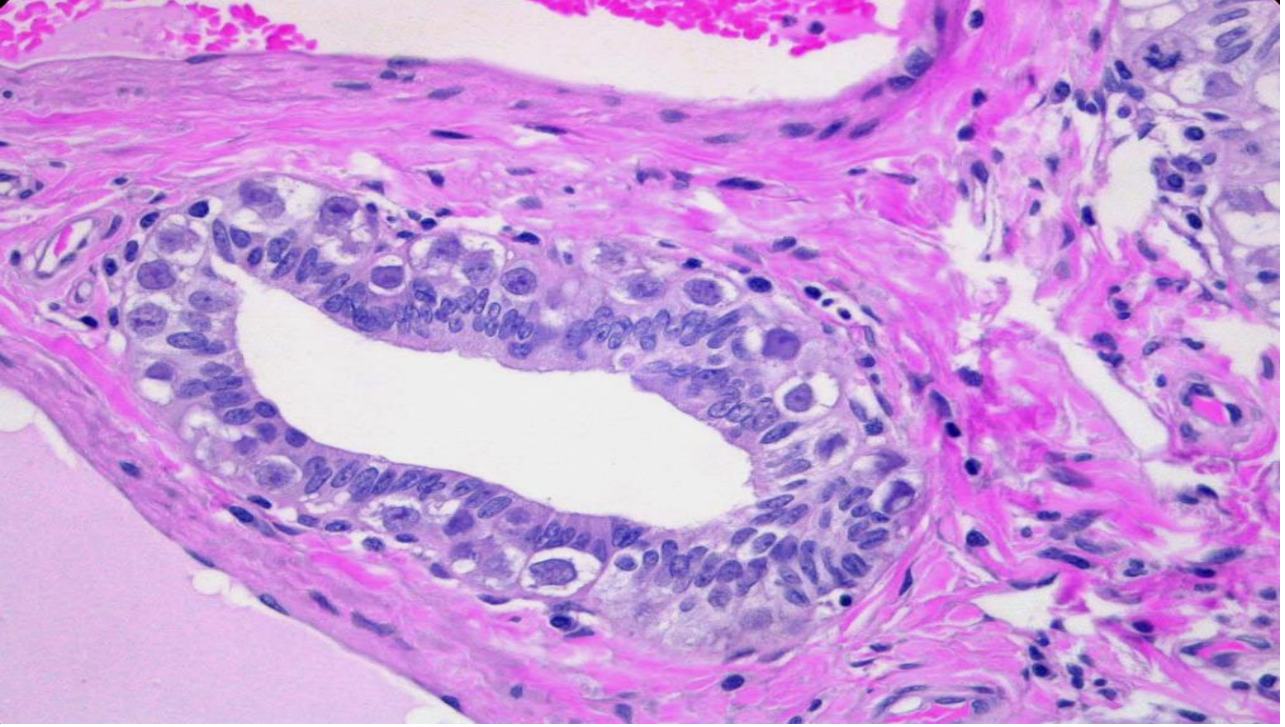
- Do you report the presence of primitive neuroectodermal elements?
- ISUP survey
  - 79% yes
  - 21% no

- No significance in terms of prognosis or treatment, if it does not meet the criteria for somatic malignancy what is the rationale for doing?
  - *Recommendation: Only report immaturity if you think there is definite or possible PNET somatic malignancy.*

