



The Royal College of Pathologists  
*Pathology: the science behind the cure*

## Standards and Datasets for Reporting Cancers

# Dataset for histological reporting of cervical neoplasia (2<sup>nd</sup> edition)

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## 1 INTRODUCTION

This document provides the datasets for the histological reporting of cervical cancers in small resection and hysterectomy specimens and replaces the previous datasets of 2001. Meticulous reporting of cervical cancers is important because gross pathological and histological parameters will determine patient treatment. Accurate recording of pathological parameters in the datasets has both direct and indirect implications for the prognosis of individual patients. The use of datasets (and the background information that forms part of the datasets) in the context of the multidisciplinary team (MDT) meeting is advocated to optimise decisions related to patient treatment, 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. It is important to have robust local mechanisms in place to ensure that the MDT Clinical Leads and Cancer Registries are apprised of supplementary or revised histology reports which may affect patient treatment and data collection.

The new datasets are largely based on the original version. The presentation of data items in the small resection specimen protocol has been re-ordered so that invasive tumours are covered before preinvasive lesions. Some data items have been removed because of recent developments in the NHSCSP (National Health Service Cervical Screening Programme) e.g. the implementation of the audit of cervical cancers, in which changes associated with HPV infection and epithelial changes of uncertain significance are included.

Details regarding tumour margins have been expanded and clarified in the dataset covering the reporting of cervical cancer in hysterectomy specimens. Perhaps the most important and controversial changes are those related to use of the term ‘microinvasive carcinoma’. Because of the lack of clarity of this term and the wide variation in the criteria that are applied in its use, the British Association of Gynaecological Pathologists (BAGP) Working Group has advocated the avoidance of this term in histological reporting and recommends using the FIGO stage as a specific descriptor of small invasive carcinomas. Measurement of multifocal carcinomas is also discussed in some detail because of the risk of over-staging FIGO stage IA1 or IA2 cancers as IB cancers, and thereby influencing treatment decisions.

Most gynaecological oncologists use the FIGO staging system for gynaecological cancers. However, TNM staging is included in this dataset to allow standardisation of staging across all cancer sites. Depending on local protocols, clinicians may elect to include TNM staging in gynaecological cancer datasets.

Evidence for the revised dataset was obtained from a review of relevant literature up to 2007.

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
- National Health Service Cervical Screening Programme (NHSCSP)
- British Society for Clinical Cytology (BSCC)
- British Society for Colposcopy and Cervical Pathology (BSCCP)
- British Gynaecological Cancer Society (BGCS).

## **2 CLINICAL INFORMATION REQUIRED ON THE SPECIMEN REQUEST FORM**

This should include full patient details, cervical screening history (if available), clinical appearance of the cervix, the results of previous biopsies and radiological investigations that have been carried out for tumour staging, colposcopic appearance and comprehensive details of the surgical procedure. The details of surgical specimens from multiple sites should be provided and specimen pots should be labelled to correspond to the specimen details on the request form.

## **3 PREPARATION OF SPECIMEN BEFORE DISSECTION**

The usual surgical procedure for cervical carcinoma is a radical hysterectomy and lymph node dissection. In cases of advanced cervical tumours, adjacent organs may be involved and specimen preparation will depend on whether adjacent organs have been resected, whether or not the tumour is visible macroscopically, and the extent of tumour spread.

If adherent or adjacent organs are attached these will need to be opened (to allow fixation) in a way that will not compromise resection margins, and margins may need to be painted with ink or appropriate dye prior to specimen opening. However, nowadays advanced cervical cancers (>FIGO IIA) are unlikely to be surgically resected and are usually treated with chemoradiation.

Preparation of radical hysterectomy specimens will depend on the size of the cervical tumour and the extent of spread. Parametrial, paracervical and vaginal margins may require painting with ink/dye before opening the uterus (this may be done before sampling to allow adequate fixation of the corpus). Opening the uterus should allow optimal visualisation of the cervical tumour and facilitate block taking to ensure that all of the core data items can be assessed. There is no one proscriptive method of opening the uterus and the BAGP Working Group was of the opinion that this can be done according to the preference of the individual pathologist. In the case of large tumours, opening the specimen in the sagittal plane may be appropriate but for very small tumours or tumours that are not obvious macroscopically it may be advantageous to open the uterus in the coronal plane. Some pathologists advocate amputation of the cervix before opening the uterus so that the cervix can be dissected and processed in a similar way to a cone or loop biopsy, but this will depend on tumour size – large, bulky tumours may not be amenable to sampling in this way.

A photographic record of the specimen may be useful.

