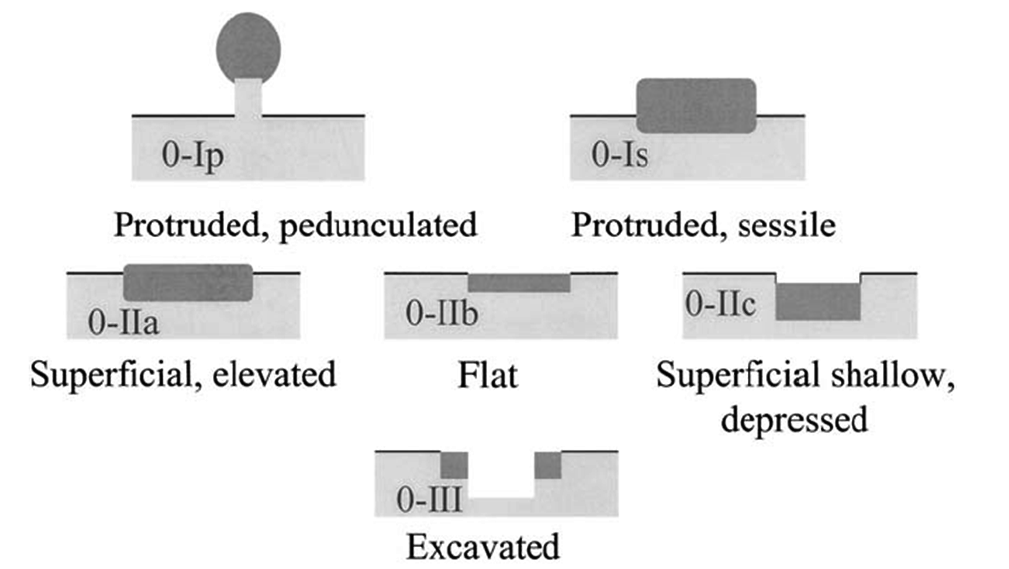


**Elements in black text are CORE Elements in grey text are NON-CORE □ indicates multi-select values** o **indicates single select values**

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| --- | --- |
| Definition of 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 III-2 or above (based on prognostic factors in the National Health and Medical Research Council levels of evidence1). In rare circumstances, where level III-2 evidence is not available an element may be made a Core element where there is unanimous agreement in the expert committee. An appropriate staging system e.g., Pathological TNM staging would normally be included as a Core element.    The summation of all core elements is considered to be the minimum reporting standard for a specific cancer.  **Reference**  1 Merlin T, Weston A and Tooher R (2009). Extending an evidence hierarchy to include topics other than treatment: revising the Australian 'levels of evidence'. *BMC Med Res Methodol* 9:34. |
| Definition of Non-core elements | Non-core elements are those which are unanimously agreed should be included in the dataset but are not supported by level III-2 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 Dataset Authoring Committee. |
| Scope of this dataset | The dataset has been developed for the reporting of local excision specimens from the colon and rectum, including polypectomies, endoscopic mucosal resections (EMR), endoscopic submucosal dissections (ESD), endoscopic full thickness resections (EFTR), transanal submucosal excisions, transanal minimally invasive surgery (TAMIS) and transanal endoscopic microsurgery (TEMS) specimens.  Surgical resection specimens from patients with primary carcinoma of the colon and rectum, including neuroendocrine carcinomas (NECs) and mixed neuroendocrine-non-neuroendocrine neoplasms (MiNENs), are dealt with in a separate dataset.  The dataset is recommended for the reporting of neuroendocrine neoplasms (neuroendocrine tumours (NETs) and (NECs)) diagnosed from local excision specimens and thus differs from the dataset for the reporting of primary carcinoma of the colon and rectum in surgical resection specimens from which NETs are excluded. |

| **Core/**  **Non-core** | **Element name** | **Values** | **Commentary** | **Implementation notes** |
| --- | --- | --- | --- | --- |
| Non-core | CLINICAL INFORMATION | * Information not provided * Screening colonoscopy * 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 * Previous polyp(s) * Previous colorectal cancer * Other, *specify* | Clinical information can be provided by the clinician on the endoscopy report or the pathology request form. Pathologists could search for additional information from possible previous pathology reports.  The presence of a known polyposis syndrome, Lynch syndrome, chronic inflammatory bowel disease (IBD) or any other relevant gastrointestinal disorder should be recorded and provided to the pathologist as awareness of such underlying conditions may influence histological interpretation.  The diagnosis of conventional adenoma or advanced serrated polyp in a patient with IBD raises the possibility of IBD-associated dysplasia in the involved segment. |  |
| Core and  Non-core | ENDOSCOPIC PROCEDURE | * Not specified * Polypectomy/Endoscopic mucosal resection (EMR) * Cautery * Not specifed * Used * Not used * Submucosal injection * Not specifed * Used (EMR) * Not used * Resection type * Not specifed * En bloc * Piecemeal * Endoscopic submucosal dissection (ESD) * Transanal endoscopic microsurgery (TEMS) * Transanal minimally invasive surgery (TAMIS) * Endoscopic full thickness resection (EFTR) * Other, *specify* | The type of endoscopic procedure is important as it may affect histological analysis, including the evaluation of resection margins.  Polypectomy removes polyps using a snare without or with submucosal injection of a solution to lift the lesion (EMR). Diminutive (1-5 millimetres (mm)) polyps and small (6-9 mm) sessile polyps are usually removed by cold snare or sometimes hot snare (mechanical transection without or with electrocautery). Hot snare polypectomy may be used for larger (10-19 mm) sessile polyps and pedunculated polyps. Depending on polyp size and configuration, en bloc or piecemeal removal is performed.1  Endoscopic submucosal dissection (ESD) consists of en bloc resection of superficial lesions of any size after submucosal injection of a solution, using specialised endoscopic knives. It is more commonly used in the upper gastrointestinal tract and sometimes performed in the large bowel for suspected superficial invasive carcinomas. One of the main advantages of ESD compared with EMR is an accurate evaluation of resection margins.  Transanal endoscopic microsurgery (TEMS) is a minimally invasive surgical procedure for en bloc removal of large rectal lesions and early rectal carcinomas not amenable to colonoscopic resection. For malignant lesions, the muscular layer of the rectum is removed with the specimen.  Transanal minimally invasive surgery (TAMIS) is a crossover procedure between laparoscopic surgery and TEMS for resection of benign and early-stage malignant lesions in the lower and mid rectum. The TAMIS technique can also be used for non-curative intent surgery of more advanced lesions in patients who are not candidates for radical surgery.  Endoscopic full thickness resection (EFTR) is a recent minimally invasive endoscopic technique that can be performed in the large bowel resulting in the full transection of all layers of the bowel. EFTR can be used for the management of challenging epithelial and subepithelial lesions that are not amenable to conventional endoscopic resection methods and previously required a surgical approach.  **Reference**  1 Ferlitsch M, Moss A, Hassan C, Bhandari P, Dumonceau JM, Paspatis G, Jover R, Langner C, Bronzwaer M, Nalankilli K, Fockens P, Hazzan R, Gralnek IM, Gschwantler M, Waldmann E, Jeschek P, Penz D, Heresbach D, Moons L, Lemmers A, Paraskeva K, Pohl J, Ponchon T, Regula J, Repici A, Rutter MD, Burgess NG and Bourke MJ (2017). Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. *Endoscopy* 49(3):270-297. |  |
| Core | POLYP NUMBERa  *(Per container)* | * Not specified   \_\_\_\_\_\_\_\_  OR   * Multiple (with no specific number given) | Polyp number is an essential component used in bowel screening registries and for surveillance guidelines. Preferably, the endoscopist should submit tissue piece(s) from each polyp resection in a separate container, so that each specimen jar will contain only one polyp sample for histological evaluation.  When multiple polyps or an unknown number of polyps are received in a specimen container, this may preclude accurate assessment of i) the number of polyps received; ii) polyp classification; iii) the number of positive polyps if carcinoma is present in more than one fragment. As polyps are often resected in multiple fragments (piecemeal resection), the number of fragments does not necessarily reflect the number of polyps removed.  In the event that fragments are received from multiple polyps in a specimen container from multiple sites, the ability to accurately record polyp features corresponding to the polyp site of origin may be compromised. This may have impacts for bowel screening registry follow up. | a As indicated on the container label, pathology request form or colonoscopy report. |
