Endometrial Cancer Histopathology Reporting Guide

International Collaboration on Cancer Reporting (ICCR)

Family/Last name

Given name(s)

Date of birth DD – MM – YYYY

Patient identifiers

Date of request DD – MM – YYYY

Accession/Laboratory number

Elements in **black text** are REQUIRED. Elements in **grey text** are RECOMMENDED.

Operative procedure

Simple hysterectomy ◯ Radical hysterectomy ◯ Other ◯

Attached anatomical structures

Vaginal cuff ☐ Left fallopian tube ☐
Left ovary ☐ Right fallopian tube ☐
Right ovary ☐ Parametria ☐

Accompanying specimens

None submitted ☐ Omentum ☐
Peritoneal biopsies ☐ Lymph nodes ☐
Other ☐

Tumour site (Note 1)

Fundus ☐ Body ☐ Isthmus/lower uterine segment ☐

Block identification key (Note 2)

(List with indication of nature and origin of tissue blocks)

Maximum tumour dimension (Note 3) mm

Histological tumour type (Note 4) **Histological subtypes** (Note 5)

Endometrioid ☐ ⇒ %
Mucinous ☐ ⇒ %
Serous ☐ ⇒ %
Clear cell ☐ ⇒ %
Undifferentiated ☐ ⇒ %
Mixed epithelial ☐
Carcinosarcoma ☐ ⇒ % (Epithelial) & % (Sarcomatous) (Note 6)
Other ☐ ⇒ Homologous ◯ Heterologous ◯

Histological grade (Note 7)

Grade 1 ◯ Grade 2 ◯ Grade 3 ◯
Not gradeable ◯ Not applicable ◯

Myometrial invasion (Note 8)

None ◯ <50% ◯ ≥ 50% ◯

Percentage of myometrium infiltrated by carcinoma (Note 9) %

Lymphovascular invasion (Note 10)

Present ◯ Not identified ◯ Indeterminate ◯

Site(s): Parametria ☐ At cervical resection margin ☐
Other ▶

Cervical stromal invasion (Note 11)

Present ◯ Not identified ◯ Indeterminate ◯

Distance of tumour to cervical resection margins (Note 12) mm

Vagina

Involved ◯ Not involved ◯ Not applicable ◯

Omentum

Involved ◯ Not involved ◯ Not applicable ◯

Peritoneal biopsy/biopsies

Involved ◯ Not involved ◯ Not applicable ◯

Uterine serosa (Note 13)

Involved ◯ Not involved ◯ Indeterminate ◯

Parametria (Note 14)

Involved ◯ Not involved ◯ Not applicable ◯

Adnexa (Note 15)

Involved ◯ Not involved ◯ Not applicable ◯

Cervical surface or crypt (Note 16)

Involved ◯ Not involved ◯ Indeterminate ◯

Distance of myoinvasive tumour to serosa (Note 17)

mm

Background endometrium (Note 18)

- ☐ Cyclical
- ☐ Atrophic
- ☐ Complex hyperplasia
- ☐ Atypical hyperplasia/Endometrial intraepithelial neoplasia
- ☐ Serous endometrial intraepithelial carcinoma
- ☐ Hormone effect
- ☐ Simple hyperplasia

Peritoneal cytology (Note 19)

Positive ◯ Atypical/suspicous ◯
Negative ◯ Not submitted ◯

LYMPH NODES STATUS (Note 20)

Involved ◯ Not involved ◯ Not applicable ◯

⇩

Left pelvic:
Number retrieved
Number involved

Right pelvic:
Number retrieved
Number involved

Para-aortic:
Number retrieved
Number involved

Extra-nodal spread:

Present ◯ Not identified ◯ Not applicable ◯

Distant Metastases

Present ◯ Not identified ◯ Indeterminate ◯

STAGING

Provisional FIGO stage (2009) (see adjacent table) (Note 21)

Pathological staging (TNM and AJCC 7th ed.)(see adjacent table)

ANCILLARY STUDIES (Note 22)

