

Colorectal Excisional Biopsy (Polypectomy) Histopathology Reporting Guide



Family/Last name		Date of birth	DD - MM - YYYY
Given name(s)			
Patient identifiers		Date of request	DD - MM - YYYY
		Accession/Laboratory number	

Elements in **black text** are **CORE**. Elements in **grey text** are **NON-CORE**.
☐ indicates multi-select values ☐ indicates single select values

SCOPE OF THIS DATASET

CLINICAL INFORMATION (Note 1)

- ☐ Information not provided
☐ Information provided (select all that apply)

☐ Neoadjuvant therapy

- ☐ Information not provided
☐ No
☐ Yes, *specify*

☐ Known polyposis syndrome

- ☐ Familial adenomatous polyposis (FAP)
☐ *MUTYH*-associated polyposis (MAP)
☐ Serrated polyposis
☐ Other, *specify*

☐ Lynch syndrome

☐ Chronic inflammatory bowel disease

- ☐ Ulcerative colitis
☐ Crohn disease
☐ Indeterminate colitis

☐ Previous biopsy

☐ Previous local resection

☐ Other clinical information, *specify*

ENDOSCOPIC PROCEDURE (select all that apply) (Note 2)

☐ Not specified

☐ Polypectomy

☐ Cautery

- ☐ Used ☐ Not used

☐ Resection type

- ☐ En bloc ☐ Piecemeal

☐ Endoscopic mucosal resection (EMR)

☐ Cautery

- ☐ Used ☐ Not used

☐ Resection type

- ☐ En bloc ☐ Piecemeal

- ☐ Endoscopic submucosal dissection (ESD)
☐ Endoscopic intermuscular dissection (EID)
☐ Endoscopic full thickness resection (EFTR)
☐ Transanal minimally invasive surgery (TAMIS)
☐ Transanal endoscopic microsurgery (TEMS)
☐ Other, *specify*

POLYP NUMBER^a (Note 3)

(Per container)

OR ☐ Multiple (with no specific number given)

☐ Not specified

^a As indicated on the container label, pathology request form or colonoscopy report.

SPECIMEN SITE(S)^a (select all that apply) (Note 4)

- ☐ Not specified
☐ Caecum
☐ Ileocaecal valve
☐ Appendiceal orifice
☐ Ascending colon
☐ Hepatic flexure
☐ Transverse colon
☐ Splenic flexure
☐ Descending colon
☐ Sigmoid colon
☐ Rectosigmoid junction
☐ Rectum
☐ Anorectal junction

mm from the anal verge

☐ Other, *specify*

ENDOSCOPIC POLYP SIZE^a (Note 5)

Size

mm

 OR

mm

 to

mm

OR

Size category

- ☐ Diminutive (1-5 mm)
- ☐ Small (6-9 mm)
- ☐ Large (>9 mm)

ENDOSCOPIC POLYP CLASSIFICATION^a (Note 5)

Polyp configuration^b

- ☐ Not provided
- ☐ Non-pedunculated (0-Is, 0-IIa, 0-IIb, 0-IIc)
- ☐ Pedunculated (0-Ip)

Polyp classification (select all that apply)

☐ Paris classification, *specify*

☐ Lateral spreading tumour classification, *specify*

☐ Optical diagnosis, *specify*

^a As indicated on the container label, pathology request form or colonoscopy report.

^b Core for malignant polyps; non-core for all others. As specifically indicated by the endoscopist or derived from the Paris classification.

MACROSCOPIC SPECIMEN DIMENSIONS (Note 6)

Intact specimens

Maximum dimensions of intact specimen

mm

 x

mm

 x

mm

Maximum dimension of lesion

mm

FOR PEDUNCULATED POLYP

- ☐ Stalk absent
- ☐ Stalk present

mm

Fragmented specimens

Number of fragments

Dimension of largest piece

mm

☐ Cannot be assessed, *specify*

BLOCK IDENTIFICATION KEY (Note 7)

(List overleaf or separately with an indication of the nature and origin of all tissue blocks)

HISTOLOGICAL TYPE OF POLYP (select all that apply) (Note 8)

(Value list based on the World Health Organization (WHO) Classification of Digestive System Tumours, 6th Edition (2026))

- ☐ No polyp identified (normal mucosa)
- ☐ Tubular adenoma
- ☐ Tubular adenoma, high grade
- ☐ Tubulovillous adenoma
- ☐ Tubulovillous adenoma, high grade
- ☐ Villous adenoma
- ☐ Villous adenoma, high grade
- ☐ Hyperplastic polyp
- ☐ Sessile serrated lesion
- ☐ Sessile serrated lesion with dysplasia
- ☐ Traditional serrated adenoma
- ☐ Traditional serrated adenoma with conventional (adenomatous) dysplasia, low grade
- ☐ Traditional serrated adenoma with conventional (adenomatous) dysplasia, high grade
- ☐ Traditional serrated adenoma with serrated high grade dysplasia
- ☐ Carcinoma^c
- ☐ Hamartomatous polyp
- ☐ Inflammatory polyp
- ☐ Mucosal prolapse polyp
- ☐ Other, *specify*

Comments

^c For carcinoma refer to HISTOLOGICAL TUMOUR TYPE describing all histological subtypes of carcinoma.

HISTOLOGICAL TUMOUR TYPE^d (Note 9)

(Value list based on the WHO Classification of Digestive System Tumours, 6th Edition (2026))

- ☐ Adenocarcinoma, not otherwise specified (NOS)
☐ Mucinous adenocarcinoma
☐ Serrated adenocarcinoma
☐ Micropapillary adenocarcinoma
☐ Medullary carcinoma
☐ Adenoma-like adenocarcinoma
☐ Signet-ring cell adenocarcinoma
☐ Adenosquamous carcinoma
☐ Squamous cell carcinoma
☐ Low grade tubuloglandular carcinoma
☐ Lymphoglandular complex-like adenocarcinoma
☐ Undifferentiated carcinoma
☐ Carcinoma with mesenchymal differentiation
☐ Neuroendocrine neoplasms^e
☐ Neuroendocrine carcinoma, NOS
☐ Large cell
☐ Small cell
☐ Mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN)

☐ Other, *specify*

☐ No evidence of residual tumour

Precursor polyp/lesion

- ☐ Absent
☐ Present, *specify type^f*

^d To complete this and all following elements ONLY if a carcinoma is present. If multiple primary carcinomas are present, separate datasets should be used to record this and all following elements for each primary carcinoma.

^e Neuroendocrine tumours are not covered in this dataset; refer to the ICCR Neuroendocrine tumours dataset.

^f Refer to HISTOLOGICAL TUMOUR TYPE.

HISTOLOGICAL TUMOUR GRADE^g (Note 10)

- ☐ Not applicable
☐ Low grade (formerly well to moderately differentiated)
☐ High grade (formerly poorly differentiated)

^g Refer to the Note for application to specific histological tumour types.

EXTENT OF INVASION (Note 11)

- ☐ Cannot be assessed
☐ No evidence of primary tumour
☐ Invasion into lamina propria (intramucosal)
☐ Invasion into submucosa
☐ Invasion into muscularis propria
☐ Invasion into subserosa or into pericolic or perirectal connective tissues
☐ Invasion onto the surface of the visceral peritoneum
☐ Invasion directly into other structure(s)/organ(s), *specify*

INVASIVE CARCINOMA DIMENSIONS (Note 12)

(Applicable only for malignant polyps with invasion limited to the submucosa)

DEPTH OF INVASION**Non-pedunculated polyps**

Maximum depth of invasion mm

- ☐ Measured from surface
☐ Measured from muscularis mucosae

KIKUCHI CLASSIFICATION^h

- ☐ Sm1 (invasion into superficial third of submucosa)
☐ Sm2 (invasion into middle third of submucosa)
☐ Sm3 (invasion into lower third of submucosa)

Pedunculated polyps**HAGGITT CLASSIFICATION**

- ☐ Level 1 (invasion limited to head of polyp)
☐ Level 2 (invasion into neck of polyp)
☐ Level 3 (invasion into stalk)
☐ Level 4 (invasion into submucosa below stalk)

Maximum depth of invasion for Haggitt levels 3 and 4 onlyⁱ mm

WIDTH OF INVASION

Maximum width of invasion mm

☐ Cannot be assessed, *specify*

^h Applicable only for intact specimens with identifiable muscularis propria.

ⁱ From a horizontal line in the stalk at the junction between the normal mucosa and the lesion to the deepest point of invasion.

LYMPHATIC AND VENOUS INVASION (Note 13)

- ☐ Not identified
☐ Present (select all that apply)
☐ Small vessel (lymphatic, capillary or venular)
☐ Large vessel (venous)^j
☐ Intramural
☐ Extramural

^j Select the deepest level.