| Core | SPECIMEN SITE(S)a | * 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* | 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. | a As indicated on the container label, pathology request form or colonoscopy report. |
| Non-core | ENDOSCOPIC POLYP SIZE AND CLASSIFICATIONa | Size (mm)   * Not specified   \_\_\_ mm  OR  Size range \_\_\_ mm to \_\_\_ mm  OR  Size category   * Diminutive * Small * Large   Classification   * Not given * Paris classification, *specify* * Lateral spreading tumour classification, *specify* * Optical diagnosis, *specify* | Polyp size is associated with risk of metachronous polyp and colorectal carcinoma, and is used to determine colonoscopy surveillance intervals. Conventional adenomas <10 millimetres (mm) are considered as low-risk lesions while conventional adenomas ≥10 mm are classified as advanced lesions. Polyps <10 mm in size are further divided into small (6-9 mm) and diminutive (1-5 mm) lesions. The size of conventional adenoma correlates with other advanced histologic features (villosity >25% of the polyp and high- grade dysplasia). Sessile serrated lesions (formerly known as sessile serrated adenoma/polyp) and hyperplastic polyps ≥10 mm are considered advanced lesions.  Information on endoscopic appearances of polyps should be recorded for endoscopy/histology correlation. This may be helpful to pathologists who may request deeper levels in tissue blocks when the first histologic impression does not match the endoscopic appearance (optical diagnosis).    Superficial and early neoplasms of the gastrointestinal tract can be assessed on the basis of their endoscopic appearance. Various classifications are used.  Using the Paris classification, type 0 neoplastic lesions are classified as polypoid (Ip and Is), non-polypoid (IIa, IIb and IIc), and non-polypoid and excavated (III) (Figure 1).1  **Figure 1** (See the end of the document for figures).  Lateral spreading tumours (LSTs) are a subgroup of the type IIa lesions, larger than 10 mm in diameter, and classified into 2 groups: granular and non-granular LSTs.2 Granular LSTs are subclassified into homogenous and nodular mixed types. Non-granular LSTs have a higher malignant potential than the granular LST and are subclassified into flat, elevated and pseudo-depressed types.  For direct optical diagnosis of colorectal lesions, usually both high-definition white light as well as image-enhanced endoscopy, are becoming increasingly used. Various strategies and classifications exist, including the Narrow-band imaging (NBI) International Colorectal Endoscopic (NICE), the Japanese NBI Expert Team (JNET) and the Workgroup serrAted polypS and Polyposis (WASP) classifications.3-5 The endoscopist’s optical diagnosis can be reported as a specific type of the classification used or as histologic category: serrated lesions/polyps (hyperplastic polyp, sessile serrated lesion, sessile serrated adenoma with dysplasia), adenoma, early adenocarcinoma, advanced adenocarcinoma, submucosal lesion, others.  **References**  1 Endoscopic Classification Review Group (2005). Update on the paris classification of superficial neoplastic lesions in the digestive tract. *Endoscopy* 37(6):570-578.  2 Kudo S (1993). Endoscopic mucosal resection of flat and depressed types of early colorectal cancer. *Endoscopy* 25(7):455-461.  3 IJspeert JE, Bastiaansen BA, van Leerdam ME, Meijer GA, van Eeden S, Sanduleanu S, Schoon EJ, Bisseling TM, Spaander MC, van Lelyveld N, Bargeman M, Wang J, Dekker E, Dutch Workgroup serrAted polyp S and Polyposis (2016). Development and validation of the WASP classification system for optical diagnosis of adenomas, hyperplastic polyps and sessile serrated adenomas/polyps. *Gut* 65(6):963-970.  4 Sano Y, Tanaka S, Kudo SE, Saito S, Matsuda T, Wada Y, Fujii T, Ikematsu H, Uraoka T, Kobayashi N, Nakamura H, Hotta K, Horimatsu T, Sakamoto N, Fu KI, Tsuruta O, Kawano H, Kashida H, Takeuchi Y, Machida H, Kusaka T, Yoshida N, Hirata I, Terai T, Yamano HO, Kaneko K, Nakajima T, Sakamoto T, Yamaguchi Y, Tamai N, Nakano N, Hayashi N, Oka S, Iwatate M, Ishikawa H, Murakami Y, Yoshida S and Saito Y (2016). Narrow-band imaging (NBI) magnifying endoscopic classification of colorectal tumors proposed by the Japan NBI Expert Team. *Dig Endosc* 28(5):526-533.  5 Hewett DG, Kaltenbach T, Sano Y, Tanaka S, Saunders BP, Ponchon T, Soetikno R and Rex DK (2012). Validation of a simple classification system for endoscopic diagnosis of small colorectal polyps using narrow-band imaging. *Gastroenterology* 143(3):599-607 e591. | a As indicated on the container label, pathology request form or colonoscopy report*.* |
| Core and Non-core | SPECIMEN DIMENSIONS | Maximum dimensions of intact specimen  \_\_\_ mm x \_\_\_ mm  Maximum dimension of intact polyp  \_\_\_ mm  Aggregated dimensions for fragmented polyps  \_\_\_ mm x \_\_\_ mm  Maximum dimension of largest piece for fragmented polyps  \_\_\_ mm | The dimensions of large en bloc resection specimens (large endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), transanal endoscopic microsurgery (TEMS), transanal minimally invasive surgery (TAMIS), endoscopic full thickness resection (EFTR)) need to be recorded. If possible, a photograph should be taken and recorded. When the specimen contains normal tissue and the polyp is macroscopically clearly visible, the maximum diameter of the polyp (without the stalk if pedunculated) should be given.  For polyps resected in piecemeal fashion, a measurement of the aggregated tissue fragments with a dimension of the largest piece of tissue can be given to provide some information about the amount of tissue submitted.  Resection specimens of sessile polyps usually include various amounts of normal surrounding colonic mucosa. The dimension of these specimens does not reflect the actual size of the polyp. The microscopic size may be more appropriate for these cases.  Various studies demonstrated some discordance between polyp sizes determined by endoscopy and pathology, with a tendency for larger endoscopy than pathology sizing.1 For all polyps resected in piecemeal fashion, the endoscopic size is used for determining surveillance intervals. For en bloc resection specimens, the pathology size may be more accurate; however, these lesions are often large with little impact of size differences for determining colonoscopy surveillance intervals.  **Reference**  1 Taylor JL, Coleman HG, Gray RT, Kelly PJ, Cameron RI, O'Neill CJ, Shah RM, Owen TA, Dickey W and Loughrey MB (2016). A comparison of endoscopy versus pathology sizing of colorectal adenomas and potential implications for surveillance colonoscopy. *Gastrointest Endosc* 84(2):341-351. |  |
