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Histopathology MT Guidelines for Gynaecological Cancers

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Management of Gynaecological Cancers:

Histopathology Network Guidelines (2025)

1. Principle

There have been several recent important molecular and immunohistochemical advances introduced into the reporting of gynaecological cancers. The general principles of the Histopathology Network Guidelines are that all pathology discussed at the specialist gynaecological MDT should have (i) undergone the appropriate processes in a timely manner, and (ii) been reviewed by a core MDT pathologist who is accredited in gynaecological pathology. **Accreditation is defined as: participating and maintaining adequate scores in the relevant quality assessment scheme (that is, the National Gynaecological Pathology EQA scheme) and sustaining a workload sufficient to uphold adequate skill in this subspeciality.** It follows that, in general, MDT reviews should be carried out by the local core MDT pathologist(s) who meet(s) the above criteria. There may also be a requirement for central specialist pathology review for certain cases where the reporting/reviewing pathologist or MDT feel this is warranted, or where the pathology falls into a category that automatically generates a central review requirement (more detail below).

2. General recommendations

2.1 *"The role of the cellular pathologist in the cancer multidisciplinary team" (September 2022)*, published by the Royal College of Pathologists, recommends that the pathologists who support a particular MDT should participate in the relevant specialist EQA scheme. ***The Pathway Board Network therefore requires that all core pathologists for Gynaecological cancer MDTs should participate in the National Gynaecological Pathology EQA scheme.***

2.2 A best practice scenario would incorporate slide review for all cases discussed at MDT by the core MDT pathologist. This is encouraged; however, due to time constraints and limited resources it may not always be possible. **It is therefore advised that slide review (by an accredited local/central pathologist) should occur by default in the following scenarios:**

- *Where review of the pathology report raises a query or requires further clarification.*
- *Where there has been a significant discrepancy between histological findings and clinical or imaging features.* These cases will be identified at the time of the MDT.
- *Where the reporting has been done by a pathologist who is non-accredited according to the above criteria.* For these cases it is strongly advised that a slide review be performed by the MDT pathologist *in advance of* MDT pathology discussion, in the event that there are changes arising from the review.
- *In areas where published audits have indicated an area of acknowledged diagnostic difficulty leading to frequent revision of diagnosis*.

- *For uncommon conditions seen within the spectrum of practice of the MDT (as a means of maintaining skills amongst the group of pathologists supporting the diagnostic area).* These cases may well necessitate central pathology review, supported by implementation of the above guidelines and by the maintenance of good communication between local and central reviewing pathologists.

2.3 Occasional cases represent cross referrals where patients under The Christie MDT service are managed within the Manchester University NHS Foundation Trust (MUFT) MDT service, and vice versa. If a central pathology review has already been performed at one of the two central Histopathology departments (either Christie or Manchester Royal Infirmary) then double reviews should not routinely take place, although some exceptions may occur.

3. Specific recommendations

It should be noted that where there is any uncertainty regarding pathological assessment of any potential malignancy following local pathology assessment, early proactive central review is encouraged to avoid undue delay.

3.1 Endometrial tumours

MMR, p53 and ER immunohistochemistry should be routinely performed on all primary diagnoses of endometrial carcinoma. POLE mutational genomic analysis is also recommended at the point of diagnosis (see below). p53, p16 and progesterone receptor immunohistochemistry are of value in the differential diagnosis of carcinoma showing endometrioid morphology with a high nuclear grade, since a proportion of these may actually represent gland-forming uterine serous carcinoma.

MMR protein immunohistochemical assessment is required in all primary endometrial malignancy diagnoses, both for the purposes of Lynch syndrome screening and because the MMR status impacts patient management. All 4 MMR proteins (MLH1, PMS2, MSH2, MSH6) should be interpreted concurrently and in line with the BAGP guidelines. MMR assessment is recommended to be performed on biopsy material wherever possible, since accurate staining is highly subject to adequate tissue fixation, and assessment is therefore often unsatisfactory on tissue blocks from large resections. Where the biopsy demonstrates atypical endometrial hyperplasia only, but carcinoma is subsequently diagnosed on the resection specimen, MMR analysis should be retrospectively carried out on the biopsy sample.