Immunohistochemical markers

Positive Abs	
Negative Abs	
Equivocal Abs	

Conclusions:

Molecular data

Test	Result

Tumour stage FIGO & pTNM##

Primary Tumour (T) (Surgical-Pathologic Findings)		
TNM	FIGO	
TX		Primary tumour cannot be assessed
T0		No evidence of primary tumour
Tis*		Carcinoma in situ (preinvasive carcinoma)
T1	I	Tumour confined to corpus uteri
T1a	IA	Tumour limited to endometrium or invades less than one-half of the myometrium
T1b	IB	Tumour invades one-half or more of the myometrium
T2	II	Tumour invades stromal connective tissue of the cervix but does not extend beyond uterus**
T3a	IIIA	Tumour involves serosa and /or adnexa (direct extension or metastasis)
T3b	IIIB	Vaginal involvement (direct extension or metastasis) or parametrial involvement.
T4	IVA	Tumour invades bladder mucosa and /or bowel mucosa (bullous oedema is not sufficient to classify a tumour as T4)
Regional Lymph Nodes (N)		
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1	IIIC1	Regional lymph nodes metastasis to pelvic lymph nodes
N2	IIIC2	Regional lymph nodes metastasis to para-aortic lymph nodes, with or without positive pelvic lymph nodes.
Distant Metastasis (M)		
M0		No distant metastasis
M1	IVB	Distant metastasis (includes metastasis to inguinal lymph nodes intraperitoneal disease, or lung, liver, or bone. It excludes metastasis to para-aortic lymph nodes, vagina, pelvic serosa, or adnexa.

* Note: FIGO no longer includes Stage 0(Tis)

** Endocervical glandular involvement only should be considered Stage I and not as Stage II.

American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer Science and Business Media LLC, www.springerlink.com. Update: 1st July 2011.

Note 1 - Tumour site

Reason/Evidentiary Support:

There may be an association between lower uterine segment/isthmic tumours and Lynch syndrome.[1-2]

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Note 2 – Block identification key

Reason/Evidentiary Support:

Complex cases are often referred for specialist review and the reviewer needs to know the origin and nature of the blocks for accurate assessment and staging of tumours.

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Note 3 - Maximum tumour dimension

Reason/Evidentiary Support:

There is a significant correlation between primary tumour diameter >20 mm and peritoneal failure. Does not yet reach III-2 evidence level.[3]

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Note 4 – Histological tumour type

Reason/Evidentiary Support:

See WHO classification of endometrial tumours below for extended list of tumour types. In cases where there is no residual tumour in the hysterectomy specimen or where there is a significant discrepancy between the reported tumour type in the biopsy and that in the hysterectomy, it may be necessary to review the prior biopsy. All morphological types in mixed carcinomas should be reported.[4]

WHO histological classification (2003)

Epithelial tumours

Endometrial carcinoma

Endometrioid adenocarcinoma

Variant with squamous differentiation

Villoglandular variant
Secretory variant
Ciliated cell variant

Mucinous adenocarcinoma
Serous adenocarcinoma
Clear cell adenocarcinoma
Mixed adenocarcinoma*
Squamous cell carcinoma
Transitional cell carcinoma
Small cell neuroendocrine carcinoma
Undifferentiated carcinoma
Others

Mixed epithelial and mesenchymal tumours

Carcinosarcoma (malignant mullerian mixed tumour, metaplastic carcinoma)

* According to the WHO, the term *mixed carcinoma* should only be used when two or more distinctive subtypes of endometrial carcinoma are identified, each representing more than 10% of the tumour. However, it is recommended that all types are recorded in the pathology report, even if the minor component comprises less than 10% of the neoplasm.

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Note 5 – Histological subtypes

Reason/Evidentiary Support:

Adequate sampling of the tumour is required (minimum of 4 blocks) to allow meaningful assessment of this data item.