## **4 SPECIMEN HANDLING AND BLOCK SELECTION**

Cone and loop biopsies are performed mainly for preinvasive lesions but occasionally an early invasive carcinoma is identified. Wedge biopsies are usually performed for the confirmation and typing of tumours.

Trachelectomy specimens tend to be performed at specialist centres and, although their detailed assessment is outwith the remit of this document, it is recommended that local protocols should incorporate examination of all of the cervical, vaginal and parametrial tissue resected in a way that ensures accurate assessment of tumour dimensions, parametrial involvement and margin status, including distances from all margins.

#### **4.1 Gross examination and dissection of excisional cervical biopsy specimens (wedge/cone/loop biopsy)**

The number of pieces of tissue must be indicated on the proforma. It has become increasingly common to receive a second, separate loop biopsy that has been taken from the apex of the more superficial loop biopsy (so called "top hat") and both specimens should be processed in the same way. In some cases, more than two pieces of tissue may be received. All specimens should be measured in three dimensions, and must be examined in their entirety. The block designation of each separate specimen must be provided (e.g. first piece: blocks A–C; second piece: blocks D–F; etc.).

There are several methods of dissection of cone and loop biopsies (whether received opened or closed), although there are two preferred, widely used methods. The first is serial slicing at 2–3mm intervals,<sup>1,2</sup> from one edge to the other in a sagittal and parasagittal plane (beginning at the 3 or 9 o'clock edge, if the 12 o'clock position has been marked by the surgeon), perpendicular to the transverse axis of the external os. This avoids the problems of interpretation that may arise when dysplastic epithelium arises on the narrow end of a wedge shaped block (if a loop/cone specimen is sectioned radially, see below), and facilitates assessment of tumour volume in small lesions or neoplasms<sup>3</sup>. However, this method does not allow direct correlation of CIN, CGIN or tumour with the specific position on a clock face<sup>4</sup> that the second, radial method of sampling permits. Using this technique, wedge shaped slices are taken according to the hours on a clock face. Although this method of sampling may be useful if accurate mapping of a lesion is desired,<sup>2</sup> in practice, determination of the position of a cervical lesion is very rarely of relevance to subsequent treatment or management.

In either case, the slices should be submitted in sequential, individually designated cassettes, and local protocols must be in place to ensure that the sequential (not the apposing) faces of consecutive slices are blocked and cut for histology to enable measurement of the third dimension of cervical tumours when necessary. In some centres, for the purpose of expediency, the excision margins of loop biopsies are assessed by embedding the outer (curved) surface of the first and last slices of the loop face down for sectioning, instead of the cut surface. This avoids having to request additional levels to assess these margins.

Although it has been suggested for reasons of convenience and economy<sup>4,5</sup> that if slices are small, two or three may be placed in one cassette, Members of the Working Party of The Royal College of Pathologists<sup>6</sup> advocate that each slice of tissue should be placed in a single cassette, so that the sequence of the slices is unambiguous thus enabling assessment of unifocal versus multifocal disease, and reliable interpretation of the order of sequential slices to establish when the third dimension of a lesion may exceed 7mm (FIGO IB1). The BAGP Working Group is of the view that if more than one slice is placed in an individual cassette, local protocols should be in place so that it is known unequivocally which slices are adjacent and consecutive.

#### **4.2 Gross examination and dissection of hysterectomy specimens**

The specimen components (usually vaginal cuff, uterus, parametria, fallopian tubes, and ovaries), their dimensions and gross appearances should be recorded. Lymph nodes are usually sent in separate pots and labelled as to their sites of origin.

After appropriate measurements have been taken, it may be necessary to trim or remove the vaginal cuff to enable assessment of the cervical tumour. If this is done, the circumferential vaginal resection margin can be blocked in strips for histological assessment of this resection margin. If there is only a short length of vaginal cuff attached to the specimen, trimming will

not be necessary and the vaginal cuff (and resection margin) is submitted in continuity with the cervix. Particular attention should be paid to the fornices. If there is macroscopic evidence of vaginal involvement the position and extent of involvement should be recorded.

If present and visible, the dimensions of a preceding loop or cone biopsy site should be recorded. Although it may be difficult to measure the cervical tumour in three dimensions, this should be attempted if possible. Tumour size remains one of the most important determinants of outcome and accurate measurement is important in ascertaining the FIGO stage.<sup>7</sup> In most studies tumour size is based on two-dimensional measurements but, in a few studies, measurements in terms of volume have been shown to predict prognosis more reliably than measurements in only one or two dimensions<sup>8,9</sup> although, in practice, management usually does not depend on tumour volume.

