



# Minimum Dataset for Colorectal Cancer

1st Edition, August 2007

This document should be read in conjunction with the minimum dataset proforma for colorectal cancer resection developed by the NSW Oncology Group for Colorectal Cancer. It is based on information contained within multiple international publications and datasets and has been developed in consultation with local practicing pathologists, oncologists, surgeons, radiologists and interested national bodies.





## TABLE OF CONTENTS

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SCOPE OF DOCUMENT .....	5
How to use this document .....	5
INTRODUCTION .....	6
Authors .....	6
MACROSCOPIC DESCRIPTION .....	7
Site of tumour.....	7
Definition of the rectum.....	7
Maximum tumour diameter.....	8
Distance of tumour to nearer cut end.....	8
Presence of tumour perforation .....	8
Relationship of rectal tumours to the anterior peritoneal reflection .....	9
MICROSCOPIC DESCRIPTION .....	11
Tumour type .....	11
Differentiation by predominant area .....	12
Local invasion .....	13
Non-peritonealised circumferential margin in rectal tumours .....	14
The non-peritonealised margin in the colon.....	15
Lymphocytic infiltration.....	15
Lymph nodes .....	16
Guidelines for small tumour deposits in lymph nodes.....	16
A note on TNM 5 <sup>th</sup> edition versus TNM 6 <sup>th</sup> edition .....	17
Lymphovascular invasion .....	18
Perineural invasion .....	18
Histologically confirmed distant metastases.....	19
Background abnormalities.....	19
Residual tumour status .....	20
Summary – TNM staging .....	20
Mismatch repair deficiency status .....	21
Appendix A – Minimum dataset proforma for colorectal cancer resections.....	22
Appendix B – Colorectal cancer surgical request .....	24
Useful Website .....	26
REFERENCES .....	26



## SCOPE OF DOCUMENT

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This document should be read in conjunction with the minimum dataset proforma for colorectal cancer resections, which was developed by the NSW Oncology Group for Colorectal Cancer. It is based on information contained within multiple international publications and datasets and has been developed in consultation with local practising pathologists, oncologists, surgeons, radiologists and interested national bodies.

## HOW TO USE THIS DOCUMENT

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To facilitate accurate and complete reporting of colorectal carcinomas, a proforma for the reporting of colorectal cancer resection specimens has been created from a set of minimum data items (Appendix A). To aid in the collection of all essential data items, a colorectal cancer surgical request form has also been prepared (Appendix B). This document is a working guide to help in the accurate reporting of the dataset items contained in the proforma. The data items are listed in the way that they would usually be reported in current laboratory practice. These guidelines reference relevant literature for each data item, including their prognostic significance or relevance to case management.

It is important to highlight that the data items presented here form a “minimum” dataset. The report is formatted with tick boxes for ease of presentation. Individual departments can alter the format to suit their working practices, add areas of free text, or incorporate the items into a free text document with the minimum dataset serving as their template.

This minimum dataset for colorectal cancer was developed after lengthy consultation with interested parties and it is hoped that all those good ideas and comments have been taken on board. It may not please everyone and is a work in progress, but it is an important first step towards the objective of improving the way we report colorectal cancer.

## INTRODUCTION

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Colorectal cancer is currently the most common cancer diagnosed in Australia and has the second highest incidence of cancer related deaths [1]. Recent advances have been made with regard to the biological understanding of this disease and its treatment, with new surgical, chemotherapeutic and radiotherapeutic strategies now available.

Histopathological reporting of resection specimens for colorectal cancer provides important information both for the clinical management of the affected patient and for the evaluation of health care as a whole. For the patient it confirms the diagnosis and describes the variables that will affect prognosis, all of which will inform future clinical management. For health care evaluation, pathology reports provide information for cancer registration and clinical audit for ensuring comparability of patient groups in clinical trials, and for assessing the accuracy of new diagnostic tests and preoperative staging techniques. In order to fulfil all of these functions, the information contained within the pathology report must be accurate and complete.

Guidelines, datasets and various documents on best practice in pathology are nothing new. There are large differences however, between available versions. Within existing datasets there is variability in the amount of information required, ranging from those that encompass vast lists of every possible data item, many without proven relevance, to the more focussed and pragmatic evidence-based minimum datasets.

Several studies have highlighted deficiencies in the content of colorectal cancer resection reports, including elements that are considered crucial for patient management [2]. Many studies have shown that adherence to a minimum dataset proforma for colorectal cancer reporting significantly improves the rate of inclusion of these crucial features [3].

## AUTHORS

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This document was written by Dr Jill Farmer, Dr Sian Munro and Associate Professor Nicholas Hawkins from the Colorectal Cancer Research Consortium. The document should be read in conjunction with the minimum dataset proforma for colorectal cancer resections, which was developed in collaboration with Dr Andrew Kneebone, the NSW Oncology Group for Colorectal Cancer and local pathologists. The Colorectal Cancer Research Consortium is supported by a Strategic Research Partnership Grant from the Cancer Council NSW.

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## MACROSCOPIC DESCRIPTION

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**All measurements should be made in millimetres**

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### SITE OF TUMOUR

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**The site of the tumour should be recorded.**

It is important to record the correct anatomical site of a tumour for the following reasons:

- It determines the appropriate staging system.
- It indicates whether a non-peritonealised (circumferential) margin is present.
- It defines the presence of regional lymph nodes versus non-regional lymph nodes.

