**Borderline tumour** (Required or recommended)

**Reason/Evidentiary Support**

**Histologic Type (Required)**
Terminology for ovarian borderline tumours has evolved over several years.¹² The preferred terminology is borderline tumour, for example serous or mucinous borderline tumour, and this has been endorsed in the 2014 WHO Classification.³ An acceptable synonym is atypical proliferative tumour.³ Serous borderline tumours which have been previously designated typical and micropapillary types, are now classified as serous borderline tumour/atypical proliferative serous tumour and micropapillary variant of serous borderline tumour/non-invasive low-grade serous carcinoma respectively, in the 2014 WHO Classification for gynecologic tumors.¹³ For mucinous, endometrioid, clear cell, Brenner, and seromucinous tumours, borderline tumour/atypical proliferative tumour terminology is also used in the 2014 WHO Classification.³⁵ The term low malignant potential is not recommended.³⁴⁹ Synonyms for seromucinous tumours include endocervical-type mucinous borderline tumour, Müllerian mucinous borderline tumour, and atypical proliferative (borderline) Müllerian tumour.⁵

**Special Features**
Determining the lowest threshold for the diagnosis of a borderline tumour in the setting of a cystadenoma/cystadenofibroma with minimal epithelial proliferation can be subjective and quantitative criteria have been suggested: cystadenomas/cystadenofibromas with qualitatively sufficient epithelial stratification/complexity involving ≥10% of the epithelial volume are designated as borderline tumours arising within a cystadenoma/cystadenofibroma.²⁴⁹ However, many would still diagnose a borderline tumour in which the epithelial stratification/complexity involves <10% of the epithelial volume.

**Micropapillary architecture (Required)**
As serous borderline tumour/atypical proliferative serous tumour can exhibit variable degrees of micropapillary architecture, a diagnosis of micropapillary variant of serous borderline tumour is based on the presence of ≥5 mm of confluent micropapillary growth.⁴

**Microinvasion (Required)**
A standardized quantitative criterion for distinguishing microinvasion from frankly invasive carcinoma within a borderline tumour has not been established, and varying definitions have been used in different studies, including 1 mm, 2 mm, 3 mm, 5 mm, and 10 mm² as the upper limits of microinvasion.¹²²⁴⁹¹⁰ The 2014 WHO Classification suggests a cut-off of 5 mm.¹ Some groups distinguish 2 patterns of stromal invasion in serous tumours which quantitatively falls short of frankly invasive carcinoma (<5mm) - conventional “microinvasion” (isolated and/or small clusters of eosinophilic cells) and “microinvasive carcinoma” (glandular or micropapillary patterns qualitatively analogous to low-grade serous carcinoma)¹²⁴ However, other investigators do not advocate this distinction. Due to insufficient numbers of cases in the literature, definitive conclusions regarding the clinical significance of this distinction cannot be drawn.¹⁴¹¹ Analogous to the situation for serous tumours, some investigators advocate the separation of “microinvasion” from “microinvasive carcinoma” in mucinous borderline tumours while others use these 2 terms synonymously.⁹¹⁰

**Intraepithelial carcinoma (Recommended)**
In mucinous borderline tumours, intraepithelial carcinoma is diagnosed in non-invasive foci with marked nuclear atypia.²⁹¹⁰ However, the reproducibility of this diagnosis has not been formally analysed.

**Implants (Required)**
Extra-ovarian implants occur in approximately 20% of serous borderline tumours and are more common with exophytic neoplasms. The most important adverse prognostic factor for serous borderline tumours is the presence of invasive implants in extra-ovarian tissues with non-invasive implants having a favourable prognosis. Specifying the location and size of implants is important for determining the FIGO stage.¹² Non-invasive and invasive implants may co-exist in the same specimen. Non-invasive implants are subclassified as epithelial or desmoplastic types.² Epithelial-type non-invasive implants resemble detached fragments of a serous borderline tumour involving extra-ovarian tissues. They do not exhibit infiltration of underlying tissue, and they are often present within mesothelial or epithelial-lined spaces although they may be adherent to the serosal surface. Desmoplastic non-invasive implants are composed of glands or papillary clusters within fibroblastic or granulation tissue-like stroma, but they do not exhibit infiltration of adjacent tissue. Often these are located on serosal surfaces or within septa in the omentum. Note that the presence of isolated individual or small clusters of eosinophilic epithelial cells within the stroma is generally considered to be within the spectrum of desmoplastic non-invasive implants rather than representing an invasive implant.¹⁴
The most widely used criterion for diagnosing invasive implants is destructive invasion of underlying tissue.\textsuperscript{13} Invasive implants often feature markedly crowded epithelial nests, glands or micropapillary clusters with a haphazard arrangement. The nests, glands and papillae are sometimes surrounded by clefts. As some peritoneal staging biopsies may be superficial without sufficient underlying tissue to assess invasion, expanded criteria for invasive implants have been proposed for cases without classic patterns of invasion.\textsuperscript{14} These criteria include micropapillary architecture resembling micropapillary serous borderline tumour and clusters of tumour within clear lacunar spaces. Not all gynaecological pathologists accept these expanded criteria,\textsuperscript{1,2} but they have been shown to correlate with poor outcome.\textsuperscript{14}

In occasional cases, it may not be possible to definitively distinguish non-invasive from invasive implants and the recommendation is to designate such implants as being of indeterminate type.\textsuperscript{15} This terminology should only be used sparingly, and obtaining a specialist gynaecological pathology opinion and submitting additional sections for histological examination (if an omentectomy specimen), may be useful.

When diagnosing invasive implants, the report should state that these represent extra-ovarian low-grade serous carcinoma; this has been endorsed in the 2014 WHO blue book.\textsuperscript{14,14} It is unclear whether invasive implants involving extra-ovarian sites in association with an ovarian serous borderline tumour represent metastases from the serous borderline tumour or an independent primary peritoneal tumour. A number of molecular studies analysing primary ovarian tumours with their associated implants have yielded varying results\textsuperscript{1} but a recent study of a large population-based cohort has shown that the vast majority of implants are clonally related to the primary ovarian tumour.\textsuperscript{16} Most of the cases from that study were non-invasive implants; however, all 10 invasive implants had the same mutational status (KRAS mutation, BRAF mutation, or wild-type KRAS/BRAF) as the corresponding serous borderline tumour, suggesting that invasive implants are clonally related to the primary ovarian tumour as opposed to representing independent primary peritoneal lesions. Nevertheless, the number of invasive implants evaluated by molecular methods in the entire literature is limited.

Implants may also be encountered in the setting of seromucinous borderline tumours, and the same issues for serous tumours pertain. In general implants do not occur in the setting of borderline mucinous, endometrioid, clear cell or Brenner tumours. In the presence of an “implant” in association with an ovarian mucinous borderline tumour, an undiagnosed or unsampled primary ovarian mucinous carcinoma or a metastasis from a non-gynaecological primary tumour involving the ovary should be excluded.

References:


