

Histological tumour type (Required)

Reason/Evidentiary Support

All ovarian epithelial malignancies and borderline tumours should be typed according to the WHO classification.¹ There are 5 major subtypes of primary ovarian carcinoma, high-grade serous, clear cell, endometrioid, mucinous and low-grade serous.²⁻⁵ There are also other uncommon minor subtypes, those listed by the WHO including malignant Brenner tumour, seromucinous carcinoma and undifferentiated carcinoma.¹ Carcinosarcoma is a mixed epithelial and mesenchymal malignancy but is included in the category of epithelial malignancies in this dataset since most are of epithelial origin and histogenesis.⁶

Although management of ovarian carcinoma is, at present, largely dependent on tumour stage and grade, accurate typing will almost certainly become more important in the future with the introduction of targeted therapies and specific treatments for different tumour types. This is in part because, although clinically often considered as one disease, there is an increasing realisation that the different morphological subtypes of ovarian carcinoma have a different pathogenesis, are associated with distinct molecular alterations and have a different natural history, response to traditional chemotherapy and prognosis.²⁻⁵ Tumour typing may also be important in identifying or initiating testing for an underlying genetic predisposition; for example, high-grade serous carcinoma may be associated with underlying *BRCA1/2* mutation while endometrioid and clear cell carcinomas can occur in patients with Lynch syndrome.⁷ The most common ovarian carcinoma is high-grade serous carcinoma (approximately 70%) followed by clear cell and endometrioid.^{8,9} Mucinous and low-grade serous are less common. Approximately 90% of advanced stage ovarian carcinomas (stage III/IV) are high-grade serous in type.^{8,9}

Most primary tubal carcinomas are high-grade serous or endometrioid and most primary peritoneal carcinomas are of high-grade serous type. As discussed in the sections on tumour site, it may be difficult to ascertain the origin of a high-grade serous carcinoma since multiple sites are often involved.

Mixed ovarian carcinomas are now considered to be uncommon. The current 2014 WHO classification does not include a category of mixed carcinoma² but the prior classification stated that a diagnosis of mixed carcinoma should only be made if the minor component represents more than 10% of the neoplasm.² However, it is recommended that all different morphological subtypes in an ovarian carcinoma are documented, even if they comprise less than 10% of the neoplasm. As stated, mixed carcinomas in the ovary are uncommon, the most prevalent combination being clear cell and endometrioid (both of these tumour types often arise in endometriosis). Most neoplasms which were previously classified as mixed serous and endometrioid and mixed serous and clear cell represent high-grade serous carcinomas with pseudoendometrioid areas and areas of cytoplasmic clearing respectively. In such cases, immunohistochemical markers, especially WT1, may be useful (see **Note 20 IMMUNOHISTOCHEMICAL MARKERS**).

Borderline tumours should also be typed according to WHO criteria. The most common subtypes are serous and mucinous (intestinal type). Seromucinous, endometrioid, clear cell and Brenner subtypes also occur.

References:

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- 2 McCluggage WG (2008). My approach to and thoughts on typing of ovarian carcinomas. *J Clin Pathol* 61:152-163.
- 3 Shih IM, Kurman RJ (2004). Ovarian tumorigenesis. A proposed model based on morphological and molecular genetic analysis. *Am J Pathol* 164:1511-1518.
- 4 Gilks CB (2004). Subclassification of ovarian surface epithelial tumors based on correlation of histologic and molecular pathologic data. *Int J Gynecol Pathol* 23:200-205.
- 5 Soslow RA (2008). Histologic subtypes of ovarian carcinoma: an overview. *Int J Gynecol Pathol* 27:161-174.
- 6 McCluggage WG (2002). Malignant biphasic uterine tumours: carcinosarcomas or metaplastic carcinomas? *J Clin Pathol* 55:321-325.
- 7 Downes MR, Allo G, McCluggage WG, Sy K, Ferguson SE, Aronson M, Pollett A, Gallinger S, Bilbily E, Shaw P, Clarke BA (2014). Review of findings in prophylactic gynaecologic specimens in Lynch syndrome with literature review and recommendations for grossing. *Histopathology* 65:228-239.
- 8 Seidman JD, Horkayne-Szakaly I, Haiba M, Boice CR, Kurman RJ, Ronnett BM (2004). The histologic type and stage distribution of ovarian carcinomas of surface epithelial origin. *Int J Gynecol Pathol* 23:41-44.
- 9 Köbel M, Kalloger SE, Huntsman DG et al (2010). Differences in tumor type in low-stage versus high-stage ovarian carcinomas. *Int J Gynecol Pathol* 29:203-211.

WHO classification of tumours

The 2014 WHO classification of tumours for carcinomas of the ovary, fallopian tube and peritoneum

Ovary

Epithelial tumours	Serous Tumours	Borderline	Serous borderline tumour /Atypical proliferative serous tumour	8442/1
			Serous borderline tumour- micropapillary variant / Non-invasive low-grade serous carcinoma	8460/2
		Malignant	Low-grade serous carcinoma	8460/3
			High-grade serous carcinoma	8461/3
	Mucinous tumours	Borderline	Mucinous borderline tumour / Atypical proliferative mucinous tumour	8472/1
		Malignant	Mucinous carcinoma	8480/3
	Endometrioid tumours	Borderline	Endometrioid borderline tumour / Atypical proliferative endometrioid tumour	8380/1
		Malignant	Endometrioid carcinoma	8380/3
	Clear cell tumours	Borderline	Clear cell borderline tumour / Atypical proliferative clear cell tumour	8313/1
		Malignant	Clear cell carcinoma	8310/3
	Brenner tumours	Borderline	Borderline Brenner tumour / Atypical proliferative Brenner tumour	9000/1
		Malignant	Malignant Brenner tumour	9000/3
	Seromucinous tumours	Borderline	Seromucinous borderline tumour / Atypical proliferative seromucinous tumour	8474/1
		Malignant	Seromucinous carcinoma	8474/3
	Undifferentiated carcinoma			8020/3
Mixed epithelial and mesenchymal tumours			Carcinosarcoma	8980/3

Fallopian tube

Epithelial tumours	Epithelial precursor lesion	Serous tubal intraepithelial carcinoma	8441/2
	Epithelial borderline tumour	Serous borderline tumour / Atypical proliferative serous tumour	8442/1
	Malignant epithelial tumours	Low-grade serous carcinoma	8460/3
		High-grade serous carcinoma	8461/3
		Endometrioid carcinoma	8380/3
		Undifferentiated carcinoma	8020/3
	Others	Mucinous carcinoma	8480/3
		Transitional cell carcinoma	8120/3
		Clear cell carcinoma	8130/3
Mixed epithelial-mesenchymal tumours		Carcinosarcoma	

Peritoneum

Epithelial tumours of Müllerian type	Serous borderline tumour / Atypical proliferative serous tumour	8442/1
	Low-grade serous carcinoma	8460/3
	High-grade serous carcinoma	8461/3
	Others	

Note: a code for mixed cell adenocarcinoma is not included in the above list but the code M8323/3 is recommended if this diagnosis is made.