



The Royal College of Pathologists

Pathology: the science behind the cure

## Standards and datasets for reporting cancers

### Dataset for histological reporting of endometrial cancer

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## Foreword

The Cancer Datasets published by the Royal College of Pathologists are guidelines that should assist pathologists in providing a high standard of care for patients. Guidelines are systematically developed statements to assist the decisions of practitioners and patients about appropriate health care for specific clinical circumstances and are based on the best available evidence at the time the dataset was prepared. It may be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. Just as adherence to the guidelines may not constitute defence against a claim of negligence, so deviation from them should not necessarily be deemed negligent.

The dataset was reviewed by the Cancer Services Working Group and was placed on the College website for consultation with the membership between 9 November and 7 December 2009. All comments received from the Working Group and membership have been addressed by the authors to the satisfaction of the Chair of the Working Group and the Director of the Professional Standards Unit.

No major organizational changes or cost implications have been identified that would hinder the implementation of the dataset.

Each year, the College will ask the authors of the dataset, in conjunction with the relevant sub-specialty advisor to the College, to consider whether or not the dataset needs to be revised.

This dataset was developed without external funding to the writing group. The College requires the authors of datasets to provide a list of potential conflicts of interest; these are monitored by the Director of the Professional Standards Unit and are available on request.

## 1 Introduction

This document provides the dataset for the histological reporting of endometrial cancers and replaces the first edition of the dataset that was published in 2001.

Meticulous reporting of endometrial cancers is important because pathological parameters determine prognosis and treatment. The cancer dataset (and the background information that forms part of the datasets) should be used in the context of the Multidisciplinary Team Meeting (MDTM) to optimise management decisions, to facilitate regular audit and review of all aspects of the service, to enable the collection of accurate data for cancer registries and to provide feedback for those caring for patients with cancer.

The new edition of the dataset is largely based on the original version. The layout of the reporting proforma has been revised for clarity. Several new core data items have been added. The diagnostic categories have been expanded to incorporate mucinous adenocarcinoma and undifferentiated carcinoma. 'Tumour-free distance to serosa', one of the new core data items, refers to the distance between the deepest demonstrated tumour and the nearest uterine serosa. Microscopic involvement of cervical glandular surface or crypt epithelium has been added. Parametrial involvement, of importance as a poor prognostic indicator and included in the new FIGO staging system, is another new data item. Finally, an item on omental involvement by tumour is added for those cases where omentectomy or omental biopsy has been carried out, usually for high grade carcinomas, e.g. uterine serous carcinoma, clear cell carcinoma, grade 3 endometrioid carcinoma, carcinosarcoma or undifferentiated carcinoma.

It is important to have robust local mechanisms in place to ensure that the MDTM Clinical Leads and other key members and Cancer Registries are informed of supplementary or revised histology reports that may affect patient treatment and data collection.

Most gynaecological oncologists use the FIGO staging system for gynaecological cancers, a new revised version of which has been published in 2009<sup>1</sup> (Appendix B). In order to allow standardisation of staging across all cancer sites, the corresponding revision of TNM<sup>2</sup> is also included in Appendix B.

The 2009 FIGO staging system for endometrial carcinoma differs from its predecessor in several respects, most notably the stages assigned to (i) depth of myometrial invasion, (ii) cervical glandular and stromal involvement, and (iii) distribution of nodal metastases. Parametrial invasion is now included in the FIGO staging system but peritoneal washings are not. The changes and the rationale underlying them are discussed in detail in the relevant paragraphs below. It is anticipated that the changeover to the new FIGO staging system will take some time, but it is recommended that the 2009 FIGO staging system is introduced as soon as is practical in MDTM settings. This will require pathologists, gynaecological, medical and clinical oncologists, radiologists and other personnel involved in the management of patients with endometrial cancer to collaborate closely. To avoid confusion and adverse patient consequences during this transition period and to help with interpretation of old pathology reports and case notes, we include the 1998 version of the FIGO staging in Appendix C; TNM staging is also included with this older version.

Evidence for this revised dataset was obtained from a review of relevant literature up to 2009 using the PubMed and Medline databases. A consensus view was taken on selection of the information to be included on grounds of robustness of evidence, reinforced by the authors' own experience.

The following organisations have been consulted during the preparation of the dataset:

- Working Group of the British Association of Gynaecological Pathologists (BAGP) comprising BAGP Council and co-opted members.
- British Gynaecological Cancer Society (BGCS).

## **2 Clinical information required on the Specimen Request Form**

This should include full patient details, clinical presentation, results of previous biopsies and radiological investigations for tumour staging, and comprehensive details of the surgical procedure. It is also highly desirable to provide details of any family history of cancer and relevant hormonal therapy.

The nature of surgical specimens from multiple sites should be carefully recorded and the specimen pots should be labelled to correspond to the specimen details on the request form.