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Note 6 – Carcinosarcoma

Reason/Evidentiary Support:

A recent study has shown that the presence of heterologous elements in stage I carcinosarcomas is an important adverse prognostic feature; does not yet reach III-2 evidence level.[5]

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Note 7 - Histological grade

Reason/Evidentiary Support:

The FIGO grading system for endometrioid adenocarcinomas of the uterine corpus is based on the following architectural features:[6]

Grade 1: 5% or less non-squamous solid growth pattern

Grade 2: 6% to 50% non-squamous solid growth pattern

Grade 3: > 50% non-squamous solid growth pattern

Notable nuclear atypia, which exceeds that which is routinely expected for the architectural grade, increases the tumour grade by 1.

In addition, the following guidelines should be used in grading:

(1) Non-gland forming squamous elements should be disregarded for grading purposes.
(2) Endometrioid and mucinous carcinomas should be graded using the FIGO grading system.
(3) Serous, clear cell and undifferentiated carcinomas and carcinosarcomas are not graded but are regarded as high grade neoplasms.[7] When the dataset is being completed, these should be designated as "not applicable" for histologic grade.
(4) In mixed carcinomas, the highest grade should be assigned.

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Note 8 – Myometrial invasion

Reason/Evidentiary Support:

Depth of invasion should be measured from the endomyometrial junction (not the surface of exophytic tumours) to the deepest focus of tumour invasion. Measurement of the depth of invasion may be rendered difficult by irregularity of the endomyometrial junction, polypoid tumour growth, intramural leiomyomas, adenomyosis and uncommonly by smooth muscle metaplasia within polypoid neoplasms.[8] Deep myometrial invasion has repeatedly been shown to be an important poor prognostic indicator in endometrial carcinoma. This is an independent predictor of haematogenous dissemination by endometrial carcinoma and it is therefore an important determinant of adjuvant therapy.[9]

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Note 9 – Percentage of myometrium infiltrated by carcinoma

Reason/Evidentiary Support:

Tumour-free distance and percentage of myometrium infiltrated are independent prognostic factors for lymph node metastasis in endometrial carcinoma; studies do not reach level III-2 evidence.[10]

The percentage of myometrium infiltrated by carcinoma is defined as the percentage of myometrium involved as determined by the depth of myometrial invasion from the endomyometrial junction to the deepest focus of invasive carcinoma in comparison to the overall myometrial thickness.

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Note 10 – Lymphovascular invasion

Reason/Evidentiary Support:

Lymphovascular invasion is a predictor of tumour recurrence and lymph node metastasis.[11] However, lymphovascular space invasion does not alter the tumour stage. For example, if an endometrial adenocarcinoma is confined to the inner half of the myometrium but shows lymphovascular invasion in the outer half of the myometrium, this should still be staged as FIGO 1A. Similarly lymphovascular invasion alone in cervical, parametrial or para-ovarian vessels does not upstage the tumour. There is an increased incidence of vascular pseudoinvasion in laparoscopic hysterectomy specimens associated with the use of an intrauterine balloon manipulator.[11-12]

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Note 11 – Cervical stromal invasion

Reason/Evidentiary Support:

Cervical stromal infiltration by endometrial carcinoma is associated with a risk of recurrence and is a predictor of pelvic lymph node metastases.[13-14]

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Note 12 – Distance of tumour to cervical resection margins

Reason/Evidentiary Support:

Close margins may indicate a need for vault brachytherapy. Vascular invasion at cervical resection margin should be documented but does not upstage the tumour.