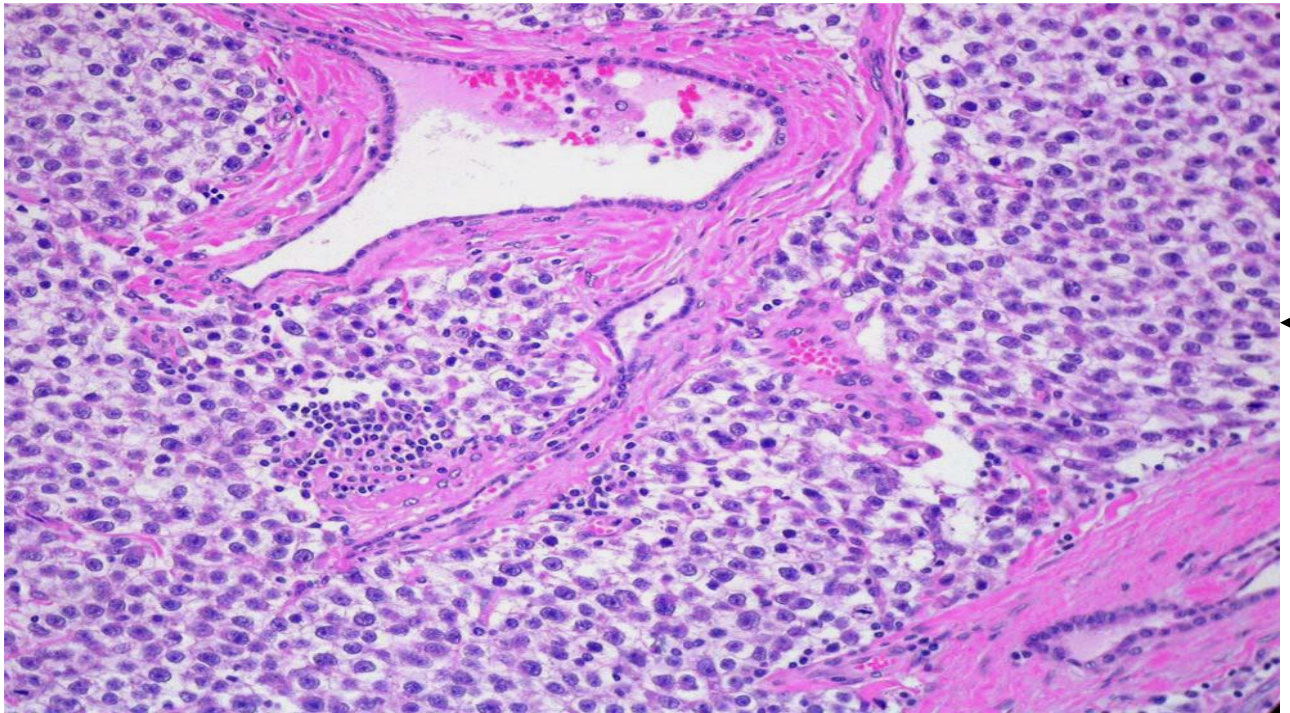
Q35 Do you distinguish between pagetoid invasion of the rete epithelium and invasion of the rete stroma ?

- ENUP expert survey
  - 96% yes
  - 4% no
- ISUP pre-meeting survey
  - 79% yes
  - 21% no