## **3 Preparation of specimen before dissection**

The usual treatment for endometrial cancer is hysterectomy and bilateral salpingo-oophorectomy. The specimen should be transported to the laboratory as soon after surgery as possible. Whether received fresh or in formalin, the uterus should be opened as soon after receipt as possible in order to facilitate fixation of the tumour and preservation of tumour morphology. Good preservation of tumour morphology is of crucial importance for accurate subtyping and grading of the tumour. If the ovaries and fallopian tubes are normal, they can be allowed to fix intact. In some cases, one or both ovaries may contain tumour; in these cases, the ovaries should be handled in the same way as an ovarian tumour. Slicing may facilitate adequate fixation but this should only be done after careful inspection of the capsule.

There are several ways of opening the uterus, depending on the preference and experience of the pathologist.<sup>3,4</sup> Some pathologists prefer to open the uterus in the sagittal plane while others open it coronally along the lateral border and between the cornua. The latter may be advantageous because it preserves the anterior and posterior uterine walls, enabling the pathologist to block the uterus in the sagittal plane both anteriorly and posteriorly. Whatever the manner of opening, it should enable accurate mapping and appropriate sampling of the tumour.

A photographic record of the specimen may be useful.

## 4 Specimen handling and block selection

Depending on the preoperative diagnosis, results of radiological staging and intraoperative findings, the hysterectomy specimen may be accompanied by lymph nodes and an omental biopsy or omentectomy. All the specimens should be received in separate pots, appropriately labelled as to site of origin.

### 4.1 Gross examination and dissection

The different components of the hysterectomy specimen (uterus, ovaries and tubes) should be specified, and their dimensions and macroscopic appearance should be recorded. The gross appearance of the tumour, its maximum diameter and the presence or absence of gross myometrial invasion, cervical involvement or serosal surface involvement should be recorded. The position of the tumour within the uterus should be documented, as there is some evidence that neoplasms arising in the isthmus are more aggressive with a worse prognosis.<sup>5,6</sup> Any ovarian or tubal abnormalities should be documented. The omentum, if received, should be measured and the presence of any gross tumour recorded.

### 4.2 Block selection

Some protocols, including the previous edition of the dataset, recommend blocking the uterus in the transverse plane.<sup>3,4</sup> An alternative method involves blocking the uterus in the sagittal plane; this preserves the continuity of the endocervical canal with the endometrial cavity for easier mapping of the tumour and more accurate evaluation of cervical involvement by tumour. Whichever method is chosen for blocking the uterus, the pathologist should ensure that the uterus is sampled in such a way as to ensure accurate staging.

In those cases where no macroscopic tumour is identified, it may be necessary to block the entire endometrial cavity. Where tumour is identified grossly, at least four blocks should be taken of the tumour, including a block to demonstrate the area of deepest myometrial invasion or serosal involvement. In order to allow evaluation of depth of myometrial invasion, the tumour blocks should include the full thickness of the uterine wall. Where the uterine wall is too thick to fit into one cassette, the block should be divided into two and the cassettes should be appropriately labelled. Where possible, at least one tumour block should be in continuity with normal endometrium in order to facilitate the evaluation of the depth of myometrial invasion. At least one other block of background endometrium should be taken if possible. Cornual blocks should be taken when the tumour is situated in the cornual region, when macroscopic examination shows tumour extending to or breaching the serosa in this region or when no macroscopic tumour is seen in the resected uterus.

At least two blocks should be taken from the cervix, one from the anterior and one from the posterior lip. Transverse blocks of the upper endocervical canal may also be taken to ensure adequate sampling of this. Additional sampling of the cervix has not been shown to identify more cases of microscopic tumour involvement.<sup>7</sup> Parametrial connective tissue, where present, should be blocked in its entirety. If the ovaries are macroscopically normal, one or two blocks should be taken. If an ovarian tumour is present, this should be blocked according to ovarian tumour protocols, which currently recommend one block per cm of the maximum tumour diameter. If the fallopian tubes are macroscopically normal, we recommend sampling two or three slices from each tube, including one slice from the fimbrial end. In addition, any grossly abnormal areas should be sampled.

Where an omentectomy specimen is submitted, this should be measured and subjected to careful macroscopic examination. One block, taken from an area of obvious tumour, is adequate in cases where macroscopically visible tumour nodules are present. If the specimen is macroscopically normal, three to five blocks should be taken.<sup>8</sup>

The number of lymph nodes retrieved from each site should be recorded. Where many lymph nodes are resected, it is not practical to record the dimensions of every lymph node, but the dimensions of the largest should be documented. The presence of macroscopic involvement

of lymph nodes should be noted. All resected lymph nodes should be sampled. Every lymph node should be examined histologically in its entirety, unless obviously grossly involved by tumour. Only one block is necessary from any grossly involved node. Nodes smaller than 5 mm can be bisected or processed intact. To enable accurate counting of lymph nodes, it is preferable that individual nodes are placed in separate cassettes, but this practice may vary between institutions. Large lymph nodes may require sampling in more than one cassette.

The origin/designation of all tissue blocks should be recorded and every block should be individually labelled so it is readily identifiable. This is particularly important should the need for internal or specialist external review arise. The reviewer needs to be clear about the origin of each block in order to provide an informed specialist opinion. It may be advantageous to record the position of tissue blocks on a photograph of the uterus.

## 5 Core histological data items

The prognosis of endometrial carcinomas depends on the pathological subtype of the tumour, the grade and its stage at presentation.<sup>9</sup>

### 5.1 Tumour type

Endometrial carcinomas should be subtyped according to the WHO classification<sup>10</sup> (see Appendix A). Endometrioid carcinomas have, in general, a better prognosis than serous and clear cell carcinomas.<sup>9,11–14</sup> Information about mucinous carcinomas is still relatively limited, but available information suggests that their clinical behaviour is similar to that of endometrioid adenocarcinoma.<sup>15</sup> Thus, accurate subtyping of endometrial carcinoma is important because this has prognostic implications and potentially aggressive tumours (such as grade 3 endometrioid carcinomas, serous, clear cell and undifferentiated carcinomas, and carcinosarcomas) are likely to undergo pelvic and/or para-aortic lymphadenectomy and omentectomy, as well as hysterectomy and bilateral salpingo-oophorectomy.

It is outside the scope of this document to provide detailed information regarding the histopathological features of endometrial carcinoma subtypes and the reader is referred to specialist textbooks of gynaecological pathology. A few points will, however, be highlighted for clarification. The term endometrioid adenocarcinoma with squamous differentiation refers to the entities previously termed adenoacanthoma and adenosquamous carcinoma. Some 30% of endometrioid adenocarcinomas of the endometrium contain squamous elements. It has been shown that the cytology of the squamous elements in such tumours is not a useful prognostic indicator and, accordingly, these tumours are now referred to as endometrioid adenocarcinoma with squamous differentiation.<sup>16</sup>

*Mucinous adenocarcinoma* refers to a subtype of endometrial adenocarcinoma in which more than 50% of the tumour cells contain intracytoplasmic mucin. The relatively recently described microglandular subtype of mucinous carcinoma can be confused with endocervical microglandular hyperplasia on biopsy specimens.<sup>17</sup>

*Carcinosarcomas (malignant mixed Mullerian tumours)* are now known to be epithelial neoplasms which have undergone sarcomatous metaplasia,<sup>18</sup> the epithelial elements being the driving force. Accordingly, they are a subtype of high grade endometrial carcinoma. Undifferentiated carcinoma has recently been highlighted as an aggressive form of uterine carcinoma which may be associated with a more differentiated component, as part of a mixed carcinoma.<sup>19</sup>

*Mixed carcinoma* refers to a tumour composed of more than one morphological subtype. Using the WHO definition, at least 10% of the tumour must comprise the non-dominant type of differentiation. However, it is recommended that all subtypes are mentioned in the pathology report, even if the minor component comprises less than 10% of the neoplasm. It is advised that the approximate percentage of all cell types should be stated in the report, although it is controversial as to what percentage of a more aggressive subtype might influence tumour behaviour.

*Pure squamous cell carcinomas* arising in the endometrium are extremely uncommon. It is much more common to see extensive squamous differentiation in an endometrioid carcinoma or uterine involvement by cervical squamous cell carcinoma. These more likely possibilities should be excluded before diagnosing a primary squamous cell carcinoma of endometrium.

## 5.2 Tumour grade

The FIGO grading system, most commonly used for grading endometrioid and mucinous carcinomas, is based upon the extent of non-gland forming tumour combined with assessment of the nuclear morphology.<sup>20</sup> These tumour types often incorporate solid squamous elements, which should be disregarded for grading purposes. If 5% or less of the non-squamous component is solid, the tumour is grade 1. A tumour in which 6–50% of the non-squamous component is solid is grade 2. A tumour in which over 50% of the non-squamous component is solid is grade 3. In adenocarcinomas exhibiting a grade 1 or grade 2 architectural pattern, the presence of grade 3 nuclei, i.e. nuclei with marked enlargement, irregular coarse chromatin and prominent nucleoli, raises the tumour grade by one. The presence of grade 3 nuclei in an architecturally well-differentiated adenocarcinoma should alert the pathologist to the possibility of a serous carcinoma; p53 and hormone receptor immunohistochemistry may be useful in this regard.

This grading system has demonstrated prognostic utility,<sup>21</sup> but is unfortunately poorly reproducible.<sup>22</sup> The poor reproducibility of FIGO grading has led to attempts to devise a two-tier grading system which is likely to be more reproducible simply by reducing the number of categories.<sup>23,24</sup> However, for the time being, it is recommended that histopathologists continue to use the generally accepted, albeit imperfect, FIGO grading system.