| Core | HISTOLOGICAL TYPE OF POLYP | * 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, high grade * Serrated adenoma unclassified * Suspicious for adenocarcinoma * Adenocarcinomab * Neuroendocrine tumour * Grade 1 * Grade 2 * Grade 3 * Neuroendocrine carcinoma * Small cell type * Large cell type * Mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN) * Hamartomatous polyp * Inflammatory polyp * Mucosal prolapse polyp * Other, *specify*   **Additional features**  ***For neuroendocrine neoplasms only***   * Not applicable   Mitotic count \_\_\_ /2 mm2  AND/OR  Ki-67 proliferation index \_\_\_%   * Adenoma with epithelial misplacement * Other, *specify* | Each polyp should be classified according to the World Health Organization (WHO) Classification of Tumours of the Digestive System 5th edition, 2019.1    Conventional adenomas are divided based on 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%) are advanced lesions. The presence of high grade dysplasia is reported. Conventional adenomas with high grade dysplasia are regarded as advanced lesions in colonoscopy surveillance guidelines. High grade dysplasia is characterised by marked architectural changes visible at low magnification (complex crowding, irregularity of glands, cribriform architecture, intraluminal necrosis), associated with cytological features (loss of cell polarity, enlarged nuclei with prominent nucleoli, often with atypical mitotic figures). Epithelial misplacement of adenomatous glands into the head or stalk of the polyp can be present in usually large pedunculated polyps. This should be recorded as a separate value in addition to the main histological subtype of polyp.  Dysplasia in sessile serrated lesion (SSLD), formerly known as sessile serrated adenoma/polyp, shows greater morphological heterogeneity than conventional adenoma. The dysplasia should not be graded because biologically advanced SSLDs may show mild morphological changes.2  Traditional serrated adenoma is considered as a low-grade dysplastic lesion with different morphology than the usual dysplasia in conventional adenomas. However, superimposed dysplasia can develop as these lesions progress. Only when high grade dysplasia is present, this be should recorded as traditional serrated adenoma (TSA), high grade.  Serrated adenoma unclassified can be used for lesions that are difficult to classify as either TSA or SSLD, not for SSL versus hyperplastic polyp.  Some advanced conventional adenomas or serrated lesions/polyps may demonstrate histological features suspicious but not definite for the diagnosis of adenocarcinoma. This can be due to limited amount of tissue, cautery artefact or cases difficult to distinguish between epithelial misplacement of adenomatous glands and invasive adenocarcinoma. Such cases should be recorded as an additional value “Suspicious for adenocarcinoma”. The clinical behaviour of these lesions is not clear. The pathologist should comment in the report when an invasive carcinoma cannot be excluded but should not complete the elements for adenocarcinoma if the diagnosis of adenocarcinoma is not definite.  Neuroendocrine neoplasms are classified into neuroendocrine tumours (NETs), neuroendocrine carcinomas (NECs) and mixed neuroendocrine-non-neuroendocrine neoplasms (MiNENs). NETs are graded 1-3 using the mitotic count and Ki-67 proliferation index (Table 1).3 If the two proliferation indicators suggest different grades, the higher grade is assigned. Most NETs of the gastrointestinal tract are grade 1 or 2.  **Table 1** (See the end of the document for tables)  For adenocarcinoma in a polyp, NEC or MiNEN, refer to additional elements specific to malignant polyps (see **HISTOLOGICAL TUMOUR TYPE**).  Other benign polyps (hamartomatous polyps, inflammatory polyps) do not have dysplasia. If superimposed dysplasia is identified in a hamartomatous polyp or if a particular subtype of hamartomatous polyp is identified (e.g., juvenile polyp, Peutz-Jeghers polyp), it should be recorded as an additional feature. Dysplasia arising in an inflammatory polyp raises the possibility of inflammatory bowel disease (IBD)-associated dysplasia.  Various types of mesenchymal polyp can be identified in polypectomy specimens, including perineurioma, Schwann cell hamartoma, schwannoma, neurofibroma, ganglioneuroma, lipoma, granular cell tumour, inflammatory fibroid polyp or gastrointestinal tumour. This should be recorded under the “other” category.  **References**  1 Nagtegaal ID, Arends MJ and Salto-Tellez M (2019). Colorectal adenocarcinoma. In: *Digestive System Tumours. WHO Classification of Tumours, 5th Edition*, Lokuhetty D, White V, Watanabe R and Cree IA (eds), IARC Press, Lyon, France.  2 Liu C, Walker NI, Leggett BA, Whitehall VL, Bettington ML and Rosty C (2017). Sessile serrated adenomas with dysplasia: morphological patterns and correlations with MLH1 immunohistochemistry. *Mod Pathol* 30(12):1728-1738.  3 Nagtegaal ID, Arends MJ, Odze RD and Lam AK (2019). Tumours of the colon and rectum. In: *Digestive System Tumours. WHO Classification of Tumours, 5th Edition*, Lokuhetty D, White V, Watanabe R and Cree IA (eds), IARC Press, Lyon, France.  4 Klimstra DS, Kloppel G, La Rosa S and Rindi G (2019). Classification of neuroendocrine neoplasms of the digestive system. In: *Digestive System Tumours. WHO Classification of Tumours, 5th Edition*, Lokuhetty D, White V, Watanabe R and Cree IA (eds), IARC Press, Lyon, France. | Value list from the World Health Organization (WHO)  Classification of Tumours of the Gastrointestinal Tract (2019)).  Note that permission to publish the WHO classification of tumours may be needed in your implementation. It is advisable to check with the International Agency for Research on Cancer (IARC).  b For adenocarcinoma, refer to HISTOLOGICAL TUMOUR TYPE describing all histological subtypes of adenocarcinomas. |
| Core and Non-core | HISTOLOGICAL TUMOUR TYPEc | * Not applicable * No evidence of residual tumour * Adenocarcinoma not otherwise specified (NOS) * Mucinous adenocarcinoma * Signet-ring cell adenocarcinoma * Medullary carcinoma * Serrated adenocarcinoma * Micropapillary adenocarcinoma * Adenoma-like adenocarcinoma * Small cell type * Large cell type * Mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN) * Other, specify   **Precursor polyp/lesion**   * Absent * Present, *specify type*d | Colorectal cancers should be typed according to the World Health Organization (WHO) Classification of Tumours of the Digestive System, 5th edition, 2019.1 This applies only in the setting of a malignant polyp and not of an endoscopic biopsy specimen. If identified, the precursor polyp/lesion from which the adenocarcinoma arose should be recorded. Some endoscopic resection specimens following a large biopsy or neoadjuvant therapy may only show a scar but no residual tumour.  Most colorectal adenocarcinomas are of no specific type (not otherwise specified (NOS)) but some subtypes of adenocarcinoma are defined as follows:  *Mucinous adenocarcinoma* classification requires greater than 50% of the tumour to comprise pools of extracellular mucin containing malignant glands or individual tumour cells. Microsatellite instability is present in a higher proportion compared to adenocarcinoma NOS. Tumours with less than 50% mucinous content are described as having a mucinous component.  *Signet-ring cell adenocarcinoma* classification requires greater than 50% of the tumour to demonstrate single malignant cells with intracytoplasmic mucin, displacing and typically indenting the nuclei, imparting signet-ring cell morphology. Signet-ring cell adenocarcinoma has stage-independent adverse prognostic significance relative to adenocarcinoma NOS.2 There is a strong association with microsatellite instability and with Lynch syndrome.3 Tumours with less than 50% signet-ring cell content are described as having a signet-ring cell component.  *Medullary carcinoma* is characterised by sheets of malignant cells with indistinct cell boundaries, vesicular nuclei, prominent nucleoli, abundant eosinophilic cytoplasm and prominent intratumoural lymphocytes and neutrophils. These tumours almost invariably demonstrate microsatellite instability and are associated with a good prognosis.4  *Serrated adenocarcinoma* shares morphological similarities with precursor serrated polyps, demonstrating glandular serrations, which are often slit-like, abundant eosinophilic or clear cytoplasm, minimal necrosis and sometimes areas of mucinous differentiation.5  *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 this feature to classify as micropapillary adenocarcinoma. This pattern is most frequently encountered alongside adenocarcinoma NOS. There is a strong association with adverse pathological features including a high risk of lymph node metastatic disease.6    *Adenoma-like adenocarcinoma* is defined as an invasive adenocarcinoma in which at least 50% of the invasive tumour has an adenoma-like appearance with villous architecture, low grade cytology, a pushing growth pattern and minimal desmoplastic stromal reaction.7 Diagnosis of adenocarcinoma on endoscopic biopsy is exceedingly difficult. This variant is associated with a good prognosis.  Neuroendocrine carcinomas (NECs) show marked cytological atypia, brisk mitotic activity, and are subclassified into small cell and large cell subtypes. NECs are considered high-grade by definition. A Ki-67 proliferation index <55% is associated with better overall survival.8 Mixed neuroendocrine-non-neuroendocrine neoplasms (MiNENs) are usually composed of a poorly differentiated NEC component and an adenocarcinoma component. If a pure or mixed NEC is suspected on morphology, immunohistochemistry is required to confirm neuroendocrine differentiation, usually applying synaptophysin and chromogranin A as a minimum.  Other epithelial tumours rarely encountered include adenosquamous carcinoma, carcinoma with sarcomatoid components, undifferentiated carcinoma, squamous cell carcinoma and non-signet-ring cell poorly cohesive adenocarcinoma. Many of these are extremely rare.  If multiple primary tumours are present, separate datasets should be used to record histological tumour type and all following elements for each primary tumour.  **References**  1 Nagtegaal ID, Arends MJ and Salto-Tellez M (2019). Colorectal adenocarcinoma. In: *Digestive System Tumours. WHO Classification of Tumours, 5th Edition*, Lokuhetty D, White V, Watanabe R and Cree IA (eds), IARC Press, Lyon, France.  2 Kang H, O'Connell JB, Maggard MA, Sack J and Ko CY (2005). A 10-year outcomes evaluation of mucinous and signet-ring cell carcinoma of the colon and rectum. *Dis Colon Rectum* 48(6):1161-1168.  3 Kakar S, Deng G, Smyrk TC, Cun L, Sahai V and Kim YS (2012). Loss of heterozygosity, aberrant methylation, BRAF mutation and KRAS mutation in colorectal signet ring cell carcinoma. *Mod Pathol* 25(7):1040-1047.  4 Pyo JS, Sohn JH and Kang G (2016). Medullary carcinoma in the colorectum: a systematic review and meta-analysis. *Hum Pathol* 53:91-96.  5 Garcia-Solano J, Perez-Guillermo M, Conesa-Zamora P, Acosta-Ortega J, Trujillo-Santos J, Cerezuela-Fuentes P and Makinen MJ (2010). Clinicopathologic study of 85 colorectal serrated adenocarcinomas: further insights into the full recognition of a new subset of colorectal carcinoma. *Hum Pathol* 41(10):1359-1368.  6 Haupt B, Ro JY, Schwartz MR and Shen SS (2007). Colorectal adenocarcinoma with micropapillary pattern and its association with lymph node metastasis. *Mod Pathol* 20(7):729-733.  7 Gonzalez RS, Cates JM, Washington MK, Beauchamp RD, Coffey RJ and Shi C (2016). Adenoma-like adenocarcinoma: a subtype of colorectal carcinoma with good prognosis, deceptive appearance on biopsy and frequent KRAS mutation. *Histopathology* 68(2):183-190.  8 Milione M, Maisonneuve P, Spada F, Pellegrinelli A, Spaggiari P, Albarello L, Pisa E, Barberis M, Vanoli A, Buzzoni R, Pusceddu S, Concas L, Sessa F, Solcia E, Capella C, Fazio N and La Rosa S (2017). The Clinicopathologic Heterogeneity of Grade 3 Gastroenteropancreatic Neuroendocrine Neoplasms: Morphological Differentiation and Proliferation Identify Different Prognostic Categories. *Neuroendocrinology* 104(1):85-93. | Value list from the WHO Classification of Tumours of the Gastrointestinal Tract (2019).  c To complete this and all following elements ONLY if an adenocarcinoma,  neuroendocrine carcinoma or MiNEN is present. If multiple primary  carcinomas are present, separate datasets should be used to record this  and all following elements for each primary carcinoma.  d Refer to HISTOLOGICAL TYPE OF POLYP. |
| Core | HISTOLOGICAL GRADE OF ADENOCARCINOMA | * Not applicable * Low grade (formerly well to moderately differentiated) * High grade (formerly poorly differentiated) | Grading applies only to malignant polyps not to endoscopic biopsy specimens. Despite low level of interobserver agreement,1 histological grade is associated with nodal status and is an independent prognostic factor used in risk assessment models for colorectal carcinoma.2-4  Various grading systems have been used over the years. A two-tiered grading system is more reproducible and more prognostically relevant than a four-tiered grading system. For consistency with the latest World Health Organization (WHO) classification,5 grading should be based on gland formation: low grade (formerly well to moderately differentiated) and high grade (formerly poorly differentiated). Grading is based on the least differentiated component of the tumour, although there is no good evidence to support this stance and a minimum area of high grade tumour required for this classification has not been defined. Grading may not be applicable if the adenocarcinoma is very small.  Tumour buds or poorly differentiated clusters, most commonly seen at the invasive tumour front, should not be considered in the evaluation of grade. Emerging data suggests that grading based on poorly differentiated clusters is superior to conventional grading with respect to both prognostic value and reproducibility.6,7  Only adenocarcinoma not otherwise specified (NOS) and mucinous adenocarcinoma should be graded. Grading is not applicable to other subtypes of adenocarcinoma, as grading by gland formation is difficult to apply to subtypes and most of these are associated with their own clinical prognosis e.g., bad for signet-ring cell adenocarcinoma, micropapillary adenocarcinoma, serrated adenocarcinoma and good for medullary carcinoma and adenoma-like adenocarcinoma. Mucinous adenocarcinoma should be graded on gland formation and epithelial maturation.5 Tumour mismatch repair (MMR) status is likely to influence clinical behaviour of some histological tumour types, including mucinous adenocarcinoma, but some studies have found morphological grading superior to MMR status for prognostication of mucinous adenocarcinomas.8,9 A cribriform pattern of invasive adenocarcinoma is associated with greater risk of nodal metastasis in malignant polyps.10  **References**  1 Chandler I and Houlston RS (2008). Interobserver agreement in grading of colorectal cancers-findings from a nationwide web-based survey of histopathologists. *Histopathology* 52(4):494–499.  