

Extent of invasion (Core)

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) and American Joint Committee on Cancer (AJCC) 8th editions^{1,2} 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 invasive neoplasia or intramucosal carcinoma) are acknowledged but, given the negligible metastatic potential of such neoplasms,³ these should be classified under the same category with high grade dysplasia/high grade non-invasive neoplasia.

pT1 indicates tumour extension beyond muscularis mucosae into submucosa, but without involvement of muscularis propria. Further consideration of pT1 colorectal carcinoma is provided in a separate local excision dataset.

pT2 indicates extension into muscularis propria but not beyond. In the low rectum, the internal sphincter represents a continuation of the muscularis propria and invasion of this also constitutes pT2. Note that skeletal muscle fibres can cross over from external to internal sphincter and invasion of skeletal muscles fibres of the internal sphincter is also classified as pT2. Such complexities of sphincter anatomy make accurate assessment of level of invasion in this region challenging.

pT3 indicates tumour spread beyond muscularis propria in continuity with the primary tumour and excluding tumour confined to the lumen of veins or lymphatic channels. Distinction from pT2 may be difficult if tumour extends to the outer edge of the muscularis propria. If no muscle separates tumour cells from mesenteric connective tissue, the tumour should be classified as pT3.⁴ Invasion beyond internal sphincter into the intrasphincteric plane, but not involving the external sphincter, is considered pT3.

pT4 encompasses either tumour infiltration of the peritoneal surface (pT4a) or tumour involvement of an adjacent organ (pT4b). Peritoneal involvement has been demonstrated by multivariate analysis to have a negative impact on prognosis.^{5,6} Although some small studies have suggested that peritoneal involvement was associated with worse outcome than invasion of adjacent organs, data from a large cohort of more than 100,000 colon cancer cases indicate that penetration of the visceral peritoneum carries a 10-20% better 5-year survival than locally invasive carcinomas for each pN category.⁷

Involvement of the peritoneal surface (pT4a) is defined as tumour breaching the serosa with tumour cells visible either on the peritoneal surface, free in the peritoneal cavity or separated from the peritoneal surface by inflammatory cells only.⁸ Should tumour pass close to the serosal surface and elicit a mesothelial reaction but no clear invasion, additional sections and/or multiple levels should be examined. If tumour does not demonstrate serosal involvement after additional evaluation, it should be categorised as pT3. Assessment of this scenario remains prone to interobserver variation.⁹ Several studies advocate the application of elastic stains to evaluate peritoneal elastic lamina invasion, as a staging or prognostic tool, but others have not found this useful.¹⁰⁻¹³ Cases with perforation through tumour should also be classified as pT4a, even in the absence of microscopic documentation of tumour cells on the peritoneal surface. This does not apply to colonic or rectal perforation distant from the tumour, for example secondary to distal obstruction.

Note pT4a implies peritoneal involvement through direct continuity with the primary tumour whereas peritoneal deposition of tumour discontinuous from the primary tumour is regarded as

distant metastatic disease (pM1c). It is also important to carefully distinguish involvement of a peritoneal surface from involvement of a non-peritonealised surgical resection margin, which is recorded separately. The first is a risk factor for intraperitoneal metastatic disease while the latter is a risk factor for local recurrence.

Tumour involvement of an adjacent organ (pT4b) may follow peritoneal invasion or represent direct extraperitoneal invasion, for example in low rectal tumours. Tumours adherent to other organs must be demonstrated microscopically to show invasion into the adjacent organ, rather than inflammatory adherence, to be classified as pT4b. Intramural (longitudinal) tumour extension into an adjacent part of the intestine does not influence pT classification, for example intramural extension of a caecal tumour into the terminal ileum or of a rectal tumour into the anal canal. Tumour involvement of greater omentum is considered pT4b if it follows transperitoneal invasion. Rarely, a transverse colonic tumour can invade greater omentum directly without breaching the serosa, meriting classification as pT3 rather than pT4b. For rectal tumours, invasion of skeletal muscle of the external sphincter and/or levator ani is classified as pT4b.

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 Jass JR, O'Brien MJ, Riddell RH and Snover DC (2007). Recommendations for the reporting of surgically resected specimens of colorectal carcinoma. *Hum Pathol* 38(4):537-545.
- 5 Puppa G, Maisonneuve P, Sonzogni A, Masullo M, Capelli P, Chilosi M, Menestrina F, Viale G and Pelosi G (2007). Pathological assessment of pericolonic tumor deposits in advanced colonic carcinoma: relevance to prognosis and tumor staging. *Mod Pathol* 20(8):843-855.
- 6 Shepherd NA, Baxter KJ and Love SB (1997). The prognostic importance of peritoneal involvement in colonic cancer: a prospective evaluation. *Gastroenterology* 112(4):1096-1102.
- 7 Gunderson LL, Jessup JM, Sargent DJ, Greene FL and Stewart AK (2010). Revised TN categorization for colon cancer based on national survival outcomes data. *J Clin Oncol* 28(2):264-271.
- 8 Petersen VC, Baxter KJ, Love SB and Shepherd NA (2002). Identification of objective pathological prognostic determinants and models of prognosis in Dukes' B colon cancer. *Gut* 51(1):65-69.
- 9 Kirsch R, Messenger DE, Shepherd NA, Dawson H and Driman DK (2018). Wide variability in assessment and reporting of colorectal cancer specimens among North American pathologists: results of a Canada-US Survey. *Can J of Pathol* 11(1):58-69.

- 10 Liang WY, Chang WC, Hsu CY, Arnason T, Berger D, Hawkins AT, Sylla P and Lauwers GY (2013). Retrospective evaluation of elastic stain in the assessment of serosal invasion of pT3N0 colorectal cancers. *Am J Surg Pathol* 37(10):1565-1570.
- 11 Kojima M, Nakajima K, Ishii G, Saito N and Ochiai A (2010). Peritoneal elastic laminal invasion of colorectal cancer: the diagnostic utility and clinicopathologic relationship. *Am J Surg Pathol* 34(9):1351-1360.
- 12 Grin A, Messenger DE, Cook M, O'Connor BI, Hafezi S, El-Zimaity H and Kirsch R (2013). Peritoneal elastic lamina invasion: limitations in its use as a prognostic marker in stage II colorectal cancer. *Hum Pathol* 44(12):2696-2705.
- 13 Puppa G, Shepherd NA, Sheahan K and Stewart CJR (2011). Peritoneal elastic lamina invasion in colorectal cancer: the answer to a controversial area of pathology? *Am J Surg Pathol* 35(3):465-468.