

Prof. Dr. Kiril Trpkov :

1. **In your experience, how frequent do you use urothelial atypia with unknown significance? Any threshold/limit to the usage i.e. <2% per total cases seen? (ZT)**

I use "urothelial atypia with unknown significance" very rarely. There is no threshold per se. Primarily I use it in the setting of first presentation of the patient (i.e. not previously known CIS of urothelial carcinoma). In the sign out I include a line "urothelial dysplasia can not be R/O and follow-up of the patient is warranted".

2. **Sometimes difficult to decide invasion into lamina propria, besides desmoplasia and irregular basement membrane. How to differentiate from tangential cut. (Anonymous)**

1. Cut deeper levels. 2. If still uncertain – can be signed out as "suspicious, but not definitive for invasion (microinvasion)". 3. If carcinoma looks low-grade, one has to be very cautious if carcinoma is labelled "invasive"

3. **Any tips in preparation and fixation of prostate tissue i.e. orientation to prevent twisted and crooked tissue especially thin ones? (ZT)**

First, it is important to talk to the techs who remove the cores from the needle biopsies and place them in containers – this has to be done gently and carefully, so fragmentation is avoided as much as possible. Second, path techs who embed the cores have to make sure that they are levelled (placed in one plane). Also we routinely place only 2 cores per block; if done carefully, this can be done for 3 or more cores, but the less cores are in the block – the easier it is to handle and orient them.

4. **Prof, do you routinely grade RCC on needle biopsies specimen?**

(Natasha Chew Bee See)

Yes, if clear cell RCC or papillary RCC type – for which the WHO/ISUP grade applies. I put (in brackets): "grading based on the core tissue sample"

5. **In inverted papilloma of bladder, you mentioned that the entity should have >80% inverted pattern. In biopsy specimen, how should we report if the inverted pattern <80% (F)**

If there is less than 80% - one can report:

High grade non-invasive (or invasive) urothelial carcinoma with (dominant) papillary growth and focal inverted growth (for example, 50% or less)

6. **Is the term atypical small acinar proliferation still used? (Anonymous)**

I have never used ASAP term – I use and prefer the term "atypical glands, suspicious (microfocus)", which is a more general term, as atypical glands can be not only small, but also

large, or cribriforming. This is usually accompanied by a note explaining why I consider the glands “atypical” or “suspicious”, with a description of the morphology, IHC results, and typically with a recommendation for repeat biopsy with increased sampling from the specific location (typically 3 cores).

**7. How to tell the difference between poorly formed glands (pattern 4) and pattern 5?** (Anonymous)

Pattern 5 should be called cautiously on biopsy, particularly when single cells or cord-like pattern are seen – one generally requires a good cluster of at least 5-10 individual cells, or cords. If the background of such glands looks mostly like small acinar pattern 3, one should be very careful not to overcall such glands that are tangentially cut as pattern 5.

Poorly formed glands pattern 4 usually look like small solid nests with no (or barely) visible lumina – with lack of larger cell sheets, or individual/single cells and cords; again a good cluster of them (at least 5-10) is needed to interpret them as “poorly formed, pattern 4”.

The general principle is – if in doubt, go with the lower (not higher!) grade.

**8. Prof, do you record number of nerve trunk in radical prostatectomy report?** (Anonymous)

No, perineural invasion is very common on RP and has no prognostic significance, so it should not be reported (included the number of nerves etc.)

Prof. Dr. Annie Cheung :

**1. Adenoid basal carcinoma look like adenoid cystic ca at a glance?** (Q)

Adenoid basal carcinoma shows milder nuclear pleomorphism and scanty mitotic figures. It does not harbour the intraluminal hyaline material commonly found in adenoid cystic carcinoma. Adenoid cystic carcinoma display more conspicuous nuclear pleomorphism and mitotic activity +/- necrosis. It often shows diffuse immunoreactivity for CD117 (c-kit) which is often absent or weak in adenoid basal carcinoma.

**2. What is the role of p16 in distinguishing HSIL from LSIL?** (Anonymous)

P16 helps as a surrogate marker for high risk HPV infection. P16 IHC is helpful in equivocal case that we have difficulty in distinguishing LSIL (negative) vs HSIL (positive) in biopsies.

However, integration with morphology is essential. P16 positive immunoreactivity may be found in HPV negative lesions.

**3. Is there endometrial carcinoma with more than one molecular abnormality such as p53 aberrant and MMR-def? How to classified according to TCGA? (Anonymous)**

Yes. Some Grade 3 endometrioid carcinoma can be both p53 aberrant and MMR-def. TCGA study demonstrated distinct patterns in endometrioid and serous carcinoma of endometrium. However, recent studies suggested that grade 3 endometrioid carcinoma with both p53 mutation and deficient MMR status behave more alike to MMR deficient carcinoma, i.e. better outcome than p53 mutated MMR proficient endometrial carcinoma.

**4. What other criteria you used in diagnosing LSIL in cervical biopsy if there is absence of koilocytes and P16 negative? (Anonymous)**

Features of mild dysplasia (CIN I) may warrant diagnosis of LSIL. The absence of koilocytes in a small biopsy may be due to sampling issue.