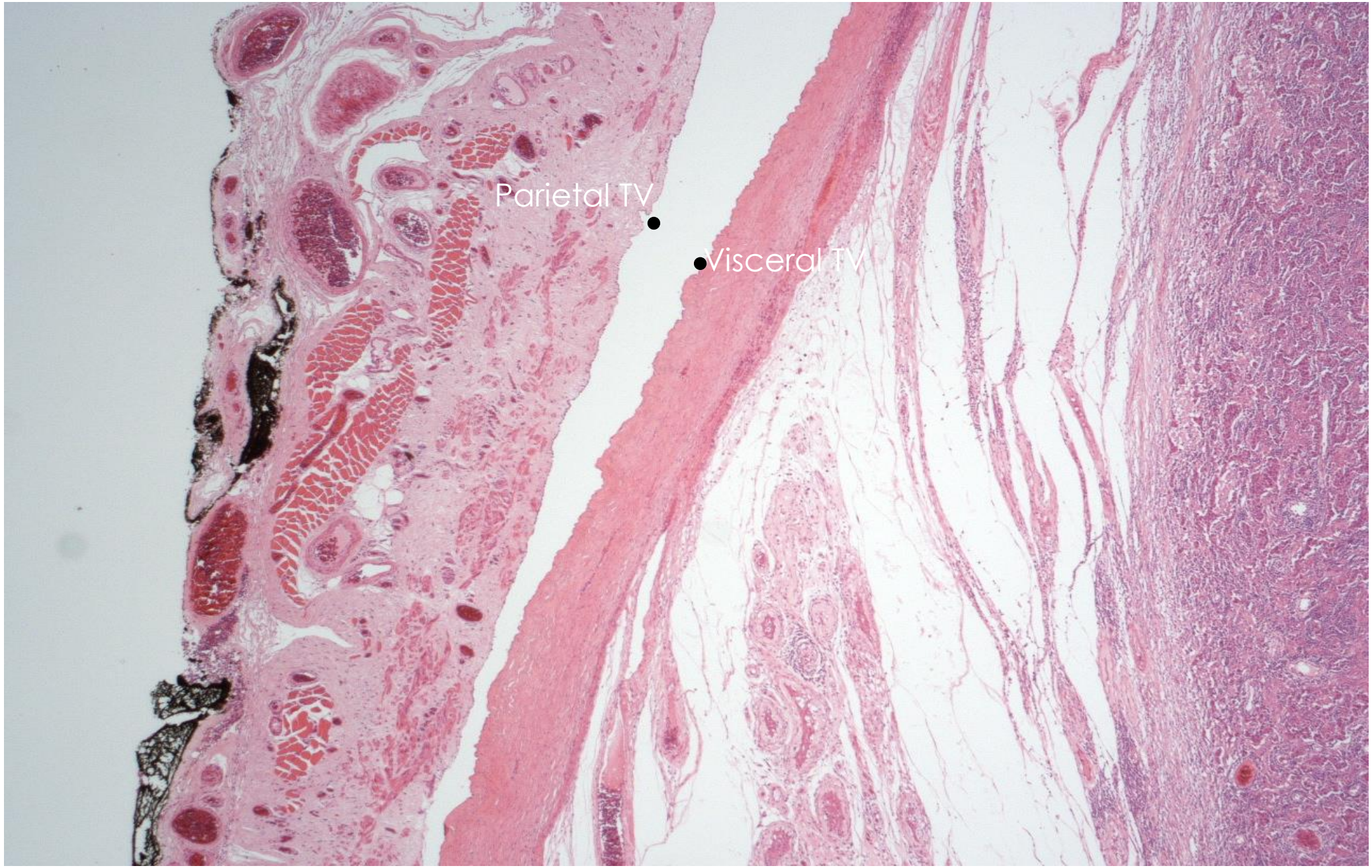
Recommendation: Pagetoid involvement of the rete epithelium and invasion of the rete stroma must be distinguished



Rete testis involvement: pagetoid pattern (IN SITU)



Rete testis invasion: direct pattern


Parietal TV
Visceral TV

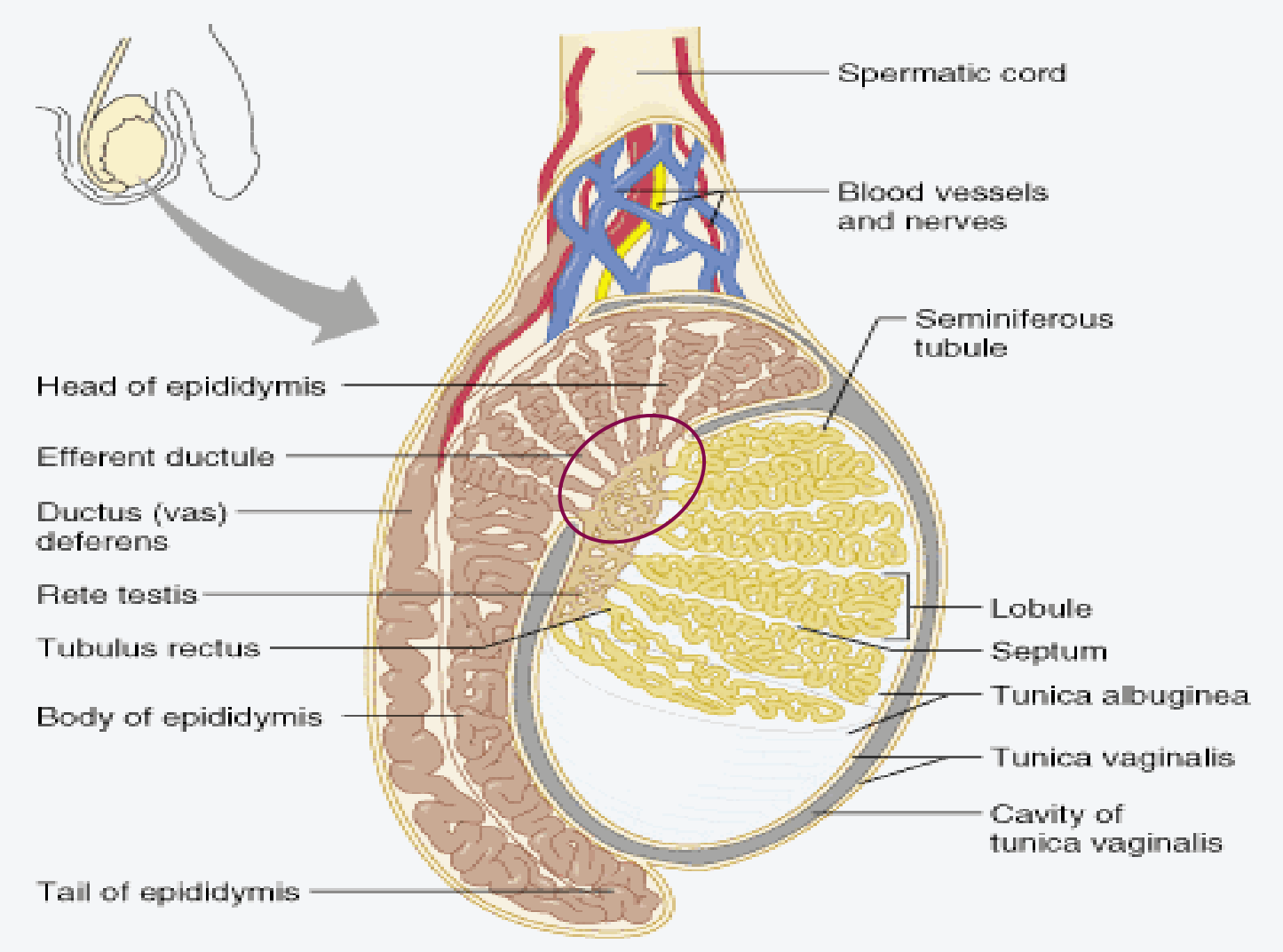
Q39 How would you stage the following: Tumour invading the inner serosal lining of the testis, not the outer layer, no vascular invasion ?