POLE gene mutational status similarly impacts patient management, depending on tumour stage and other parameters that may only be known at the point of final MDT discussion; however, it should be noted that molecular analysis may take several weeks to yield a report. As such, the Pathway Board recommends that reflex POLE molecular analysis be requested on all endometrial cancers at the point of diagnosis (i.e. on the initial tumour sample), to avoid potential delays in management. This test is performed and funded by the regional Genomic Laboratory Hub (GLH). The request form for the North West (Manchester) GLH can be found via the following link on their website:

https://mft.nhs.uk/nwglh/test-information/cancer/solid-tumour/sample-requirements/referral-form/

It should be noted that, at the time of publication of these guidelines, the BAGP and BGCS recommend continuing the use of the 2009 FIGO endometrial cancer staging system in the UK; the 2023 updated FIGO staging is not currently approved for clinical use. This recommendation has been endorsed by the regional Pathway Board Network.

3.2 Cervical tumours

Early invasive cervical carcinomas can be difficult to diagnose and stage on a loop biopsy, particularly Silva pattern A lesions, which can be misdiagnosed as CGIN. Where there is any uncertainty regarding the pathological assessment, early central review is advised.

p16 immunohistochemistry is recommended to classify carcinomas as HPV-independent or HPV-associated, since abnormal “block-type” expression of p16 is a reliable marker for high-risk HPV.

Small cancers involving the margins of excision biopsies should be assigned a provisional stage and this should be clearly stated in the text of the report, rather than allocating an automatic FIGO 2018 Stage IB to such lesions which may subsequently be downstaged after further excision. Final complete staging should be assigned upon correlation with full radiological/histological findings. This approach avoids overstaging and is endorsed in the 2021 RCPath dataset (see link below).

Biomarkers including PD-L1 may be required for targeted drug therapy and immunohistochemical testing should be performed at certified centres where clinically indicated.

3.3 Vulval tumours

p16 and p53 immunohistochemistry should be performed on all cases of vulval squamous cell carcinomas and VIN, even where the morphology appears typical in the latter. Abnormal “block-type” expression of p16 is a reliable marker for HPV-driven aetiology, which has prognostic significance. HPV-independent tumours should be further stratified into p53 mutation-type or p53 wild-type, since these tumours also have differing prognostic implications. Further information on the recognition of different patterns of p53 immunohistochemical expression can be found in the RCPath guidance document (link provided below).

3.4 Suspected sarcomas

All diagnosed/suspected sarcomas arising in the female genital tract, including low-grade endometrial sarcomas, should be sent for central pathology review at the earliest opportunity. Most patients with confirmed sarcoma will subsequently require referral to the central regional sarcoma (GMOSS) MDT via the gynaecology oncology MDT. At the initial assessment of small biopsies where sarcoma is suspected, 12 unstained sections should be cut to ensure adequate tissue preservation and to facilitate subsequent immunohistochemistry.

3.5 Peritoneal biopsies

Since peritoneal carcinomatosis usually arises from gynaecological or gastrointestinal malignancy, it is recommended that biopsy assessment of peritoneal malignancy includes the immunohistochemistry panel below:

- CK7
- PAX8
- ER
- WT1
- p53
    - The combination of PAX8 and WT1 positivity together with ER staining (albeit patchy) is highly specific for serous carcinomas of tubo-ovarian origin; moreover, mutational-type expression of p53 will be present in 95% of high-grade serous carcinomas
- +/- GATA-3, CDX2, CK20, TTF-1, calretinin – depending on degree of suspicion for a non-gynaecological primary
- +/- Ki-67, p16 – if there is uncertainty between low-grade and high-grade serous carcinoma

4. Guidance documents

4.1 National reporting guidelines for gynaecological malignancies issued by the Royal College of Pathologists (RCPath) can be found at the following link:
https://www.rcpath.org/profession/guidelines/cancer-datasets-and-tissue-pathways.html

4.2 Site and tumour specific RCPath guidelines can be accessed via the following links:

RCPath Tissue pathways for gynaecological reporting (2023)

RCPath Dataset for histopathological reporting of vulval carcinomas (2023)

RCPath Dataset for the reporting of cervical neoplasia (2021)

RCPath Dataset for histopathological reporting of carcinomas of the ovaries, fallopian tubes and peritoneum (2019; currently under review at the time of issuing this document)

RCPath Dataset for histopathological reporting of endometrial cancer (2017; currently under review at the time of issuing this document)

RCPath Dataset for histopathological reporting of uterine sarcomas (2018; currently under review at the time of issuing this document)

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