The position of the tumour in the cervix should be recorded. If tumour involves more than one quadrant of the cervix, the appropriate boxes should be marked on the proforma (e.g. anterior and right should be marked if both the anterior and right quadrants are involved). In one study, the risk of lymph node involvement was shown to increase progressively with involvement of one, two, three or four cervical quadrants (from 2% if one quadrant is involved to 13% if three or four quadrants are involved).<sup>10</sup> Furthermore, systematic recording of the position of the tumour within the cervix enables audit of, and correlation with, radiological findings.

Macroscopic tumour involvement of the parametrial and paracervical tissues should be noted and recorded and may determine the method of dissection and block taking. It may be preferable to sample the tumour in continuity with the involved parametrial or paracervical tissues, rather than remove these to begin with, but either method can be used. There are few published data about the processing and sampling of parametrial and paracervical tissues whose volume and extent are dictated by the surgical procedure, but these were included as separate data items in the previous datasets for the reporting of cervical neoplasia of The Royal College of Pathologists (RCPath).<sup>11</sup> It recommended that this practice should continue to enable studies to be carried out to assess whether paracervical margin involvement simply reflects a correlate of radial margin involvement, or has the same prognostic implications as parametrial involvement. In one study, assessment of paracervical tissues was included with parametrial tissues<sup>12</sup> in order to determine the pattern of parametrial spread. This study, which involved the processing of hysterectomy specimens of 69 patients with early cervical carcinoma (FIGO stage IB1, IB2 and IIA) with a 'giant section technique' and separating paracervical and parametrial tissues to obtain a thorough three-dimensional assessment of these, revealed clinically undetected involvement in a significant percentage of cases, and metastasis to the pelvic lymph nodes was always associated with parametrial disease. Parametrial involvement is a poor prognostic indicator for early stage cervical carcinoma, regardless of lymph node status,<sup>13</sup> and is an adverse prognostic indicator for advanced stage cervical carcinomas.<sup>14</sup>

Extension of the tumour into the uterine corpus should be recorded although this does not alter the stage of the cervical carcinoma.

#### **4.3 Block selection for excisional cervical biopsy specimens (wedge/cone/loop biopsy)**

These specimens should be blocked in their entirety. Cassettes should be separately identified, with a block designation to indicate their origin.

#### **4.4 Block selection for hysterectomy specimens**

Blocks of the cervix must be taken to demonstrate the maximum depth of invasion and the relationship of the tumour to the surgical resection margins, notably the vaginal, anterior cervix/bladder reflection, posterior cervix/rectovaginal septum and parametrial/paracervical margins.

For small tumours, or in cases where no macroscopic tumour is identified, the whole of the cervix should be blocked as in the case of cone/loop biopsies. For large, bulky tumours at least one section per centimetre of greatest tumour dimension should be blocked<sup>15</sup> to include, if possible, the point of deepest invasion, i.e. full thickness of the cervical wall. Additional blocks should include the interface with adjacent cervix in order to demonstrate any CIN or CGIN from which the carcinoma may have arisen.<sup>5</sup> Full thickness sections from the lower uterine segment, immediately proximal and adjacent to the tumour should be taken to identify upward extension.

Blocks of the vaginal resection margin may be taken in continuity with the tumour if the vaginal cuff is short (see above) or separate blocks of the trimmed circumferential vaginal resection margin should be blocked in specifically designated cassettes according to their origin (e.g. from the anatomical quadrants from which they have originated).

The parametria and paracervical tissues should be blocked in their entirety. The laterality of the blocks must be recorded and inking may be helpful to define the true surgical margins.<sup>5</sup>

The uterine corpus and adnexa should be sampled according to standard protocols<sup>1,2,4,5</sup> if uninvolved, but additional blocks may be required if there is evidence of involvement by tumour.

The number of lymph nodes retrieved from each site should be recorded. The presence of macroscopic involvement of lymph nodes should be noted together with the dimensions of involved nodes. All resected lymph node tissue should be sampled and all lymph nodes from each location must be blocked. Each individual 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 5mm can be bisected or processed whole and large lymph nodes may require sampling in more than one block.

In departments where the facility for processing of oversize blocks is available a good overview of the tumour and resection margins can be obtained, but standard blocks of tumour should also be processed, to enable immunohistochemistry or other special stains to be performed more readily should these be required.

The origin/designation of all tissue blocks should be recorded. This is particularly important should the need for internal or specialist external review arise. The reviewer needs to be clear about the origin, relevant resection margin/s and laterality of each block in order to provide an informed specialist opinion.