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### DEFINITION OF THE RECTUM

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In 1999 representatives of the American Society of Colon and Rectal Surgeons and the Association of Coloproctology of Great Britain and Ireland met with their Australian counterparts to define the rectum and the procedures to treat cancer of the rectum [4].

The treatment of rectal cancer differs from the treatment of colonic cancer in some important respects, particularly in the areas of surgery and radiotherapy. It is thus essential to have a clear anatomical definition of the rectum.

Strictly the rectum is that part of the large bowel distal to the sigmoid colon and its upper limit is indicated by the end of the sigmoid mesocolon. Standard anatomical texts put this at the level of the 3<sup>rd</sup> sacral vertebra [5], but it is generally agreed by surgeons that the rectum starts at the sacral promontory [6]. It was agreed by the Expert Advisory Committee that any tumour whose distal margin is seen at 15cm or less from the anal verge using a rigid sigmoidoscope should be classified as rectal. Clearly, in the excised specimen these anatomical landmarks are not available for the pathologist, hence the importance of the site of the tumour being stated by the surgeon on the clinical request form.

## MAXIMUM TUMOUR DIAMETER

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**The maximum tumour diameter should be recorded. The diameter is measured from the luminal aspect of the bowel. The thickness of the tumour is ignored for this measurement.**

The definitive determination of tumour size is made on gross pathological examination.

Several studies have shown that tumour size is of no prognostic significance in colorectal cancer [7,8]. However, it is recorded for purposes of documentation and for correlation with measurements made by various imaging modalities.

## DISTANCE OF TUMOUR TO NEARER CUT END

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**This is the measurement from the nearer cut end of the specimen and not the non-peritonealised (circumferential, radial) margin.**

Tumour at a longitudinal margin has always been considered a poor prognostic feature but it occurs very rarely [9,10]. The necessity of sampling this margin has therefore been questioned [11-13]. It may be prudent to sample this margin if the tumour is close to the margin, or if the tumour is found by histology to have an exceptionally infiltrative growth pattern, to show extensive vascular invasion or lymphatic permeation or to be a pure signet ring, small cell or undifferentiated carcinoma [11].

NB. It is useful to have normal tissue for control purposes and uninvolved margins can provide this.

## PRESENCE OF TUMOUR PERFORATION

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**The presence or absence of tumour perforation should be recorded.**

Tumour perforation is defined as a macroscopically visible defect through the tumour, such that the bowel lumen is in communication with the external surface of the intact resection specimen. Perforation through the tumour into the peritoneal cavity is a well established adverse prognostic factor in colonic [14] and rectal cancer [15]. It is suggested that a block be taken from the area of perforation for histological confirmation. If perforation is present then this is regarded as pT4 in the TNM staging system, regardless of other factors [16].

Perforation of the proximal bowel as a result of a distal obstructing tumour should not be recorded as tumour perforation.