PERINEURAL INVASION^k (Note 14)

- ☐ Not identified
☐ Present^j
☐ Intramural
☐ Extramural

^k Core only for carcinomas invading beyond the submucosa (pT2-4).

TUMOUR BUDDING (Note 15)☐ Not applicable^lNumber of tumour buds^m**Tumour budding score**

- ☐ Bd1 (0-4 buds)
- ☐ Bd2 (5-9 buds)
- ☐ Bd3 (≥ 10 buds)

^l For intramucosal adenocarcinoma, for carcinoma following neoadjuvant therapy and for mucinous and signet-ring adenocarcinomas where tumour cells are only present within extracellular mucin pools.

^m After scanning 10 fields on a 20x objective lens, the hotspot field normalised to represent a field of 0.785 mm².

POORLY DIFFERENTIATED CLUSTERS (PDCs) (Note 16)

Number of PDCs

PDC score

- ☐ Grade 1 (0-4 PDCs)
- ☐ Grade 2 (5-9 PDCs)
- ☐ Grade 3 (≥ 10 PDCs)

MARGIN STATUS (Note 17)**Deep margin**☐ Cannot be assessedⁿ

Distance to invasive carcinoma

mm

☐ Involved (distance to invasive carcinoma=0 mm)**Lateral margin**☐ Cannot be assessedⁿ

Distance to neoplasia

mm

☐ Involved, specify

ⁿ For piecemeal resection specimens with carcinoma present in multiple fragments, or specimens with extensive cautery artefact.

ANCILLARY STUDIES (Note 18)**Mismatch repair (MMR) immunohistochemistry**

- ☐ Not performed
- ☐ Not interpretable
- ☐ Proficient
- ☐ Deficient
- ☐ *MLH1/PMS2* loss
- ☐ *MSH2/MSH6* loss
- ☐ *MSH6* loss
- ☐ *PMS2* loss
- ☐ Other, specify

OR**Microsatellite instability (MSI) testing**

- ☐ Not performed
- ☐ MS-stable
- ☐ MSI-high

BRAF V600E mutation testing

- ☐ Not performed
- ☐ Mutated
- ☐ Wild type

MLH1 promoter methylation testing

- ☐ Not performed
- ☐ Inconclusive
- ☐ Methylated
- ☐ Not methylated

Other, record test(s), methodology and result(s)

Representative blocks for ancillary studies, specify those blocks best representing tumour and/or normal tissue for further study

HIGH GRADE NEUROENDOCRINE NEOPLASMS ONLY^o**Neuroendocrine markers**

- ☐ Not performed
- ☐ Performed (select at least two of the following core options)

☐ Synaptophysin☐ Chromogranin-A☐ INSM1☐ Other, specify

Specify test(s) performed and result(s) if available

Ki-67 proliferation index

- ☐ Not performed
- ☐ Performed

%

p53

- ☐ Not performed
- ☐ Performed

☐ Abnormal, specify test(s) performed and result(s) if available

☐ Wildtype pattern**RB1**

- ☐ Retained
- ☐ Deficient

Low molecular weight cytokeratin(s)

- ☐ Positive
- ☐ Negative

^o Neuroendocrine tumours are not covered in this dataset; refer to the ICCR Neuroendocrine tumours dataset.

Definitions

CORE elements

CORE elements are those which are essential for the clinical management, staging or prognosis of the cancer. These elements will either have evidentiary support at Level P2 or above (based on the Hierarchy of Research Evidence for Tumour Pathology¹). In rare circumstances, where level P2 evidence is not available an element may be made a CORE element where there is unanimous agreement in the Dataset Authoring Committee (DAC). An appropriate staging system, e.g., Pathological TNM staging would normally be included as a CORE element.

Molecular and immunohistochemical testing is a growing feature of cancer reporting. However, in many parts of the world this type of testing is limited by the available resources. In order to encourage the global adoption of ancillary tests for patient benefit, International Collaboration on Cancer Reporting (ICCR) includes the most relevant ancillary testing in ICCR Datasets as CORE elements, especially when they are necessary for the diagnosis. Where the technical capability does not yet exist, laboratories may consider temporarily using these data elements as NON-CORE items.

The summation of all CORE elements is considered to be the minimum reporting standard for a specific cancer.

NON-CORE elements

NON-CORE elements are those which are unanimously agreed should be included in the dataset but are not supported by level P2 evidence. These elements may be clinically important and recommended as good practice but are not yet validated or regularly used in patient management.

Key information other than that which is essential for clinical management, staging or prognosis of the cancer such as macroscopic observations and interpretation, which are fundamental to the histological diagnosis and conclusion e.g., macroscopic tumour details, may be included as either CORE or NON-CORE elements by consensus of the DAC.

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Scope

The dataset has been developed for the reporting of local excision specimens from the colon and rectum, including neuroendocrine carcinomas (NECs) and mixed neuroendocrine-non-neuroendocrine neoplasms (MiNENs). The dataset covers polypectomies, endoscopic mucosal resections (EMR), endoscopic submucosal dissections (ESD), endoscopic intermuscular dissection (EID), endoscopic full thickness resections (EFTR), transanal submucosal excisions, transanal minimally invasive surgery (TAMIS) and transanal endoscopic microsurgery (TEMs) specimens.

It is not applicable to neuroendocrine tumours (NETs) or non-epithelial malignancies. NETs are covered in a separate ICCR dataset.

Surgical resection specimens from patients with primary colorectal carcinoma, including NECs and MiNENs, are also addressed in a separate ICCR dataset.

The second edition of this dataset has been updated to align with the World Health Organization (WHO) Classification of Digestive System Tumours, 6th edition, 2026.²

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Note 1 – Clinical information (Core and Non-core)

Clinical information may be provided by the clinician on the endoscopy report or pathology request form. Pathologists may seek additional relevant information from the electronic health record, previous pathology reports, or other clinical records.

The presence of a known polyposis syndrome, Lynch syndrome, chronic inflammatory bowel disease (IBD) or any other relevant gastrointestinal disorder should be recorded and communicated to the pathologist, as awareness of these underlying conditions may influence histological interpretation. In patients with IBD (Crohn disease or ulcerative colitis), lesions arising within segments affected by inflammation may represent IBD-associated dysplasia and may require management that differs from that of sporadic lesions.³

Information regarding previous biopsy or local excision should also be recorded, as it may influence histological interpretation. Epithelial misplacement secondary to a previous biopsy may be difficult to distinguish from true submucosal invasion.^{4,5} Similarly, a local excision specimen following a previous incomplete resection may show only scar tissue with no residual tumour.

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Note 2 – Endoscopic procedure (Core and Non-core)

The type of endoscopic procedure is important because it may affect histological analysis, including evaluation of resection margins.⁶

Conventional polypectomy using snare resection remains the standard technique for most colorectal polyps. Cold snare polypectomy is the preferred method for diminutive (≤ 5 millimetres (mm)) polyps and is increasingly used for non-malignant polyps up to 9 mm in size. Compared with hot snare techniques, cold snare polypectomy avoids thermal artefact, shortens procedure time, and may reduce the risk of delayed bleeding.⁶

Endoscopic mucosal resection (EMR) is an established technique for the removal of colorectal polyps and can provide curative resection for superficial colorectal neoplasia. The procedure involves submucosal injection to lift the lesion, followed by snare resection. EMR is particularly suitable for non-pedunculated colorectal polyps 20 mm or larger, which account for approximately 1% of all colorectal lesions. Cold-snare EMR has shown promise as an alternative approach for larger polyps, although additional high-quality studies are required to better define its limitations. Conventional EMR may be performed piecemeal for larger lesions, although this approach is associated with a higher risk of recurrence than en bloc resection techniques.^{7,8}

Endoscopic submucosal dissection (ESD) consists of en bloc resection of large lesions through marking, submucosal injection, circumferential mucosal incision, and submucosal dissection using specialised endoscopic knives. ESD is particularly indicated for colorectal lesions 20 mm or larger, lesions with high suspicion of limited submucosal invasion, lesions not amenable to snare-based techniques, lesions with

submucosal fibrosis, locally residual or recurrent lesions after endoscopic resection, and sporadic lesions arising in the context of chronic inflammation.⁸ Compared with EMR, ESD achieves higher en bloc and complete resection rates, lower rates of lateral margin involvement, and lower recurrence rates.^{9,10} However, ESD requires increased procedural time and carries higher perforation risk.

Endoscopic intermuscular dissection (EID) is an endoscopic resection technique that involves dissection within the intermuscular plane between the longitudinal and circular layers of the muscularis propria. It is particularly suited to en bloc resection of rectal adenocarcinomas invading into deep submucosa.^{10,11} The main advantage of EID is the higher rate of complete resection in this setting compared to ESD.

