Cancer of the Exocrine Pancreas, Ampulla of Vater and Distal Common Bile Duct

STRUCTURED REPORTING PROTOCOL

(1st Edition 2014)

Core Document versions:

- AJCC Cancer Staging Manual 7th edition (including errata corrected with 5th reprint 10th Aug 2010).
- World Health Organization Classification of Tumours Pathology and Genetics of Tumours of the Digestive System, 2010, 4th edition

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The Royal College of Pathologists of Australasia ("College") has developed these protocols as an educational tool to assist pathologists in reporting of relevant information for specific cancers. While each protocol includes "standards" and "guidelines" which are indicators of 'minimum requirements' and 'recommendations', the protocols are a first edition and have not been through a full cycle of use, review and refinement. Therefore, in this edition, the inclusion of "standards" and "guidelines" in each document are provided as an indication of the opinion of the relevant expert authoring group, but should not be regarded as definitive or as widely accepted peer professional opinion. The use of these standards and guidelines is subject to the clinician's judgement in each individual case.

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Contents

Scope

This protocol contains standards and guidelines for the preparation of structured reports for cancer of the exocrine pancreas, ampulla of Vater and distal common bile duct. It excludes cancer of the duodenum apart from those occurring in the periampullary region and neuroendocrine tumours.

Structured reporting aims to improve the completeness and usability of pathology reports for clinicians, and improve decision support for cancer treatment.

This document is based on information contained within multiple international publications and datasets and has been developed in consultation with local practising pathologists, oncologists, surgeons and interested national bodies.

Abbreviations

AJCC	American Joint Committee on Cancer
LIS	laboratory information system
PD	pancreaticoduodenectomy
RCPA	Royal College of Pathologists of Australasia
SMA	superior mesenteric artery
SMV	superior mesenteric vein
TNM	tumour-node-metastasis
WHO	World Health Organization

Definitions

The table below provides definitions for general or technical terms used in this protocol. Readers should take particular note of the definitions for 'standard', 'guideline' and 'commentary', because these form the basis of the protocol.

Ancillary study	An ancillary study is any pathology investigation that may form part of a cancer pathology report but is not part of routine histological assessment.
Clinical information	Patient information required to inform pathological assessment, usually provided with the specimen request form. Also referred to as 'pretest information'.
Commentary	Commentary is text, diagrams or photographs that clarify the standards (see below) and guidelines (see below), provide examples and help with interpretation, where necessary (not every standard or guideline has commentary). Commentary is used to: • define the way an item should be reported, to foster reproducibility • explain why an item is included (e.g. how does the item assist with clinical management or prognosis of the specific cancer). • cite published evidence in support of the standard or guideline • clearly state any exceptions to a standard or guideline. • In this document, commentary is prefixed with 'CS' (for commentary on a standard) or 'CG' (for commentary on a guideline), numbered to be consistent with the relevant standard or guideline, and with sequential alphabetic lettering within each set of commentaries (e.g. CS1.01a, CG2.05b).
General commentary	General commentary is text that is not associated with a specific standard or guideline. It is used: • to provide a brief introduction to a chapter, if necessary • for items that are not standards or guidelines but are included in the protocol as items of potential importance, for which there is currently insufficient evidence to recommend their inclusion. (Note: in future reviews of protocols, such items may be reclassified as either standards or guidelines, in line with diagnostic and prognostic advances, following evidentiary review).
Guideline	Guidelines are recommendations; they are not mandatory, as indicated by the use of the word 'should'. Guidelines cover items that are not essential for clinical management, staging or prognosis of a cancer, but are recommended. Guidelines include key observational and interpretative findings that are fundamental to the diagnosis and conclusion. Such