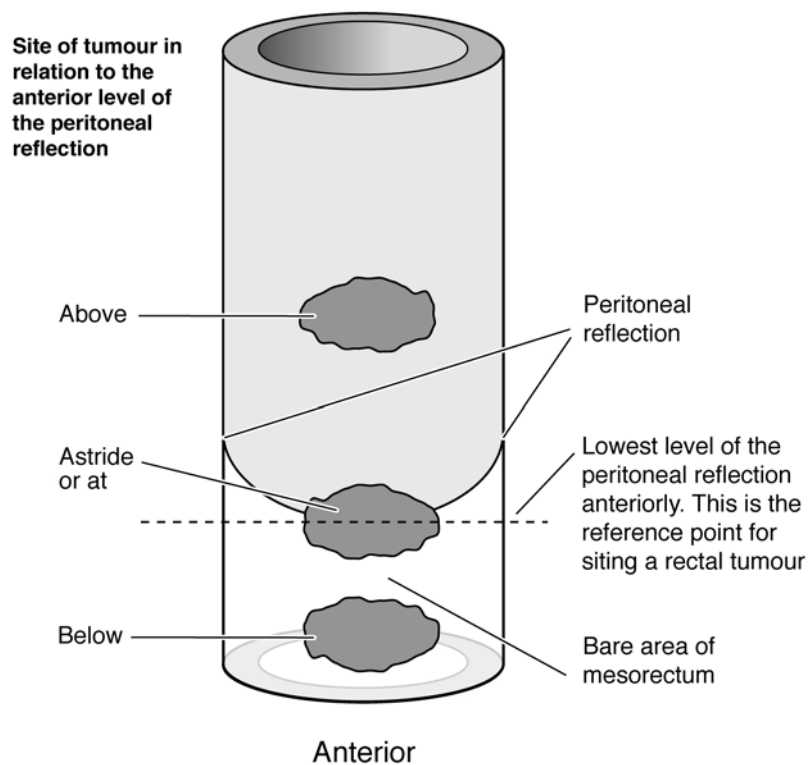
## RELATIONSHIP OF RECTAL TUMOURS TO THE ANTERIOR PERITONEAL REFLECTION

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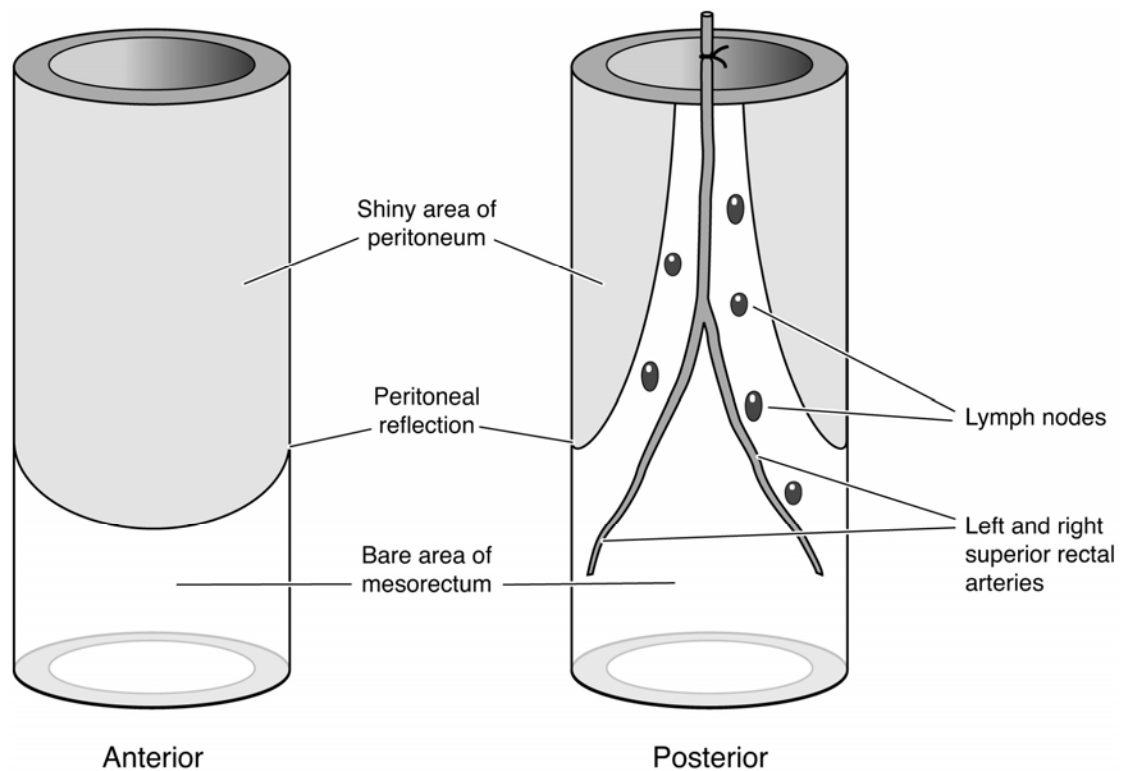
The relationship of rectal tumours to the anterior peritoneal reflection should be recorded.

Rectal tumours are classified according to whether they are

- a. Entirely above the level of the peritoneal reflection anteriorly.
- b. Astride (or at) the level of the peritoneal reflection anteriorly.
- c. Entirely below the level of the peritoneal reflection anteriorly.



The non-peritonealised margin is also known as the radial or circumferential resection margin. It represents the “bare” area in the connective tissue at the surgical plane of excision that is not covered by a serosal surface. Low rectal tumours will be completely surrounded by a non-peritonealised margin (the circumferential margin), while upper rectal tumours have a non-peritonealised margin posterolaterally and a peritonealised (serosal) surface anteriorly. Tumours below the peritoneal reflection have the highest rates of local recurrence [15,17-19].



**Anteriorly the rectum is covered by peritoneum down to the peritoneal reflection. Posteriorly the non-peritonealised margin extends upwards as a triangular shaped bare area containing the rectal arteries, which then continues up to the start of the sigmoid mesocolon.**

## MICROSCOPIC DESCRIPTION

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### TUMOUR TYPE

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**The tumour type should be described according to WHO International Histological Classification of Tumours ICD-10 (the “Blue Book”) [20].**

Virtually all colorectal cancers are adenocarcinomas. The term “Adenocarcinoma NOS” on the proforma is used in this instance to indicate conventional adenocarcinoma without any of the special features of the tumour types listed below it.

For convenience the tumour types are summarised:

- Adenocarcinoma
- Mucinous adenocarcinoma
- Signet-ring carcinoma
- Small cell carcinoma
- Squamous cell carcinoma
- Adenosquamous carcinoma
- Medullary carcinoma
- Undifferentiated carcinoma

For most tumours, histologic type is not prognostically significant. Exceptions include tumour types that are, by definition, high grade e.g. small cell carcinoma; and the medullary subtype, which is invariably associated with high microsatellite instability (MSI-H) and has a favourable prognosis when compared to other poorly differentiated and undifferentiated colorectal carcinomas [20].

## DIFFERENTIATION BY PREDOMINANT AREA

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**The assessment of differentiation should be based on the predominant degree of differentiation present in the primary tumour [21].**

Assessment of differentiation should be based on the percentage of tumour showing the formation of glands, as described in WHO International Histological Classification of Tumours [20]:

- Well differentiated adenocarcinoma shows glands in 95% of the tumour.
- Moderately differentiated adenocarcinoma shows 50-95% glands.
- Poorly differentiated adenocarcinoma shows 5-50% glands.
- Undifferentiated carcinoma shows <5% glands.

Histologic grade is a stage independent prognostic factor [17,22]. Multiple grading systems with variation in the number of strata within them have been suggested over the past few years. The distinction between well and moderately differentiated adenocarcinoma (low grade) versus poorly differentiated or undifferentiated carcinoma (high grade) has been shown to be prognostically useful [23]. The terms well, moderate and poor differentiation are equivalent to Grades 1-3 in the TNM staging system [16].