- ENUP expert survey
  - T1 52%
  - T2 48%
- ISUP survey
  - T1 61%
  - T2 38%
  - T3 1%

No consensus

There is no consensus as to whether the visceral TV / inner serosal lining represents pT2 disease, although this is a rare route of ETE and of dubious prognostic significance

Testicular Hilum?

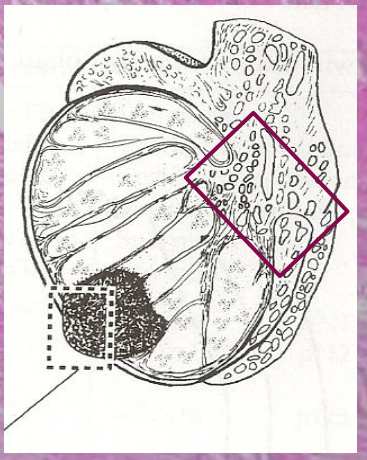


Extratesticular extension of germ cell tumors preferentially occurs at the hilum

Testicular hilum

Hilar soft tissue

Rete testis



Hilar Soft Tissue Invasion

Multivariate analysis: Both rete testis and hilar soft tissue invasion were strong independent predictors of metastasis at presentation

Half of the cases showing hilar ETE were staged pT1 which may represent a potential understaging

Yilmaz A, Cheng T, Zhang J, Tpkov K. Testicular hilum and vascular invasion predict advanced clinical stage in nonseminomayous germ cell tumors. Mod Pathol 2013; 26 (579-586)

Q41 How would you stage the following: tumour invading the hilar fatty tissue adjacent to the epididymis, no vascular invasion ?

- ISUP pre-meeting survey
  - T1 48%
  - T2 25%
  - T3 27%
- ENUP expert survey
  - T1 40%
  - T2 36%
  - T3 24%

Q40 How would you stage the following: Tumour invading the epididymis, no vascular invasion ?

- ENUP expert survey
  - T1 88%
  - T2 12%
- ISUP
  - T1 83%
  - T2 14%
  - T3 3%

Possible revisions to TNM to be considered:

- *Epididymis or hilar soft tissue invasion ?T2*
- *Subdivision of T1 to reflect rete testis invasion*

Thank you

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P Humphrey;
M Zhou;
A Lopez Beltran;
J Srigley.

Mahul Amin
Eva Compérat
Jonathan Epstein
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Asli Yilmaz