	findings are essential from a clinical governance perspective, because they provide a clear, evidentiary decision-making trail. Guidelines are not used for research items. In this document, guidelines are prefixed with 'G' and numbered consecutively within each chapter (e.g. G1.10).
Predictive factor	A *predictive factor* is a measurement that is associated with response or lack of response to a particular therapy.
Prognostic factor	A *prognostic factor* is a measurement that is associated with clinical outcome in the absence of therapy or with the application of a standard therapy. It can be thought of as a measure of the natural history of the disease.
Macroscopic findings	Measurements, or assessment of a biopsy specimen made by the unaided eye.
Microscopic findings	In this document, the term 'microscopic findings' refers to histological or morphological assessment.
Standard	Standards are mandatory, as indicated by the use of the term 'must'. Their use is reserved for core items essential for the clinical management, staging or prognosis of the cancer and key information (including observations and interpretation) which is fundamental to the diagnosis and conclusion. These elements must be recorded and at the discretion of the pathologist included in the pathology report according to the needs of the recipient of the report. The summation of all standards represents the minimum dataset for the cancer. In this document, standards are prefixed with 'S' and numbered consecutively within each chapter (e.g. **S1.02**).
Structured report	A report format which utilises standard headings, definitions and nomenclature with required information.
Synoptic report	A structured report in condensed form (as a synopsis or precis).
Synthesis	Synthesis is the process in which two or more pre-existing elements are combined, resulting in the formation of something new. The Oxford dictionary defines synthesis as "the combination of components or elements to form a connected whole". In the context of structured pathology reporting, synthesis represents the integration and interpretation of information from two or more modalities to derive new information.

Introduction

Cancer of the exocrine pancreas, ampulla of Vater and distal common bile duct

Pancreatic, ampullary, distal common bile duct and duodenal cancers occurring within the region of the duodenal papilla are often collectively referred to as periampullary cancers. The vast majority (90%) of these cancers are adenocarcinomas, which arise in the exocrine pancreas (43-77%), followed by adenocarcinomas of the ampulla (11-12%), distal common bile duct (10-11%) and duodenum (4-5%).[1-3]

Australian data for 'pancreatic cancer' show that it is the 6th highest cause of cancer related deaths with a dismal 5 year survival of 6%. Although separate Australian mortality data is not available for ampullary, distal common bile duct and duodenal cancer, reports from the literature indicate that patients with ampullary and distal common bile duct adenocarcinoma have significantly improved 5 year overall survival rates (53-66% and 50-74% respectively) after resection, in contrast to patients with pancreatic adenocarcinoma (13-55%).[1,4] Tumour staging and eligibility for adjuvant therapy also depend on tumour origin, emphasising the need to accurately identify and report these tumours accordingly.[1,2,4-9]

The true origin of carcinomas arising in this region may be difficult to determine due to the size of these tumours relative to normal structures, the 'field effect' of dysplasia and the ability of carcinomas to colonise epithelial surfaces and mimic dysplasia.[10] Nevertheless, an informed decision can be made in many cases through detailed macroscopic and microscopic assessment.[11]

Recent advances in the understanding of the biology of these tumours has driven requirements for detailed assessment and reporting of these surgical specimens. Endocrine, haematological and mesenchymal neoplasms occurring within the pancreas have different requirements for reporting and these will be covered by separate protocols.

Benefits of structured reporting

Structured pathology reports with standardised definitions for each component have been shown to significantly improve the completeness and quality of data provided to clinicians, and has been recommended both in North America and the United Kingdom.[12-15]

The College of American Pathologists and the Royal College of Pathologists (United Kingdom) have recently published useful protocols for the reporting of cancer.[16] These have been widely used in recent years in Australia and New Zealand, usually in modified formats to suit local requirements and preferences. A protocol endorsed by the Royal College of Pathologists of Australasia and other local organisations involved in the management of periampullary cancer is therefore needed. The authors have not attempted to 're-invent the wheel' but have borrowed freely from pre-existing publications. The intention is to provide pathologists with a minimum dataset and guidelines that are comprehensive, easy to use, and in keeping with local capacity and practice.

Design of this protocol

This protocol defines the relevant information to be assessed and recorded in a pathology report for cancer of the exocrine pancreas, ampulla of Vater, distal common bile duct and duodenum in the periampullary region. Mandatory elements (standards) are differentiated from those that are not mandatory but are recommended (guidelines). Also, items suited to tick boxes are distinguished from more complex elements requiring free text or narrative. The structure provided by the following chapters, headings and subheadings describes the elements of information and their groupings, but does not necessarily represent the format of either a pathology report (Chapter 7) or checklist (Chapter 6). These, and the structured pathology request form (Appendix 1), are templates representing information from this protocol, organised and formatted differently to suit their respectively different purposes.

It should be noted that if the resection specimen contains two or more primary carcinomas (as indicated by the term 'synchronous carcinomas' on the reporting checklist) then a separate reporting checklist must be completed for each primary carcinoma.