2 Weiser MR, Gonen M, Chou JF, Kattan MW and Schrag D (2011). Predicting survival after curative colectomy for cancer: individualizing colon cancer staging. *J Clin Oncol* 29(36):4796-4802.  3 Renfro LA, Grothey A, Xue Y, Saltz LB, Andre T, Twelves C, Labianca R, Allegra CJ, Alberts SR, Loprinzi CL, Yothers G, Sargent DJ and Adjuvant Colon Cancer Endpoints G (2014). ACCENT-based web calculators to predict recurrence and overall survival in stage III colon cancer. *J Natl Cancer Inst* 106(12):1-9.  4 Chapuis PH, Dent OF, Fisher R, Newland RC, Pheils MT, Smyth E and Colquhoun K (1985). A multivariate analysis of clinical and pathological variables in prognosis after resection of large bowel cancer. *British Journal of Surgery* 72(9):698–702.  5 Nagtegaal ID, Arends MJ and Salto-Tellez M (2019). Colorectal adenocarcinoma. In: *Digestive System Tumours. WHO Classification of Tumours, 5th Edition*, Lokuhetty D, White V, Watanabe R and Cree IA (eds), IARC Press, Lyon, France.  6 Konishi T, Shimada Y, Lee LH, Cavalcanti MS, Hsu M, Smith JJ, Nash GM, Temple LK, Guillem JG, Paty PB, Garcia-Aguilar J, Vakiani E, Gonen M, Shia J and Weiser MR (2018). Poorly differentiated clusters predict colon cancer recurrence: an in-depth comparative analysis of invasive-front prognostic markers. *Am J Surg Pathol* 42(6):705-714.  7 Ueno H, Kajiwara Y, Shimazaki H, Shinto E, Hashiguchi Y, Nakanishi K, Maekawa K, Katsurada Y, Nakamura T, Mochizuki H, Yamamoto J and Hase K (2012). New criteria for histologic grading of colorectal cancer. *Am J Surg Pathol* 36(2):193-201.  8 Kakar S, Aksoy S, Burgart LJ and Smyrk TC (2004). Mucinous carcinoma of the colon: correlation of loss of mismatch repair enzymes with clinicopathologic features and survival. *Mod Pathol* 17(6):696-700.  9 Yoshioka Y, Togashi Y, Chikugo T, Kogita A, Taguri M, Terashima M, Mizukami T, Hayashi H, Sakai K, de Velasco MA, Tomida S, Fujita Y, Tokoro T, Ito A, Okuno K and Nishio K (2015). Clinicopathological and genetic differences between low-grade and high-grade colorectal mucinous adenocarcinomas. *Cancer* 121(24):4359-4368.  10 Brown IS, Bettington ML, Bettington A, Miller G and Rosty C (2016). Adverse histological features in malignant colorectal polyps: a contemporary series of 239 cases. *J Clin Pathol* 69(4):292-299. | Only adenocarcinoma NOS and mucinous adenocarcinoma should be graded. |
| Core | EXTENT OF INVASION | * Non-invasive neoplasia/high grade dysplasia * Invasion into submucosa * Invasion into muscularis propria * Invasion through the muscularis propria into pericolorectal connective tissue * Invasion onto the surface of the visceral peritoneum * Invasion into adjacent structure(s)/organ(s), *specify* | The anatomic extent of tumour invasion, based on a combination of macroscopic and microscopic assessment of an excision specimen, is the most important prognostic factor in colorectal cancer. pT classification indicates the extent of invasion of the primary tumour in the absence of application of neoadjuvant therapy. Criteria of the Union for International Cancer Control (UICC)1 and American Joint Committee on Cancer (AJCC)2 8th editions are applied, with the exception that pT in situ is not recognised. Rare cases of colorectal neoplasia confined to invasion of the lamina propria (intramucosal carcinoma) are acknowledged but, given the negligible metastatic potential of such neoplasms, including those with a poorly differentiated morphology,3,4 these should be classified under high grade dysplasia/non-invasive neoplasia.  Some rare polyps will remain difficult to classify as either invasive or non-invasive neoplasia, in particular when epithelial misplacement is present. Some adenomas may involve submucosal lymphoglandular complexes, mimicking invasive carcinoma,5 but the distinction with an adenocarcinoma invading the submucosa can be challenging. In other cases, signet-ring cells limited to the mucosa may be identified in an adenoma.6 The clinical behaviour of such lesions is not clear. The pathologist should comment in the report when an invasive carcinoma cannot be excluded or for rare cases with unknown clinical behaviour.  For endoscopic resection of early colorectal carcinoma, tumours are usually invading no deeper than into the submucosa (pT1). For rectal carcinoma removed by transanal endoscopic microsurgery (TEMS)/transanal minimally invasive surgery (TAMIS), invasion into the muscularis propria (pT2) or the perirectal fat tissue (pT3) can be present. Further consideration of colorectal carcinoma invading beyond the submucosa is provided in a separate surgical resection dataset.  **References**  1 Brierley JD, Gospodarowicz MK and Wittekind C (eds) (2016). *UICC TNM Classification of Malignant Tumours, 8th Edition*, Wiley-Blackwell.  2 Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, Jessup JM, Brierley JD, Gaspar LE, Schilsky RL, Balch CM, Winchester DP, Asare EA, Madera M, Gress DM and Meyer LR (eds) (2017). *AJCC Cancer Staging Manual. 8th ed.*, Springer, New York.  3 Kojima M, Shimazaki H, Iwaya K, Nakamura T, Kawachi H, Ichikawa K, Sekine S, Ishiguro S, Shimoda T, Kushima R, Yao T, Fujimori T, Hase K, Watanabe T, Sugihara K, Lauwers GY and Ochiai A (2017). Intramucosal colorectal carcinoma with invasion of the lamina propria: a study by the Japanese Society for Cancer of the Colon and Rectum. *Hum Pathol* 66:230-237.  4 Lewin MR, Fenton H, Burkart AL, Sheridan T, Abu-Alfa AK and Montgomery EA (2007). Poorly differentiated colorectal carcinoma with invasion restricted to lamina propria (intramucosal carcinoma): a follow-up study of 15 cases. *Am J Surg Pathol* 31(12):1882-1886.  5 Lee HE, Wu TT, Chandan VS, Torbenson MS and Mounajjed T (2018). Colonic adenomatous polyps involving submucosal lymphoglandular complexes: a diagnostic pitfall. *Am J Surg Pathol* 42(8):1083-1089.  6 Bellan A, Cappellesso R, Lo Mele M, Peraro L, Balsamo L, Lanza C, Fassan M and Rugge M (2016). Early signet ring cell carcinoma arising from colonic adenoma: the molecular profiling supports the adenoma-carcinoma sequence. *Hum Pathol* 50:183-186. |  |