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Note 13 – Uterine serosa

Reason/Evidentiary Support:

Carcinoma should penetrate through the serosa in order to be classified as serosal involvement. Involvement of the serosa (FIGO stage IIIA) carries a higher risk of locoregional recurrence than does adnexal involvement (also FIGO stage IIIA).[15]

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Note 14 – Parametria

Reason/Evidentiary Support:

Most hysterectomies for endometrial cancer will be simple hysterectomies and will not have parametrial resections. Endometrial carcinomas with parametrial invasion are staged as FIGO IIIB. Although not an independent prognostic indicator, parametrial involvement by direct extension is a poor prognostic factor and also correlates with other poor prognostic factors. The presence of lymphovascular invasion in parametrial tissues should be documented but does not constitute parametrial involvement.[16-17]

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Note 15 – Adnexa

Reason/Evidentiary Support:

FIGO staging is based on tumour involvement of either the fallopian tube or ovary (stage IIIA). Especially with low-grade endometrioid adenocarcinomas, involvement of the uterine corpus and adnexa may indicate synchronous, independent neoplasms rather than metastasis from the endometrium to the adnexa; a variety of pathological parameters is useful in the distinction between synchronous independent and metastatic neoplasms. As for other sites in the gynaecological tract in which lymphovascular invasion by endometrial adenocarcinoma may be identified e.g., myometrium and parametrial tissue, the identification of lymphovascular space invasion alone in adnexal structures does not alter the tumour stage i.e. endometrial carcinoma should not be upstaged if there is vascular involvement in the adnexa in the absence of tumour outwith vascular channels.

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Note 16 – Cervical surface or crypt

Reason/Evidentiary Support:

Not necessary for staging but some oncologists administer vault brachytherapy if this is identified. Level III-2 evidence currently not available.

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Note 17 – Distance of myoinvasive tumour to serosa

Reason/Evidentiary Support:

Tumour-free distance and percentage of myometrium infiltrated are independent prognostic factors for lymph node metastasis in endometrial carcinoma; studies do not reach level III-2 evidence.[10]

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Note 18 – Background endometrium

Reason/Evidentiary Support:

The appearance of the background endometrium and the presence of abnormalities such as hyperplasia or polyps, should be documented. If present, the type of endometrial hyperplasia should be specified. In cases of serous carcinoma, the presence of serous endometrial intraepithelial carcinoma (serous EIC) the presumed precursor of uterine serous carcinoma should be recorded. [18]

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Note 19 – Peritoneal cytology

Reason/Evidentiary Support:

This data item is not necessary for staging but there is lack of consensus in the literature regarding the prognostic significance of positive peritoneal washings in the absence of other evidence of extrauterine spread. A recommendation is made by FIGO and UICC to record positive peritoneal washings without altering the tumour stage.[19-20]

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Note 20 – Lymph node status

Reason/Evidentiary Support:

Pelvic and para-aortic node status should be recorded separately since this affects tumour stage. Pelvic node involvement without para-aortic involvement is stage IIIC1 while para-aortic node involvement is stage IIIC2.[21-22]

The number of nodes involved and the site of involvement is prognostically important and may direct adjuvant treatment.

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Note 21 – Provisional FIGO Stage

Reason/Evidentiary Support:

Staging is provisional since final stage should be determined at multidisciplinary team/tumour board meeting when all relevant clinical and radiological information is available.[7,23]

The reference document TNM Supplement: A commentary on uniform use, 4th Edition (C Wittekind editor) may be of assistance when staging.[24]

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Note 22 – Ancillary studies

Reason/Evidentiary Support:

Immunohistochemistry may be useful in certain diagnostic scenarios. For example, a panel of markers (ER, PR, vimentin, CEA, p16) may be useful in the distinction between a primary endometrial and cervical adenocarcinoma.[25-26] Other markers (ER, PR, p53, p16) may be useful in the distinction between an endometrioid and a serous adenocarcinoma.[27-28] Immunohistochemistry for mismatch repair proteins (MLH1, MSH2, MSH6, PMS2) may be useful in helping to establish whether endometrial carcinomas are associated with underlying mismatch repair gene abnormalities and hereditary non-polyposis colorectal cancer (Lynch) syndrome. [29-30]

Different morphological subtypes of endometrial adenocarcinomas are associated with distinct molecular abnormalities. However, at present molecular analysis has little role in diagnosis or as an independent prognostic or predictive factor. However, this may change in the future and targeted therapies may be developed against carcinomas exhibiting specific molecular abnormalities.

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