Key documentation

- Tumours of the exocrine pancreas In: *Pathology and Genetics of Tumours of the Digestive System.* World Health Organization Classification of Tumours, 2010[17]
    - Tumours of the pancreas, p.280
    - Tumours of the ampullary region, p.82
    - Tumours of the gallbladder and extrahepatic bile ducts, p.264
    - Tumours of the small intestine, p.96
- *AJCC Cancer Staging Manual*, 7th edition, American Joint Committee on Cancer, 2010[9]
- *Guidelines for Authors of Structured Cancer Pathology Reporting Protocols*, Royal College of Pathologists of Australasia, 2009[18]
- *The Pathology Request–Test–Report Cycle — Guidelines for Requesters and Pathology Providers*, Royal College of Pathologists of Australasia, 2004[19]

Changes since last edition

Not applicable.

Authority and development

This section provides details of the committee involved in developing this protocol and the process by which it was developed.

Protocol developers

This protocol was developed by an expert committee, with assistance from relevant stakeholders.

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Acknowledgements

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Stakeholders

ACT Health
Anatomical Pathology Advisory Committee (APAC)
Australian Association of Pathology Practices Inc (AAPP)
Australian Cancer Network
Australian Commission on Safety and Quality in Health Care
Australasian Pancreatic Club
Cancer Australia
Cancer Council ACT
Cancer Council NSW
Cancer Council Queensland
Cancer Council SA
Cancer Council Tasmania
Cancer Council Victoria
Cancer Council Western Australia
Cancer Institute NSW
Cancer Services Advisory Committee (CanSAC)

Cancer specific expert groups – engaged in the development of the protocols
Cancer Voices
Colorectal Cancer Research Consortium
Clinical Oncology Society of Australia (COSA)
Colorectal Surgical Society of Australia and New Zealand (CSSANZ)
Department of Health and Ageing
Grampians Integrated Cancer Services (GICS)
Health Informatics Society of Australia (HISA)
Independent Review Group of Pathologists
Medical Software Industry Association (MSIA)
National Breast and Ovarian Cancer Centre (NBOCC)
National Coalition of Public Pathology (NCOPP)
National E-Health Transition Authority (NEHTA)
National Pathology Accreditation Advisory Council (NPAAC)
National Round Table Working Party for Structured Pathology Reporting of Cancer.
New Zealand Guidelines Group (NZGG)
NSW Department of Health
NZ Ministry of Health
Peter MacCallum Cancer Institute
Queensland Cooperative Oncology Group (QCOG)
Representatives from laboratories specialising in anatomical pathology across Australia
Royal Australasian College of Physicians (RACP)
Southern Cancer Network, Christchurch, New Zealand
Southern Melbourne Integrated Cancer Service (SMICS)
Standards Australia
Sydney Upper Gastrointestinal Surgical Society (SUGSS)
The Australasian Gastro-Intestinal Trials Group (AGITG)
The Medical Oncology Group of Australia
The Royal Australasian College of Surgeons (RACS)
The Royal Australian and New Zealand College of Radiologists (RANZCR)
The Royal Australian College of General Practitioners (RACGP)
The Royal College of Pathologists of Australasia (RCPA)
Victorian Cooperative Oncology Group (VCOG)
Western Australia Clinical Oncology Group (WACOG)

Secretariat

Meagan Judge, Royal College of Pathologists of Australasia

Development process

This protocol has been developed following the seven-step process set out in *Guidelines for Authors of Structured Cancer Pathology Reporting Protocols*.[18]

Where no reference is provided, the authority is the consensus of the expert group.

1 Pre-analytical

This chapter relates to information that should be recorded on receipt of the specimen in the laboratory.

The pathologist is reliant on the quality of information received from the clinicians or requestor. Some of this information may be received in generic pathology request forms, however, the additional information required by the pathologist specifically for the reporting of periampullary cancers is outlined in Appendix 1. Appendix 1 also includes a standardised request information sheet that may be useful in obtaining all relevant information from the requestor**.**

Surgical handling procedures affect the quality of the specimen and recommendations for appropriate surgical handling are included in Appendix 1.

S1.01 All demographic information provided on the request form and with the specimen must be recorded.

CS1.01a The Royal College of Pathologists of Australasia (RCPA) *The Pathology Request-Test-Report Cycle — Guidelines for Requesters and Pathology Providers* must be adhered to.[19] This document specifies the minimum information to be provided by the requesting clinician for any pathology test.