For the most part the pathological distinction between moderately and poorly differentiated or undifferentiated tumours is consistent and interobserver variability is small. Distinction between well and moderately differentiated carcinomas is less reproducible and associated with significant interobserver variability. Thus, a two tiered grading system that eliminates this distinction is recommended:

- Well differentiated and moderately differentiated – low grade
- Poorly differentiated and undifferentiated – high grade

Small foci of apparent poor differentiation are not uncommon at the advancing edge of tumours but these are insufficient to classify the tumour as poorly differentiated [21].

There is recent interest in the phenomenon of tumour budding at the advancing margin of colorectal cancers with accumulating evidence that it might have prognostic significance [24]. However, this is not yet considered sufficient to justify the inclusion of this item the minimum dataset.

## LOCAL INVASION

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**The maximum degree of local invasion into or through the bowel wall should be recorded. This is based on the T component of the TNM staging system.**

- pTis**    **Carcinoma in-situ: intraepithelial or invasion of lamina propria.**
- pT1**    **Tumour invades submucosa.**
- pT2**    **Tumour invades muscularis propria.**
- pT3**    **Tumour invades through muscularis propria into subserosa or into non-peritonealised pericolic or perirectal tissues.**
- pT4**    **Tumour directly invades other organs or structures (pT4a) and/or perforates visceral peritoneum (pT4b).**
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**pTis:** The TNM classification includes a level pTis to represent either in-situ carcinoma or carcinoma showing invasion of the lamina propria (intramucosal carcinoma). This practice is based primarily on the aim of achieving a uniform staging system across all organ systems. Colorectal neoplasia has not been shown to have metastatic potential until it has invaded through the muscularis mucosae. The term pTis is thus avoided in the lower gastrointestinal tract and the term high grade dysplasia is preferred. pTis tumours should be regarded as adenomas and not as carcinomas for the purpose of diagnosis and cancer registration.

**pT1:** Tumour invades submucosa but not muscularis propria.

**pT2:** Tumour invades into, but not through muscularis propria.

**pT3:** Tumour invades through muscularis propria into subserosa or into non-peritonealised pericolic or perirectal tissues.

pT3 indicates spread in continuity beyond the bowel wall. The microscopic presence of tumour cells confined within the lumen of lymph vessels or veins does not qualify as local spread in the T classification [16]. Occasionally cancer has spread as far as the outer edge of the muscularis propria but not beyond. If no muscle separates the cancer from the mesenteric tissue then the muscle coat should be interpreted as breached (pT3) [25].

**pT4a:** Tumour directly invades other organs or structures **AND/OR**

**pT4b:** Tumour invades through serosa with tumour cells on the peritoneal surface or free in the peritoneal cavity. Cases showing perforation should be classified as pT4b.

Direct invasion in pT4 includes invasion of other segments of the colorectum by way of the serosa, e.g. invasion of sigmoid colon by a carcinoma of the caecum [16,26]. Intramural or longitudinal extension of tumour into an adjacent part of the bowel e.g. extension of a caecal tumour into the terminal ileum does not affect the pT stage.

Serosal involvement through direct continuity with the primary tumour (pT4) is recorded differently from peritoneal tumour deposits that are separate from the primary. These latter deposits are regarded as distant metastases (pM1).

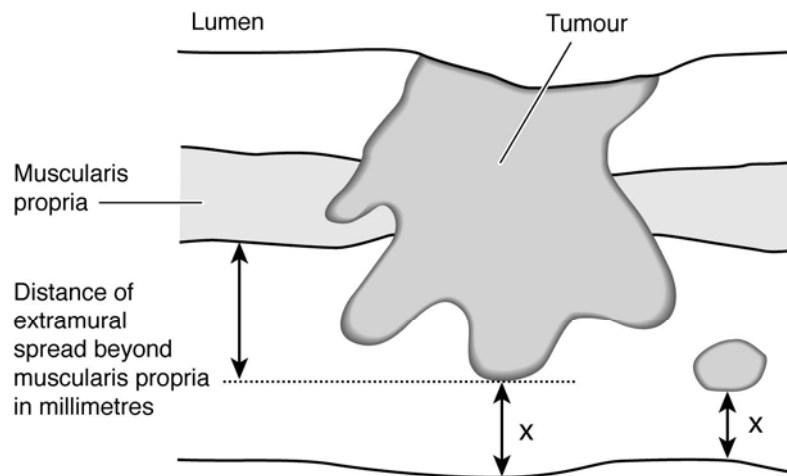
## NON-PERITONEALISED CIRCUMFERENTIAL MARGIN IN RECTAL TUMOURS

**In rectal tumours the minimum distance in millimetres between the tumour and the non-peritonealised, (circumferential, radial) margin should be recorded from the histological slides.**

Tumour frequently (5-36%) involves the non-peritonealised surgical circumferential resection margin (CRM) in the rectum and is associated with significantly higher rates of local recurrence and cancer-related death [27-34].

The frequency of involvement of the CRM depends on the quality of surgery, advancing TNM stage and whether the patient has undergone preoperative neoadjuvant therapy. The closer the tumour is to the CRM the worse the prognosis [35]. The vast majority of studies, including clinical trials and population studies, have used a cut off of 1mm or less to define margin involvement. The Dutch total mesorectal excision (TME) study suggests this measurement should be 2mm [31].

CRM involvement may be through direct continuity with the main tumour, by tumour deposits discontinuous from the main tumour or by tumour in veins, lymphatics or lymph nodes. All types of involvement confer a poor prognosis [28,31].



**x = minimum clearance in mm of primary tumour, extramural or nodal deposit or tumour in vessel etc, whichever is the closest.**

Confusingly, the residual tumour status (R) used in the TNM staging system requires that tumour be identified at the resection margin for the margin to be considered involved [16]. Thus, in TNM staging if tumour is not actually seen at this margin it is coded as R0. Therefore, recording the distance between the tumour and the CRM will alert the clinician to those patients who may benefit from being treated as though they were margin positive.

## THE NON-PERITONEALISED MARGIN IN THE COLON

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The importance of non-peritonealised margin involvement in colonic tumours, particularly those of caecum and ascending colon has recently been recognised [14,36]. Studies indicate the frequency of margin involvement is 7-10% [36]. It is recommended that tumour involvement of the non-peritonealised resection margin in colonic tumours should be recorded when this is present as this may facilitate the selection of patients with colonic tumours for postoperative adjuvant therapy [11].

## LYMPHOCYTIC INFILTRATION

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Intraepithelial lymphocytes (IEL) are those that are in direct contact with tumour cells or are located directly between tumour cell clusters. For standardised detection, routine histological methods should be used. Only a high density of lymphocytes ( $\geq 5$  IEL per hpf) should be considered significant. It has been suggested that a minimum of 10 standard fields including both the centre and periphery of the tumour should be included in the count [37].

Intraepithelial lymphocytes are thought to be indicative of a host immune response against cancer cells. They are also associated with a favourable outcome in terms of both recurrence and overall survival [38-40].

While the extent of lymphocytic infiltrates at the margins of the tumour (peritumoural lymphocytes) and the prominence of lymphoid follicles (Crohn's-like reaction) in adjacent tissues are also features of MMR deficient tumours, most studies have found the strongest correlation between IELs and MMR deficiency [41,42]. IEL counts are therefore not necessary if MMR deficiency status is to be assessed formally, by MMR immunohistochemistry or MSI testing.

## LYMPH NODES

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### **All lymph nodes should be harvested from the specimen and examined histologically.**

The finding of positive lymph nodes is a major determinant of whether the patient receives adjuvant therapy. The probability of finding a positive node increases with the number of nodes found although this probability curve flattens out after finding 12-15 nodes [43,44]. However, for practical purposes all lymph nodes present should be harvested from the specimen.

The AJCC recommendations state that if the examined lymph nodes are negative, but only a small number of nodes has been found, then the case should be classified as pN0 rather than pNX [16].

The N3 staging category, which described cases with a positive apical node, has been shown not to be prognostic [45] and so has been removed from the 6th edition of the AJCC guidelines.

Direct extension of a colorectal tumour into a lymph node is considered nodal metastasis. Metastasis in any lymph nodes other than regional nodes is classified as distant metastasis [16].

There is no consensus that occult metastatic disease detected by immunohistochemistry or other methods discriminates between high- and low-risk groups of patients. Data are thus insufficient to recommend routine use of tissue levels or ancillary special techniques [23,25].

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## GUIDELINES FOR SMALL TUMOUR DEPOSITS IN LYMPH NODES

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Isolated tumour deposits are single tumour cells or small cell clusters, generally less than 0.2mm in diameter, present within a lymph node. They may be visible in H&E stained sections or detected by immunohistochemistry. The literature suggests that the finding of such cells is not a marker of an adverse prognosis for the patient [46-48].

The TNM 6<sup>th</sup> edition recommends that cases in which isolated tumour cells are the only form of nodal involvement should be classified as pN0, although the presence of the isolated tumour cells should be noted. Optional designation as pN0(i+) is suggested for this situation [26], although a free-text description might provide clearer communication.

Micrometastasis refers to nodal metastatic deposits less than 2 mm in diameter. Such deposits differ from isolated tumour cells not only in size, but also in that they show evidence of growth, for example glandular differentiation, distension of the sinus or a stromal desmoplastic reaction [25].

The TNM 6<sup>th</sup> edition suggests that cases where micrometastasis is the only form of metastatic spread, be classified as pN1(mi), although again some explanatory free text would be advisable in this situation.

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## A NOTE ON TNM 5<sup>TH</sup> EDITION VERSUS TNM 6<sup>TH</sup> EDITION

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Isolated tumour deposits in the pericolic or perirectal fat, separate from the main tumour and lacking evidence of pre-existing lymph node or vessel, are common. TNM 5<sup>th</sup> edition classified such deposits as involved lymph nodes if they were >3mm in diameter. TNM 6<sup>th</sup> edition replaced this criterion with another, namely that such deposits were classified as involved lymph nodes if they showed a rounded contour, regardless of size. Deposits of irregular shape are to be coded as T3 and recorded as vascular invasion. This change has been the subject of some criticism, as it has replaced a relatively objective criterion (a measurement) with a subjective one (assessment of shape). The assessment of the nodal contour has been shown to be poorly reproducible [49] and it has therefore been suggested that the 5<sup>th</sup> edition criteria should be adhered to.

Other commentators [50] have pointed out that, reproducible or not, both criteria are essentially arbitrary and that such deposits may derive from nodes, vascular invasion, perineural invasion or a combination of these within a single case. Most examples occur in situations where there are unequivocally involved nodes anyway (in only 8% of cases were they the only form of deposit) and, where present, are in themselves associated with an adverse prognosis. It would therefore seem reasonable to adhere to the TNM 6<sup>th</sup> edition criteria, stating in free-text if isolated tumour deposits are the only form of nodal deposits identified.

## LYMPHOVASCULAR INVASION

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**For all tumours, including malignant polyps, venous and lymphatic invasion should be reported as present or absent and its anatomic location specified as mural or extramural.**

Venous invasion by tumour has been repeatedly shown by multivariate [17,51,52] and univariate analyses to be a stage independent adverse prognostic factor. However some studies identifying venous invasion as an adverse factor on univariate analysis have failed to confirm its independent impact on prognosis on multivariate breakdown [52-54]. Similar disparate results have also been reported for lymphatic invasion [54]. In other reports vascular invasion as a general feature was prognostically significant, but no distinction between lymphatic and venous vessels was made. In a few studies the location as well as the type of the involved vessels (e.g. extramural veins) were both considered strong determinants of prognostic impact [23,55]. Data from existing studies are difficult to amalgamate but nevertheless, the importance of venous and lymphatic invasion by tumour is strongly suggested and largely confirmed.

Some groups have recommended that only extramural vascular invasion be recorded [11], while others have recommended that the site of any vascular invasion should be recorded, along with its location, intra or extramural [23]. Both intramural and extramural vascular invasion have been shown to have similar prognostic value [14]. Evidence is also lacking or is inconclusive for preferential recording of vascular versus lymphatic invasion. It is thus recommended that both items are combined as lymphovascular invasion and a comment made on its location.

It is debatable whether special techniques, such as histochemical and immunohistochemical stains, to identify elastic tissue or endothelium increase the ease or accuracy of evaluation. Because these techniques are also labour intensive and time consuming they are not performed routinely. Accordingly, special stains are not recommended.

The prognostic importance of involvement of small (thin-walled, presumably lymphatic) vessels in the submucosa has been well documented with respect to polypectomies of malignant polyps. Such involvement has been shown to be associated with an increased risk of regional lymph node metastasis [56].

## PERINEURAL INVASION

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**Perineural invasion should be reported as present or absent.**

There is some evidence that perineural infiltration by tumour is an important indicator of spread, particularly in rectal tumours where it may involve the sacral plexus and this may be an indication for radiotherapy [57].

The presence or absence of perineural invasion should be assessed using routine histology alone.

## HISTOLOGICALLY CONFIRMED DISTANT METASTASES

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**The presence of histologically confirmed distant metastases and their site should be recorded.**

Pathological M staging can only be based on distant metastases that are submitted for histological assessment by the surgeon and will therefore tend to underestimate the true (clinical) M stage. Pathologists will only be able to use pM1 (distant metastases present) or pMX (distant metastases unknown). However at the request of the oncologists, a box marked cM has been included in the staging summary to record the presence of *clinically* diagnosed metastases as stated by the submitting surgeon and captured by the clinical request form.

Disease classifiable as distant metastasis may sometimes be present within the primary tumour resection specimen, e.g. a serosal or mesenteric deposit that is distant from the primary tumour mass.

Metastatic deposits in lymph nodes distant from those surrounding the main tumour or its main artery in the specimen will usually be submitted separately by the surgeon (e.g. deposits in para-aortic nodes or nodes surrounding the external iliac or common iliac arteries). Metastatic deposits in lymph nodes distant from those surrounding the main tumour or its main artery in the specimen are regarded as distant metastases (pM1) [26].

## BACKGROUND ABNORMALITIES

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**The presence of any pathological abnormalities in the background bowel should be recorded. Those listed are particularly of note.**

If the resection specimen contains two or more carcinomas (as indicated by the term “synchronous carcinomas” on the minimum dataset proforma) then a separate minimum dataset should be completed for each primary carcinoma. Where possible lymph nodes should be assigned and assessed for each cancer separately, based on topographical distribution.

## RESIDUAL TUMOUR STATUS

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**The completeness of resection should be recorded.**

**R0 No margin involvement (or residual disease).**

**R1 Microscopic but not macroscopic margin involvement.**

**R2 Macroscopic margin involvement.**

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Residual tumour classification (R status) is not limited to the primary tumour. The R classification not only considers locoregional residual tumour, but also distant residual tumour in the form of unresected or incompletely resected metastases (R2) [58].

For example, a metastasis in the liver from a primary colorectal carcinoma would be M1 and R0 if the metastasis was solitary and resected with tumour-free margins. This case would be M1 and R2 if the metastasis was not resected.

The resection status rule also applies to lymph nodes. If a clinically positive lymph node is left behind it is classified as R2.

Tumour cells that are confined to the lumen of blood vessels or lymphatics at the resection margin are classified as R0 [58].

Peritoneal involvement alone is not a reason to categorise the tumour as incompletely excised.

With regard to the presence of residual disease in areas which have not been resected (e.g. involvement of other organs by trans-coelomic spread), it is the responsibility of the surgeon to recognise and report these deposits. Such information will be collected by the surgical request form.

## SUMMARY - TNM STAGING

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**TNM 6<sup>th</sup> edition is used.**

The prefix “p” is used to indicate pathological staging.

If neoadjuvant chemotherapy or radiotherapy has been given, the prefix “yp” should be used to indicate that the original p stage may have been modified by therapy. Tumour remaining in a resection specimen following neoadjuvant therapy should always be classified by ypTNM to distinguish it from untreated tumour [26].

## MISMATCH REPAIR DEFICIENCY STATUS

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A mutation in mismatch repair genes (mainly MLH1, PMS2, MSH2 and MSH6) can cause an accumulation of DNA mutations that result in the initiation of cancer. Mismatch repair deficient (MMRD) cancers occur either sporadically (~12%) or less commonly (~2%) because the individual suffers from hereditary non-polyposis colorectal cancer (HNPCC). Tumours which show loss of MMR proteins by immunohistochemistry are almost always characterised by microsatellite instability (MSI), which is determined by analysis of tumour DNA. This finding is important for the following reasons:

MMRD has been shown to be a favourable prognostic factor in colorectal cancer, in terms of both recurrence-free survival and overall survival [41,59,60].

MMRD tumours may be less responsive to adjuvant chemotherapy compared to other colorectal cancers [61-63] although this has not been shown conclusively in all studies [64-66].

In 2% of cases MMRD is associated with underlying HNPCC which raises cancer issues for all family members.

Immunohistochemical (IHC) analysis of mismatch repair proteins is used to detect MMRD in colorectal cancer, with an absence of one or more of the mismatch repair proteins considered an abnormal result [67,68]. MMRD can also be determined by microsatellite analysis, which is the amplification and analysis of selected microsatellite loci within the genome of the tumour cells. However, this later technique is not used routinely in diagnostic pathology settings. MMR testing is currently recommended for all cases of colorectal cancer arising in individuals less than 50 years of age, although this cut off is arbitrary.



## NOTES ON MINIMUM DATA SET PROFORMA FOR COLORECTAL CARCINOMA

### Maximum tumour diameter

This is measured in mm from the luminal aspect of the bowel.

### Distance of tumour to nearer cut end

This is the measurement in mm from the nearer cut end of the specimen and not the non-peritonealised or circumferential margin.

### Presence of tumour perforation

Perforation is defined as a macroscopically visible defect through the tumour such that the bowel lumen is in communication with the external surface of the intact resection specimen. Such cases are always regarded as pT4 in the TNM staging system. Perforation of the proximal bowel wall as a result of a distal obstructing tumour does not count as tumour perforation.

### Relationship of rectal tumours to the anterior peritoneal reflection

The peritoneal reflection is identified from the exterior surface of the anterior aspect of the specimen. Rectal tumours are classified according to whether they are entirely above, astride (or at), or entirely below the level of the peritoneal reflection anteriorly.

### Tumour type

Virtually all colorectal cancers are adenocarcinomas. Type is described according to WHO International Histological Classification of Tumours ICD-10.

### Differentiation by predominant area

Differentiation should be assessed on the predominating degree of differentiation represented in the primary tumour. Poorly differentiated (high grade) tumours should be separated from well or moderately differentiated (low grade) tumours. Small foci of apparent poor differentiation are not uncommon at the advancing edge of tumours but these are insufficient to classify the tumour as poorly differentiated.

### Local invasion

The maximum degree of local invasion into or through the bowel wall should be recorded. The pT4 stage encompasses either tumour infiltration of an adjacent organ (pT4a) or involvement of the serosal surface (pT4b). Accordingly pT4 tumours may have either or both the pT4 boxes marked.

### Histological measurement from tumour to non-peritonealised margin

For rectal tumours the minimum distance in millimetres between the tumour and the non-peritonealised, (circumferential, radial) margin should be recorded from the histological slides. This measurement may be taken from the primary tumour, nodal or perineural deposits or tumour in vessels, whichever is closest. The importance of tumour involvement of the non-peritonealised margin in certain colonic tumours (e.g. caecum) is the subject of ongoing research. Record when appropriate.

### Lymphocytic infiltrate

Only count lymphocytes that are in direct contact with tumour cells, or are located directly between tumour cell clusters (intraepithelial lymphocytes). For standardised detection methodology, routine histology should be used. Only high density (> 5 TIL per hpf) should be considered significant.

A minimum of 10 random fields including both the centre and periphery of the tumour should be included in the count. While the extent of lymphocytic infiltrates at the margins of the tumour (peritumoural lymphocytes) and the prominence of lymphoid follicles (Crohn's like reaction) in adjacent tissues are also features of MMR deficient tumours, most

studies have found the strongest correlation between IELs and MMRD.

### Lymph nodes

All lymph nodes should be harvested from the specimen and examined histologically. A reduced number of lymph nodes may be found in limited resections and after pre-operative radiotherapy or chemotherapy.

Extramural deposits of tumour that have no lymph node structure are classified according to the recommendations of the 6<sup>th</sup> edition of the TNM classification.

### Lymphovascular invasion

Lymphovascular invasion should be assessed and recorded for all tumours, including malignant polyps. Record its type (venous, lymphatic) and its location (mural, extramural).

### Perineural invasion

Record as present or absent.

### Histologically confirmed distant metastases

The absence or presence of histologically confirmed distant metastases and their site should be recorded. If this cannot be assessed histologically pMX should be recorded. If however, the clinical request form indicates metastases are present clinically or on imaging etc, then a cM classification can be assigned.

### Background abnormalities

The presence of any pathological abnormalities in the background bowel should be recorded. Those listed are particularly of note. If the resection contains two or more carcinomas then a separate minimum data set should be completed separately for each primary carcinoma. Where possible lymph nodes should be assigned and assessed for each cancer separately, based on topographical distribution.

### Residual tumour

The absence or presence of residual tumour after treatment is described by the symbol R. For the purposes of TNM staging, if tumour is not actually at a margin it is recorded as R0. However, if the distance between the tumour and the circumferential margin is  $\leq$  1mm (some studies suggest 2mm) this has been shown to be indicative of a high risk of tumour recurrence.

### TNM staging

The 6<sup>th</sup> edition of TNM is used.

The prefix "p" is used to indicate pathological staging.

If neoadjuvant preoperative chemotherapy or radiotherapy has been given the prefix "yp" is used to indicate that the original p stage may have been modified by therapy.

### Reporting of a resection specimen in which the primary tumour was completely removed by previous polypectomy

Record all data assessable from the resection specimen. The type, degree of differentiation, presence of vascular invasion and MMR status of the primary tumour should be recorded and cross referenced with the original specimen, if known.

### Mismatch Repair Deficiency Status

Absence of staining for one or more of any mismatch repair genes (mainly MLH1, PMS2, MSH2 & MSH6) is considered abnormal. This abnormality is associated with microsatellite instability phenotype (MSH-I) and may reflect the presence of a germ line mutation or somatic inactivation of that mismatch repair enzyme.

## APPENDIX B – COLORECTAL CANCER SURGICAL REQUEST

### COLORECTAL CANCER SURGICAL REQUEST FORM

Affix patient details here

Affix doctor details here

**Patient presentation at surgery**

- Screening
- Symptoms
- Emergency due to obstruction, perforation (with abscess/peritonitis), excessive bleeding or in conjunction with resuscitation
- Unknown

*Please tick boxes and/or indicate on diagram tumour location and lines of resection*

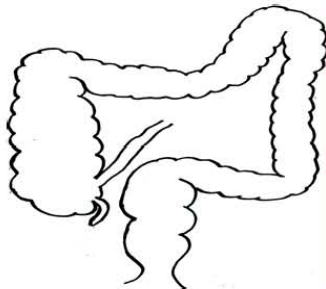
**Tumour Location**

- Caecum
- Ascending colon
- Hepatic flexure
- Transverse colon
- Splenic flexure
- Descending colon
- Sigmoid colon
- Rectum
- Multi-focal

Distance from anal verge .....cm  
(Rigid sigmoidoscopy – rectal cancer only)

**Operation Performed**

- Right hemicolectomy
- Extended right hemicolectomy
- Left hemicolectomy
- Sigmoid colectomy
- Transverse colectomy
- Anterior resection:  TME
- Abdominoperineal resection:  TME
- Hartmann's
- Other (specify) .....



**Pre-operative radiotherapy (rectal cancer only)**

- Not given
- Pre-operative short course radiotherapy
- Pre-operative long course radiotherapy or chemo-irradiation
- Unknown

**Method of surgery**

- Open resection
- Laparoscopic resection
- Laparoscopic resection converted to open
- Local excision (e.g. TEMS)

**Surgeon's opinion of nature of surgery**

- Curative (no obvious tumour remaining)
- Indeterminate due to local excision
- Indeterminate due to inadequate lymph node clearance
- Palliative (tumour transected)
- Palliative (metastases remaining)
- Palliative (both)

**Adjacent organs involved?**

- No
- Yes (specify).....

**Distant metastases present?**

- None
- Lymph nodes
- Peritoneal
- Hepatic
- Other.....

Surgeon's name: .....

Signature: .....

Date: .....

**Please attach form to pathology request for collection with bowel specimen**

## SURGICAL REQUEST GUIDELINES

### **Presentation at Surgery:**

Emergency surgery is a prognostic factor in determining postoperative mortality and long-term survival. It is important to note that many patients who have an emergency admission do not have emergency surgery and their risk of dying from surgery approximates to that of an elective case. The term emergency therefore refers to surgery rather than the mode of admission. Patient presentation at surgery should be determined by the surgeon.

### **Distance from Anal Verge**

Measured in centimetres using the best available information; rigid sigmoidoscopy measurements are preferred over digital rectal examination, operative findings or colonoscopy measurements. This measurement allows for the classification of rectal cancers into upper, mid and lower third categories, which significantly impacts on case management.

### **Method of surgery**

Informs on current practice patterns as laparoscopic surgical techniques are becoming increasingly utilised.

### **Surgeon's opinion of nature of surgery**

This item pertains to the overall completeness of resection of the tumour, including evidence of residual disease at surgical margins or within regions in which resection has not been attempted. It allows for residual tumour status (R) to be assessed. R0 classification may include M1 cases if both the primary tumour and the distant metastasis are completely resected by curative surgery.

### **Adjacent organs involved?**

With regard to presence of residual disease in areas which have not been resected (e.g. involvement of other organs by trans-coelomic spread), it is the responsibility of the surgeon to recognise and report these deposits.

### **Distant metastases present?**

The reporting of metastatic deposits, either resected or not resected, is required for accurate assessment of the metastatic (M) stage of the tumour.

## TISSUE HANDLING GUIDELINE

Through consultation with pathologists the following tissue handling guidelines have been requested where possible:

- Please keep the tissue as intact as possible.
- Please do not cut through the mesorectal tissue. If it is necessary to view a rectal tumour, please open the specimen away from the tumour from the proximal end.

## USEFUL WEBSITE

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<http://www.uicc.org/>

The UICC website has a dedicated TNM page, which includes a frequently asked questions (FAQ) section and a link to a helpdesk, for questions not covered by the FAQ.

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