Endoscopic full thickness resection (EFTR) is a minimally invasive endoscopic technique that results in full thickness excision of the bowel wall.¹² This method is particularly useful for difficult-to-resect lesions up to 20 mm in size, recurrent lesions with scar formation after previous endoscopic resections, and circumscribed lesions in the middle and upper rectum.¹³ EFTR allows curative endoscopic resection of selected lesions that would otherwise require surgical intervention.

Transanal minimally invasive surgery (TAMIS) is an advanced transanal platform for high-quality local excision of rectal neoplasia. Indications include endoscopically unresectable benign lesions and selected early rectal carcinomas with favourable histological features.¹⁴ Compared with conventional transanal excision, TAMIS is associated with lower rates of positive resection margins and tumour recurrence.¹⁵ TAMIS may also be used for palliative or non-curative treatment of more advanced lesions in patients who are not candidates for radical surgery.

Transanal endoscopic microsurgery (TEMs) is an established transanal technique that allows en bloc excision of rectal lesions.¹⁵ TEMs and TAMIS provide comparable oncological outcomes for benign and early malignant rectal neoplasms, and the choice of technique is generally determined by surgeon preference, local expertise, availability and cost.¹⁶ Meta-analysis comparing ESD with transanal endoscopic surgery for early rectal tumours has demonstrated no significant differences in recurrence rates, en bloc resection rates, R0 resection rates, or complication rates.¹⁷

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Note 3 – Polyp number (Core)

Polyp number is an essential component of bowel screening registries and is used for post-polypectomy risk stratification and surveillance recommendations. The surveillance studies validating current guidelines generally assume that individual polyps can be characterised separately, although specimen submission practices are rarely specified in detail.¹⁸⁻²¹

When multiple polyps, or an unknown number of polyps, are received in a single specimen container, this may preclude accurate assessment of i) the number of polyps received; ii) the classification of individual polyps, and iii) the number of malignant polyps when carcinoma is present in more than one fragment may not be possible. This may adversely affect post-polypectomy risk stratification and surveillance recommendations and compromise the quality of data recorded in bowel cancer screening programmes and pathology databases.

Submission of each polyp in a separate specimen container is recommended whenever feasible, allowing accurate histological assessment of individual lesions. However, in routine clinical practice, multiple polyps, particularly when diminutive or small, from the same anatomical location, and considered endoscopically innocuous, may be submitted together in a single container.

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Note 4 – Specimen site(s) (Core)

Determination of specimen site is based on clinical information provided on the container label, the pathology request form or the endoscopy report. Any discrepancy should be discussed with the endoscopist.

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Note 5 – Endoscopic polyp size (Non-core) and Endoscopic polyp classification (Core and Non-core)

Endoscopic polyp size

Polyp size is associated with risk of metachronous polyps and colorectal carcinoma and is used to determine colonoscopy surveillance intervals.

A conventional adenoma measuring <10 mm, with low grade dysplasia and <25% villosity is considered a low-risk lesion, whereas a conventional adenoma measuring ≥10 mm is considered an advanced lesion in current surveillance guidelines. Polyps <10 mm in size are further classified as small (6-9 mm) or diminutive (1-5 mm). The size of conventional adenoma correlates with other advanced histologic features, including villosity >25% of the polyp and high grade dysplasia. Sessile serrated lesions and hyperplastic polyps measuring ≥10 mm are also considered advanced lesions.

However, endoscopic measurement of polyp size is subject to substantial interobserver variability and may result in misclassification across clinically important surveillance thresholds. Visual estimation remains the most common method in clinical practice but demonstrates limited accuracy across all levels of endoscopic experience. In one study, visual estimation achieved only 63.6% accuracy compared with caliper measurement of resected specimens.²² Notably, 17.3% of polyps measuring ≥10 mm were incorrectly classified as <10 mm, potentially affecting surveillance recommendations. A systematic review of 61 studies similarly demonstrated considerable variability in endoscopic size estimation and identified visual and snare-based methods as the least accurate techniques.²³

Despite these limitations, endoscopic polyp size remains an integral component of current surveillance algorithms and should therefore be recorded when available.

Endoscopic polyp classification

Information regarding the endoscopic appearance of polyps should be recorded to facilitate endoscopic-histological correlation. This information may be particularly helpful when histological findings do not correspond to the endoscopic impression and additional tissue levels or further review are required. The distinction between pedunculated and non-pedunculated lesions is particularly important in the assessment of malignant polyps.

Superficial neoplastic lesions of the gastrointestinal tract can be classified according to their endoscopic appearance using several established classification systems. The most widely used is the Paris classification, in which type 0 neoplastic lesions are categorised as polypoid (Ip and Is), non-polypoid (IIa, IIb and IIc), and excavated (III) lesions (Figure 1).²⁴ Information regarding pedunculated or non-pedunculated configuration may be provided directly by the endoscopist or inferred from the Paris classification. Pedunculated polyps are classified as type 0-Ip. Non-pedunculated polyps include sessile (0-Is) and non-polypoid (0-IIa, 0-IIb and 0-IIc) lesions.

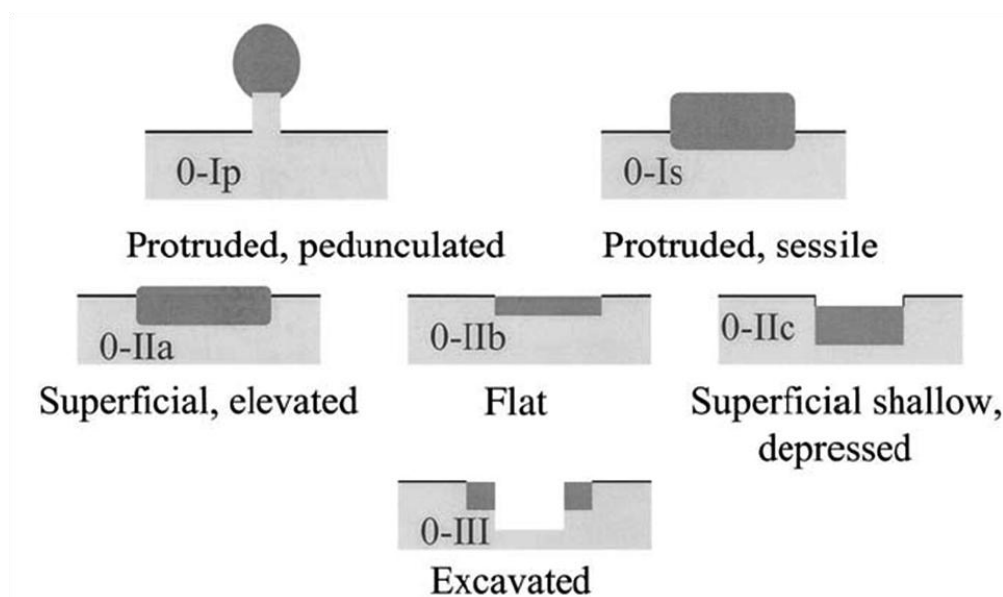


Figure 1: Schematic representation of the major variants of type 0 neoplastic lesions of the digestive tract: polypoid (Ip and Is), non-polypoid (IIa, IIb, and IIc), non-polypoid and excavated (III). Terminology as proposed in a consensus macroscopic description of superficial neoplastic lesions. Reproduced with permission from Paris workshop participants (2003). The Paris endoscopic classification of superficial neoplastic lesions: oesophagus, stomach, and colon: November 30 to December 1, 2002. *Gastrointest Endosc* 58(6 Suppl):S3-43.²⁴

Lateral spreading tumours (LSTs) are a subgroup of type IIa lesions, larger than 10 mm in diameter, and divided into granular and non-granular types.²⁵ Granular LSTs are subclassified into homogenous and nodular mixed types. Non-granular LSTs are associated with a higher risk of malignancy and are subdivided into flat, elevated and pseudo-depressed types.

For direct optical diagnosis of colorectal lesions, both high-definition white-light endoscopy and image-enhanced endoscopy are increasingly used. Several classification systems have been developed, including the Narrow-band imaging (NBI) International Colorectal Endoscopic (NICE), the Japanese NBI Expert Team (JNET) and the Workgroup serrated polyp and Polyposis (WASP) classifications.²⁶⁻²⁸ The endoscopist's optical diagnosis may be reported as either a classification category or a predicted histological diagnosis: serrated lesions/polyps (hyperplastic polyp, sessile serrated lesion, sessile serrated lesion with dysplasia), adenoma, early adenocarcinoma, advanced adenocarcinoma, submucosal lesion, others.