| Core and Non-core | INVASIVE CARCINOMA DIMENSIONS | * Cannot be assessed   Maximum depth of invasion \_\_\_ mm   * Cannot be assessed   Maximum width of invasion \_\_\_ mm | Depth of invasion is one of the main histological risk factors associated with clinical outcome and used for patient management.1,2 Submucosal invasion ≥1 millimetre (mm) is associated with an increased risk of lymph node metastasis.3-5 Depth of invasion is the maximum thickness of invasive carcinoma, measured in mm, from the deepest aspect of the invasive tumour in the submucosa to either the overlying muscularis mucosae or the surface of the polyp, if the carcinoma is ulcerated or has overgrown the precursor polyp. This requires well-oriented sections perpendicular to the surface. If the resection is piecemeal, the maximum depth of invasion in any fragment is used.  A semi-quantitative evaluation of the depth of invasion into 3 or 4 levels may still be used in some parts of the world as  follows:  Haggitt levels 1 (head), 2 (neck), 3 (stalk) and 4 (beyond stalk) for pedunculated polyps, with significant increased risk of lymph metastasis for level 4 polyps.2,6 This requires intact polyp with well-oriented sections from the head to the base.  Kikuchi levels sm1 (superficial submucosa), sm2 (mid submucosa) and sm3 (deep submucosa) for sessile polyps, with significant increased risk of nodal metastasis for sm3 polyps.7,8 This requires the presence of the muscularis propria to define the deep boundary of the submucosa, which is often absent in endoscopic resection specimens. The Kikuchi system can be more reliably applied in transanal endoscopic microsurgery (TEMS), transanal minimally invasive surgery (TAMIS) and endoscopic full thickness resection (EFTR) specimens.  The maximum width of invasive carcinoma can also be recorded. Tumours with an invasive component ≥4 mm are more likely to be associated with lymph node metastasis.9,10 If the resection is piecemeal, the maximum width of invasion in any fragment is used.  **References**  1 Williams JG, Pullan RD, Hill J, Horgan PG, Salmo E, Buchanan GN, Rasheed S, McGee SG, Haboubi N and Association of Coloproctology of Great Britain Ireland (2013). Management of the malignant colorectal polyp: ACPGBI position statement. *Colorectal Dis* 15 Suppl 2:1-38.  2 Backes Y, Elias SG, Groen JN, Schwartz MP, Wolfhagen FHJ, Geesing JMJ, Ter Borg F, van Bergeijk J, Spanier BWM, de Vos Tot Nederveen Cappel WH, Kessels K, Seldenrijk CA, Raicu MG, Drillenburg P, Milne AN, Kerkhof M, Seerden TCJ, Siersema PD, Vleggaar FP, Offerhaus GJA, Lacle MM, Moons LMG and Dutch TCRCWG (2018). Histologic factors associated with need for surgery in patients with pedunculated T1 colorectal carcinomas. *Gastroenterology* 154(6):1647-1659.  3 Bosch SL, Teerenstra S, de Wilt JH, Cunningham C and Nagtegaal ID (2013). Predicting lymph node metastasis in pT1 colorectal cancer: a systematic review of risk factors providing rationale for therapy decisions. *Endoscopy* 45(10):827-834.  4 Beaton C, Twine CP, Williams GL and Radcliffe AG (2013). Systematic review and meta-analysis of histopathological factors influencing the risk of lymph node metastasis in early colorectal cancer. *Colorectal Dis* 15(7):788-797.  5 Ueno H, Hase K, Hashiguchi Y, Shimazaki H, Yoshii S, Kudo SE, Tanaka M, Akagi Y, Suto T, Nagata S, Matsuda K, Komori K, Yoshimatsu K, Tomita Y, Yokoyama S, Shinto E, Nakamura T and Sugihara K (2014). Novel risk factors for lymph node metastasis in early invasive colorectal cancer: a multi-institution pathology review. *J Gastroenterol* 49(9):1314-1323.  6 Haggitt RC, Glotzbach RE, Soffer EE and Wruble LD (1985). Prognostic factors in colorectal carcinomas arising in adenomas: implications for lesions removed by endoscopic polypectomy. *Gastroenterology* 89(2):328–336.  7 Kikuchi R, Takano M, Takagi K, Fujimoto N, Nozaki R, Fujiyoshi T and Uchida Y (1995). Management of early invasive colorectal cancer. Risk of recurrence and clinical guidelines. *Dis Colon Rectum* 38(12):1286-1295.  8 Nascimbeni R, Burgart LJ, Nivatvongs S and Larson DR (2002). Risk of lymph node metastasis in T1 carcinoma of the colon and rectum. *Dis Colon Rectum* 45(2):200-206.  9 Brown IS, Bettington ML, Bettington A, Miller G and Rosty C (2016). Adverse histological features in malignant colorectal polyps: a contemporary series of 239 cases. *J Clin Pathol* 69(4):292-299.  10 Ueno H, Mochizuki H, Hashiguchi Y, Shimazaki H, Aida S, Hase K, Matsukuma S, Kanai T, Kurihara H, Ozawa K, Yoshimura K and Bekku S (2004). Risk factors for an adverse outcome in early invasive colorectal carcinoma. *Gastroenterology* 127(2):385-394. |  |
| Core | LYMPHATIC AND VENOUS INVASION | * Not identified * Present * Small vessel (lymphatic, capillary or venular) * Large vessel (venous) * Intramural * Extramural | For colorectal cancer, it is important to report the presence or absence of lymphovascular invasion and to classify this further according to the type of vessels involved and, for veins, their intramural or extramural location, as these features may have different clinical and prognostic implications.  Small vessel invasion should be reported separately from venous (large vessel) invasion. 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 immuno-histochemistry, which only stains lymphatic endothelial cells, not venular, but this is not routinely recommended in reporting polypectomy specimens. All forms of small vessel invasion are considered under the ‘L’ classification under Union for International Cancer Control (UICC)/American Joint Committee on Cancer (AJCC) TNM 8th editions.1,2 Small vessel invasionis associated with lymph node metastatic disease and has been shown to be an independent indicator of adverse outcome in several studies.3-5 A higher prognostic significance of extramural small vessel invasion has been suggested, but the importance of anatomic location in small vessel invasion is not well established.4 In malignant polyps, lymphatic invasion is associated with an increased risk of lymph node metastasis.6,7  Venous invasion is defined as tumour present within an endothelium-lined space that is either surrounded by a rim of muscle or contains red blood cells.8 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.9,10 A circumscribed tumour nodule 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.  Extramural (beyond muscularis propria) venous invasion has been demonstrated by multivariate analysis in multiple studies to be a stage independent adverse prognostic factor for colonic and rectal cancer.4,11 However, it would only be identified in transanal minimally invasive surgery (TAMIS) or endoscopic full thickness resection (EFTR) specimens. There is also evidence from several studies that intramural (intramuscular or submucosal) venous spread is also of prognostic importance but the evidence is much weaker than for extramural venous invasion.12  **References**  1 Brierley JD, Gospodarowicz MK and Wittekind C (eds) (2016). *UICC TNM Classification of Malignant Tumours, 8th Edition*, Wiley-Blackwell.  2 Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, Jessup JM, Brierley JD, Gaspar LE, Schilsky RL, Balch CM, Winchester DP, Asare EA, Madera M, Gress DM and Meyer LR (eds) (2017). *AJCC Cancer Staging Manual. 8th ed.*, Springer, New York.  3 Santos C, Lopez-Doriga A, Navarro M, Mateo J, Biondo S, Martinez Villacampa M, Soler G, Sanjuan X, Paules MJ, Laquente B, Guino E, Kreisler E, Frago R, Germa JR, Moreno V and Salazar R (2013). 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| Non-core | TUMOUR BUDDING | * Cannot be assessed   Number of tumour budse \_\_\_\_  **Tumour budding score**   * Bd1 - low budding (0-4 buds) * Bd2 - intermediate budding (5-9 buds) * Bd3 - high budding (≥10 buds) | Tumour budding is defined as single cells or clusters of up to 4 tumour cells at the invasive front of invasive carcinomas. It is considered to be the morphological manifestation of epithelial mesenchymal transition.1 Tumour budding is different from tumour grade (based on gland formation) and poorly differentiated clusters (≥5 cells).  There is increasing evidence that tumour budding is an independent adverse prognostic factor in colorectal carcinoma. Several studies have shown that pT1 colorectal carcinomas, including malignant polyps, with tumour budding score Bd2 and Bd3 (≥5 buds) are associated with an increased risk of lymph node metastasis.2-6 For stage II colorectal carcinomas, tumour budding score Bd3 is associated with increased risk of recurrence and mortality.7-9  Tumour budding is reported as the number of buds and scored using a three-tiered system. According to the recommendations from a consensus conference on tumour budding,10 the number of tumour buds is the highest count after scanning 10 separate fields (20x objective lens) along the invasive front of the tumour or the entire lesion for malignant polyps (‘hotspot’ approach). The count of tumour buds is only performed in non-mucinous, non-signet-ring cell adenocarcinoma areas. The number of tumour buds is counted on haematoxylin and eosin (H&E). If the invasive front of the tumour is obscured by inflammatory cells, immunohistochemistry using pan-cytokeratin can be used to help identifying the buds, but the final count is performed on H&E. Depending on the eyepiece field number diameter of the microscope, the number of buds may need to be normalised to represent the number for a field of 0.785 mm2 (objective lens 20x with eyepiece diameter of 20 mm).  Tumour budding should only be reported in non-mucinous and non-signet-ring cell adenocarcinoma areas.  **References**  1 Zlobec I and Lugli A (2010). Epithelial mesenchymal transition and tumor budding in aggressive colorectal cancer: tumor budding as oncotarget. *Oncotarget* 1(7):651-661.  2 Ueno H, Hase K, Hashiguchi Y, Shimazaki H, Yoshii S, Kudo SE, Tanaka M, Akagi Y, Suto T, Nagata S, Matsuda K, Komori K, Yoshimatsu K, Tomita Y, Yokoyama S, Shinto E, Nakamura T and Sugihara K (2014). Novel risk factors for lymph node metastasis in early invasive colorectal cancer: a multi-institution pathology review. *J Gastroenterol* 49(9):1314-1323.  3 Tateishi Y, Nakanishi Y, Taniguchi H, Shimoda T and Umemura S (2010). Pathological prognostic factors predicting lymph node metastasis in submucosal invasive (T1) colorectal carcinoma. *Mod Pathol* 23(8):1068-1072.  4 Suh JH, Han KS, Kim BC, Hong CW, Sohn DK, Chang HJ, Kim MJ, Park SC, Park JW, Choi HS and Oh JH (2012). Predictors for lymph node metastasis in T1 colorectal cancer. *Endoscopy* 44(6):590-595.  5 Pai RK, Cheng YW, Jakubowski MA, Shadrach BL, Plesec TP and Pai RK (2017). Colorectal carcinomas with submucosal invasion (pT1): analysis of histopathological and molecular factors predicting lymph node metastasis. *Mod Pathol* 30(1):113-122.  6 Beaton C, Twine CP, Williams GL and Radcliffe AG (2013). Systematic review and meta-analysis of histopathological factors influencing the risk of lymph node metastasis in early colorectal cancer. *Colorectal Dis* 15(7):788-797.  7 van Wyk HC, Park J, Roxburgh C, Horgan P, Foulis A and McMillan DC (2015). The role of tumour budding in predicting survival in patients with primary operable colorectal cancer: a systematic review. *Cancer Treat Rev* 41(2):151-159.  8 Petrelli F, Pezzica E, Cabiddu M, Coinu A, Borgonovo K, Ghilardi M, Lonati V, Corti D and Barni S (2015). Tumour budding and survival in stage II colorectal cancer: a systematic review and pooled analysis. *J Gastrointest Cancer* 46(3):212-218.  9 Rogers AC, Winter DC, Heeney A, Gibbons D, Lugli A, Puppa G and Sheahan K (2016). Systematic review and meta-analysis of the impact of tumour budding in colorectal cancer. *Br J Cancer* 115(7):831-840.  10 Lugli A, Kirsch R, Ajioka Y, Bosman F, Cathomas G, Dawson H, El Zimaity H, Flejou JF, Hansen TP, Hartmann A, Kakar S, Langner C, Nagtegaal I, Puppa G, Riddell R, Ristimaki A, Sheahan K, Smyrk T, Sugihara K, Terris B, Ueno H, Vieth M, Zlobec I and Quirke P (2017). Recommendations for reporting tumor budding in colorectal cancer based on the International Tumor Budding Consensus Conference (ITBCC) 2016. *Mod Pathol* 30(9):1299-1311. | Should only be reported in non-mucinous and non-signet ring cell adenocarcinoma areas.  e After scanning 10 fields on a 20x objective lens, the hotspot field  normalised to represent a field of 0.785 mm2*.* |
| Core | PERINEURAL INVASION | * Not identified * Present | Multiple independent studies and one meta-analysis have demonstrated the adverse prognostic implication of perineural invasion in colorectal cancer, particularly in stage II disease.1,2 One large multicentre study reported adverse prognostic significance of both intramural and extramural perineural invasion.1 However, the importance of anatomic location in perineural invasion is not well established.  In malignant polyps, perineural invasion is extremely rare. It can sometimes be found in endoscopic resection or transanal endoscopic microsurgery (TEMS)/transanal minimally invasive surgery (TAMIS) for early rectal carcinomas.  **References**  1 Ueno H, Shirouzu K, Eishi Y, Yamada K, Kusumi T, Kushima R, Ikegami M, Murata A, Okuno K, Sato T, Ajioka Y, Ochiai A, Shimazaki H, Nakamura T, Kawachi H, Kojima M, Akagi Y, Sugihara K and Study Group for Perineural Invasion projected by the Japanese Society for Cancer of the Colon and Rectum (2013). Characterization of perineural invasion as a component of colorectal cancer staging. *Am J Surg Pathol* 37(10):1542-1549.  2 Liebig C, Ayala G, Wilks J, Verstovsek G, Liu H, Agarwal N, Berger DH and Albo D (2009). Perineural invasion is an independent predictor of outcome in colorectal cancer. *J Clin Oncol* 27(31):5131-5137. |  |
| Core | MARGIN STATUS | **Deep margin**   * Cannot be assessed * Involved * Not involved   Distance to invasive carcinoma  \_\_\_ mm  **Lateral margin**   * Cannot be assessed * Involved, *specify* * Not involved   Distance to neoplasia  \_\_\_ mm | The margin status is an essential component of the histological examination. Assessment of margins can only be done for en bloc polypectomy, endoscopic submucosal dissection (ESD), endoscopic full thickness resection (EFTR), transanal minimally invasive surgery (TAMIS) and transanal endoscopic microsurgery (TEMS) specimens. Margins cannot be reliably assessed for specimens resected in piecemeal fashion.  An involved (positive) deep resection margin is a predictor for adverse outcome.1 However, if no other adverse histological features are present, an involved deep margin is associated with a risk of local recurrence but not lymph node or distant metastasis. Various cut-offs have been used to define an involved deep margin. Most studies have shown that a clearance of <1 millimetre (mm) should be regarded as a positive margin.2,3 Pathologists should report the deep margin as either involved if carcinoma cells are present directly at the margin, or record the clearance distance to nearest 0.1 mm between the deep margin and the closest invasive carcinoma. If the invasive carcinoma is within a diathermy zone, the distance between the outer aspect of the diathermy zone and the closest carcinoma should be reported if possible. In cases for which extensive diathermy artefacts obscure the presence of possible carcinoma at the margin, immunohistochemistry for CDX2 or pancytokeratin may be helpful in this assessment. If measurement is not possible, the margin status should be reported as non-assessable.  Lateral margin is less critical for patient management but needs to be recorded. A positive lateral margin does not influence local recurrence rate.4 The status of the lateral margin should be recorded as either involved or by measuring the distance to nearest 0.1 mm between the closest lateral margin and the neoplasm (dysplasia or carcinoma). If possible, the component of the malignant polyp present at the margin (carcinoma or benign precursor polyp/lesion) should be specified. However, this distinction is not always possible.  **References**  1 Bujanda L, Cosme A, Gil I and Arenas-Mirave JI (2010). Malignant colorectal polyps. *World J Gastroenterol* 16(25):3103-3111.  2 Hackelsberger A, Fruhmorgen P, Weiler H, Heller T, Seeliger H and Junghanns K (1995). Endoscopic polypectomy and management of colorectal adenomas with invasive carcinoma. *Endoscopy* 27(2):153-158.  3 Cooper HS, Deppisch LM, Gourley WK, Kahn EI, Lev R, Manley PN, Pascal RR, Qizilbash AH, Rickert RR, Silverman JF and Wirman JA (1995). Endoscopically removed malignant colorectal polyps: clinicopathologic correlations. *Gastroenterology* 108(6):1657-1665.  4 Lee S, Kim J, Soh JS, Bae J, Hwang SW, Park SH, Ye BD, Byeon JS, Myung SJ, Yang SK and Yang DH (2018). Recurrence rate of lateral margin-positive cases after en bloc endoscopic submucosal dissection of colorectal neoplasia. *Int J Colorectal Dis* 33(6):735-743. |  |
| Core and  Non-core | ANCILLARY STUDIES | ***For neuroendocrine neoplasms only***   * Not applicable * Neuroendocrine markers, *specify result(s) if available*   AND  Ki-67 proliferation index \_\_\_ %    **Mismatch repair (MMR) immunohistochemistry**   * Not tested * Not interpretable * MMR proficient * MMR deficient * *MLH1/PMS2* loss * *MSH2/MSH6* loss * *MSH6* loss * *PMS2* loss * Other, *specify*   **MMR status by microsatellite instability (MSI) testing**   * Not tested * Test failed * MSI-high * MSI-low * MS-stable   ***BRAF* V600E mutation testing**   * Not tested * Test failed * Mutated * Wild type   ***MLH1* promoter methylation testing**   * Not tested * Test failed * Methylated * Not methylated * Inconclusive   **Other, *specify*** | If a pure or mixed neuroendocrine neoplasm is suspected on morphology, immunohistochemistry is required to confirm neuroendocrine differentiation, usually applying synaptophysin and chromogranin A as a minimum. As with other gastrointestinal tract and pancreatic neuroendocrine neoplasms, assessment of proliferation index by Ki-67 immunohistochemistry is fundamental to grading of the neuroendocrine component. A Ki-67 proliferation index <55% is associated with better overall survival in neuroendocrine carcinomas.1  Testing colorectal carcinoma for mismatch repair (MMR) protein deficiency is standard of care for Lynch syndrome screening and provides therapeutic decision information for patient management.2 MMR deficiency is associated with good prognosis, poor response to 5-Fluorouracil and predicts response to immune checkpoint blockage therapy.3,4  *BRAF* mutation testing and *MLH1* promoter methylation analysis are performed to help distinguish sporadic MLH1-deficient colorectal carcinomas from Lynch syndrome associated tumours, caused by constitutional *MLH1* mutation. The presence of either *BRAF* V600E mutation or *MLH1* promoter methylation effectively excludes Lynch syndrome. *BRAF* mutation status may also have predictive/therapeutic value.  **References**  1 Milione M, Maisonneuve P, Spada F, Pellegrinelli A, Spaggiari P, Albarello L, Pisa E, Barberis M, Vanoli A, Buzzoni R, Pusceddu S, Concas L, Sessa F, Solcia E, Capella C, Fazio N and La Rosa S (2017). The Clinicopathologic Heterogeneity of Grade 3 Gastroenteropancreatic Neuroendocrine Neoplasms: Morphological Differentiation and Proliferation Identify Different Prognostic Categories. *Neuroendocrinology* 104(1):85-93.  2 Vasen HF, Blanco I, Aktan-Collan K, Gopie JP, Alonso A, Aretz S, Bernstein I, Bertario L, Burn J, Capella G, Colas C, Engel C, Frayling IM, Genuardi M, Heinimann K, Hes FJ, Hodgson SV, Karagiannis JA, Lalloo F, Lindblom A, Mecklin JP, Moller P, Myrhoj T, Nagengast FM, Parc Y, Ponz de Leon M, Renkonen-Sinisalo L, Sampson JR, Stormorken A, Sijmons RH, Tejpar S, Thomas HJ, Rahner N, Wijnen JT, Jarvinen HJ, Moslein G and Mallorca group (2013). Revised guidelines for the clinical management of Lynch syndrome (HNPCC): recommendations by a group of European experts. *Gut* 62(6):812-823.  3 Le DT, Durham JN, Smith KN, Wang H, Bartlett BR, Aulakh LK, Lu S, Kemberling H, Wilt C, Luber BS, Wong F, Azad NS, Rucki AA, Laheru D, Donehower R, Zaheer A, Fisher GA, Crocenzi TS, Lee JJ, Greten TF, Duffy AG, Ciombor KK, Eyring AD, Lam BH, Joe A, Kang SP, Holdhoff M, Danilova L, Cope L, Meyer C, Zhou S, Goldberg RM, Armstrong DK, Bever KM, Fader AN, Taube J, Housseau F, Spetzler D, Xiao N, Pardoll DM, Papadopoulos N, Kinzler KW, Eshleman JR, Vogelstein B, Anders RA and Diaz LA, Jr. (2017). Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade. *Science* 357(6349):409-413.  4 Popat S and Houlston RS (2005). A systematic review and meta-analysis of the relationship between chromosome 18q genotype, DCC status and colorectal cancer prognosis. *Eur J Cancer* 41(14):2060-2070. |  |

**Figure**

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**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):S3-43.1

**Reference**

1 Endoscopic Classification Review Group (2005). Update on the paris classification of superficial neoplastic lesions in the digestive tract. *Endoscopy* 37(6):570-578.

**Table**

**Table 1: Classification and grading for neuroendocrine neoplasms.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Terminology** | **Differentiation** | **Grade** | **Mitotic count**  **(mitoses/2 mm2)** | **Ki-67 index** |
| NET, grade 1 | Well differentiated | Low | <2 | <3% |
| NET, grade 2 | Intermediate | 2-20 | 3-20% |
| NET, grade 3 | High | >20 | >20% |
| NEC, small cell type | Poorly differentiated | High | >20 | >20% |
| NEC, large cell type | >20 | >20% |
| MiNEN | Well or poorly differentiated | Variable | Variable | Variable |

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**Reference**

4 Klimstra DS, Kloppel G, La Rosa S and Rindi G (2019). Classification of neuroendocrine neoplasms of the digestive system. In: *Digestive System Tumours. WHO Classification of Tumours, 5th Edition*, Lokuhetty D, White V, Watanabe R and Cree IA (eds), IARC Press, Lyon, France.