## **5 CORE HISTOLOGICAL DATA ITEMS**

In the case of loop/cone/wedge biopsies and hysterectomy specimens the presence or absence of cervical intraepithelial neoplasia (CIN) must be reported, and the grade provided (CIN 1, 2, 3). Cervical glandular intraepithelial neoplasia (CGIN) must be recorded and graded (low or high grade), as should stratified mucin-producing intraepithelial lesion (SMILE).<sup>16</sup> It should

be remembered that in loop/cone biopsies a final FIGO stage cannot be provided for incompletely excised lesions, including cases with CIN or CGIN at a margin; only a provisional FIGO stage can be applied.

### **Tumour type**

Tumour type should be designated according to the WHO classification (see Section 7). There is controversy in the literature as to whether different tumour types are associated with different prognoses and, while some studies have reported a poorer prognosis for adenocarcinoma and adenosquamous carcinoma as opposed to squamous carcinoma,<sup>13,17,18</sup> other studies have shown that the apparent poor prognosis of these tumour types may be due to the presence of bulkier disease and greater resistance to radiotherapy.<sup>19–21</sup> Neuroendocrine carcinomas (both small and large cell types) must be separately identified because of their poor prognosis and the need for neo-adjuvant or adjuvant chemotherapy.<sup>22,23</sup>

### **Tumour grade**

Tumour grade is a controversial prognostic factor in cervical carcinoma. This is likely to reflect the variety of grading systems in use and lack of agreement on how to apply them. The systems that have shown close correlation with prognosis are those in which multiple criteria are assessed and individually scored, such as the Stendahl system<sup>24</sup> or invasive front grading.<sup>25</sup> These have been shown to work well when used by individuals, but have not been tested widely for reproducibility and are too cumbersome for routine use. It is currently recommended that squamous carcinomas should be graded according to a modified version of Broders as well differentiated (keratinising), moderately or poorly differentiated.<sup>26</sup> There is no agreed grading system for cervical adenocarcinoma. It has, however, been recommended that these tumours be graded according to the FIGO system for endometrial adenocarcinoma,<sup>6</sup> but in cervical adenocarcinoma the nuclear grade may be more significant.<sup>27</sup> Grading of adenosquamous carcinomas as well, moderately or poorly differentiated according to the degree of differentiation of the squamous and glandular components is suggested by the Working Group.<sup>6</sup> Neuroendocrine carcinomas are not graded and are, by definition, high grade carcinomas.

### **Tumour dimensions**

The term ‘microinvasive carcinoma’ does not appear in the FIGO staging system for cervical cancer. Furthermore, use of the term ‘microinvasive carcinoma’ has different connotations in the United Kingdom and North America. In the United Kingdom, microinvasive carcinoma is considered to be synonymous with FIGO stage IA1 and IA2 disease in most, but not all, institutions (some use the term microinvasive carcinoma to indicate FIGO stage IA1). In the United States, the term is synonymous with stage IA1 disease.<sup>28</sup> The American Society of Gynecologic Oncology (SGO) has its own definition of FIGO stage IA tumours that is limited not only by the depth of tumour invasion, but also by the presence of lymphovascular invasion. According to the SGO, cancers that invade more than 3mm or those invading less than 3mm with lymphovascular involvement are classified as FIGO stage IB.<sup>29</sup> In order to avoid confusion, the BAGP Working Group has indicated a preference for avoiding the term ‘microinvasive carcinoma’ and for using the specific FIGO stage as a descriptor.

Depth of invasion must be measured in all cases. This measurement is taken from the base of the epithelium (surface or glandular) from which the carcinoma arises, as specified in the FIGO classification. If there is no obvious epithelial origin, the depth should be measured from the tumour base (deepest focus of tumour invasion) to the base of the nearest surface epithelium.

According to the FIGO classification two tumour dimensions are required but there is no guidance from FIGO with regard to measurement of the second dimension of horizontal spread. Several studies have suggested that tumour volume is the most reliable prognostic factor for early stage tumours.<sup>8,30-32</sup> For practical purposes, measurement of tumours in two dimensions (depth and maximal horizontal extent) is adequate, although a third dimension to calculate volume may be required in individual cases.

In unifocal tumours the maximum horizontal dimension/width of tumour is measured in the section in which the width is greatest (from the edge at which invasion is first seen, to the most distant edge at which invasion is identified). There is controversy about this measurement because according to NHSCSP Publication Number 10 the measurement of width is not limited to the confluent component of the tumour.<sup>6</sup> This becomes problematical because up to 12% of carcinomas with early invasion may be multifocal in origin.<sup>33</sup> It is unclear how the horizontal dimension of lesions with multiple invasive foci should be measured. In such circumstances it is important to distinguish multifocal FIGO stage IA1 or IA2 disease from clinically occult stage IB disease<sup>34</sup> although there is both anecdotal evidence and accumulating evidence in the literature that the prognosis of small FIGO stage IB tumours does not differ significantly from stage IA2 tumours.<sup>29,31</sup> There is a paucity of published data about the measurement and subsequent staging of multifocal tumours,<sup>34</sup> and until further data emerge, the BAGP Working Group recommends that such cases are discussed individually and staged at the MDT meeting. If the small invasive foci are clearly separate, then some of these neoplasms may be regarded as multiple foci of stage IA1 disease while in other cases, where the foci are not clearly separate, then the measurement of horizontal spread may be taken from one edge of the whole lesion to the other. If invasive carcinoma is present in three or more adjacent sections of tissue the diameter of the lesion may exceed 7mm, i.e. the carcinoma may be more than FIGO stage IA2. An estimate of the thickness of the blocks can be calculated from the macroscopic description of the specimen, and the number of blocks taken, although pathologists should be mindful that thickness of large/outsize blocks can vary from block to block, as compared with standard-sized blocks.

All grossly visible lesions, even those with only superficial invasion, are clinical stage IB. Large tumours must also be measured in at least two dimensions.

Early invasive adenocarcinoma is a controversial entity and is not specifically mentioned in the 1995 FIGO staging, but nonetheless it is recommended that the FIGO classification be applied.<sup>23</sup> Identification of early invasion in a glandular lesion may be more difficult than in a squamous lesion. Early invasive adenocarcinoma is diagnosed on the basis of obvious invasion to 5mm or less, extension beyond the normal endocervical gland field and often a stromal response characteristic of invasive carcinoma.<sup>35</sup> The width of the tumour must be measured in a similar way to that described for squamous neoplasms, but in most cases the depth is measured from the epithelial surface, rather than the point of origin which can be difficult to establish in many cases<sup>23,36</sup> i.e. the thickness, rather than the true depth of invasion is measured, and this should be indicated when completing the dataset proforma. There is now emerging evidence that the behaviour of early invasive adenocarcinoma is similar to its squamous counterpart.

### **Lymphovascular invasion**

The presence or absence of lymphovascular space invasion must be recorded for tumours of all types and stages, be they tumours that show only early invasion or more than FIGO stage IA2. The significance of lymphovascular invasion is covered in detail in a review by Singh *et al*<sup>37</sup> but briefly, this finding is in itself a strong adverse prognostic indicator and correlates highly with other adverse prognostic indicators such as tumour type and stage.<sup>18,22</sup> In patients

with early invasive tumours the quantity of lymphovascular space invasion has been shown to be an independent prognostic factor for time to recurrence.<sup>38</sup>

### **Resection margins**

The status of all resection margins must be documented in the proforma. Depending upon its position, the closest radial margin may consist only of the minimum thickness of uninvolved cervical stroma. In hysterectomy specimens, if the closest radial margin is lateral, the thickness of any previously trimmed paracervical tissue must be added to the measurements that are taken from the relevant histological section. The position of closest margins must be indicated. In cone/loop biopsies, the status of ectocervical, endocervical and deep resection margins should be recorded as should their involvement by CIN, CGIN, SMILE or invasive carcinoma.

### **Lymph nodes**

The number of nodes that are retrieved and involved at each site must be recorded, and the presence of extranodal spread must be sought and reported if present.

### **Staging**

Tumours should be staged according to the FIGO and TNM staging systems.<sup>39</sup> It is recommended that final staging of cervical tumours should take place at the MDT meeting to ensure correlation with previous cone/loop specimens and other relevant radiological and clinical findings.

### **Summary of core data items**

For excisional biopsies and hysterectomy specimens:

- tumour type
- tumour grade
- tumour size (in at least two dimensions)
- status of resection margins
- presence or absence of lymphovascular invasion.

Additional core data items for hysterectomy specimens:

- minimum tumour-free cervical stroma (tumour-free rim) and position
- closest radial resection margin
- presence or absence of lymph node metastases and extranodal spread
- involvement of other organs or tissues.

## **6 NON-CORE DATA ITEMS**

These may be recorded as a separate comment or within a complementary text report. Such items may include the presence of a cone/loop biopsy site within the cervix, extension of the carcinoma into the endometrial cavity, the results of histochemical stains for mucin on poorly differentiated tumours and the results of any immunohistochemical studies.

An additional parameter that has been reported to be of prognostic significance in cervical carcinomas and may be included within a complementary text report is the depth of infiltration in thirds of the cervical wall.<sup>40,41</sup> In one study the disease-free interval was found

to be 94.1% for tumours that infiltrated the superficial one third of the cervix, 84.5% for those that infiltrated the middle third, and 73.6% for those infiltrating the deep third.

In a study of FIGO stage I adenocarcinomas, univariate analysis showed that the thickness of the remaining cervical wall<sup>40</sup> was found correlate with overall survival. Where thickness of the remaining wall was >3mm, five-year survival was 82%, but in cases where the remaining wall thickness was 1–3mm, five-year survival fell to 62%.

## 7 WHO CLASSIFICATION OF CERVICAL EPITHELIAL TUMOURS AND SNOMED MORPHOLOGY CODING<sup>23</sup>

### Squamous tumours and precursors

Squamous carcinoma, not otherwise specified	80703
Keratinizing	80713
Non-keratinizing	80723
Basaloid	80833
Verrucous	80513
Warty	80513
Papillary	80523
Lymphoepithelioma-like	80823
Squamotransitional	81203
Early invasive (microinvasive) squamous cell carcinoma	80763
Squamous intraepithelial neoplasia	
Cervical intraepithelial neoplasia (CIN) 3	80772**
Squamous cell carcinoma <i>in situ</i>	80702

### Glandular tumours and precursors

Adenocarcinoma	81403
Mucinous adenocarcinoma	84803
Endocervical type	84823
Intestinal	81443
Signet-ring cell	84903
Minimal deviation	84803
Villoglandular	82623
Endometrioid adenocarcinoma	83803
Clear cell adenocarcinoma	83103
Serous adenocarcinoma	84413
Mesonephric adenocarcinoma	91103
Early invasive adenocarcinoma	81403
Adenocarcinoma <i>in situ</i>	81402

### Other epithelial tumours

Adenosquamous carcinoma	85603
Glassy cell carcinoma variant	80153
Adenoid cystic carcinoma	82003
Adenoid basal carcinoma	80983

Neuroendocrine tumours	
Carcinoid tumour	82403
Atypical carcinoid	82493
Small cell carcinoma	80413
Large cell neuroendocrine carcinoma	80133
Undifferentiated carcinoma	80203

\*\* In the United Kingdom, the preferred SNOMED code for CIN 3 is 74008.

## 8 SMALL BIOPSY SPECIMENS

Small colposcopically directed punch biopsies may be up to several millimetres long, and 2–4mm thick. The number of pieces received should be recorded, as should their size (in 3 dimensions). Specimens that are mounted on filter paper before fixation are more likely to be optimally oriented, have a preserved squamocolumnar junction, and intact surface epithelium.<sup>42</sup> Fixation in eosin-tinted formalin may facilitate their identification and orientation.<sup>6,42</sup> It is important to search the container and the under surface of its lid to ensure that stray fragments of tissue are recovered, and care should be taken to avert tissue loss of very small fragments – these should be wrapped, placed between layers of foam sponge, placed in mesh bags or wire baskets according to local practice.

If biopsies are >5mm in dimension, they may be bisected transversely, perpendicular to the mucosal surface, to produce two pieces. All of the biopsy fragments should be processed.

The report should incorporate the macroscopic description of the specimen, and identify the area/s of the cervix from which the biopsy has originated, i.e. ectocervix, endocervix, transformation zone.

Where artefact or epithelial loss impairs interpretation of the biopsy, this must be stated in the report. The pathologist must report all grades of CIN and/or CGIN; invasive lesions should be reported, typed and graded according to national protocols and guidelines.<sup>6</sup>

It is recommended that koilocytosis and koilocytosis-associated changes also be reported. The pathologist must be mindful of the cytology/smear history, the result of the most recent smear when writing the histology report, and include all pathological lesions (neoplastic and non-neoplastic) that may be associated with, or account for, the reported cytological abnormalities. When a biopsy fails to reveal the source of the abnormal cells in a smear, it is important to differentiate between a biopsy that is technically adequate but fails to identify a lesion, and a biopsy that is technically inadequate. The limitations of small punch biopsies in the detection of high-grade CIN should be recognised<sup>43</sup>. If invasive disease is suspected on the basis of the cytological, colposcopic, or histological features further levels should be examined.<sup>44</sup>

## 9 REPORTING OF FROZEN SECTIONS

In most institutions, frozen sections are not used routinely for the assessment of resection margins. However, in some specialist centres frozen sections may be used where trachelectomies are carried out and the upper limit of the specimen may be examined intra-operatively. Intra-operative frozen sections may be performed on clinically suspicious lymph nodes to look for metastasis before proceeding with or abandoning radical surgery. Clinicians

should be aware of the limitations of frozen sections in general, and of sampling and interpretational errors as they apply to lymph node frozen sections in particular.

## 10 SPECIFIC ASPECTS OF INDIVIDUAL TUMOURS NOT COVERED ELSEWHERE

In small biopsy samples, it may be necessary to differentiate between primary endocervical adenocarcinoma and endocervical extension from a primary endometrial adenocarcinoma. A panel of immunohistochemical markers is recommended.<sup>45–47</sup> Occasionally metaplastic processes in the endocervix, such as tuboendometrioid metaplasia, may mimic CGIN. The use of p16, MIB1 and bcl2 immunostaining may prove helpful in this regard.<sup>48</sup>

Both small and large cell neuroendocrine carcinomas may require a range of immunohistochemical markers to confirm the diagnosis. Small cell neuroendocrine carcinomas may not stain with most of the commonly used neuroendocrine markers and this does not preclude the diagnosis. p63 is a useful marker of squamous cervical neoplasms and may be of use in differentiating small cell neuroendocrine carcinoma (p63 negative) from small cell squamous carcinoma (p63 positive).<sup>49</sup> It is beyond the scope of this publication to describe in detail immunohistochemical markers of use in cervical neoplasia but the reader is referred to a recent review on this subject.<sup>49</sup>

## 11 ACKNOWLEDGEMENTS

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## APPENDIX A      TNM AND FIGO PATHOLOGICAL STAGING OF CERVICAL CARCINOMA

<b>TNM category</b>	<b>FIGO stage</b>	<b>Definition</b>
TX		Primary tumour cannot be assessed
T0		No evidence of primary tumour
Tis	0	Carcinoma <i>in situ</i>
T1	I	Cervical carcinoma confined to the uterus (extension to the corpus should be disregarded)
T1a	IA	Invasive carcinoma, diagnosed by microscopy only (all macroscopically visible lesions even those with superficial invasion are pT1b/Stage IB)
T1a1	IA1	Stromal invasion 3.0 mm or less in depth* and 7.0 mm or less in horizontal spread
T1a2	IA2	Stromal invasion more than 3.0 mm in depth and not more than 5.0 mm with a horizontal spread 7.0 mm or less
T1b	IB	Clinically visible lesion confined to the cervix or microscopic lesion greater than T1a2/IA2
T1b1	IB1	Clinically visible lesion 4.0 cm or less in greatest dimension
T1b2	IB2	Clinically visible lesion more than 4.0 cm in greatest dimension
T2	II	Tumour invades beyond the uterus but not to pelvic wall or to lower third of vagina
T2a	IIA	Tumour without parametrial invasion
T2b	IIB	Tumour with parametrial invasion
T3	III	Tumour extends to the pelvic wall and/or involves the lower third of the vagina, and/or causes hydronephrosis or non-functioning kidney
T3a	IIIA	Tumour involves lower third of vagina, no extension to pelvic wall
T3b	IIIB	Tumour extends to pelvic wall and/or causes hydronephrosis or non-functioning kidney
T4	IVA	Tumour invades the mucosa** of bladder or rectum and/or extends beyond true pelvis
M1	IVB	Distant metastasis

\* The depth of invasion is measured from the base of the epithelium, either surface or glandular, from which it originates. The depth of invasion is defined as the measurement of the tumour from the epithelial-stromal junction of the adjacent most superficial epithelial papilla to the deepest point of invasion. Vascular space involvement, either venous or lymphatic, does not alter the staging.

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

### **Regional lymph nodes (N)\*\*\* (TNM staging system)**

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

\*\*\* Regional lymph nodes include paracervical, parametrial, hypogastric (obturator); common, internal and external iliac; presacral and lateral sacral nodes. Metastasis to lymph nodes outside of the regional nodal group is classified as distant metastasis.

### **Distant metastasis (M) (TNM staging system)**

- MX Distant metastasis cannot be assessed
- M0 No distant metastasis
- M1 Distant metastasis (excludes peritoneal metastasis)

**APPENDIX B1 REPORTING PROFORMA FOR CERVICAL CANCER IN  
EXCISIONAL CERVICAL BIOPSIES**

Surname..... Forenames..... Date of birth.....  
 Hospital..... Hospital no..... NHS no.....  
 Date of receipt..... Date of reporting..... Report no.....  
 Pathologist..... Surgeon.....

**Description of specimen and core macroscopic items**

Wedge  Cone  Loop  biopsy of cervix:.....mm x .....mm and ..... mm thick/deep  
 Number of fragments received, measurement of each and block designation:.....  
 .....

**Core microscopic items**

**Invasive malignancy:**

Type: squamous carcinoma  adenosquamous carcinoma  adenocarcinoma   
 neuroendocrine carcinoma  other  specify.....  
 Differentiation of invasive carcinoma: well/grade 1  moderate/grade 2  poor/grade 3   
 not applicable   
 Distribution of invasive component: unifocal  multifocal   
 Tumour size: maximum horizontal dimension.....mm  
 maximum thickness/depth of invasion(delete as appropriate) .....mm  
 Are invasive foci present in three or more sequential slices of tissue\*: yes  no

**Other features:**

CIN (cervical intra-epithelial neoplasia): present  absent   
 grade: CIN 1  CIN 2  CIN 3   
 CGIN (cervical glandular intraepithelial neoplasia): present  absent   
 grade: low  high   
 SMILE (stratified mucin-producing intra-epithelial lesion): present  absent

**Excision margins: (specify whether involved by CIN, CGIN or SMILE)**

Ectocervical resection margin: clear  involved  by (specify).....  
 Endocervical resection margin: clear  involved  by.....  
 Deep lateral/radial resection margin: clear  involved  by.....  
 Lymphovascular space invasion: present  absent

*\*Note:* If invasive foci are seen in three or more sequential sections of tissue, the third dimension of the lesion (which is not routinely measured) may exceed 7 mm (i.e. more than Stage IA2).

Provisional pathological FIGO stage.....pTNM stage: pT.....pN.....M.....

SNOMED codes: T.....M.....  
 T.....M.....

Signature of pathologist: ..... Date.....

**APPENDIX B2 REPORTING PROFORMA FOR CERVICAL CANCER IN  
HYSTERECTOMY SPECIMENS**

Surname..... Forenames..... Date of birth.....  
 Hospital..... Hospital no..... NHS no.....  
 Date of receipt..... Date of reporting..... Report no.....  
 Pathologist..... Surgeon.....

**Description of specimen and core macroscopic items**

Vaginal cuff: present  absent  length.....mm diameter.....mm

Dimensions of uterus: length.....mm transverse.....mm  
 anteroposterior.....mm

Adnexa: present  absent   
 normal  abnormal (specify).....

No tumour seen  Maximum dimensions of tumour: .....mm x .....mm

Position of cervical tumour: anterior  posterior  right  left  circumferential   
 ectocervix  endocervix

Macroscopic involvement of vagina: yes  no

Macroscopic involvement of parametria: yes  no

Macroscopic involvement of paracervical tissues yes  no

**Core microscopic items**

Type: squamous carcinoma  adenosquamous carcinoma  adenocarcinoma   
 neuroendocrine carcinoma  other  specify.....

Differentiation: well/grade 1  moderate/grade 2  poor/grade 3   
 not applicable

Tumour size: maximum horizontal dimension.....mm  
 thickness/depth of invasion (delete as appropriate).....mm

Minimum thickness of uninvolved cervical stroma (minimum tumour-free rim):.....mm

Position of this:.....

Closest radial resection margin (include paracervical tissue thickness):.....mm

Position of this:.....

Vaginal involvement: yes  no  Distance from distal vaginal epithelial margin:.....mm

Position of this:.....

Paracervical involvement: yes  no  If involved: left  right

Parametrial involvement: yes  no  If involved: left  right

Lymphovascular invasion: yes  no

CIN: present  absent  Grade 1/2/3 CGIN: present  absent  Grade: low/high

SMILE: present  absent

*Continued on next page*

**APPENDIX B2 REPORTING PROFORMA FOR CERVICAL CANCER IN HYSTERECTOMY SPECIMENS (CONTINUED)**

**Nodes:** (pelvic group includes obturator, internal and external iliac)

<b>Nodes (site and number)</b>	Right	left	<b>Common iliac</b>	right	left
Total number	.....	.....		.....	.....
Number involved	.....	.....		.....	.....

Extranodal spread:                    yes     no

Para-aortic nodes:                    positive                     negative                     not sampled

    total number of nodes                     number of positive nodes

Extranodal spread:                    yes     no

<b>Other tissues and organs:</b>	Normal	Abnormal (describe)
Endometrium	<input type="checkbox"/>	.....
Myometrium	<input type="checkbox"/>	.....
Right adnexum	<input type="checkbox"/>	.....
Left adnexum	<input type="checkbox"/>	.....

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Provisional pathological FIGO stage\*.....pTNM stage: pT.....pN.....M.....

(\*Correlate with previous cone/loop specimen/s – final staging may follow MDT review)

SNOMED codes:                    T.....M.....

    T.....M.....

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**Signature of pathologist:** .....                    **Date**.....

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