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Note 6 – Macroscopic specimen dimensions (Core and Non-core)

The dimensions of large en bloc resection specimens (large EMR, ESD, EID, TEMS, TAMIS, EFTR) should be recorded, at least in one dimension. When the lesion is macroscopically identifiable within the specimen, the maximum diameter of the lesion should be recorded. For pedunculated polyps, the presence and length of the stalk should also be documented. Measurement of the size of a pedunculated polyp excludes the stalk. Where feasible, a macroscopic photograph should also be taken and recorded.

In some cases, the pedunculated nature of a lesion may not be apparent in the pathology specimen, particularly when the polyp has been transected at the neck and most of the stalk remains in situ.

Communication with the endoscopist is therefore essential when information regarding polyp configuration is not provided, as distinction between pedunculated and non-pedunculated lesions may significantly influence histological risk assessment and management of malignant polyps.

For polyps resected piecemeal, the number of fragments received, and the size of the largest individual fragment may be recorded to provide an estimate of the amount of tissue submitted.

Several studies have demonstrated discordance between endoscopic and histological measurements of polyp size, with endoscopic measurements generally tending to be larger than histological measurements.²⁹ For all polyps removed piecemeal, the endoscopic size is used for surveillance recommendations and should therefore be considered the reference measurement. For en bloc resection specimens, histological measurement may be more accurate; however, these lesions are often sufficiently large that minor discrepancies are unlikely to affect surveillance recommendations.

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Note 7 – Block identification key (Non-core)

The origin/designation of all tissue blocks should be recorded. This information should ideally be documented in the final pathology report and is particularly important when further internal or external review arises. The reviewer needs to have unequivocal description of the origin of each block to provide an informed specialist opinion. If this information is not included in the final pathology report, it should be available on the laboratory computer system and relayed to the reviewing pathologist. It is highly encouraged to have a digital image (photograph) of the specimen and record of the tumour block key.

Recording the origin/designation of tissue blocks also facilitates retrieval of blocks for further immunohistochemical or molecular analysis, research studies, or clinical trials.

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Note 8 – Histological type of polyp (Core and Non-core)

Each polyp should be classified according to the WHO Classification of Digestive System Tumours, 6th edition, 2026 (Table 1).²

Conventional adenomas are classified according to both the degree of dysplasia and the proportion of villous component: tubular adenoma (villous component <25% of the polyp), villous adenoma (villous component >75% of the polyp) and tubulovillous adenoma for all other cases.

Conventional adenomas with a significant villous component (>25%) and/or high grade dysplasia are generally regarded as advanced adenomas.

Several studies have demonstrated only moderate interobserver agreement in the assessment of villous architecture among both specialist and general pathologists (kappa values 0.15-0.55).³⁰⁻³² Furthermore, villous architecture may not independently predict colorectal cancer risk.^{21,33} Consequently, some international guidelines, including those from the European Society of Gastrointestinal Endoscopy (ESGE) and the British Society of Gastroenterology, no longer use villous histology as an indication for shortened

surveillance intervals.^{34,35} In contrast, the United States Multi-Society Task Force continues to classify tubulovillous and villous adenomas as high risk lesions.³⁶

High grade dysplasia in conventional adenomas is characterised primarily by architectural complexity, including gland crowding, irregular gland architecture, cribriform growth and intraluminal necrosis, with or without accompanying cytological atypia, such as loss of polarity, nuclear enlargement, prominent nucleoli, and atypical mitotic figures.

Mucosal (“epithelial”) misplacement of adenomatous glands into the head or stalk of the polyp can be present, particularly in large pedunculated adenomas. This finding may be documented in the comment section but should not alter classification of the lesion. Intramucosal adenocarcinoma is now recognised as a separate entity and should be distinguished from high grade dysplasia (refer to **Note 9 – HISTOLOGICAL TUMOUR TYPE**).

Dysplasia in **sessile serrated lesion (SSL)** shows greater morphological heterogeneity than dysplasia in conventional adenoma, including adenomatous, serrated and minimal-deviation dysplasia.^{37,38} Dysplasia in SSLD should not be graded because biologically advanced lesions may show only subtle morphological changes.

Traditional serrated adenoma (TSA) is diagnosed based on a combination of architectural features (slit-like serrations and ectopic crypt foci formations) and cytological features (columnar cells with abundant eosinophilic cytoplasm and pencillate nuclei with pale chromatin), with the relative contributions of these features varying among morphological variants.³⁹ TSAs frequently exhibit mixed morphology, either through association with precursor serrated lesions or through progression to more advanced forms of dysplasia, including conventional adenomatous and serrated dysplasia. Conventional adenomatous dysplasia arising within a TSA should be graded as low-grade or high grade using the same criteria applied to conventional adenomas. A lesion demonstrating unequivocal TSA morphology together with an adjacent SSL should be classified as TSA (arising in SSL), rather than SSL with dysplasia. TSA of any size is considered an advanced lesion in most surveillance guidelines. However, the clinical significance of conventional adenomatous dysplasia within TSA, particularly with respect to surveillance recommendations, remains uncertain, and further studies are required to determine whether grading of this component provides additional prognostic information.

Some advanced conventional adenomas or serrated lesions may demonstrate histological features suspicious for, but not diagnostic of, invasive adenocarcinoma. This can be due to limited amount of tissue, cautery artefact or difficulty distinguishing epithelial misplacement from true invasion. In such cases, the lesion should be classified according to the highest-grade confirmed diagnosis, with an explanatory comment indicating that invasive adenocarcinoma cannot be excluded. The elements relating to adenocarcinoma should not be completed unless invasion is definitively identified.

Hamartomatous polyps and inflammatory polyps are not inherently dysplastic. If dysplasia is identified within a hamartomatous polyp or if a specific subtype of hamartomatous polyp is identified (e.g., juvenile polyp, Peutz-Jeghers polyp), this should be documented as an additional feature. Dysplasia arising within an inflammatory polyp should prompt consideration of IBD-associated dysplasia.

Mesenchymal polyps, including perineurioma, Schwann cell hamartoma, schwannoma, neurofibroma, ganglioneuroma, lipoma, granular cell tumour, inflammatory fibroid polyp and gastrointestinal stromal tumour, should be recorded under the “other” category.

For carcinoma in a polyp, refer to additional elements specific to malignant polyps (refer to **Note 9 – HISTOLOGICAL TUMOUR TYPE**).

Table 1: 6th edition of the World Health Organization Classification of tumours of the colon and rectum.²

Descriptor	ICD-O codes ^a
Benign epithelial tumours and precursors	
Colorectal hyperplastic polyp	82134/0
Hyperplastic polyp, microvesicular type*	82135/0
Hyperplastic polyp, goblet cell-rich type*	82136/0
Sessile serrated lesion, not otherwise specified (NOS)	82130/0
Sessile serrated lesion with dysplasia	82130/2
Traditional serrated adenoma, NOS	82131/0
Traditional serrated adenoma, low-grade dysplasia	82132/0
Traditional serrated adenoma, high-grade dysplasia	82132/2
Serrated polyposis	82201/0
Adenoma, intestinal type, low-grade	81441/0
Tubular adenoma, low-grade	82111/0
Villous adenoma, low-grade	82611/0
Tubulovillous adenoma, low-grade	82632/0
Adenoma, intestinal type, high-grade	81441/2
Tubular adenoma, high-grade	82111/2
Villous adenoma, high-grade	82611/2
Tubulovillous adenoma, high-grade	82632/2
Glandular intraepithelial neoplasia, low-grade	81480/0
Glandular intraepithelial neoplasia, high-grade	81480/2
Malignant epithelial tumours	
Adenocarcinoma, NOS	81400/3
Mucinous adenocarcinoma	84800/3
Serrated adenocarcinoma	82130/3
Micropapillary adenocarcinoma	82651/3
Medullary carcinoma	85100/3
Adenoma-like adenocarcinoma	82620/3
Signet-ring cell adenocarcinoma	84900/3
Adenosquamous carcinoma	85600/3
Squamous cell carcinoma	80700/3
Low-grade tubuloglandular carcinoma*	82114/3
Lymphoglandular complex-like adenocarcinoma*	80823/3
Undifferentiated carcinoma	80200/3
Carcinoma with mesenchymal differentiation	80330/3

^a These morphology codes are from the International Classification of Diseases for Oncology, fourth edition, (ICD-O-4.0).⁴⁰ Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; /3 for malignant tumours, primary site; and /6 for malignant tumours, metastatic site. Behaviour code /6 is not generally used by cancer registries.

*Codes marked with an asterisk were approved by the IARC/WHO Committee for ICD-O at its meetings during the production of this volume.

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The second part of this dataset applies to malignant polyps and colorectal carcinoma removed by local excision. Key histological parameters that predict lymph node metastasis and guide patient management include histological tumour type, histological grade, polyp configuration, depth of submucosal invasion in non-pedunculated polyps, Haggitt level in pedunculated polyps, lymphatic and venous invasion, tumour budding, margin status, and, to a lesser extent, width of invasion, poorly differentiated clusters, perineural invasion, and mismatch repair/microsatellite instability status.