Serous carcinoma, clear cell carcinoma, undifferentiated carcinoma and carcinosarcoma are not graded and are, by definition, regarded as high grade (grade 3) carcinomas. The rare small cell carcinomas (small cell neuroendocrine carcinoma) of endometrial origin are similarly not graded and are considered high grade. In mixed carcinomas with a component of serous carcinoma, clear cell carcinoma or undifferentiated carcinoma, the more aggressive component may influence the tumour behaviour.

## 5.3 Depth of myometrial invasion

Deep myometrial invasion by tumour has repeatedly been shown to be an important poor prognostic indicator in endometrial carcinoma. This is the only independent predictor of haematogenous dissemination by endometrial carcinoma<sup>25</sup> and it is therefore an important determinant of adjuvant therapy.

The 2009 FIGO staging for endometrial cancer no longer requires the pathologist to distinguish between those carcinomas confined to the endometrium and those showing invasion of the inner half of the myometrium. The tumour is FIGO Stage IA if myometrial invasion is absent or confined to less than the inner half (< 50% myoinvasion). The tumour is staged as IB if it involves the outer half of the uterine wall ( $\geq$  50% myoinvasion). This modification in staging is based on statistical analysis of data from more than 42,000 women with endometrial cancer, which showed no difference in 5-year survival for grade 1 and 2 endometrioid cancers confined to the endometrium and similar grades of myoinvasive tumour confined to less than the inner half of the uterine wall.<sup>26</sup> It also takes into account reports in the literature of significant problems in the pathological determination of depth of myometrial invasion. Two separate groups have reported disagreement with the primary pathological evaluation of the depth of myometrial invasion.<sup>27,28</sup> In many of these cases, there was overdiagnosis of early myometrial invasion because of the irregularity of the endometrial–myometrial junction and because of extension of tumour into adenomyotic foci. Other discrepancies were caused by exophytic tumours and, in some cases, extensive smooth muscle metaplasia within the stroma of the neoplasm.<sup>28</sup>

Maximum depth of tumour invasion is best assessed in a well-orientated, full thickness block of the uterine wall from the site of deepest tumour infiltration. For comparison, the block should include uninvolved endometrium, if possible. Involvement of adenomyosis by tumour does not constitute myoinvasion and should not influence the stage. The uterine wall in the cornual region is thin and therefore blocks from the cornual region should not be used for evaluation of depth of invasion unless the tumour is located wholly in this region or it reaches/breaches the serosa only in this region.

In cases where percentage depth of myometrial invasion cannot be ascertained, myometrial infiltration that reaches the arcuate vascular plexus of the uterus usually indicates > 50% myometrial invasion.<sup>29</sup>

#### **5.4 Tumour-free distance to serosa**

This term refers to the distance between the deepest portion of tumour within the myometrium and the nearest serosal surface. It is a way of assessing myometrial invasiveness of the tumour which is unaffected by the confounding factors discussed above. This measurement has been identified as an independent prognostic factor in endometrial adenocarcinoma.<sup>30,31</sup>

#### **5.5 Cervical involvement by tumour**

In most studies, involvement of the cervical stroma by endometrial carcinoma is associated with a worse prognosis than involvement confined to the endocervical glands.<sup>32,33</sup> Fanning *et al* reported that none of 12 patients (0%) with cervical glandular involvement developed recurrence, while five of eight (63%) with cervical stromal involvement recurred ( $p < 0.01$ ).<sup>31</sup> Cervical stromal invasion is also a predictor of pelvic lymph node metastases.<sup>34</sup>

In the 2009 FIGO Staging System, cervical stromal involvement by endometrial carcinoma is regarded as Stage II. Endocervical surface or crypt involvement without cervical stromal invasion is now regarded as Stage I (IA or IB depending on the depth of myometrial invasion).

Assessment of cervical stromal invasion may be difficult and may take the form of a confluent back-to-back arrangement of glands with distortion of the crypt architecture, sometimes accompanied by a desmoplastic stromal reaction or rarely, show a subtle 'burrowing' or 'adenoma malignum-like' pattern of infiltration.<sup>35</sup>

Although cervical glandular involvement, in itself, no longer results in upstaging of an endometrial cancer, this information has been retained in the reporting proforma (see Appendix D), as this finding may still influence adjuvant therapy.

#### **5.6 Adnexal involvement**

The presence or absence of ovarian or fallopian tube involvement should be documented. Adnexal involvement (FIGO Stage IIIA) may occur as a result of direct extension or metastatic spread by tumour. The distinction is irrelevant for staging purposes, but should be attempted in the interest of accuracy. It is usually possible to distinguish between direct extension and metastatic disease by careful macroscopic examination and judicious block taking. The microscopic findings of a high grade endometrial tumour and lymphovascular invasion favour metastatic disease.

Approximately 5% of women with endometrial adenocarcinoma of endometrioid type have a synchronous ovarian carcinoma of the same morphological type.<sup>36,37</sup> It is important to distinguish between a synchronous ovarian carcinoma and a metastasis in the ovary as women with the former have a much better prognosis than women with the latter.<sup>38</sup> The features in the uterine neoplasm which favour a synchronous rather than a metastatic ovarian carcinoma are low tumour grade, no or superficial myometrial invasion and absence

of lymphovascular invasion. Features in the ovarian neoplasm which favour a synchronous rather than a metastatic neoplasm include a low grade tumour and associated endometriosis or borderline tumour. In the presence of a high grade or deeply invasive endometrial carcinoma, close attention should be paid to the macroscopic and microscopic features of the ovarian tumour. Bilaterality, a nodular growth pattern, extensive necrosis and lymphovascular permeation favour an ovarian metastasis.<sup>39</sup>

### **5.7 Serosal involvement**

The uterine serosa should be examined carefully and the presence of microscopic disease documented (FIGO Stage IIIA).

### **5.8 Parametrial involvement**

The presence or absence of parametrial involvement should be documented. In the 2009 FIGO staging system, an endometrial carcinoma with parametrial invasion is regarded as Stage IIIB. This departure from the 1988 FIGO staging system is based on evidence that parametrial involvement, whether by direct tumour extension or as a result of lymphovascular invasion, is a poor prognostic factor in endometrial adenocarcinoma. It is not an independent prognostic indicator, but correlates with other poor prognostic factors.<sup>40,41</sup>

### **5.9 Lymphovascular invasion**

The presence or absence of lymphovascular invasion should be documented. It is important to note, however, that the presence of lymphovascular invasion, whether within the uterus or outside it, does *not* upstage the tumour. For example, an endometrial adenocarcinoma confined to the inner half of the myometrium but with vascular involvement in the outer half, should be staged as IA. However, as lymphovascular space invasion is a predictor of tumour recurrence and lymph node metastasis,<sup>42,43</sup> such cases should be carefully discussed at MDTMs where the need for adjuvant therapy or further staging should be determined based on all the information available. Lymphovascular invasion is a relatively unusual finding in endometrioid carcinoma in which it generally correlates with deep myometrial invasion and other poor prognostic factors. It is a much more common finding in uterine serous carcinoma where it may be present in superficially myoinvasive or even non-myoinvasive tumours.

### **5.10 Background endometrium**

The nature 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 commented upon.<sup>44</sup>

### **5.11 Peritoneal washings**

The identification of malignant cells in peritoneal washings no longer influences the 2009 FIGO staging of endometrial carcinoma. This item is nevertheless included in the dataset as the staging guidelines state that peritoneal washings should be reported separately. The significance of positive peritoneal washings in an individual case should be discussed at the MDTM.

This modification is based on the lack of consensus in the literature regarding the prognostic significance of positive peritoneal washings in the absence of other evidence of extrauterine spread. Some investigators have reported a high rate of positive peritoneal washings following preoperative manipulations and investigations; they attributed this to tumour spillage from the fallopian tubes rather than true peritoneal involvement by tumour.<sup>45</sup> Other

investigators have disagreed with the suggestion that prior manipulation causes a high false-positive rate in peritoneal washings.<sup>46,47</sup> Moreover, some investigators have questioned the value of peritoneal washing cytology as an independent prognostic indicator.<sup>48,49</sup>

## 5.12 Lymph nodes

The 2009 FIGO staging system subdivides Stage IIIC into two substages depending on the distribution of lymph node metastases. An endometrial carcinoma with pelvic lymph node metastases is categorised as Stage IIIC1. Involvement of para-aortic lymph nodes with or without pelvic lymph nodes is staged as IIIC2. Inguinal lymph node involvement is categorised as Stage IVB. This modification is based on observations that patients with para-aortic nodal involvement have a worse disease-free survival and overall survival than those with pelvic lymph node involvement.<sup>50,51</sup> In one study,<sup>50</sup> disease-free 5-year survival was 35% for patients with para-aortic lymph node metastases *versus* 85% for those with pelvic but without para-aortic lymph node metastases. Hoekstra *et al*<sup>51</sup> found that the 5-year disease-free survival with para-aortic lymph node involvement was 44.4% compared to 65.6% for pelvic lymph node metastases.

The number of nodes retrieved from each site should be recorded. The number of lymph nodes containing metastatic tumour should likewise be recorded. The presence of extranodal spread should be documented.

## 5.13 Staging

Tumours should be staged according to the 2009 FIGO staging system (Appendix B). Although it may be useful to record the provisional tumour stage on the dataset, the final definitive stage should be determined at the MDTM, taking into account all clinical, radiological and pathological findings.

## 5.13 Summary of core data items

- tumour type
- tumour grade
- depth of myometrial invasion
- tumour-free distance to serosa
- presence or absence of microscopic cervical surface or crypt involvement
- presence or absence of cervical stromal invasion
- presence or absence of adnexal involvement
- presence or absence of uterine serosal involvement
- presence or absence of lymphovascular invasion
- presence or absence of parametrial involvement
- background endometrium:
  - normal or abnormal
  - type of hyperplasia (if present)
  - any other abnormality
- adnexal structures:
  - normal or abnormal
  - specify any abnormality present
- peritoneal washings:

- whether taken or not
- malignant cells present or absent
- lymph nodes:
  - whether sampled or not
  - number identified from each site and number involved
- omentum:
  - whether sampled or not
  - presence or absence of metastasis

## 6 Non-core data items

These are data items that are of uncertain prognostic or therapeutic relevance. They may be included as a comment in the dataset or within an accompanying text report. These might include:

- uterine weight
- features noted on gross examination:
  - gross architecture of tumour
  - smooth or rough surface
  - presence or absence of necrosis
- in carcinosarcomas, the subtypes of the epithelial component, the presence or absence of heterologous mesenchymal elements and the relative percentage of the epithelial and stromal components
- in mixed carcinomas, the relative percentages of different components present
- weight of the omentum

## 7 WHO classification of endometrial epithelial tumours and SNOMED Coding

Primary endometrial tumours should be subtyped according to the WHO classification<sup>10</sup> and coded using SNOMED codes (Appendix A).

## 8 Small biopsy specimens

Most endometrial carcinomas are diagnosed on endometrial biopsy, obtained using an outpatient endometrial sampling procedure or by cervical dilatation and endometrial curettage under general anaesthesia. The Pipelle sampler, one of the most commonly used in the United Kingdom for outpatient endometrial sampling, samples approximately 4% of the endometrial surface area. In the majority of patients, endometrial curettage samples between 25% and 50% of the uterine cavity. In general, outpatient procedures yield less endometrial tissue than curettage.

When handling endometrial biopsy specimens, a sieve or mesh basket may be useful to ensure that all the material is retrieved. All the submitted tissue should be processed. The presence of a grossly obvious polyp should be stated. It may be useful to weigh the submitted tissue.

Where the biopsy shows features of an epithelial neoplasm, the report should clearly specify the subtype of tumour present and the FIGO grade on the basis of this tissue. It is recognised that in a significant proportion of cases there will be some disparity in tumour grade between the endometrial biopsy and the subsequent hysterectomy specimen. This is attributed to sampling problems inherent in blind endometrial biopsy procedures and is

unavoidable as the final FIGO grade depends on thorough sampling of tumour from the surgical specimen and assessment of the overall architectural and nuclear features.

If the biopsy is deemed to show atypical endometrial hyperplasia rather than carcinoma, the report should specify this clearly. It is outside the scope of this dataset to provide information about the pathological distinction between atypical hyperplasia and grade 1 endometrioid adenocarcinoma and the reader is referred to specialist gynaecological pathology textbooks. There is poor reproducibility in the diagnosis of atypical endometrial hyperplasia, which is applicable to specialist gynaecological pathologists, as well as to non-specialists. However, in a significant proportion of cases (ranging from 23% to 48% in several studies)<sup>52-54</sup> diagnosed as atypical hyperplasia on endometrial biopsy, the resected uterus contains adenocarcinoma. The histopathology report should therefore indicate that concurrent endometrioid adenocarcinoma cannot be ruled out. Patients diagnosed as having atypical endometrial hyperplasia will benefit from discussion at the gynaecological oncology MDTM and their management should be based on the results of clinical, pathological and imaging findings.

## **9 Reporting of frozen sections**

In most institutions in the United Kingdom, intraoperative frozen sections are rarely used in patients with endometrial carcinoma. Frozen sections may be performed to:

- determine the nature of unexpected and clinically suspicious extrauterine lesions
- evaluate suspicious lymph nodes
- evaluate depth of myometrial invasion

It is important that clinicians who request frozen sections are cautioned about the potential limitations of the technique, such as problems associated with poor morphology and sampling errors.

## **10 Specific aspects of individual tumours not covered elsewhere**

Immunohistochemistry can be useful in certain clearly defined situations. It is beyond the scope of this document to discuss in detail the various uses of immunohistochemistry in the evaluation of an endometrial carcinoma and the reader is referred to several reviews.<sup>55,56</sup> The results of immunohistochemistry should always be interpreted in conjunction with the clinical and morphological findings. A panel of markers including p53, oestrogen receptor (ER) and progesterone receptor may be helpful in distinguishing between uterine serous carcinoma and endometrioid adenocarcinoma. A panel comprising ER, vimentin, monoclonal carcinoembryonic antigen (CEA) and p16 may be useful in distinguishing between a primary endometrial and endocervical adenocarcinoma. Markers such as chromogranin A, synaptophysin and CD56 may be useful in confirming neuroendocrine differentiation in a neoplasm.

## **11 Acknowledgements**

Members of the British Association of Gynaecological Pathologists (BAGP) Working Group.  
Professor M Wells, author of the 2001 dataset for the reporting of endometrial cancers.

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## Appendix A: WHO classification of endometrial tumours and SNOMED M coding

### Adenocarcinoma

Endometrioid	M83803
Variant with squamous differentiation	M85703
Villoglandular variant	M82623
Secretory variant	M83823
Ciliated cell variant	M83833
Mucinous	M84803
Serous	M84413
Clear cell	M83103
Mixed cell carcinoma	M83233
Squamous cell carcinoma	M80703
Transitional carcinoma	M81203
Small cell carcinoma	M80413
Undifferentiated carcinoma	M80203
Carcinosarcoma	M89803

## Appendix B: 2009 FIGO and TNM staging of endometrial carcinoma

FIGO stage	TNM category	Definition
–	TX	Primary tumour cannot be assessed
–	T0	No evidence of primary tumour
–	Tis	Carcinoma <i>in situ</i> (preinvasive carcinoma)
I	T1	Tumour confined to corpus uteri
IA	T1a	No or less than half of myometrial invasion
IB	T1b	Invasion equal to or more than half of the myometrium
II	T2	Tumour invades cervical stroma, but does not extend beyond the uterus*
III	T3 and/or N1	Local and/or regional spread of the tumour
IIIA	T3a	Tumour invades uterine serosa and/or adnexa <sup>#</sup>
IIIB	T3b	Vaginal and/or parametrial involvement <sup>#</sup>
IIIC	N1	Metastases to pelvic and/or para-aortic lymph nodes <sup>#</sup>
IIIC1		Positive pelvic nodes
IIIC2		Positive para-aortic lymph nodes (± positive pelvic nodes)
IV		Tumour invades bladder and/or bowel mucosa, and/or distant metastases
IVA	T4	Invasion of bladder and/or bowel mucosa <sup>##</sup>
IVB	M1	Distant metastases, including intra-abdominal metastases and/or inguinal lymph nodes

### Notes:

Stage groupings apply to all grades of carcinoma.

\*Endocervical glandular involvement only should be considered as Stage I and no longer as Stage II.

<sup>#</sup>Positive cytology has to be reported separately without changing the stage.

<sup>##</sup>The presence of bullous oedema is not sufficient evidence to classify T4. This lesion should be confirmed by biopsy.

## **N – Regional lymph nodes**

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Regional lymph node metastasis

## **M – Distant metastasis**

- M0 No distant metastasis
- M1 Distant metastasis (excluding metastasis of vagina, pelvic serosa, or adnexa, including metastasis to inguinal lymph nodes, intra-abdominal lymph node other than para-aortic or pelvic nodes)

## **pTNM pathological classification**

The pT and pN categories correspond to the T and N categories.

- pN0** Histological examination of a pelvic lymphadenectomy specimen will ordinarily include six or more lymph nodes.

If the lymph nodes are negative but the number ordinarily examined is not met, classify as pN0. (FIGO considers such cases aspNX.)

## **Histopathological grading**

For histopathological grading use G1, G2, or G3.<sup>25</sup>

## **Stage grouping**

Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3a	N0	M0
Stage IIIB	T3b	N0	M0
Stage IIIC	T1, T2, T3	N1	M0
Stage IVA	T4	Any N	M0
Stage IVB	Any T	Any N	M1

## Appendix C: 1998 TNM and FIGO staging of endometrial carcinoma

TNM category	FIGO stage	Description
TX		Primary tumour cannot be assessed
T0		No evidence of primary tumour
Tis	0	Carcinoma <i>in situ</i> (preinvasive carcinoma)
T1	I	Tumour confined to corpus uteri
T1a	IA	Tumour limited to endometrium
T1b	IB	Tumour invades less than one half of myometrium
T1c	IC	Tumour invades one half or more of myometrium
T2	II	Tumour invades cervix but does not extend beyond uterus
T2a	IIA	Endocervical surface epithelial involvement only
T2b	IIB	Cervical stromal invasion
T3 and/or N1	III	Local and/or regional spread as specified in T3a, b, N1, and FIGO IIIA, B, C below
T3a	IIIA	Tumour involves serosa and/or adnexa (direct extension or metastasis) and/or cancer cells in ascites or peritoneal washings
T3b	IIIB	Vaginal involvement (direct extension or metastasis)
N1	IIIC	Metastasis to pelvic and/or para-aortic lymph nodes
T4	IVA	Tumour involves bladder mucosa and/or bowel mucosa*
M1	IVB	Distant metastasis (excluding metastasis to vagina, pelvic serosa, or adnexa)

\*The presence of bullous oedema is not sufficient evidence to classify a tumour as T4. The lesion should be confirmed by biopsy.

### N – Regional lymph nodes

NX Regional lymph nodes cannot be assessed  
 N0 No regional lymph node metastasis  
 N1 Regional lymph node metastasis

### M – Distant metastasis

MX Distant metastasis cannot be assessed  
 M0 No distant metastasis  
 M1 Distant metastasis

## Appendix D: Reporting proforma for endometrial cancer in hysterectomy specimens

Surname ..... Forenames ..... Date of birth .....

Hospital ..... Hospital no ..... NHS no .....

Date of request ..... Date of reporting..... Sex .....

Pathologist ..... Surgeon ..... Report no. ....

---

### Gross description

Dimensions of uterus Length (mm): ..... Transverse (mm):..... Antero-posterior (mm):.....

Maximum dimension of tumour: .....mm

Position of tumour in uterus: Fundus  Body  Isthmus  Cornu

Myometrial invasion: Yes  No  Serosal involvement: Yes  No

Maximum dimension of left ovary (mm): ..... Right ovary (mm):.....

Dimensions of omentum (if received) (mm): .....

Presence of gross tumour nodules: Yes  No

Other omental pathology (specify): .....

### Histology

Type: Endometrioid  Mucinous  Serous  Clear cell  Carcinosarcoma   
 Undifferentiated  Other (specify) .....

FIGO grade: 1  2  3

Myometrial invasion: None or < 50%  ≥ 50%  Tumour-free distance to serosa (mm): ....

Is there microscopic involvement of:

endocervical surface or crypt epithelium	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
cervical stroma	Yes <input type="checkbox"/>	No <input type="checkbox"/>		
right ovary	Yes <input type="checkbox"/>	No <input type="checkbox"/>	left ovary	Yes <input type="checkbox"/> No <input type="checkbox"/>
right fallopian tube	Yes <input type="checkbox"/>	No <input type="checkbox"/>	left fallopian tube	Yes <input type="checkbox"/> No <input type="checkbox"/>
uterine serosa	Yes <input type="checkbox"/>	No <input type="checkbox"/>	parametrium	Yes <input type="checkbox"/> No <input type="checkbox"/>

Lymphovascular invasion: present  absent

Background endometrium: Normal  Abnormal  (specify) .....

Right ovary: normal  abnormal  (specify) .....

Left ovary: normal  abnormal  (specify) .....

Right tube: normal  abnormal  (specify) .....

Left tube: normal  abnormal  (specify) .....

Peritoneal washings: not submitted  positive  negative

Lymph nodes: Not sampled

Sampled

Right pelvic lymph nodes: total no. nodes ..... no. positive nodes: .....

Left pelvic lymph nodes: total no. nodes ..... no. positive nodes: .....

Right para-aortic lymph nodes: total no. nodes ..... no. positive nodes: .....

Left para-aortic lymph nodes: total no. nodes ..... no. positive nodes: .....

Omentum Not sampled  involved by tumour  not involved by tumour

Comments

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PROVISIONAL FIGO and TNM Stage:

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Signature .....

Date...../...../.....

## Appendix E: Endometrial carcinoma dataset monitoring sheet

The Cancer Datasets of the Royal College of Pathologists comply with the AGREE standards for good quality clinical guidelines ([www.agreecollaboration.org](http://www.agreecollaboration.org)). The sections of this dataset that indicate compliance with each of the AGREE standards are indicated in the table.

AGREE Standard	Section of dataset
<b>SCOPE AND PURPOSE</b>	
1. The overall objective(s) of the guideline is (are) specifically described	1
2. The clinical question(s) covered by the guidelines is (are) specifically described	1
3. The patients to whom the guideline is meant to apply are specifically described	1
<b>STAKEHOLDER INVOLVEMENT</b>	
4. The guideline development group includes individuals from all the relevant professional groups	1
5. The patients' views and preferences have been sought	N/A
6. The target users of the guideline are clearly defined	1
7. The guideline has been piloted among target users	See previous edition
<b>RIGOR OF DEVELOPMENT</b>	
8. Systematic methods were used to search for evidence	1
9. The criteria for selecting the evidence are clearly described	1
10. The methods used for formulating the recommendations are clearly described	1
11. The health benefits, side effects and risks have been considered in formulating the recommendations	1
12. There is an explicit link between the recommendations and the supporting evidence	5
13. The guideline has been externally reviewed by experts prior to its publication	1
14. A procedure for updating the guideline is provided	Foreword
<b>CLARITY OF PRESENTATION</b>	
15. The recommendations are specific and unambiguous	5
16. The different options for management of the condition are clearly presented	5
17. Key recommendations are easily identifiable	5
18. The guideline is supported with tools for application	Appendix D
<b>APPLICABILITY</b>	
19. The potential organizational barriers in applying the recommendations have been discussed	Foreword
20. The potential cost implications of applying the recommendations have been considered	1
21. The guideline presents key review criteria for monitoring and/audit purposes	1
<b>EDITORIAL INDEPENDENCE</b>	
22. The guideline is editorially independent from the funding body	1
23. Conflicts of interest of guideline development members have been recorded	1

**Standard 20 is currently regarded as not directly applicable to this dataset.**