CS1.01b The patient's ethnicity must be recorded, if known. In particular whether the patient is of aboriginal or Torres Strait islander origin. This is in support of a government initiative to monitor the health of indigenous Australians particularly in relation to cancer.

CS1.01c The patient's health identifiers may include the patient's Medical Record Number as well as a national health number such as a patient's Medicare number (Australia), Individual Healthcare Identifier (IHI) (Australia) or the National Healthcare Identifier (New Zealand).

S1.02 All clinical information as documented on the request form must be recorded verbatim.

CS1.02a The request information may be recorded as a single text (narrative) field or it may be recorded in a structured format.

S1.03 The pathology accession number of the specimen must be recorded.

G1.01 Any clinical information received in other communications from the requestor or other clinician should be recorded.

2 Specimen handling and macroscopic findings

This chapter relates to the procedures required after the information has been handed over from the requesting clinician and the specimen has been received in the laboratory.

Tissue banking

- Pathologists may be asked to provide tissue samples from fresh specimens for tissue banking or research purposes. The decision to provide tissue should only be made if ethics approval has been obtained and the pathologist is sure that the diagnostic process and pathological evaluation will not be compromised. As a safeguard, research use of the tissue samples may be put on hold until the diagnostic process is complete.

Specimen handling

- **The specimen must be handled in a systematic and thorough fashion to ensure completeness and accuracy of pathological data.**

  - **Specimen reception:** Specimens are ideally received fresh and without delay. This allows timely frozen section analysis, optimal orientation and sampling of fresh tissue e.g. tumour bank, research. Where receipt of fresh specimen is impractical, the specimen should be sent in an adequate volume of formalin.

  - **Specimen inspection:** Based on the preoperative diagnosis, pancreaticoduodenectomy (PD) specimens often require frozen section analysis of the pancreatic neck and/or proximal bile duct margin. The specimen is orientated, preferably with the assistance of markers to key margins and/or by a surgical team member. The macroscopic impression of tumour distance to the relevant frozen section margin(s) is assessed and appropriate sampling of the margin undertaken.

    Transduodenal or endoscopic ampullectomies may be performed in some institutions for ampullary adenocarcinoma in highly selected patients.[20-22] These specimens are often best received pinned onto a board to facilitate identification of the ampullary duct at the crucial deep margin. Surgical marking of the duct is again optimal for orientation.

  - **Marking of resection margins/surfaces**: The margins (see Figure SH1 and SH2) that require identification in PD specimens include:

    - pancreatic transection (neck or body) margin,
    - posterior pancreatic margin,
    - superior mesenteric artery (otherwise known as uncinate) margin,
    - superior mesenteric vein (otherwise known as vascular groove) margin,

- bile duct margin,
- proximal gastric or duodenal margin and
- distal duodenal or jejunal margin.

The anterior portion of the pancreas is identified as a surface rather than a true margin, as surgical transection or dissection is not required. Involvement of this surface implies risk of peritoneal dissemination, whereas tumour at a dissected margin implies residual disease.[23] In some cases, the anterior surface is adherent to other structures, such as the mesocolon and requires en bloc resection. In such cases, the anterior surface may in fact comprise other structures and require reporting as a 'true' margin rather than a surface.

Other structures which may be included as margins, such as portal or superior mesenteric vein should be identified and inked (see Figure S3.09 in Chapter 3) to facilitate identification in microscopic sections. If there is a segment of superior mesenteric vein or portal vein attached to the vascular groove, the ends of the segment represent true resection margins. Likewise, if only a portion of the circumference of the vessel is included (tangential resection), the sides are also resection margins (see Figure S3.09 in Chapter 3).

The transected bile duct and/or pancreatic (neck/body) margins may have been sampled en face at the time of frozen section. If not, these and the remaining margins should be covered in different coloured inks, routine to each department prior to further dissection (see Fig SH1 and SH2).

The anterior surface, posterior margin and pancreatic transection margin of distal pancreatectomy specimens may be painted in different coloured inks, again according to each department's routine.

Ampullectomy specimens, unless specifically orientated by the surgical team, should have ink applied to the deep margin of the specimen. Invasive carcinoma at this margin may dictate the need for salvage PD in surgically fit patients.[20]

- **Tumour inspection and banking:** The stomach if present and duodenum can be opened along the lesser curvature and ante-mesenteric border respectively in order to avoid the duodenal papillae. Leaving the duodenal papillae intact facilitates assessment of tumour origin.

  Procedures required for tumour banking of fresh tissue (see section on Tissue banking) can now be performed and the specimen partially sectioned to aid fixation. The method of partial dissection will depend on the method adopted for final dissection. The fresh specimen after partial dissection may be pinned onto a board and placed into a large volume of formalin to fix for 24-48 hours.

- **Specimen Dissection:** Several different techniques are used for dissection of PD specimens and are illustrated in Fig SH3.[24,25] These include:

  1. Sectioning along the plane of the pancreatic and common bile

ducts.

2. Sectioning perpendicular to the main pancreatic duct or 'bread-loaf' slicing.

3. Sectioning the entire pancreatic head and duodenum perpendicular to the long axis of the duodenum ('axial sectioning').

4. Sectioning perpendicular to the common bile duct up to the periampullary region, followed by sectioning along the plane of the ampullary duct in the immediate periampullary region.

Advantages and disadvantages exist for all the aforementioned techniques. Importantly, the dissection method and subsequent blocking of specimens should be standardised by individual departments. The selected technique should allow detailed viewing of tumour relationship to key anatomical structures as well as resection margins and surfaces. Recent studies highlight the value of standardised macroscopic dissection of PD specimens for improved recognition of tumour origin and R1 rates.[24,26-28]

Distal pancreatectomy specimens can be serially sectioned transversely after painting and fixation. Total pancreatectomy specimens can be handled by combining the technique adopted for PD followed by serial transverse sectioning of the distal pancreas.

It is recommended that serial transverse sections of ampullectomy specimens be taken with attention to demonstrating the ampullary duct extending to the deep margin.

- **Block selection:** The tumour and surrounding parenchyma should be examined at 3-4mm intervals. Blocks are selected to show the relationship of tumour to anatomical structures relevant to T-staging such as the duodenum, ampulla, peripancreatic tissues and common bile duct.[9]

  Blocks should also be taken to show the tumour's closest distance to resection margins and surfaces. Pancreatic tumours have a dispersed pattern of growth, the full extent of which may not be appreciated macroscopically,[26] therefore extensive sampling of the tumour and margins may be required.

  Samples of uninvolved ampulla of Vater, common bile duct, duodenum and pancreas should be taken. Sections of these structures adjacent to the invasive tumour can facilitate the identification of preinvasive lesions, which in turn may assist in defining tumour origin.

  Representative sections of any other attached or separately received organs such as gallbladder, omentum or spleen should be taken.

  Ampullectomy specimens in most instances require submission of the entire specimen for histology.

- **Lymph node sampling:** All lymph nodes should be submitted. Macroscopically uninvolved lymph nodes need to be entirely embedded. Macroscopically involved lymph nodes require only 1 block for

confirmation.

Regional lymph nodes are the same for distal common bile duct, head and neck of pancreas cancers; i.e., nodes along the common bile duct, common hepatic artery, portal vein, posterior and anterior pancreaticoduodenal arcades and along the superior mesenteric vein and right lateral wall of the superior mesenteric artery.[9] For cancers located in the body and tail, regional lymph nodes include lymph nodes along the common hepatic artery, coeliac axis, splenic artery and splenic hilum.

For cancers located in the ampulla of Vater, regional lymph nodes are the peripancreatic lymph nodes including lymph nodes along the hepatic artery and portal vein.

Anatomic separation of regional lymph nodes is not necessary, however separately submitted lymph nodes should be reported as labelled.

A standard Whipple's or pylorus preserving PD resection should yield a minimum of 12 lymph nodes from the main specimen.[9,29,30] Fewer lymph nodes may be found following neoadjuvant therapy.

Fig SH1 Pancreaticoduodenectomy specimen. A. The retroperitoneal surgical margin. B. A diagrammatic mapping of the same specimen highlighting its various elements; 1. Posterior surface, 2. Uncinate margin, 3. The medial part of the vascular groove (the more lateral part is obscured by the uncinate process tip, 4. The medial aspect or posterior surface of pancreatic neck/body (only in cases with extended pancreatic resection), 5. A superior mesenteric lymph node that is not part of the retroperitoneal margin but happened to be excessively enlarged in this particular case. