

Derek C. Allen  
R. Iain Cameron  
*Editors*

# Histopathology Specimens

Clinical, Pathological  
and Laboratory Aspects

**Third Edition**

 Springer

---

# Histopathology Specimens

---

Derek C. Allen • R. Iain Cameron  
Editors

# Histopathology Specimens

Clinical, Pathological and  
Laboratory Aspects

Third Edition

 Springer

*Editors*

Derek C. Allen  
Belfast City Hospital  
Belfast  
UK

R. Iain Cameron  
Altnagelvin Hospital  
Londonderry  
UK

ISBN 978-3-319-57359-5      ISBN 978-3-319-57360-1 (eBook)  
DOI 10.1007/978-3-319-57360-1

Library of Congress Control Number: 2017950223

© Springer International Publishing AG 2017

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, express or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Printed on acid-free paper

This Springer imprint is published by Springer Nature  
The registered company is Springer International Publishing AG  
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

*To Alison, Katie, Rebecca, and Amy*

---

## Preface

Since the publication of the second edition of *Histopathology Specimens: Clinical, Pathological, and Laboratory Aspects*, pathology has further consolidated its position at the core of clinical multidisciplinary teams and their attendant meetings. These forums are pivotal nodal discussion points in patient investigation, treatment planning, and prognostication. Pathologists are required to produce and comment on reports that are timely, accurate, and relevant. To this end, the UK Royal College of Pathologists and other organisations (International Collaboration on Cancer Reporting (ICCR)) continue to publish standards of professional practice such as the Cancer Datasets and Tissue Pathways for the handling and reporting of cancer and non-cancer specimens, respectively. Indeed, the UK Royal College of Pathologists has established key performance indicators incorporated into UKAS accreditation standards aimed at ensuring laboratory processes and outcomes are beneficial to patients. These include >90% targets for attendance at multidisciplinary team meetings, coding and use of proforma histopathology reports, and 80–90% report turnaround times of 7–10 days, respectively. The College has also produced a standardised user satisfaction survey in metric form that should allow assessment of measureable pathology performance and team communication. This may also potentially be considered alongside colleague and user multisource feedback as part of annual appraisal and medical revalidation.

One other standard is that laboratories should aim to have a significant minority (15–30%) of their medical and scientific staff in training grades. The structure and content of this book not only facilitates delivery of high performance standards but also reflects the clinically integrated approach to the teaching of pathology as determined by the Royal College postgraduate training curriculum and the General Medical Council medical student undergraduate curriculum. Its content is also directly relevant to Biomedical Scientists in their devolved role of consultant supervised specimen dissection as evidenced by the collaborative IBMS/RCPATH diploma of extended practice and advanced specialist diplomas in histological dissection.

Belfast, UK  
Londonderry, UK

Derek C. Allen  
R. Iain Cameron

---

## Acknowledgements

The authors gratefully acknowledge the use of illustrations from Wittekind C., Greene L., Hutter R.V.P., Klimfingher M., and Sobin L.H. *TNM Atlas: Illustrated Guide to the TNM/pTNM Classification of Malignant Tumours*. 5th edition. Berlin, Heidelberg: Springer-Verlag, 2005.

Grateful appreciation is expressed to Joanna Renwick (Editor, Clinical Medicine), Andre Tournois, and the staff at Springer.

---

# Contents

## Part I Gastrointestinal Specimens

<b>1 Gastrointestinal Specimens: General Comments</b> . . . . .	3
Derek C. Allen and R. Iain Cameron	
<b>2 Oesophagus</b> . . . . .	13
Damian T. McManus, Derek C. Allen, and R. Iain Cameron	
<b>3 Stomach</b> . . . . .	25
Damian T. McManus, Derek C. Allen, and R. Iain Cameron	
<b>4 Pancreas, Duodenum, Ampulla of Vater and Extrahepatic Bile Ducts</b> . . . . .	37
Paul J. Kelly, Derek C. Allen, R. Iain Cameron, and Maurice B. Loughrey	
<b>5 Small Intestine</b> . . . . .	55
Derek C. Allen, R. Iain Cameron, and Maurice B. Loughrey	
<b>6 Colorectum</b> . . . . .	67
Derek C. Allen, R. Iain Cameron, and Maurice B. Loughrey	
<b>7 Appendix</b> . . . . .	87
Derek C. Allen, R. Iain Cameron, and Maurice B. Loughrey	
<b>8 Anus</b> . . . . .	95
Derek C. Allen, R. Iain Cameron, and Maurice B. Loughrey	
<b>9 Gallbladder</b> . . . . .	103
Paul J. Kelly, Derek C. Allen, R. Iain Cameron, and Maurice B. Loughrey	
<b>10 Liver</b> . . . . .	111
Paul J. Kelly, Derek C. Allen, R. Iain Cameron, and Maurice B. Loughrey	
<b>11 Abdominal Wall, Umbilicus, Hernias, Omentum, and Peritoneum</b> . . . . .	125
Derek C. Allen, R. Iain Cameron, and Maurice B. Loughrey	



## Part II Breast Specimens

- 12 Breast** ..... 133  
Shauna Casey and R. Iain Cameron

## Part III Head and Neck Specimens

- 13 Nasal Cavities and Paranasal Sinuses** ..... 149  
Seamus S. Napier and Ramzan M. Ullah
- 14 Lips, Mouth, and Tongue** ..... 157  
Seamus S. Napier and Derek J. Gordon
- 15 Maxilla, Mandible, and Teeth** ..... 169  
Seamus S. Napier and with clinical comments  
by John J. Marley
- 16 Pharynx and Larynx** ..... 179  
Seamus S. Napier and with clinical comments  
by Barry Devlin
- 17 Salivary Glands** ..... 193  
Seamus S. Napier and with clinical comments  
by John J. Marley
- 18 Thyroid Gland** ..... 203  
Caroline L. Coghlin and Seamus S. Napier
- 19 Parathyroid Glands** ..... 213  
Caroline L. Coghlin and Seamus S. Napier
- 20 Neck: Cysts, Tumours, and Dissections** ..... 219  
Seamus S. Napier and with clinical comments  
by Derek J. Gordon

## Part IV Eye

- 21 Eye** ..... 231  
Roy W. Lyness

## Part V Gynaecological Specimens

- 22 Ovary** ..... 243  
Oisín P. Houghton and W. Glenn McCluggage
- 23 Fallopian Tube** ..... 255  
Oisín P. Houghton and W. Glenn McCluggage
- 24 Uterus** ..... 261  
Oisín P. Houghton and W. Glenn McCluggage
- 25 Cervix** ..... 273  
Oisín P. Houghton and W. Glenn McCluggage

---

<b>26</b>	<b>Vagina</b> .....	283
	Oisín P. Houghton and W. Glenn McCluggage	
<b>27</b>	<b>Vulva</b> .....	289
	Oisín P. Houghton and W. Glenn McCluggage	
<b>28</b>	<b>Placenta</b> .....	295
	Oisín P. Houghton	
<b>Part VI Urological Specimens</b>		
<b>29</b>	<b>Kidney, Renal Pelvis, and Ureter</b> .....	301
	Declan M. O'Rourke and Derek C. Allen	
<b>30</b>	<b>Bladder</b> .....	321
	Declan M. O'Rourke and Derek C. Allen	
<b>31</b>	<b>Prostate</b> .....	337
	Declan M. O'Rourke and Derek C. Allen	
<b>32</b>	<b>Urethra</b> .....	353
	Declan M. O'Rourke and Derek C. Allen	
<b>33</b>	<b>Testis, Epididymis, and Vas</b> .....	363
	Declan M. O'Rourke and Derek C. Allen	
<b>34</b>	<b>Penis</b> .....	379
	Declan M. O'Rourke and Derek C. Allen	
<b>Part VII Pelvic and Retroperitoneal Specimens</b>		
<b>35</b>	<b>Pelvic Exenteration Specimens</b> .....	393
	Damian T. McManus and Derek C. Allen	
<b>36</b>	<b>Retroperitoneum</b> .....	399
	Oisín P. Houghton and Damian T. McManus	
<b>37</b>	<b>Adrenal Gland</b> .....	405
	Maurice B. Loughrey and Caroline L. Coghlin	
<b>Part VIII Skin Specimens</b>		
<b>38</b>	<b>Skin</b> .....	415
	Maureen Y. Walsh	
<b>Part IX Cardiothoracic Specimens and Vessels</b>		
<b>39</b>	<b>Lung</b> .....	435
	Kathleen M. Mulholland	
<b>40</b>	<b>Pleura</b> .....	447
	Kathleen M. Mulholland	

---

<b>41 Mediastinum</b> .....	453
Kathleen M. Mulholland	
<b>42 Heart</b> .....	461
Kathleen M. Mulholland	
<b>43 Vessels</b> .....	469
Kathleen M. Mulholland	
<b>Part X Osteoarticular and Soft Tissue Specimens</b>	
<b>44 Joint Space, Bone, Soft Tissues, and Special Techniques</b> .....	477
Oisin P. Houghton	
<b>Part XI Haemopoietic Specimens</b>	
<b>45 Lymph Nodes, Spleen, and Bone Marrow</b> .....	495
Lakshmi Venkatraman and Damian T. McManus	
<b>Part XII Miscellaneous Specimens and Ancillary Techniques</b>	
<b>46 Miscellaneous Specimens and Ancillary Techniques</b> .....	519
Damian T. McManus	
<b>Clinical Request Form Abbreviations</b> .....	533
<b>Resection Specimen Blocking Summary</b> .....	543
<b>Index</b> .....	547

---

## Contributors

**Derek C. Allen** Histopathology Laboratory, Belfast City Hospital, Belfast Health and Social Care Trust, Belfast, UK

**R. Iain Cameron** Histopathology Laboratory, Altnagelvin Hospital, Western Health and Social Care Trust, Londonderry, UK

**Shauna Casey** Histopathology Laboratory, Belfast City Hospital, Belfast Health and Social Care Trust, Belfast, UK

**Caroline L. Coghlin** Histopathology Laboratory, Belfast City Hospital, Belfast Health and Social Care Trust, Belfast, UK

**Barry Devlin** ENT Surgery, Royal Victoria Hospital, Belfast Health and Social Care Trust, Belfast, UK

**Derek J. Gordon** Regional Plastics and Maxillofacial Unit, Ulster Hospital, Southeastern Health and Social Care Trust, Dundonald, UK

**Oisín P. Houghton** Histopathology Laboratory, Institute of Pathology, Royal Victoria Hospital, Belfast Health and Social Care Trust, Belfast, UK

**Paul J. Kelly** Histopathology Laboratory, Institute of Pathology, Royal Victoria Hospital, Belfast Health and Social Care Trust, Belfast, UK

**Maurice B. Loughrey** Histopathology Laboratory, Institute of Pathology, Royal Victoria Hospital, Belfast Health and Social Care Trust, Belfast, UK

**Roy W. Lyness** Histopathology Laboratory, Belfast City Hospital, Belfast Health and Social Care Trust, Belfast, UK

**John J. Marley** Department of Oral Surgery, School of Dentistry, Royal Victoria Hospital, Belfast Health and Social Care Trust, Belfast, UK

**W. Glenn McCluggage** Histopathology Laboratory, Institute of Pathology, Royal Victoria Hospital, Belfast Health and Social Care Trust, Belfast, UK

**Damian T. McManus** Histopathology Laboratory, Belfast City Hospital, Belfast Health and Social Care Trust, Belfast, UK

**Kathleen M. Mulholland** Histopathology Laboratory, Altnagelvin Hospital, Western Health and Social Care Trust, Londonderry, UK

**Seamus S. Napier** Histopathology Laboratory, Institute of Pathology, Royal Victoria Hospital, Belfast Health and Social Care Trust, Belfast, UK

**Declan M. O'Rourke** Histopathology Laboratory, Belfast City Hospital,  
Belfast Health and Social Care Trust, Belfast, UK

**Ramzan M. Ullah** Directorate of ENT Surgery, Royal Victoria Hospital,  
Belfast Health and Social Care Trust, Belfast, UK

**Lakshmi Venkatraman** Histopathology Laboratory, Institute of Pathology,  
Royal Victoria Hospital, Belfast Health and Social Care Trust, Belfast, UK

**Maureen Y. Walsh** Histopathology Laboratory, Institute of Pathology,  
Royal Victoria Hospital, Belfast Health and Social Care Trust, Belfast, UK

---

# Introduction

---

## The Role of Histopathology Specimens

Histopathology specimens are a vital cornerstone in patient care. They not only establish a tissue diagnosis but are crucial in clinical management decisions and provide important prognostic data. They are nodal events in a patient's illness shaping the choice of relevant medical and surgical therapies and determining follow-up strategy. The data they provide are used to assess the efficiency of current and new investigation and treatment regimes and to monitor the impact of population screening programmes. Clinical governance has recognised their key role in auditing not only individual clinicians but also the patterns and quality of overall health care provision. Biomedical research with advances in investigations and therapy would flounder without them. They are therefore a precious resource to be handled with great care by sufficient numbers of appropriately trained and experienced personnel. The data generated are of a confidential nature privy to the patient, consultant clinician or general practitioner, and the reporting pathologist. This information may be shared as appropriate with other directly involved health care professionals, for example, in the context of multidisciplinary team meetings, but laboratory practice (e.g., telephoned results and report authorisation) must be geared to protect patient confidentiality at all times. The patient not only has a right to see and have explained the information in his/her specimen but must undergo a process of informed consent prior to the clinical procedure. Thus the nature, purpose, extent, and side effects of the procedure are explained in understandable terms. This process extends to the laboratory as patients can express their wish for disposal and use of the tissue not only for diagnosis but also for educative, audit, and research purposes. Additionally research projects should be verified by an appropriate research ethics committee. Patient denial of any of these uses must then be communicated to the laboratory and incorporated into the handling and disposal procedures. The histopathology specimen report forms a permanent part of the patient's medical record and as such may be used as medico-legal evidence in negligence and compensation cases. These various factors serve to emphasise the importance of the care that should be taken with these specimens by histopathology laboratory personnel.

---

## The Handling of Histopathology Specimens

Specimen transportation, accession, clinical prioritisation, dissection, audit, and reporting are considered.

---

### Specimen Transportation

There must be close liaison between pathology and clinical staff to ensure appropriate transportation of specimens between the outpatient department, operating theatre, and the laboratory, for example, prompt transport of fresh specimens or the provision of special fixatives. This must be reflected in shared protocols, a user information manual, and education of the clinical and portering staff.

---

### Specimen Accession

Allocation of a unique laboratory number and accurate computer registration of patient details are fundamental to maintenance of a meaningful and practicable histopathology database. This is important not only to individual patient care (e.g., a sequence of biopsies) but also for provision of statistics, for example, download to cancer registries.

---

### Specimen Prioritisation

With ever increasing workload and limited staffing resources, pathologists may find it necessary to put in place a specimen pull-through protocol related to clinical need to ensure that diagnostic results are available within an appropriate time frame. This can be based on various criteria such as specimen type and request form information (Appendix A). Suggested overall turnaround times for histopathology specimens are 80% and 90% of cases reported within 7 and 10 working days, respectively, subject to individual case needs and in agreement with local clinical teams.

---

### Specimen Dissection

Traditionally the role of a medical pathologist specimen dissection is now also being performed by an increasing number of biomedical scientists (BMSs) as has been the situation for several decades in some laboratories in America (Pathologist Assistants) and the UK. BMSs, trainee, and consultant pathologists are all appropriate to the task provided that several principles are adhered to:

- The histopathology specimen and its report remain the overall responsibility of the reporting consultant pathologist.
- There is close proximity and ready availability of active consultant pathologist supervision before, during, and after handling of the specimen.

- There is workforce stability and staff are prepared to work together as a team. The working unit comprises a variable combination of two people (junior/senior, medic/BMS) fulfilling the roles of dissector/writer/supervisor with active overarching consultant pathologist supervision.
- Staff recognise that acquisition of dissection skills is an at-the-bench apprenticeship based on sufficient knowledge, time, experience, and supervision. This knowledge base requires insight into normal anatomy, clinical presentation, and investigations relevant to request form information, common pathological conditions, and their effect on specimens, surgical considerations in production of the specimen, and core report data tailored to patient management and prognostic information. Consequently the chapters in this book are structured accordingly under these headings. The cut-up supervisor plays a vital role in passing on verbal knowledge but this is supplemented by various means, for example, publications (in-house protocols, ACP broadsheets, College datasets, and textbooks) or training courses. A structured training programme facilitates learning and progression.

Staff must also be familiar with the laboratory process of checking patient details, specimen labelling, and past history (cytology, biopsy, and treatment), the importance of specimen opening for adequate fixation, demonstration of resection margins, and use of macroscopic and microscopic digital photography. Knife etiquette and sampling blocks of appropriate thickness and fixation are crucial. The supervising pathologist must provide active feedback as to the significance and adequacy of these blocks. Line diagrams are an invaluable communication tool between dissector and reporters. Specimens not infrequently need to be revisited prior to report authorisation or following new information gained from the multidisciplinary team meeting. Retention of “wet” specimens must be sufficiently long (minimum 4 weeks) to allow this process to happen.

- Dissectors should only work to their individual level of experience and competence—this is determined by the structured training programme, audit process (see below), and categorisation of specimens according to their complexity.
- Dissectors should actively seek supervisor input if a specimen is complex, novel, shows an unusual variation on a usual theme, or if they have any doubt.
- The principles and a working practice of surgical cut-up are referred to in Appendices **B** and **C**.

---

## **Specimen Dissection Audit**

The quality of specimen dissection must be meaningfully monitored, and the majority of this is done actively at the laboratory bench by the consultant pathologist/BMS supervisor team as part of the specimen dissection pre-/peri-/post-view and reporting feedback procedures. In addition, this team should carry out formal periodic audit and assessment of dissectors’ skills.



This combination of approaches forms the basis for an individual dissector's continued practice and progression between specimen categories (see Appendix D). It also identifies the areas of subspecialist expertise or in need of further training. It must be recognised that category progression cannot be proscribed by rigid time frames but rather related to the aptitude of the individual dissector and spectrum of workload that is encountered.

---

## Specimen Reporting

Histopathology specimen reports remain the responsibility of an appropriately trained and experienced medical pathologist. Increasingly Royal College of Pathologist Cancer Datasets are mandating key audit data to assess the standards of specimen dissection and reporting, for example, colorectal cancer mean lymph node harvest and the reported percentages of serosal and extramural vascular involvement by tumour. Other key service quality indicators include pathologist participation in relevant interpretive histopathology external quality assurance (EQA) schemes and appropriate continuing professional development (CPD) activity. These issues are discussed at annual appraisal and are foundational to medical revalidation. The overall quality of a surgical pathology service depends on a number of key performance indicators summarised in a Royal College of Pathologists document (Key performance indicators—proposals for implementation. <http://www.rcpath.org/>). They include availability and timeliness of clinical advice, participation at multidisciplinary meetings, coding of histopathology reports, use of cancer resection report proformas, documentation of second opinions, results transmission, communication of critical and unexpected results, report turnaround times, monitoring of outstanding reports, appraisal, CPD, participation in appropriate EQA schemes, user satisfaction surveys, staff qualification, teaching, training, supervision, and succession planning (Appendix E).

The principles and practice of surgical cut-up and sample protocols for general specimen handling, categorisation, and laboratory abbreviations (Appendices F and G) are included in the appendices to this section.

Other aspects of service quality and safety are also actively addressed by appropriate guidance documents available on the Royal College of Pathologists website (Appendix H).

---

## The Core Data in Histopathology Specimens

Specimen dissection must be geared to provide information relevant to the clinician who is managing the patient. Reports must be timely, that is, prompt, but in the context of an adequate period of fixation so that acquisition of accurate data is not compromised. The report content must not only come to an interpretationally accurate diagnosis but also be qualified by assessment of various evidence-based prognostic indicators. In the field of surgical cancer pathology, this is reflected by the trend towards set format reports or datasets for the common cancers. Thus the core content should include gross specimen

description, tumour histological type and grade, extent of local tumour spread, lymphovascular invasion, lymph node involvement, relationship to primary excision margins, and any associated pathology.

---

## **Gross Description**

Clear distinction should be made between biopsy and resection specimens as they are handled differently and represent different nodal points in a patient's illness. This should be reflected in use of appropriate SNOMED T (topography) and P (procedure) codes—this also facilitates audit of biopsy and resection—proven cancer numbers and correlation with other techniques such as cytology, radiology, and serum markers. The site, distribution, size, edge, and appearance of a tumour within an organ greatly influence the specimen handling and creation of a diagnostic shortlist for microscopy. For example, a gastrointestinal malignant lymphoma may be multifocal, pale, and fleshy with prominent mesenteric lymphadenopathy, whereas a carcinoma is more usually ulcerated and annular, firm and irregular with more localised lymph node disease and vascular involvement.

---

## **Histological Tumour Type**

There are marked prognostic and therapeutic differences between the diagnoses of carcinoma, sarcoma, germ cell tumour, and malignant lymphoma. This is further highlighted within a given anatomical site, for example, lung, where a diagnosis of carcinoma can be of various subtypes requiring either primary surgical (squamous cell carcinoma) or chemo-/radiotherapeutic (small cell carcinoma) approaches and with very different biological outcomes.

---

## **Histological Tumour Differentiation or Grade**

Tumour differentiation or grade reflects the similarity to the ancestral tissue of origin and degree of cellular pleomorphism, mitoses, and necrosis. It too greatly influences choice of therapy and prognosis, for example, low-grade versus high-grade gastric lymphoma (antibiotics versus chemotherapy/surgery) or grade I (surgery alone) versus grade III (surgery and chemotherapy) breast cancer.

An accurate histological tumour type and grade cannot be ascertained unless there is appropriate specimen handling with adequate fixation.

---

## **Extent of Local Tumour Spread**

Prognosis of a given cancer may be influenced by the character of its invasive margin (circumscribed/infiltrative) but is largely determined by its pathological stage, that is, the depth or extent of spread in the organ and degree of lymph node involvement. This is then updated by other information, for

example, evidence of distant metastases, to formulate a clinical stage upon which management is based. The TNM (Tumour Nodes Metastases) classification is the international gold standard for the assessment of spread of cancer and translates into hard data some of the descriptive language used in histopathology reports facilitating communication within the multidisciplinary team. The post-surgical histopathological classification is designated pTNM and is based on pre-treatment, surgical, and pathological information. The staging is formalised and agreed at the relevant multidisciplinary team meeting thereupon forming a permanent part of the patient's medical record.

pT	Requires resection of the primary tumour or biopsy adequate for evaluation of the highest pT category or extent of local tumour spread. Due to tumour heterogeneity, this is contingent upon adequate numbers of well-orientated blocks. Where possible multiple tumours are individually staged and the highest pT category used for management decisions
pT0	No histological evidence of primary tumour
pTis	Carcinoma in situ
pT1-4	Increasing size and/or local extent of the primary tumour histologically
pN	Requires removal of nodes sufficient to evaluate the absence of regional node metastasis and also the highest pN category. Where possible all regional nodes in a resection specimen should be sought and harvested for histology
pN0	No regional lymph node metastasis histologically
pN1-3	Increasing involvement of regional lymph nodes histologically
pM	Requires microscopic examination of positive body cavity fluid cytology or distant metastases—the latter may not be available to the pathologist and therefore designated on clinical or radiological grounds

Other descriptors include unifocality (pT1a) versus multifocality (pT1b), lymphatic invasion (L), venous invasion (V), perineural invasion (Pn), classification during or after multimodality therapy (ypT), recurrent tumour (rpT), residual tumour (R0/R1/R2), and multiple primary tumours (pTm). Subdivisions of some categories exist to allow for greater specificity, for example, pN2a and pN2b.

The post-surgical pathological stage not only gives an estimate of disease prognosis but is also used to guide adjuvant therapy. Other prognostic and predictive factors are also taken into account on an individual basis, e.g., the hormonal expression, molecular features, or gene expression of the tumour in question. Qualifying tumours in the TNM system are carcinoma, malignant mesothelioma, malignant melanoma, gastrointestinal neuroendocrine and stromal tumours, gestational trophoblastic tumours, germ cell tumours, and retinoblastoma. The 8th edition TNM classification published in December 2016 (and subject to ongoing review - herein referred to as TNM 8) is used throughout this book unless otherwise stated.

---

## Lymphovascular Invasion

Usually defined histologically in blocks from the tumour edge or slightly away from it and more likely to be associated with cancers that show local recurrence, lymph node involvement, submucosal spread, and

satellite lesions. This has implications for blocking of resection specimens and their margins. Some cancers (hepatocellular carcinoma and renal cell carcinoma) have a propensity for vascular involvement and care should be taken to identify this on gross specimen dissection and microscopy as it alters the tumour stage and is a marker for distant haematogenous spread.

---

## Lymph Nodes

The pN category relates to the total node yield and the number that are involved. Nodal yields are used to audit the care of dissection by the pathologist, adequacy of resection by the surgeon, and the choice of operation, for example, axillary node sampling versus clearance in breast cancer. All regional nodes should be sampled and although ancillary techniques (xylene clearance and revealing solutions) can play a useful supplementary role, there is no substitute for time spent on careful dissection. The TNM system makes a numerical recommendation for what is considered an appropriate regional lymphadenectomy for each type of cancer resection. Care should be taken not to double count the same node, and those small nodes ( $>1$  mm with an identifiable subcapsular sinus) in the histological slides immediately adjacent to the tumour should not be ignored. TNM rules state that direct extension of primary tumour into a regional node is counted as a nodal metastasis as is a tumour nodule with the form and smooth contour of a lymph node in the connective tissue of a lymph drainage area (e.g., mesorectum) even if there is no histological evidence of residual lymphoid tissue. This probably represents a totally replaced lymph node, provided it is not recognisable as tumour in a vascular structure or perineural space. A tumour nodule with an irregular contour could be classified in the pT category, that is, as discontinuous extension, or is designated as a soft tissue tumour deposit or satellite. Dissection and submission of separate deposits is therefore important. When size is a criterion for pN classification, for example, vulval carcinoma, measurement is made of the metastasis, not of the entire node and will usually be made from the histological slides. Micrometastases ( $\leq 2$  mm) are designated pN1 (mi) and isolated tumour cells ( $\leq 0.2$  mm) pN0(i+) as they are not regarded as having metastatic potential. Most busy general laboratories submit small nodes ( $<5$  mm) intact or bisected and a mid-slice of larger ones. Additional slices are processed pending microscopy. Alternatively lymph nodes are serially sliced at 2–3 mm intervals and allocated a specific cassette. Sentinel nodes are handled in this way supplemented by use of block levels and immunohistochemistry. The limit node is the nearest node to the longitudinal and/or apical resection limits and suture ties. Some specimens, for example, transverse colectomy, will have more than one and they should be identified as such. Extracapsular spread is an adverse indicator more usually recognised histologically but should be noted on gross inspection if near to or impinging upon a resection margin, for example, axillary clearance in breast carcinoma. Non-regional lymph node involvement represents metastatic disease (pM).

## Excision Margins

The clearance of excision margins has important implications for patient follow-up, adjuvant therapy, and local recurrence of tumour. Measurements should be made on the gross specimen and checked against the histological slide. Painting of the margins by ink supplemented by labelling of the blocks is important. Paint adheres well to fresh specimens but also works on formalin-fixed tissue. India ink or alcian blue is commonly used. Commercially available multicoloured inks are helpful particularly if there are multiple margins as in breast carcinoma. If the intensity of the colour on the slide is low, it can be easily checked against the paraffin block. Paint is usually applied to margins prior to dissection but can be re-applied for further emphasis after obtaining the block along its edge. The relevance of particular margins (longitudinal, quadrant, transverse, circumferential, and anatomical) varies according to specimen and cancer type and is further discussed in their respective organ systems. In general terms, involvement of longitudinal margins can be by direct, discontinuous, or multifocal spread, for example, oesophageal carcinoma. Positive circumferential radial margins are an indicator of potential local recurrence and a gauge of cancer spread, local anatomy, and the extent of surgical excision. Peritoneal or pleural serosal disease allows potential trans-coelomic spread to other abdominopelvic organs or transpleural spread to the chest wall.

TNM classifies local resection as:

R0	No residual tumour
R1	Microscopic residual tumour (tumour transection or proven by tumour bed biopsy or cytology)
R2	Macroscopic residual tumour

## Other Pathology

Predisposing, concurrent, and associated conditions should be noted, blocked, and documented, for example, colorectal carcinoma and adenomatous polyps, gastric carcinoma and gastric atrophy or synchronous malignant lymphoma (MALToma).

## Ancillary Techniques in Histopathology Specimens

The vast majority of histopathology specimens can be adequately reported by close attention to careful gross description, dissection and block selection and microscopy of good quality formalin-fixed paraffin sections stained with haematoxylin and eosin. However, key ancillary techniques are required in a proportion of cases (see Chap. 46). Some examples are

*Frozen sections:* confirmation of parathyroidectomy, assessment of operative resection margins in cancer surgery, and cancer versus inflammatory lesions at laparotomy or thoracotomy.

*Histochemical stains:* demonstration of mucin in adenocarcinoma, congophilia in amyloid, iron in haemochromatosis, and organisms (pyogenic bacteria, tubercle, and fungus) in infection.

*Immunofluorescence:* glomerular deposits in renal biopsies, deposition of immunoglobulin, and complement in blistering skin disorders.

*Immunohistochemistry:* the surgical pathologist's "second H and E" and invaluable in assessing tumour type, prognosis, and predictive factors in treatment, for example, carcinoma (cytokeratins) versus malignant lymphoma (CD45) and malignant melanoma (S100), or better prognostic and hormone responsive breast cancer (oestrogen receptor positive). Tumour antigenic profile is often crucial in specifying the site of origin for a metastasis, for example, prostate carcinoma (PSA/PSAP positive).

*Electron microscopy:* valuable in medical renal biopsy diagnosis, and tumours where morphology and immunohistochemistry are inconclusive, for example, malignant melanoma (pre-/melanosomes) and neuroendocrine carcinoma (neurosecretory granules).

*Molecular and chromosomal studies:* immunoglobulin heavy chain and T cell receptor gene rearrangements in the confirmation of malignant lymphoma and the characterisation of various cancers (malignant lymphoma, sarcoma, and some carcinomas, e.g., renal) by specific chromosomal changes. Distinctive molecular findings in a wide range of solid tumours are being increasingly used with regard to diagnosis, prognosis, and predicting response to specific targeted therapies. This trend towards personalised oncological medicine also requires consideration of the pre-analytical phase with regard to optimal tissue preservation, fixation, and processing.

*Quantitative methods:* prognostic indicators include the Breslow depth of invasion in malignant melanoma, muscle fibre typing and diameter in myopathies, and the mitotic activity index in breast carcinoma.

---

## Diagnostic Cytology

Fine needle aspiration, exfoliative and body cavity fluid cytology all provide valuable complementary information in diagnosis and staging (see Chap. 46). The direct smear/cytospin/liquid based preparations are supplemented by formalin-fixed paraffin processed cell blocks of cell sediments and needle core fragments (mini-biopsies) which can combine good morphology and robust immunohistochemistry. Correlation between the cytology and histopathological findings is pivotal to accurate diagnosis (e.g., lung cancer) and staging (e.g., pelvic washings in gynaecological cancer). Cytology may also provide a diagnosis where biopsy fails due to sampling error, inaccessibility of the lesion, or biopsy crush artefact.

## Appendices

### Appendix A

#### Histopathology Specimen Pull-Through Protocol Specimen Type

- Urgent
- Frozen section
- Cell block—to correlate with corresponding cytology preparations
- Needle core biopsy
- Lymph node (diagnostic/sentinel)
- Bronchial/transbronchial/lung/pleural/mediastinal biopsy
- Temporal artery
- Cancer resection, wide local excision (WLE), endoscopic mucosal resection (EMR), GI polypectomy, TURBT, trachelectomy, microdochectomy, nipple biopsy
- Multidisciplinary Team Meeting (MDM/MDTM) cases
- Extras on cases pending (levels, blocks, stains)

ANY endoscopic or diagnostic biopsy specimen marked Red Flag/fast track or with the following *clinical* or *symptom terminology*:

#### Clinical Terminology (Abbreviations in Brackets)

* Mass	* Tumour	* Neoplasm (NG)
* Suspicious	* Malignant	* Carcinoma (Ca)
* Primary (1°)/Secondary (2°)	* Lymphoma (HD/NHL)	* Leukaemia
* Melanoma (MM)	* Sarcoma	* Mesothelioma
* Myeloma	* Seminoma/teratoma	* Stricture/ ulcer(ation)/ obstruction/ perforation
* SCC, TCC, AdCa, GCT, NSCLC, (P)NET, Carcinoid	* Paget's disease	* Severe/high grade dysplasia/carcinoma in situ
* Vasculitis/arteritis/ Wegener's	* Ectopic/molar gestation	* GvsHD/BMT
* ARF (acute renal failure)	* SLE/PAN	* Pneumonia/ consolidation
* Pyrexia		

#### Symptom Terminology

* Dysphagia	* Melaena	* Haematemesis
* PR bleed	* PMB	* Haemoptysis
* Haematuria	* Jaundice	

*Footnotes:*

TURBT	Transurethral resection bladder tumour
NG	New growth
MM	Malignant melanoma
HD	Hodgkin's disease
NHL	Non-Hodgkin's lymphoma
SCC	Squamous cell carcinoma or small cell carcinoma
TCC	Transitional cell carcinoma
AdCa	Adenocarcinoma
GCT	Germ cell tumour
NSCLC	Non-small cell lung cancer
(P)NET	Primitive neuroectodermal tumour
SLE	Systemic lupus erythematosus
PAN	Polyarteritis nodosa
GvsHD	Graft versus host disease
BMT	Bone marrow transplant

Dysphagia: difficulty in swallowing

Melaena: altered blood in the faeces

Haematemesis: vomiting blood

PR bleed: passage of blood per rectum

PMB: post-menopausal bleed

Haemoptysis: coughing up blood

Haematuria: blood in the urine

Jaundice: elevated bilirubin levels due to red blood cell destruction (haemolysis), hepatic damage, or bile duct obstruction

**Appendix B****Surgical Cut-Up: Principles and Practice**

Apprenticeship	Attitude/application/accountability
	Look/listen/lifelong learning—team work
	Do—focus/organisation
Patient details	Name/date of birth/health care number
Specimen details	Number of specimens/site/laterality/type
Form details	Clinical information/abbreviations
Clinical priority	Frozen/urgent/treatment decision/MDM case
Past and present	History/history/history
Knowledge base	Context/context/context
	Anatomy/clinical investigations/surgical procedures/pathology
Targeted dissection	<i>Tumour</i> : type/grade/stage/margins
	Fixation/sampling
	pT/pN/LVI
	Longitudinal, circumferential margins
	Diagrams and photographs



---

 Resources
 

---

1. Pull-through protocols
  2. Specimen dissection laboratory procedures/blocking summary sheets
  3. RCPATH Tissue Pathways/Cancer Dataset documents (audit standards)
  4. TNM8
  5. Local tissue pathology cancer report protocols
  6. Texts—Lester/Westra/Rosai/Allen
- 
- Reassess in light of further clinical information (MDM)/audit
- 

## Appendix C

### *Specimen dissection—a working practice*

1. Log the specimen into the computer and allocate a laboratory number.
2. Point out any urgent, fresh, or inadequately fixed specimens to a supervisory BMS so that appropriate action can be taken. Record on the request form.
3. With a supervisory BMS categorise the specimens (see Appendix D) and make a provisional allocation of work.
4. Send the request form of specimen categories C, D, and E to the secretarial office for registration and attachment of any computer back history. Return the forms to the laboratory staff so that specimen dissection can proceed. Categories A and B are usually loaded into the processing cassettes before registration.
5. Preview—consult with the supervisory medical pathologist about the more complex specimens (mainly categories C, D, and E) to confirm categorisation, reassign categorisation, or to discuss the special needs/work allocation of particular specimens. The medical pathologist authorises request forms at this stage.
6. Cut-up
  - Work in pairs, one to dissect and describe, the other to write, prepare cassettes, cross check data, observe, and confirm findings. The second person can also have a supervisory, training role as appropriate.
  - Check and sign off request form and specimen container label details, i.e.,
    - Patient name
    - Patient date of birth
    - Patient unit number
    - Specimen type, parts, and numbering
    - Laboratory reference number and cassette labels.
  - Dissect to your level of experience and competence to obtain an accurate description and relevant blocks and also to allow a subsequent meaningful review process.
  - Float out the cassettes with their blocks in formalin.
  - Set the specimens (mainly categories C, D, and E) aside on and covered by appropriately numbered wet paper towels with the corresponding request form beside them.