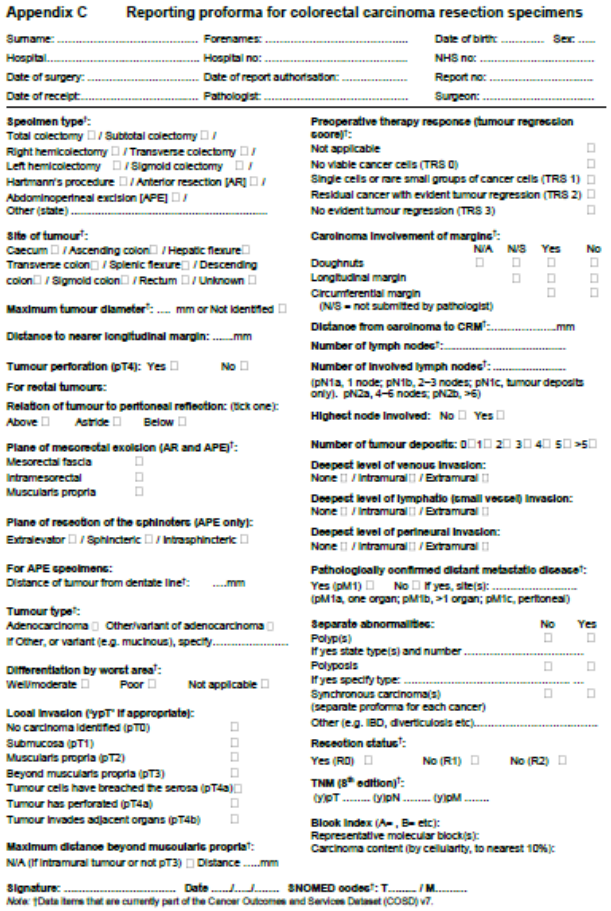
Updates in colonic cancer: surgical and pathological views

Dr. Mohammed Natiq

Usage of pathology report



Appendix C Reporting proforma for colorectal carcinoma resection specimens

Surname: ..... Forenames: ..... Date of birth: ..... Sex: .....
Hospital..... Hospital no: ..... NHS no: .....
Date of surgery: ..... Date of report authorisation: ..... Report no: .....
Date of receipt:..... Pathologist: ..... Surgeon: .....

Specimen type†:
Total colectomy ☐ / Subtotal colectomy ☐ /
Right hemicolectomy ☐ / Transverse colectomy ☐ /
Left hemicolectomy ☐ / Sigmoid colectomy ☐ /
Hartmann's procedure ☐ / Anterior resection [AR] ☐ /
Abdominoperineal excision [APE] ☐ /
Other (state) .....

Site of tumour†:
Caecum ☐ / Ascending colon☐ / Hepatic flexure☐
Transverse colon☐ / Splenic flexure☐ / Descending colon☐ / Sigmoid colon☐ / Rectum ☐ / Unknown ☐

Maximum tumour diameter†: .... mm or Not identified ☐

Distance to nearer longitudinal margin: .....mm

Tumour perforation (pT4): Yes ☐ No ☐

For rectal tumours:

Relation of tumour to peritoneal reflection: (tick one):
Above ☐ Astride ☐ Below ☐

Plane of mesorectal excision (AR and APE)†:
Mesorectal fascia ☐
Intramesorectal ☐
Muscularis propria ☐

Plane of resection of the sphincters (APE only):
Extralevator ☐ / Sphincteric ☐ / Intrasphincteric ☐

For APE specimens:
Distance of tumour from dentate line†: .....mm

Tumour type†:
Adenocarcinoma ☐ Other/variant of adenocarcinoma ☐
If Other, or variant (e.g. mucinous), specify.....

Differentiation by worst area†:
Well/moderate ☐ Poor ☐ Not applicable ☐

Local invasion ('ypT' if appropriate):
No carcinoma identified (pT0) ☐
Submucosa (pT1) ☐
Muscularis propria (pT2) ☐
Beyond muscularis propria (pT3) ☐
Tumour cells have breached the serosa (pT4a)☐
Tumour has perforated (pT4a) ☐
Tumour invades adjacent organs (pT4b) ☐

Maximum distance beyond muscularis propria†:
N/A (if intramural tumour or not pT3) ☐ Distance .....mm

Preoperative therapy response (tumour regression score)†:
Not applicable ☐
No viable cancer cells (TRS 0) ☐
Single cells or rare small groups of cancer cells (TRS 1) ☐
Residual cancer with evident tumour regression (TRS 2) ☐
No evident tumour regression (TRS 3) ☐

Carcinoma involvement of margins†:

	N/A	N/S	Yes	No
Doughnuts	☐	☐	☐	☐
Longitudinal margin		☐	☐	☐
Circumferential margin			☐	☐

(N/S = not submitted by pathologist)

Distance from carcinoma to CRM†:.....mm

Number of lymph nodes†:.....

Number of involved lymph nodes†: .....
(pN1a, 1 node; pN1b, 2–3 nodes; pN1c, tumour deposits only). pN2a, 4–6 nodes; pN2b, >6)

Highest node involved: No ☐ Yes ☐

Number of tumour deposits: 0☐1☐ 2☐ 3☐ 4☐ 5☐ >5☐

Deepest level of venous invasion:
None ☐ / Intramural☐ / Extramural ☐

Deepest level of lymphatic (small vessel) invasion:
None ☐ / Intramural☐ / Extramural ☐

Deepest level of perineural invasion:
None ☐ / Intramural☐ / Extramural ☐

Pathologically confirmed distant metastatic disease†:
Yes (pM1) ☐ No ☐ If yes, site(s): .....
(pM1a, one organ; pM1b, >1 organ; pM1c, peritoneal)

Separate abnormalities:	No	Yes
Polyp(s)	☐	☐
If yes state type(s) and number		
Polyposis	☐	☐
If yes specify type:		
Synchronous carcinoma(s) (separate proforma for each cancer)	☐	☐

Other (e.g. IBD, diverticulosis etc).....

Resection status†:
Yes (R0) ☐ No (R1) ☐ No (R2) ☐

TNM (8th edition)†:
(y)pT ..... (y)pN ..... (y)pM .....

Block index (A=, B= etc):
Representative molecular block(s):
Carcinoma content (by cellularity, to nearest 10%):

Signature: ..... **Date** ...../...../..... **SNOMED codes†: T**..... **/ M**.....

Note: †Data items that are currently part of the Cancer Outcomes and Services Dataset (COSD) v7.

- All reporting pathologists should provide pathology reports that are accurate, complete, understandable and timely. The use of proformas has been demonstrated to facilitate these requirements and their use is strongly recommended

Usage of pathology report

- confirm the diagnosis
- inform the prognosis
- plan the treatment of individual patients
- audit pathology services
- evaluate the quality of other clinical services, notably radiology, surgery, oncology and screening programs
- collect accurate data for cancer registration and epidemiology
- facilitate high-quality research
- provide education
- plan service delivery

Diagnosis

The WHO classification 5th edition (2019), is recommended. Virtually all colorectal cancers are adenocarcinomas, mostly of no specific subtype, but some subtypes of adenocarcinoma are recognized:

- mucinous carcinoma (variant of adenocarcinoma with >50% composed of extracellular mucin)
- signet ring cell carcinoma (variant of adenocarcinoma with >50% signet ring cells)
- medullary carcinoma
- serrated adenocarcinoma
- micropapillary adenocarcinoma
- adenoma-like adenocarcinoma.

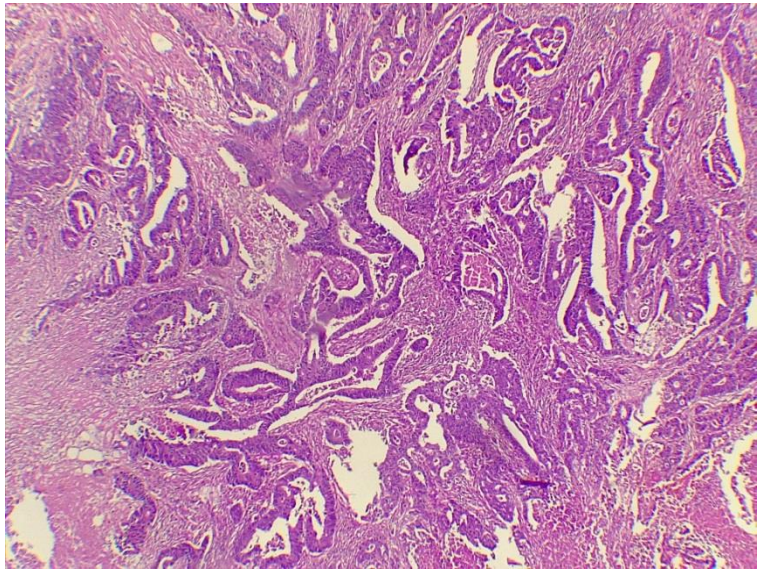
Tumour type†:

Adenocarcinoma ☐ Other/variant of adenocarcinoma ☐

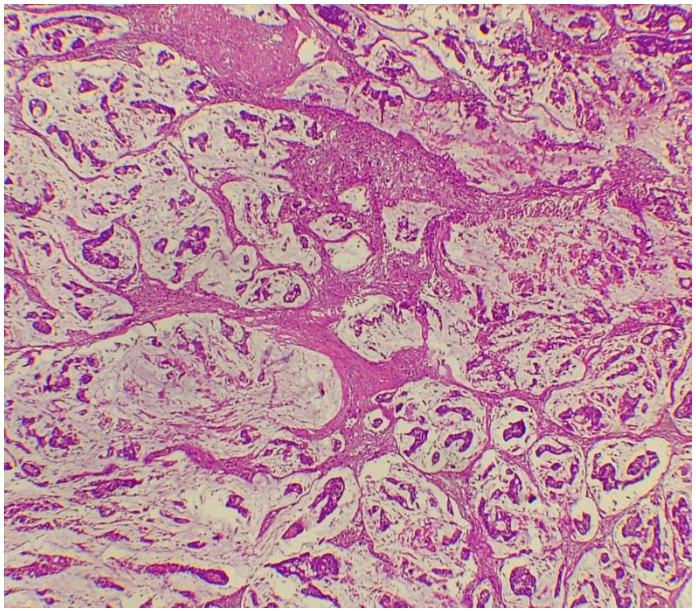
If Other, or variant (e.g. mucinous), specify……

Differentiation by worst area†:

Well/moderate ☐ Poor ☐ Not applicable ☐



Moderately diff. adenocarcinoma



Mucinouc adenocarcinoma

Union for International Cancer Control
TNM 8 classification of colorectal tumors

pT	**Primary tumour**
pTX	Primary tumour cannot be assessed
pT0	No evidence of primary tumour
pT1	Tumour invades submucosa
pT2	Tumour invades muscularis propria
pT3	Tumour invades into subserosa or into non-peritonealised pericolic or perirectal tissues
pT4	Tumour perforates visceral peritoneum (4a) and/or directly invades other organs or structures (4b)
pN	**Regional lymph nodes**
pNX	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastatic disease
pN1	Metastatic disease in 1–3 regional lymph nodes
pN1a	Metastasis in 1 regional lymph node
pN1b	Metastases in 2–3 regional lymph nodes
pN1c	Tumour deposit(s), i.e. satellites,* in the subserosa, or in non-peritonealised pericolic or perirectal soft tissue without regional lymph node metastatic disease (tumour deposits are ignored if there is nodal metastatic disease)
pN2	Metastatic disease in 4 or more regional lymph nodes
pN2a	Metastases in 4–6 regional lymph nodes
pN2b	Metastases in 7 or more regional lymph nodes
pM	**Distant metastatic disease**
pM1	Distant metastatic disease
pM1a	Metastasis confined to 1 organ without peritoneal metastases
pM1b	Metastases in more than 1 organ
pM1c	Metastases to the peritoneum with or without other organ involvement

Prognosis

- *Depth of local invasion predicts recurrence and prognosis*

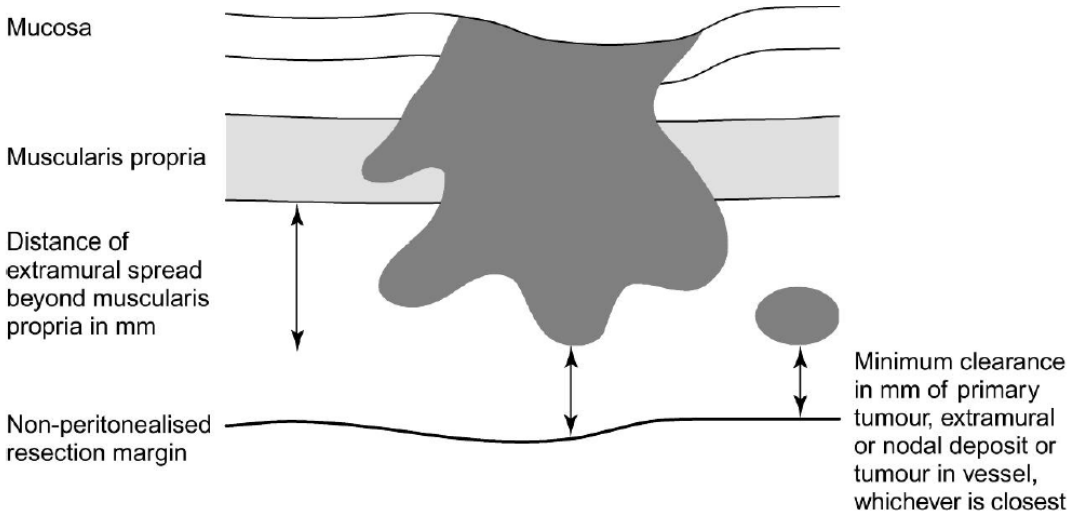


Figure 6. Measuring extramural spread and clearance of tumour from the circumferential margin.

Prognosis

- Perforation through the tumor into the peritoneal cavity is a well-established adverse prognostic factor in colonic and rectal cancer and should be recorded (pT4a)

Local invasion ('ypT' if appropriate):

No carcinoma identified (pT0) ☐

Submucosa (pT1) ☐

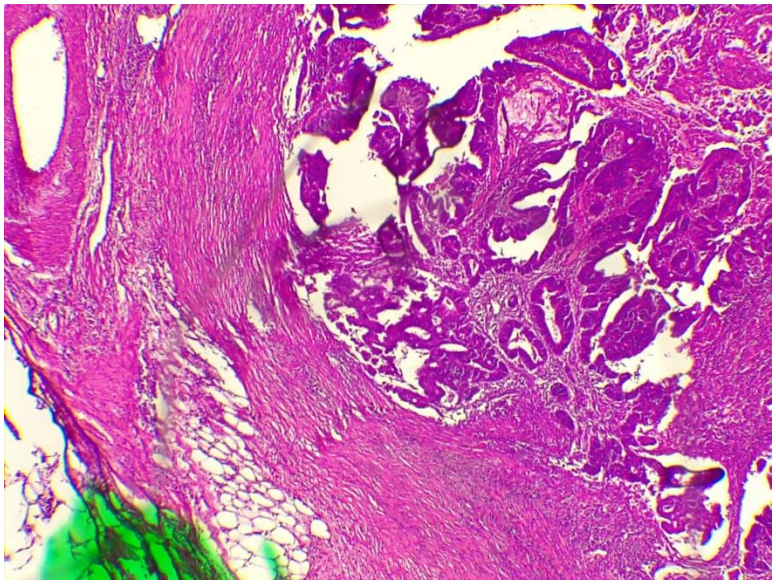
Muscularis propria (pT2) ☐

Beyond muscularis propria (pT3) ☐

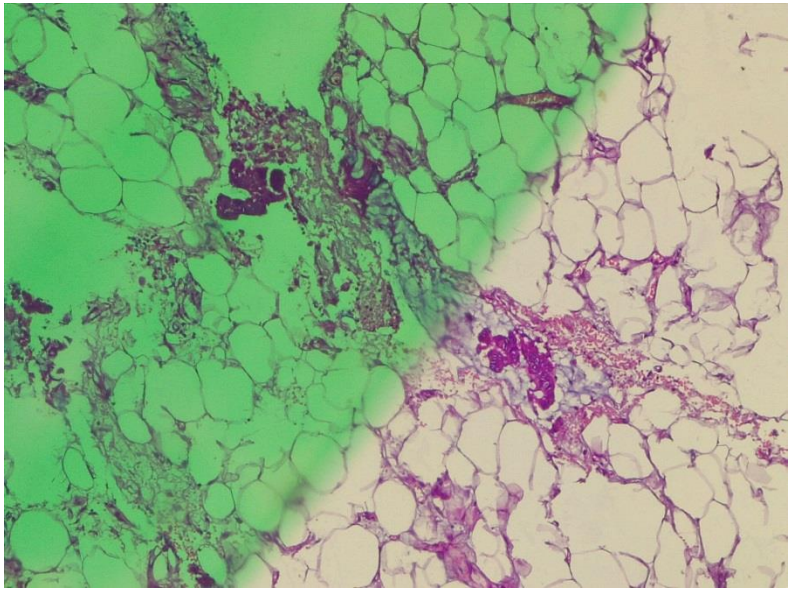
Tumour cells have breached the serosa (pT4a) ☐

Tumour has perforated (pT4a) ☐

Tumour invades adjacent organs (pT4b) ☐



T2



T3

Prognosis

- histological grade has been shown in numerous studies to be an independent prognostic factor for colorectal carcinoma
- grading should be based on the least differentiated tumor component
- differentiation of colorectal tumors applies only to ‘adenocarcinoma, NOS’ and mucinous carcinoma

Prognosis

- *Grade of regression in rectal cancer after preoperative therapy is important for prognosis*

Table 1. Four-tier system for evaluating tumour regression.

Evaluation (of primary tumour site)	**Tumour regression score**
No viable cancer cells (complete response)	0
Single cells or rare small groups of cancer cells (near-complete response)	1
Residual cancer with evident tumour regression, but more than single cells or rare small groups of cancer cells (partial response)	2
Extensive residual cancer with no evident tumour regression (poor or no response)	3

Prognosis

Nodal status predict prognosis

TNM 8 has further sub classified pN1/2 stage as follows:

- N1: Metastatic disease in 1–3 regional lymph nodes
  - N1a: Metastasis in 1 regional lymph node
  - N1b: Metastases in 2–3 regional lymph nodes
- N2: Metastatic disease in 4 or more regional lymph nodes
  - N2a: Metastases in 4–6 regional lymph nodes
  - N2b: Metastases in 7 or more regional lymph nodes.

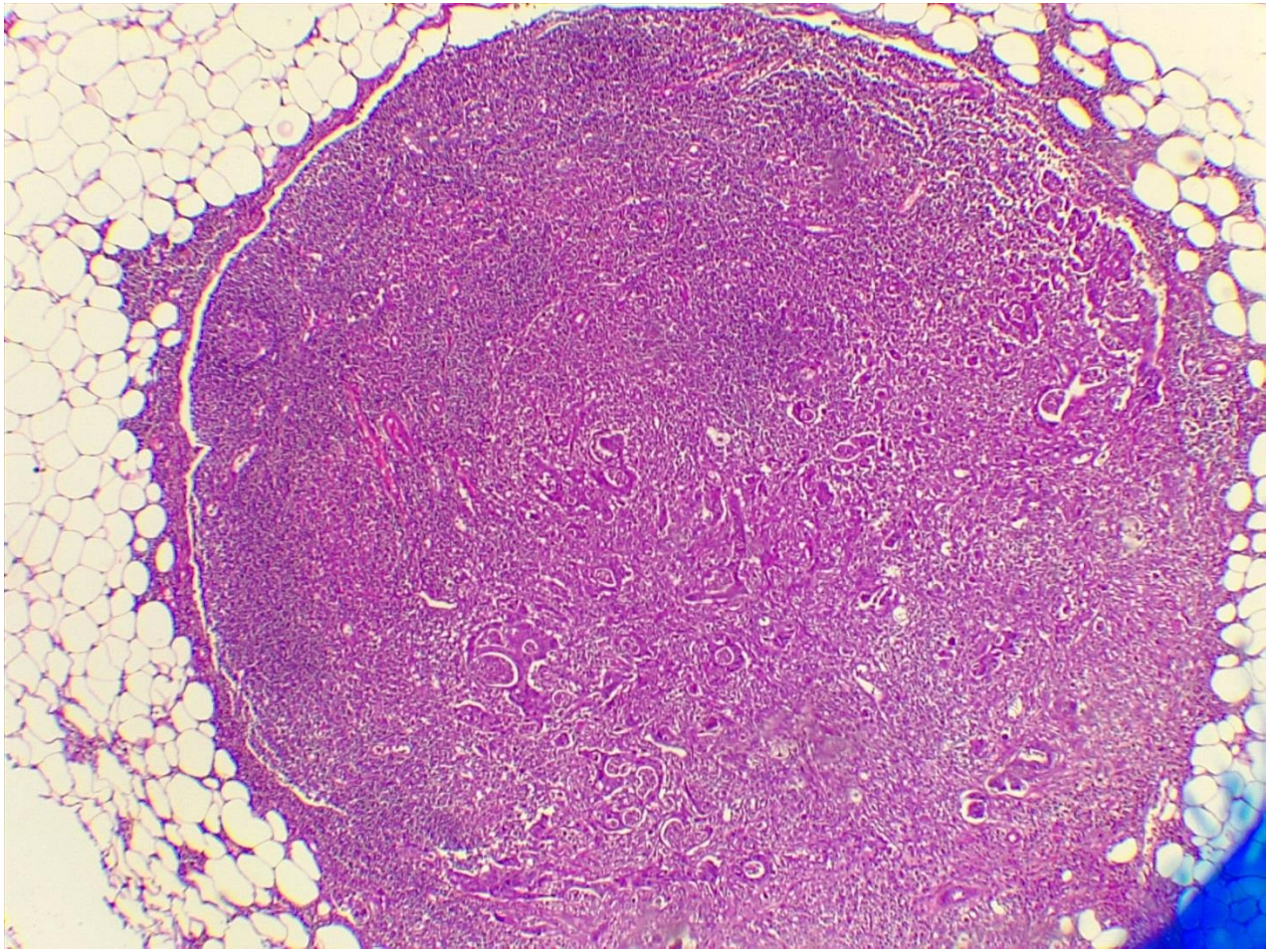
Prognosis

Number of lymph nodes†:.....

Number of involved lymph nodes†: .....

(pN1a, 1 node; pN1b, 2–3 nodes; pN1c, tumour deposits only). pN2a, 4–6 nodes; pN2b, >6)

Highest node involved: No ☐ Yes ☐



Prognosis

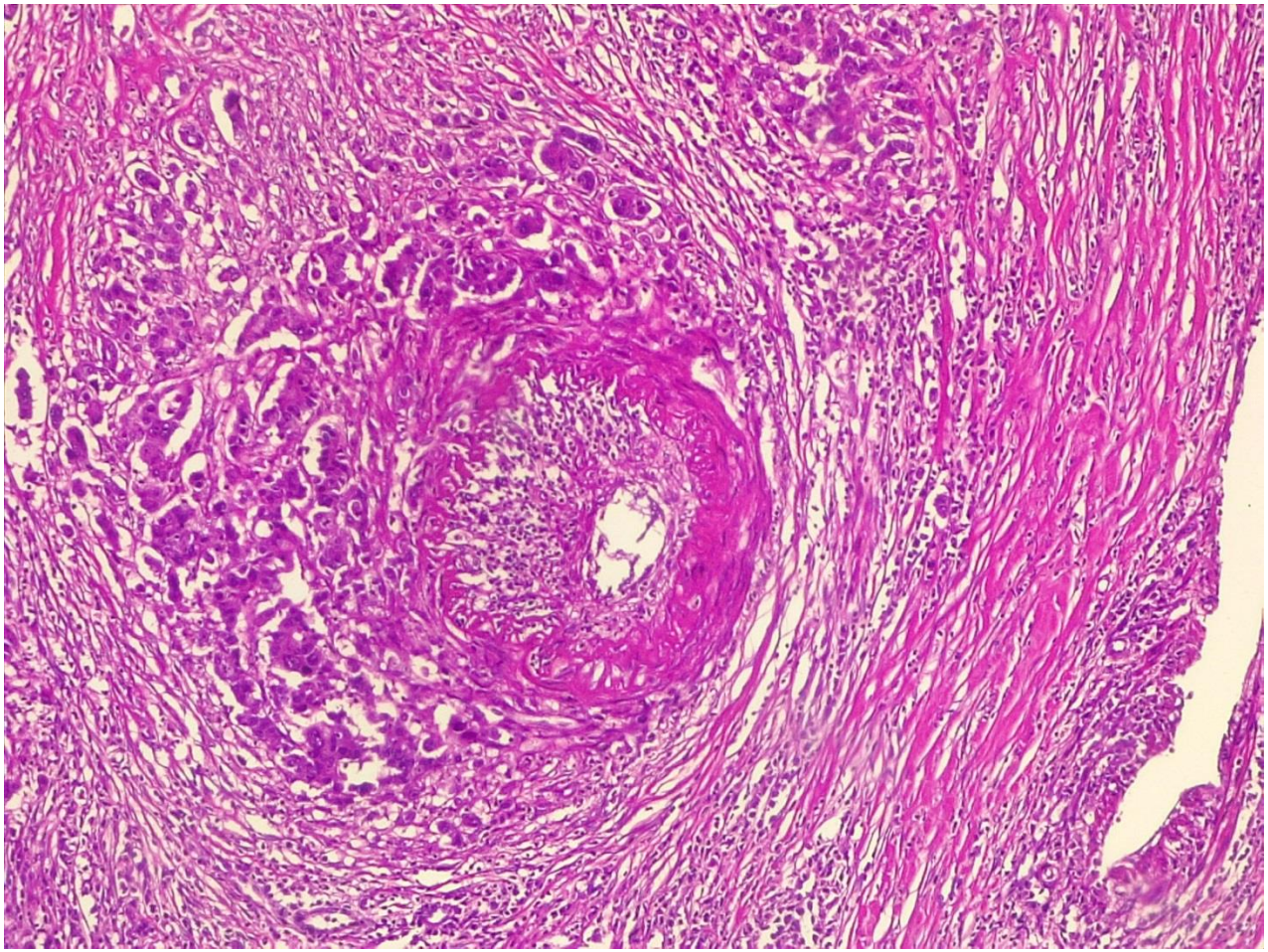
Venous, lymphatic and perineural invasion predict prognosis

Deepest level of venous invasion:
None □ / Intramural□ / Extramural □

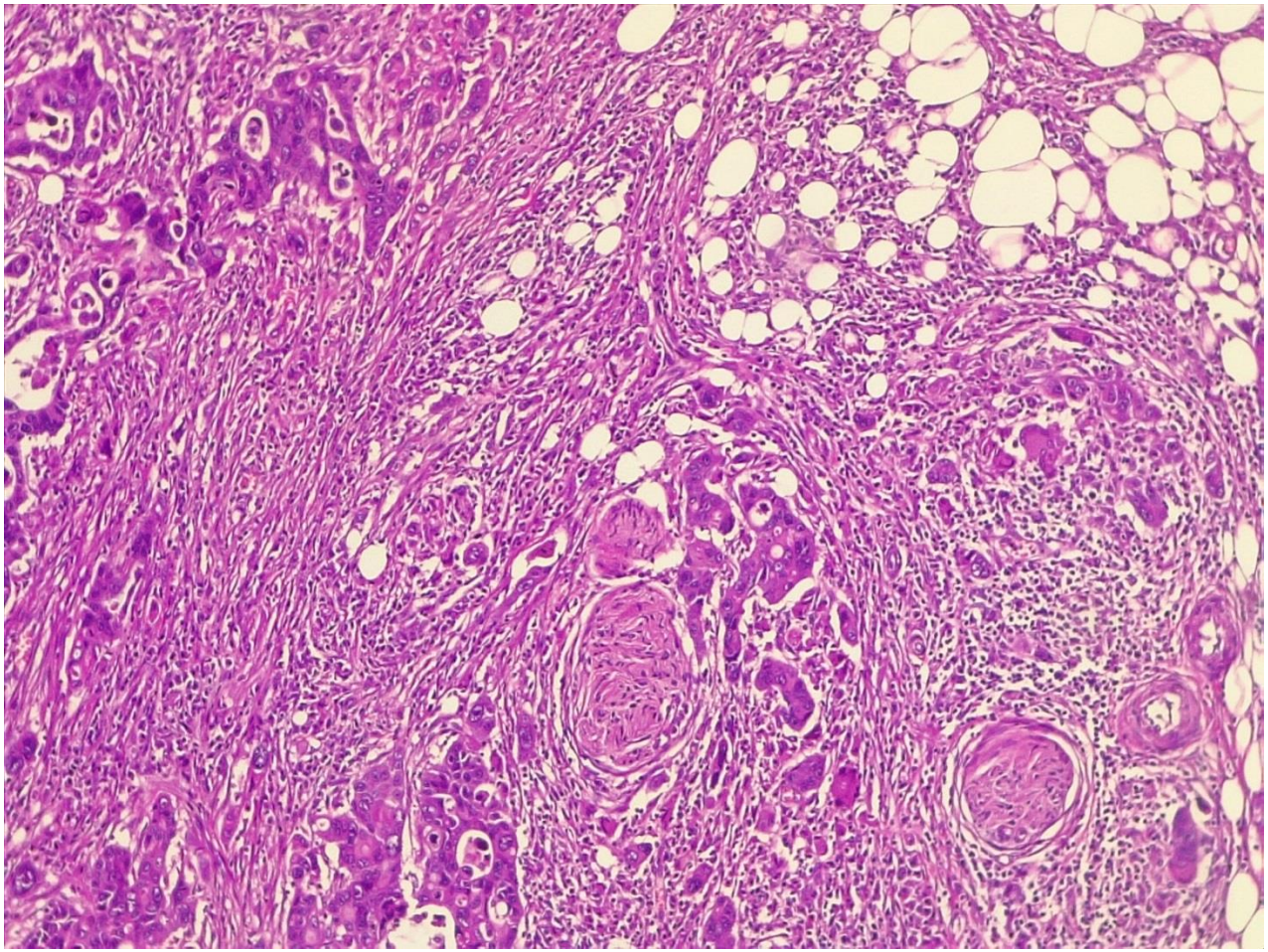
Deepest level of lymphatic (small vessel) invasion:
None □ / Intramural□ / Extramural □

Deepest level of perineural invasion:
None □ / Intramural□ / Extramural □

LV invasion



Perineural invasion



Treatment

- Those without lymph node metastatic disease but with adverse pathological features (venous invasion, perforation, peritoneal involvement, margin involvement or extensive local spread) may also be offered adjuvant therapy for small but probable benefit

Treatment

- Lynch syndrome accounts for approximately 2–3% of all colorectal cancers.
- Some studies have predicted a lack of response to 5-fluorouracil-based chemotherapy with possible abrogation by the addition of oxaliplatin to the chemotherapy regime (such as in FOLFOX), but other studies have not demonstrated this. MMR deficiency predicts response to immune checkpoint blockade therapy

Treatment

- mutations in *KRAS and NRAS* predict lack of response to anti-epidermal growth factor receptor (EGFR) targeted therapy.
- The TRK inhibitors larotrectinib and entrectinib are now approved by NICE for the treatment of solid tumors, including colorectal cancer, which harbor NTRK fusions, where there are no other satisfactory systemic treatment options

Treatment

Appendix E **Reporting proforma for further investigations for colorectal carcinoma**

Surname: ..... Forenames: ..... Date of birth: ..... Sex: ....
Hospital..... Hospital no: ..... NHS no: .....
Date of surgery: ..... Date of report authorisation: ..... Report no: .....
Date of receipt:..... Pathologist: ..... Surgeon: .....

Mismatch repair (MMR) protein immunohistochemistry

	Yes	No	Equivocal	Test failed	Not performed
MLH1 nuclear expression intact	☐	☐	☐	☐	☐
PMS2 nuclear expression intact	☐	☐	☐	☐	☐
MSH2 nuclear expression intact	☐	☐	☐	☐	☐
MSH6 nuclear expression intact	☐	☐	☐	☐	☐

Microsatellite instability (MSI) testing
MSI-high ☐ MSI-low ☐ MS-stable ☐ Test failed ☐ Not performed ☐

MLH1 promoter hypermethylation testing
Present ☐ Absent ☐ Test failed ☐ Not performed ☐

BRAF V600E mutation testing
Present ☐ Absent ☐ Test failed ☐ Not performed ☐

KRAS mutation testing
Present ☐ Absent ☐ Test failed ☐ Not performed ☐
Specify mutation.....

NRAS mutation testing
Present ☐ Absent ☐ Test failed ☐ Not performed ☐
Specify mutation.....

NTRK fusion immunohistochemistry screening
Present ☐ Absent ☐ Test failed ☐ Not performed ☐

NTRK fusion NGS testing
Present ☐ Absent ☐ Test failed ☐ Not performed ☐
Specify fusion.....

Multi-gene panel testing

Performed: Yes ☐ No ☐

Method used .....

Actionable molecular aberrations detected not listed above .....

Exome sequencing

Performed: Yes ☐ No ☐

Method used .....

Actionable molecular aberrations detected not listed above .....

Whole genome sequencing

Performed: Yes ☐ No ☐

Method used .....

Actionable molecular aberrations detected not listed above .....

Signature: ..... Date ...../...../..... SNOMED codes: T..... / M.....

Mismatch repair (MMR) protein immunohistochemistry

	Yes	No	Equivocal	Test failed	Not performed
MLH1 nuclear expression intact	☐	☐	☐	☐	☐
PMS2 nuclear expression intact	☐	☐	☐	☐	☐
MSH2 nuclear expression intact	☐	☐	☐	☐	☐
MSH6 nuclear expression intact	☐	☐	☐	☐	☐

Microsatellite instability (MSI) testing
MSI-high ☐ MSI-low ☐ MS-stable ☐ Test failed ☐ Not performed ☐

MLH1 promoter hypermethylation testing
Present ☐ Absent ☐ Test failed ☐ Not performed ☐

BRAF V600E mutation testing
Present ☐ Absent ☐ Test failed ☐ Not performed ☐

KRAS mutation testing
Present ☐ Absent ☐ Test failed ☐ Not performed ☐
Specify mutation.....

NRAS mutation testing
Present ☐ Absent ☐ Test failed ☐ Not performed ☐
Specify mutation.....

NTRK fusion immunohistochemistry screening
Present ☐ Absent ☐ Test failed ☐ Not performed ☐

NTRK fusion NGS testing
Present ☐ Absent ☐ Test failed ☐ Not performed ☐
Specify fusion.....

Audit

- It is therefore recommended that MDTs and pathology departments audit their reports at regular intervals to ensure that their overall results are not significantly different from what might be expected. The following three standards are recommended:

Audit

- the median number of lymph nodes examined should be at least 15.

‘’ the prognosis of stage II colorectal cancer is directly related to the number of lymph nodes examined pathologically, with the implication that some of these patients are ‘understaged’ and that, if more lymph nodes had been examined, metastatic disease would have been found’’

- the frequency of peritoneal involvement should be at least 20% for colonic cancers.
- the frequency of venous invasion should be at least 30%.

Audit

These parameters should be evaluated on a series of at least 50 resection specimens from symptomatic (i.e. non-screening) patients, who have not undergone preoperative therapy.

Audit

- Turnaround time of pathology reports should also be audited. The recommended minimum standard for endoscopic cases is 90% authorized within five working days from the date of specimen receipt in the histopathology laboratory.
- The recommended minimum standard for surgical resection cases is 90% authorized within ten working days from the date of specimen receipt in the histopathology laboratory.

Clinical services

- Patients with rectal adenocarcinoma and involvement of the circumferential resection margin (CRM) are at high risk of local recurrence, and may receive preoperative or postoperative radiotherapy or chemotherapy, which are toxic but decrease the likelihood of this unpleasant and nearly uniformly fatal complication.The frequency of CRM involvement found may indicate the quality of rectal cancer surgery being performed.

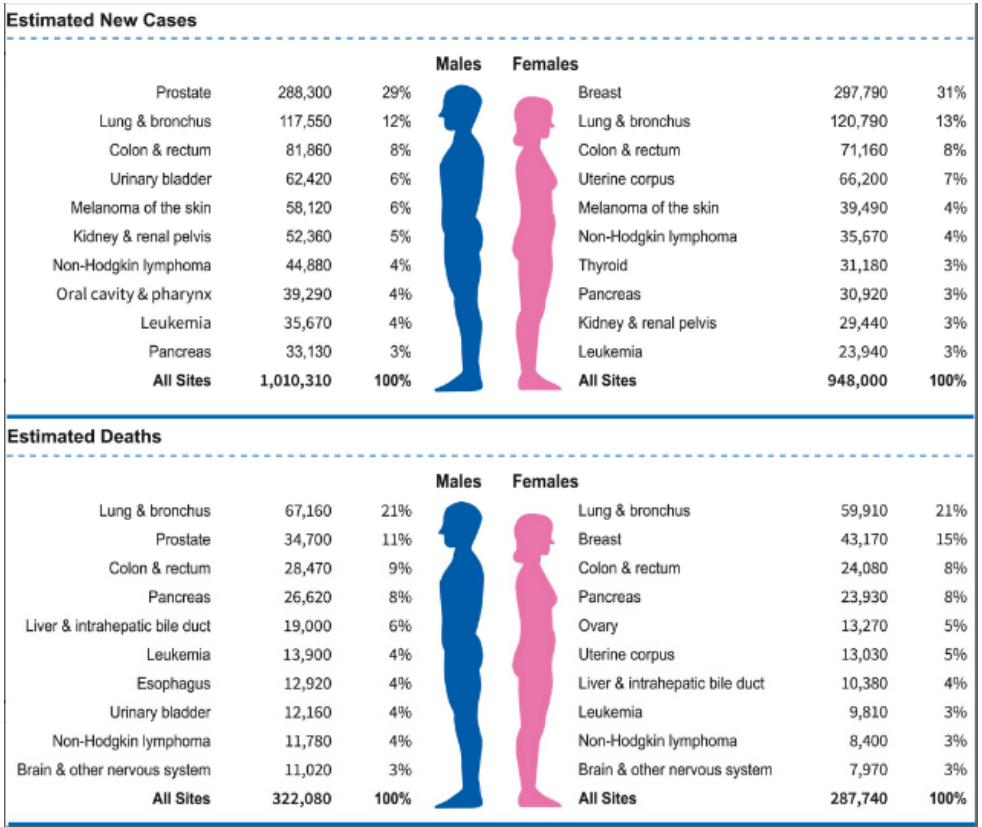
Clinical services

- Tumor size is not considered of prognostic relevance for colorectal cancer and does not influence staging. However, size allows correlation with pre-operative imaging, endoscopic and surgical assessments, and evidence of response to preoperative therapy if smaller than the initial MRI/CT estimate.

cancer registration

- For statistics
- For screening programs

Siegel, R. L., Miller, K. D., Wagle, N. S., & Jemal, A. (2022). Cancer statistics, 2023. CA: A Cancer Journal for Clinicians, 73(1), 17-48. https://doi.org/10.3322/caac.21763



Estimated New Cases

	Males			Females	
Prostate	288,300	29%		Breast	297,790	31%
Lung & bronchus	117,550	12%		Lung & bronchus	120,790	13%
Colon & rectum	81,860	8%		Colon & rectum	71,160	8%
Urinary bladder	62,420	6%		Uterine corpus	66,200	7%
Melanoma of the skin	58,120	6%		Melanoma of the skin	39,490	4%
Kidney & renal pelvis	52,360	5%		Non-Hodgkin lymphoma	35,670	4%
Non-Hodgkin lymphoma	44,880	4%		Thyroid	31,180	3%
Oral cavity & pharynx	39,290	4%		Pancreas	30,920	3%
Leukemia	35,670	4%		Kidney & renal pelvis	29,440	3%
Pancreas	33,130	3%		Leukemia	23,940	3%
All Sites	**1,010,310**	**100%**		**All Sites**	**948,000**	**100%**

Estimated Deaths

	Males			Females	
Lung & bronchus	67,160	21%		Lung & bronchus	59,910	21%
Prostate	34,700	11%		Breast	43,170	15%
Colon & rectum	28,470	9%		Colon & rectum	24,080	8%
Pancreas	26,620	8%		Pancreas	23,930	8%
Liver & intrahepatic bile duct	19,000	6%		Ovary	13,270	5%
Leukemia	13,900	4%		Uterine corpus	13,030	5%
Esophagus	12,920	4%		Liver & intrahepatic bile duct	10,380	4%
Urinary bladder	12,160	4%		Leukemia	9,810	3%
Non-Hodgkin lymphoma	11,780	4%		Non-Hodgkin lymphoma	8,400	3%
Brain & other nervous system	11,020	3%		Brain & other nervous system	7,970	3%
All Sites	**322,080**	**100%**		**All Sites**	**287,740**	**100%**

Research

- To identify new molecular targets for novel therapies

Education

Service delivery

- Given expanding molecular testing requirements, greater engagement of cellular pathology services with both molecular pathology and clinical laboratory genetics services is advised, to optimize local arrangements for testing pathways. Although most bowel cancer somatic tumor testing is currently performed using assays directed at specific genes, this is likely to migrate in coming years to a NGS panel-based approach to testing, covering a wider range of cancer-related genes of interest.

- **ACKNOWLEDGMENT**
- The presenter wishes to thank Dr. *Azza N. Al-jaleeli* for providing the photos of her work at Gastroenterology and hepatology diseases teaching hospital.

References

- Standards and datasets for reporting cancers
- Dataset for histopathological reporting of colorectal cancer
- April 2023
- Authors: Professor Maurice B Loughrey, Belfast Health and Social Care Trust and Queen's University Belfast
- Professor Philip Quirke, Leeds Teaching Hospitals NHS Trust and Leeds University
- Professor Neil A Shepherd, Gloucestershire Hospitals NHS Foundation Trust and University of Exeter