Management of patients with malignant colorectal polyps should involve a multidisciplinary approach. Close collaboration between the endoscopist, pathologist, colorectal surgeon, oncologist, and other members of the multidisciplinary team is essential for accurate diagnosis, risk stratification, and selection of the most appropriate treatment and surveillance strategy.

Several multivariable risk prediction models and nomograms have recently been developed to provide individualised estimates of lymph node metastasis risk in pT1 colorectal carcinoma by integrating multiple clinicopathological variables.⁴¹⁻⁴⁶ These models commonly incorporate combinations of depth of submucosal invasion, lymphatic or venous invasion, tumour budding, histological grade, margin status, tumour morphology, and anatomical location. Most models demonstrate moderate discriminatory performance (area under the receiver operating characteristic curve approximately 0.70-0.80) and generally outperform assessment based on individual adverse features alone.

However, most models have been developed retrospectively within single geographic regions, particularly East Asian and European populations, and there remains considerable variability in pathological assessment methods and definitions of adverse features. Consequently, these risk calculators have not yet undergone sufficient international external validation or prospective evaluation to support their incorporation into routine clinical practice or this dataset.

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Note 9 – Histological tumour type (Core and Non-core)

Colorectal carcinomas should be classified according to the WHO Classification of Digestive System Tumours, 6th edition, 2026 (Table 1).² This element applies only to local excision specimens containing invasive or intramucosal carcinoma and not to endoscopic biopsy specimens. Where identifiable, the precursor lesion from which the carcinoma arose should be recorded. In some specimens obtained after extensive biopsy sampling or neoadjuvant therapy, only scar tissue may be present without residual tumour. Compared with adenocarcinoma, not otherwise specified (NOS), mucinous adenocarcinoma and signet-ring cell carcinoma are associated with an increased risk of lymph node metastasis in malignant polyps.^{47,48}

Most colorectal carcinomas are **adenocarcinomas NOS**. However, several histological subtypes are associated with distinct morphological, molecular, and clinical features.

Mucinous adenocarcinoma is defined by the presence of extracellular mucin comprising more than 50% of the tumour volume, with malignant glands or individual tumour cells, including signet-ring cells, floating within mucin pools. Microsatellite instability is more common in mucinous adenocarcinoma than adenocarcinoma NOS. Tumours with less than 50% mucinous differentiation should be reported as adenocarcinoma with a mucinous component.

Serrated adenocarcinoma demonstrates morphological features reminiscent of precursor serrated polyps, including glandular serration, often slit-like in configuration, abundant eosinophilic or clear cytoplasm, minimal necrosis, and occasional mucinous differentiation with cell balls or papillary rods.⁴⁹ Not all adenocarcinomas arising in serrated lesions demonstrate serrated morphology.

Micropapillary adenocarcinoma is characterised by small, rounded clusters of tumour cells lying within stromal spaces mimicking vascular channels. At least 5% of the tumour should demonstrate a micropapillary growth pattern for classification as micropapillary adenocarcinoma.^{50,51} This subtype is most frequently encountered alongside adenocarcinoma NOS. There is a strong association with adverse pathological features, particularly of lymph node metastasis.⁵²

Medullary carcinoma is characterised by sheets of malignant cells with indistinct cell boundaries, vesicular nuclei, prominent nucleoli, abundant eosinophilic cytoplasm and a prominent intratumoural infiltrate composed of predominantly of lymphocytes. At least 50% of the tumour should demonstrate these features for classification as a medullary carcinoma. These tumours almost invariably demonstrate microsatellite instability and generally have a favourable prognosis.⁵³

Adenoma-like adenocarcinoma is defined as an invasive adenocarcinoma in which at least 50% of the invasive component demonstrates adenoma-like morphology, including villous architecture, low grade cytology, a pushing growth pattern, and minimal desmoplastic stromal reaction.⁵⁴ Diagnosis on endoscopic biopsy may be exceedingly difficult because of its deceptively bland appearance. This subtype is associated with a favourable prognosis.

Signet-ring cell carcinoma is defined by signet-ring cells comprising more than 50% of the tumour cell population. These cells contain abundant intracytoplasmic mucin, displacing and typically indenting the nuclei, imparting signet-ring cell morphology. Signet-ring cell carcinoma is associated with adverse stage-independent prognosis and demonstrate increased frequencies of microsatellite instability and Lynch syndrome.⁵⁵⁻⁵⁶ Tumours containing less than 50% signet-ring cells should be reported as adenocarcinoma with a signet-ring cell component. Tumours containing both > 50% extracellular mucin and > 50% signet-ring cell morphology should be termed mucin-rich signet-ring cell carcinomas.

Adenosquamous carcinoma demonstrates unequivocal glandular and squamous differentiation and is typically associated with advanced-stage disease and poor prognosis.⁵⁷

Primary colorectal **squamous cell carcinoma** is rare and lack glandular differentiation.⁵⁸ Associated squamous metaplasia or dysplasia can be evident in adjacent mucosa. Reported associations include HPV infection and ulcerative colitis.^{59,60}

Low grade tubuloglandular adenocarcinoma occurs almost exclusively in patients with chronic inflammatory bowel disease. It is characterised by haphazardly arranged, well-differentiated infiltrative glands with little or no desmoplastic response and may not form a discrete mass lesion.⁶¹ This subtype frequently demonstrates a favourable prognosis.

Lymphoglandular complex-like adenocarcinoma (also known as dome carcinoma or gut-associated lymphoid tissue carcinoma) is characterised by prominent associated lymphoid tissue reminiscent of normal lymphoglandular complexes.^{62,63} Evidence of malignancy includes haphazard glandular architecture, desmoplasia, necrosis, and/or infiltrating single tumour cells. Most cases are confined to the submucosa and are associated with a favourable prognosis, although lymph node metastases may occur.

Undifferentiated carcinoma lacks morphological, immunohistochemical and molecular evidence of glandular, squamous or neuroendocrine differentiation. These tumours frequently contain discohesive rhabdoid cells with abundant eosinophilic cytoplasm and are commonly associated with inactivation of

members of the SWI/SNF chromatin-remodelling complex, including SMARCA2 (BRM), SMARCA4 (BRG1), SMARCB1 (INI1), and ARID1A, with corresponding loss of nuclear immunostaining for the related proteins.⁶⁴ There is an association with microsatellite instability.⁶⁵ Prognosis is generally poor.

Carcinoma with mesenchymal differentiation demonstrates both epithelial and mesenchymal differentiation, with each component comprising at least 30% of the tumour. Mesenchymal differentiation may be spindle cell, heterologous or homologous in nature.⁶⁶ These tumours are exceedingly rare.

Colorectal neoplasms with neuroendocrine differentiation may be classified as NEC, mixed neuroendocrine-non-neuroendocrine (MiNEN) or amphicrine-like carcinoma.² Pure NETs are outside the scope of this dataset; please refer to the ICCR NETs dataset.

Neuroendocrine carcinomas (NECs) are high grade by definition and demonstrate marked cytological atypia, brisk mitotic activity, and either small-cell or large-cell morphology. MiNENs most commonly comprise a poorly differentiated NEC component and an adenocarcinoma NOS component. Amphicrine-like carcinoma differs from MiNEN in that individual tumour cells demonstrate both neuroendocrine and non-neuroendocrine differentiation, resulting in a morphologically homogeneous tumour population.

If a pure or mixed neuroendocrine neoplasm is suspected on morphology, immunohistochemistry is required to confirm neuroendocrine differentiation (refer to **Note 18 – ANCILLARY STUDIES**).

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Note 10 – Histological tumour grade (Core)

Grading applies only to malignant polyps not to endoscopic biopsy specimens. Despite low level of interobserver agreement,⁶⁷ histological high grade is associated with lymph node status and is an independent prognostic factor incorporated into risk assessment models for colorectal carcinoma.^{34,68}

The risk of lymph node metastasis is consistently higher in high grade (poorly differentiated) than in low-grade (moderately or well-differentiated) carcinomas. A meta-analysis of 13 studies including 7,066 patients who underwent radical surgery for early colorectal carcinoma demonstrated that high grade was strongly associated with lymph node metastasis (odds ratio (OR) 8.27; 95% confidence interval (CI) 4.6-14.6).⁶⁹ A second meta-analysis of 31 studies including approximately 1,900 patients with malignant polyps managed by endoscopic or surgical resection confirmed this association, demonstrating that high grade was associated with lymph node metastasis in the surgical subgroup (OR 3.9; 95% CI 2-7.9).⁷⁰

In accordance with the WHO Classification of Digestive System Tumours, 6th edition, a two-tier grading system should be used: low grade (formerly well differentiated and moderately differentiated) and high grade (formerly poorly differentiated). A tumour should be classified as high grade when it contains at least one focus lacking gland formation occupying a minimum area of 0.196 mm² (approximately equivalent to the field of view of a 40× objective lens and 20 mm eyepiece).⁷¹ Tumours lacking such a focus should be classified as low grade. Tumour budding and poorly differentiated clusters at the invasive front should not be considered in the evaluation of grade. Cribriform architecture is regarded as a form of glandular differentiation and should not be interpreted as evidence of high grade morphology.

The grading system is applicable to adenocarcinoma NOS, mucinous adenocarcinoma, serrated adenocarcinoma and lymphoglandular complex-like adenocarcinoma.

The following tumour types should generally be regarded as high grade: Signet-ring cell adenocarcinoma, micropapillary adenocarcinoma, adenosquamous carcinoma.

The following tumour types should generally be regarded as low grade: Adenoma-like adenocarcinoma and low grade tubuloglandular adenocarcinoma.

Grading is not applicable to medullary carcinoma, squamous cell carcinoma, undifferentiated carcinoma, carcinoma with mesenchymal differentiation and neuroendocrine carcinoma.

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Note 11 – Extent of invasion (Core)

In malignant polyps, the anatomical extent of invasion is a key determinant of prognosis and subsequent management. Pathological tumour (pT) classification describes the extent of invasion of the primary tumour in patients who have not received neoadjuvant therapy. Staging should be assigned according to the current Union for International Cancer Control (UICC) 9th edition⁷² and the American Joint Committee on Cancer (AJCC) 8th edition TNM.⁷³

The vast majority of malignant polyps demonstrate unequivocal invasion into the submucosa and are therefore classified as **pT1** (or pTx if the deep margin is involved).

Rarely, invasion is confined to the lamina propria. Such lesions are classified as intramucosal adenocarcinoma (**pTis**).^{74,75} Histological features supporting this diagnosis may include intramucosal signet-ring cells, tumour buds or poorly differentiated tubules confined to the mucosa. Intramucosal adenocarcinoma is exceedingly uncommon, accounting for <0.1% of all colorectal carcinomas. Available evidence suggests an association with microsatellite instability and Lynch syndrome.^{75,76} Given the negligible risk of lymph node metastasis associated with intramucosal adenocarcinoma, histological risk factors used for pT1 risk stratification are generally not applicable and need not be routinely assessed.

pT2 indicates tumour invasion into, but not beyond, the muscularis propria.

pT3 indicates tumour invasion through the muscularis propria into pericorectal tissues. Tumour present within veins or lymphatic channels beyond the muscularis propria should not be considered pT3 unless there is direct continuity with the primary tumour. Distinction between pT2 and pT3 may occasionally be difficult when tumour extends to the outer border of the muscularis propria. In such cases, if no residual muscle fibres separate tumour cells from pericorectal connective tissue, the tumour should be classified as pT3.⁷⁷

pT4 encompasses either tumour infiltration of the visceral peritoneal surface (**pT4a**) or direct invasion of adjacent organs or structures (**pT4b**). Such findings would be exceedingly uncommon in local excision specimens.

Further discussion on pT staging in colorectal carcinomas extending beyond the submucosa is provided in the ICCR dataset for surgical resection specimens.

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Note 12 – Invasive carcinoma dimensions (Core and Non-core)

Measurement of invasive carcinoma dimensions is one of the most important histological risk factors in malignant polyps, is associated with clinical outcome, and is used to guide patient management.^{68,78} If assessable, the depth of invasion should be recorded in all malignant polyps (core), whereas the width of invasion may provide additional prognostic information (non-core).

For colorectal carcinomas invading beyond the submucosa (>pT1), measurement of invasive carcinoma dimensions is generally not clinically useful, as local excision alone is not considered adequate oncological treatment for these stages. The average risk of lymph node metastasis increases substantially with increasing tumour stage, being approximately 18.5% for pT2 tumours, 42% for pT3 tumours, and 50% for pT4 tumours.⁷⁹

Depth of invasion Accurate measurement requires en bloc resection, intact specimen and appropriate specimen handling. Pinning the specimen to a firm surface facilitates proper orientation and allows sectioning perpendicular to the resection plane. When an en bloc specimen is received with limited fragmentation, accurate assessment may still be possible, provided that the invasive carcinoma is confined to a single fragment and the orientation permits reliable measurement of the depth and width of invasion. In piecemeal resections, particularly when invasive carcinoma is present in multiple fragments, only the maximum depth of invasion identified in any individual fragment can be recorded, and accurate assessment of the overall depth of invasion and margin status is generally not possible.

Methods for assessing depth of invasion depend on the configuration of the lesion (non-pedunculated or pedunculated) and include both semi-quantitative and quantitative approaches. If information regarding polyp configuration is not provided, communication with the endoscopist is essential, as a pedunculated polyp transected high within the stalk may be difficult to distinguish histologically from a non-pedunculated lesion, potentially affecting the method used for measuring submucosal invasion and subsequent risk stratification.

Non-pedunculated malignant lesions (Paris 0-Is, 0-IIa, 0-IIb and 0-IIc)

Traditionally, depth of submucosal invasion in sessile malignant polyps has been assessed using the Kikuchi classification, which subdivides the submucosa into three levels: sm1 (superficial third), sm2 (middle third), and sm3 (lower third). Increasing depth of invasion is associated with an increasing risk of lymph node metastasis, with the highest risk observed in sm3 lesions.^{80,81} However, because the full thickness of the submucosa is usually not represented in endoscopic resection specimens, the Kikuchi classification has largely been replaced by direct microscopic measurement using an optical micrometre or measurement from digital images. The Kikuchi system may be more reliably applied in TEMS, TAMIS, and EFTR specimens, where the entire bowel wall is more frequently represented.

Two methods are used to measure the depth of invasion, depending on the status of the muscularis mucosae. For lesions with an intact or partially preserved muscularis mucosae, the depth of invasion should be measured from the lower border of the muscularis mucosae to the deepest point of tumour invasion.⁸² When the muscularis mucosae is completely obliterated by tumour, measurement should be made from the tumour surface to the deepest invading tumour cell. The method used should be recorded.

A depth of submucosal invasion of ≥ 1 mm is the most widely accepted threshold defining deep submucosal invasion and is associated with an increased risk of lymph node metastasis in non-pedunculated malignant lesions.^{78,83,84} Some studies have suggested that a threshold of ≥ 2 mm may provide more accurate risk stratification.^{85,86} Superficial submucosal invasion (< 1 mm) is associated with a very low risk of lymph node metastasis (approximately 0-4%) when other adverse histological features are absent. In contrast, deep submucosal invasion (≥ 1 mm) is associated with a 10-18% risk of residual disease within the bowel wall or

regional lymph nodes following endoscopic resection. Multiple meta-analyses have confirmed deep submucosal invasion ≥ 1 mm as an independent predictor of lymph node metastasis (OR 3.00-3.87).⁶⁸ However, in a recent meta-analysis, deep submucosal invasion ≥ 1 mm, as a solitary risk factor, was not an independent predictor of lymph node metastasis with an absolute risk of 2.6% and pooled incidence rate of 2.83 (95% CI 1.66-4.78).⁸⁷

Although deep submucosal invasion is an established adverse histological feature, its independent significance when present as the sole risk factor remains controversial. Current evidence suggests that depth of invasion should be interpreted in conjunction with other adverse histological features rather than in isolation. Further studies are required to clarify the optimal threshold for defining high-risk invasion (≥ 1 mm versus ≥ 2 mm) and its role in guiding management decisions.

Pedunculated malignant lesions (Paris 0-Ip)

In pedunculated malignant polyps, depth of invasion is commonly assessed using the Haggitt classification, a semi-quantitative system that divides invasion into four levels:⁸⁸

- Level 1: invasion limited to the head of the polyp
- Level 2: invasion into the neck of the polyp
- Level 3: invasion into the stalk
- Level 4: invasion into the submucosa of the bowel wall below the stalk

Application of the Haggitt classification requires an intact polyp with well-oriented sections extending from the head of the lesion to its base. All non-pedunculated malignant polyps with submucosal invasion are considered equivalent to Haggitt level 4 lesions.

The risk of lymph node metastasis is very low following complete excision of pedunculated malignant polyps with Haggitt level 1-3 invasion, provided that no additional adverse histological features, such as lymphovascular invasion or poor differentiation, are present. In contrast, Haggitt level 4 pedunculated lesions are associated with a risk of lymph node metastasis of up to 25%.⁸⁸

Quantitative measurement of submucosal invasion can also be performed in pedunculated polyps by measuring from the Haggitt line (virtual horizontal plane at the junction between the normal mucosa and the lesion) to the deepest point of invasion. However, this measurement is often difficult to perform reproducibly and is not routinely used in clinical practice.

Width of invasion

The maximum width of invasion may also be recorded but is not routinely included in most contemporary risk stratification algorithms because the supporting evidence is less robust than that for depth of submucosal invasion. Tumours with an invasive component measuring ≥ 4 mm in maximum width are associated with an increased risk of lymph node metastasis.^{85,86} In piecemeal resections, the maximum width of invasion identified in any individual fragment may be recorded.

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Note 13 – Lymphatic and venous invasion (Core)

Vascular invasion is one of the most important histological risk factors for lymph node metastasis in malignant colorectal polyps and is widely regarded as a high-risk feature that may warrant completion surgical resection when present. It is important to distinguish between small vessel (mostly lymphatic) invasion and large vessel (venous) invasion, and for venous invasion to record whether involvement is intramural or extramural, as these features may have different prognostic and clinical implications.

Small vessel invasion is defined as tumour involvement of thin-walled structures lined by endothelium, without an identifiable smooth muscle layer or elastic lamina. Small vessels may represent lymphatics, capillaries or post-capillary venules. Lymphatics and venules may be distinguished by D2-40 immunohistochemistry, which only stains lymphatic endothelial cells, not venular, but this is not routinely recommended in reporting all polypectomy specimens. All forms of small vessel invasion are considered under the 'L' classification under UICC 9th edition/AJCC 8th edition TNM.^{72,73}

Small vessel invasion is a strong independent predictor of lymph node metastasis in pT1 colorectal carcinoma. A recent systematic review identified lymphovascular invasion as the strongest histological predictor of lymph node metastasis, with a relative risk of 5.2 (95% CI 4.0-6.8).⁴⁷ Multiple additional studies support this association, including a meta-analysis of 31 studies involving approximately 1,900 patients that demonstrated an OR of 7.0 (95% CI 2.6-19.2)⁷⁰ and a systematic review reporting an OR of 5.47 (95% CI 2.46-12.17).⁶⁹

Venous (large vessel) invasion is defined as tumour present within an endothelium-lined space that is either surrounded by a rim of muscle or identifiable elastic lamina.⁸⁹ It should be suspected in the presence of a rounded or elongated deposit of tumour beside an artery. Interpretation of such features is subjective and can be improved by the application of immunohistochemical and histochemical stains, in particular elastic staining to identify venous elastic lamina.^{90,91} A circumscribed tumour nodule wholly or partially surrounded by a smooth muscle wall or an identifiable elastic lamina, evident on haematoxylin & eosin (H&E) or elastic stains, is considered sufficient to classify as venous invasion. Examination of multiple levels in blocks showing features suspicious of venous invasion can also be helpful in borderline cases. Distinction should be made between intramural and extramural venous invasion.

Intramural venous invasion is an independent risk factor for lymph node metastasis in pT1 colorectal carcinoma, although available evidence suggests that its predictive value may be lower than that of lymphatic invasion. In a nationwide Danish cohort of 1,167 patients with pT1 colorectal carcinoma, venous invasion was an independent predictor of lymph node metastasis (OR 3.42; p<0.001), whereas lymphatic invasion showed a stronger association (OR 4.26; p<0.001).⁹² In addition to its association with lymph node metastasis, venous invasion is an established adverse prognostic factor associated with haematogenous dissemination and reduced cancer-specific survival. A meta-analysis demonstrated that intramural venous invasion was an independent predictor of poorer cancer-specific survival, with its adverse effect appearing to be mediated predominantly through systemic disease progression rather than local recurrence.⁹³

Extramural venous invasion (EMVI) is defined as tumour involvement of veins located beyond the muscularis propria. Multiple studies have demonstrated EMVI to be a stage-independent adverse prognostic factor in both colonic and rectal carcinoma.^{94,95} However, EMVI is rarely encountered in local excision specimens and would generally only be assessable in specimens containing tissue beyond the muscularis propria, such as transanal minimally invasive surgery (TAMIS) or EFTR specimens. Where present, EMVI should be specifically documented.

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Note 14 – Perineural invasion (Core)

Although perineural invasion (PNI) appears to be an independent adverse prognostic factor in colorectal carcinoma, the available evidence in pT1 tumours remains relatively limited compared with other established risk factors, such as lymphatic or venous invasion, tumour grade, depth of submucosal invasion, tumour budding, and margin status. Furthermore, PNI is not consistently incorporated into current risk stratification models or international management guidelines for malignant polyps. For these reasons, PNI is considered a non-core element in the setting of malignant polyps (invasion limited to the submucosa) and a core element for carcinomas invading deeper into the bowel wall.

Perineural invasion (PNI) is defined as tumour cells involving a nerve and in direct contact with the nerve sheath, without intervening connective tissue.⁹⁶ Assessment is primarily based on routine haematoxylin and eosin-stained sections. Although immunohistochemical stains such as S100 may facilitate identification of nerves in selected cases, their routine use for the assessment of PNI is not recommended.

Perineural invasion (PNI) is relatively uncommon in pT1 colorectal carcinoma compared with other adverse histological features. Nevertheless, several studies have demonstrated an association between PNI and lymph node metastasis. In a large population-based Swedish and Danish cohort of 1,439 patients with pT1 colorectal carcinoma, PNI was identified as an independent predictor of lymph node metastasis in multivariate analysis.⁹⁷ Similarly, an analysis of 14,663 patients with malignant colonic polyps from the National Cancer Database demonstrated that PNI was associated with an increased risk of lymph node metastasis (OR 1.70; $p < 0.001$), although the magnitude of this association was lower than that observed for lymphovascular invasion.⁹⁸

The adverse prognostic significance of PNI has been demonstrated in more advanced colorectal carcinomas, particularly Stage II disease, where it is associated with an increased risk of recurrence and reduced survival.⁹⁹ A large multicentre study further reported that both intramural and extramural PNI were independently associated with adverse outcome.¹⁰⁰

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Note 15 – Tumour budding (Core)

Tumour budding is an independent adverse prognostic factor and predictor of lymph node metastasis in malignant polyps. It is defined as single tumour cells or clusters of up to four tumour cells at the invasive front of the carcinoma and is considered a morphological manifestation of epithelial mesenchymal transition.¹⁰¹ Tumour budding is distinct from tumour grade, which is based on gland formation, and from poorly differentiated clusters, which is defined as clusters of five or more tumour cells.

Tumour budding should be assessed and reported according to the recommendations of the International Tumour Budding Consensus Conference (ITBCC).¹⁰² Budding is scored using a three-tier system based on the number of tumour buds identified within a hotspot field at the invasive front: Bd 1 (0-4 buds), Bd 2 (5-9 buds) and Bd 3 (≥ 10 buds). The hotspot is defined as the field showing the highest density of tumour buds along the invasive front. Immunohistochemistry using a cytokeratin marker may assist in identifying the hotspot and highlighting individual tumour buds in difficult cases. However, the final tumour bud count should be performed on haematoxylin and eosin-stained sections. Where necessary, tumour bud counts should be normalised to an area of 0.785 mm², corresponding to the standard ITBCC field size. Although this approach was introduced to improve interobserver consistency, recent studies have suggested that field-size normalisation may influence bud counts and Bd category assignment.¹⁰³ Further validation is required before alternative approaches can be recommended.

Tumour buds should not be counted in areas of neutrophil-rich inflammation or gland rupture, as these changes may produce isolated tumour cells or small tumour clusters that mimic true tumour buds (“pseudobuds”).¹⁰⁴ Unlike true tumour buds, which infiltrate the surrounding desmoplastic stroma, pseudobuds arise secondary to inflammation or gland fragmentation and are typically associated with inflammatory debris and disrupted glandular structures.

In mucinous adenocarcinoma and signet-ring cell adenocarcinoma, tumour cells should only be counted as buds when located within non-mucinous stroma. Tumour cells floating within extracellular mucin pools should not be included in the tumour bud count. Tumour budding should not be assessed in colorectal carcinomas following neoadjuvant therapy.

Tumour budding is a clinically important adverse prognostic feature. Multiple studies have demonstrated that pT1 colorectal carcinomas, including malignant polyps, with 5 or more buds (Bd2 and Bd3) have an increased risk of lymph node metastasis.¹⁰⁵⁻¹⁰⁹ A meta-analysis reported an OR of 2.83 for lymph node metastasis in tumours with tumour budding.⁸⁷ In Stage II and III colorectal carcinomas, high grade tumour budding is also associated with an increased risk of recurrence and poorer disease-free, overall, and cancer-specific survival.¹¹⁰⁻¹¹³

Tumour budding should be considered in conjunction with other adverse histological features, including lymphatic invasion, high grade, deep submucosal invasion, and margin status.

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Note 16 – Poorly differentiated clusters (PDCs) (Non-core)

Poorly differentiated clusters (PDCs) are defined as clusters of five or more tumour cells lacking glandular lumen formation.¹¹⁴ PDCs are distinct from tumour budding, which is defined as single tumour cells or clusters of up to four tumour cells. However, both features appear to exist along a biological continuum and demonstrate substantial morphological, molecular, and prognostic overlap.¹¹⁵

Poorly differentiated clusters (PDCs) are graded using a three-tier system based on the number of clusters identified within a hotspot field examined using a 20x objective lens: Grade 1 (≤ 4 clusters), Grade 2 (5-9 clusters) and Grade 3 (≥ 10 clusters). All tumour sections should be examined to identify the hotspot containing the highest density of PDCs. Although the hotspot may occur anywhere within the tumour, it is most commonly located at or near the invasive front. To be counted as a PDC, the entire cluster should be present within the hotspot field and lack evidence of gland formation. Cancer cell clusters containing small intracytoplasmic lumina but lacking a true glandular lumen may still be counted as PDCs. Clusters arising from gland fragmentation secondary to inflammation, necrosis, degeneration, or mechanical artefact should be excluded from assessment. In accordance with the original Ueno methodology, cancer cell clusters meeting the criteria for PDCs should be counted regardless of whether they are located within the tumour stroma or within a lymphovascular space.¹¹⁴ PDC counts should be normalised to an area of 0.785 mm², using the same method as the one used for tumour budding.

In mucinous or mucin-rich adenocarcinomas, tumour cells floating within mucin should be excluded. PDCs should not be reported in colorectal carcinomas following neoadjuvant therapy, as their prognostic significance in this setting has not been adequately established.

Growing evidence supports PDCs as an independent adverse prognostic factor in pT1 colorectal carcinoma, including malignant polyps.^{105,116,117} In a study of 42 non-pedunculated malignant polyps, PDCs were identified in 54.2% of node-positive cases compared with 22.2% of node-negative cases, corresponding to an

OR of 4.1 for lymph node metastasis.¹¹⁸ A subsequent systematic review and meta-analysis demonstrated an OR of 14.61 for lymph node metastasis associated with PDCs, exceeding the corresponding OR of 4.99 reported for tumour budding.¹¹⁹ Furthermore, the combined presence of high grade tumour budding and PDCs appears to confer particularly high risk, and combined scoring systems may provide improved risk stratification.^{115,120} In Stage II colorectal carcinoma, higher PDC grade is also associated with an increased risk of recurrence and cancer-specific mortality.¹²¹

Poorly differentiated clusters and tumour budding should be regarded as complementary rather than competing measures of tumour aggressiveness.

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Note 17 – Margin status (Core)

Margin status is an essential component of the histological assessment of malignant colorectal polyps and larger local excision specimens. Reliable margin assessment requires en bloc resection. When an en bloc specimen is received with limited fragmentation, accurate assessment may still be possible, provided that the invasive carcinoma is confined to a single fragment and the orientation permits reliable measurement of the distance to the deep resection margin. In piecemeal resections, particularly when invasive carcinoma is present in multiple fragments, margins cannot be reliably assessed.

Complete (R0) resection requires both lateral (horizontal) and deep (vertical) resection margins to be free of carcinoma. The clinical significance of margin involvement depends on the site of the involved margin. Involvement of the lateral margin is primarily associated with local residual or recurrent neoplasia,¹²² whereas involvement of the deep margin is associated with an increased risk of residual invasive carcinoma and adverse clinical outcome.

Assessment of margin status requires microscopic measurement of the shortest distance between invasive carcinoma and the nearest resection margin. In pedunculated polyps, this is typically the stalk margin, whereas in non-pedunculated lesions it corresponds to the deep (vertical) resection margin. The minimum clearance should be reported to the nearest 0.1 mm whenever possible.

The deep margin should be reported as involved when invasive carcinoma is present at the resection margin, or non-assessable when specimen fragmentation or extensive cautery artefact precludes reliable assessment. Cautery artefact may obscure the relationship between tumour and the resection edge. In such cases, the distance between invasive carcinoma and the outer limit of the diathermy zone should be recorded where possible. Immunohistochemistry using pancytokeratin or CDX2 may occasionally assist in difficult cases, although routine use is not recommended. If accurate measurement remains impossible, the margin should be reported as non-assessable.

The definition of a positive resection margin remains controversial.^{123,124} Historically, a clearance of less than 1 mm has been regarded as margin involvement and has been incorporated into many management algorithms.¹²⁵ Several observational studies have demonstrated increased rates of residual carcinoma and recurrence in patients with margins less than 1 mm.¹²⁶ Consequently, a margin clearance of <1 mm is considered an adverse histological feature by several international guidelines. More recent studies have questioned the clinical significance of the 1 mm threshold. In the absence of other adverse histological features, patients with a margin clearance between 0.1 mm and 1 mm may have a very low risk of local recurrence, particularly when tumour budding is absent.¹²⁷

Several studies have demonstrated substantially increased rates of residual disease when carcinoma is present at the resection margin. In the Northern Colorectal Cancer Audit Group (NORCCAG) study, residual carcinoma at the polypectomy site or regional lymph nodes was identified in 34% of patients with a 0 mm margin compared with 5% of patients with a clear margin.¹²⁸ Similarly, a Scottish national study reported higher rates of residual disease following incomplete excision, although a margin clearance of ≥ 1 mm did not appear to confer additional benefit compared with a clear margin of >0 mm.¹²⁹

The significance of margin status should be interpreted in conjunction with other adverse histological features and discussed within a multidisciplinary team. When margin involvement is the only adverse feature present, particularly in patients with significant comorbidity or operative risk, careful surveillance may be an alternative to immediate surgical resection. However, when positive margins coexist with other adverse histological features, the risk of residual disease and lymph node metastasis is substantially increased, generally favouring completion surgical resection.

The lateral margin should also be assessed and reported. Where possible, the minimum distance between the lateral margin and the neoplastic lesion should be recorded. If the margin is involved, the type of tissue present at the margin should be specified, distinguishing invasive carcinoma from residual precursor lesion (conventional adenoma, sessile serrated lesion, or dysplasia) whenever possible.

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Note 18 – Ancillary studies (Core and Non-core)

Assessment of mismatch repair (MMR) protein deficiency or microsatellite instability (MSI) is recommended in colorectal carcinoma for Lynch syndrome screening and to provide prognostic and therapeutic information.¹³⁰ MMR-deficient tumours are associated with significantly lower rates of both lymph node and distant metastases compared to microsatellite stable (MSS) tumours.¹³¹ However, the available evidence on MMR status and lymph node metastasis risk specifically in malignant polyps is limited.¹³² In malignant colorectal polyps, the principal indication is identification of patients who may have Lynch syndrome.

In colorectal carcinomas demonstrating loss of MLH1 and PMS2 expression, additional testing for *BRAF* mutation testing and/or *MLH1* promoter methylation may assist in distinguishing sporadic MLH1-deficient colorectal carcinomas from Lynch syndrome-associated tumours caused by a germline *MLH1* pathogenic variant. The presence of either a *BRAF* V600E mutation or *MLH1* promoter hypermethylation strongly supports a sporadic origin and makes Lynch syndrome unlikely. In contrast, MLH1/PMS2-deficient tumours lacking both *BRAF* mutation and *MLH1* promoter hypermethylation should prompt consideration of Lynch syndrome and referral for genetic counselling where appropriate.

In addition to its role in Lynch syndrome screening, MMR/MSI status provides important prognostic and therapeutic information. MMR-deficient/MSI-high colorectal carcinomas are associated with distinct biological behaviour and may predict response to immune checkpoint inhibitor therapy in advanced disease. Although these therapeutic implications are generally less relevant in the setting of malignant polyps, MMR/MSI status should still be recorded when tested.

If a pure or mixed neuroendocrine neoplasm is suspected on morphology, positivity for at least two markers of neuroendocrine differentiation by immunohistochemistry is required (core) to confirm neuroendocrine differentiation, usually synaptophysin, chromogranin A and/or INSM1. As with other gastrointestinal tract and pancreatic neuroendocrine neoplasms, assessment of proliferation index by Ki-67 immunohistochemistry is a core component as it is fundamental to grading of the neuroendocrine component.² For the differential diagnosis with grade 3 NET, p53 (core) and Rb1 (non-core) can be applied.

Low molecular weight cytokeratins can be used (non-core). MMR stains may also be considered for NECs (non-core). A Ki-67 proliferation index <55% is associated with better overall survival in NECs.¹³³ *TP53* mutations are found in over 69% of NEC compared to 10-15% of NET grade 3 (G3),^{134,135} while RB1 loss is found in 40-60% of NEC and only very rarely in NET G3.¹³⁶

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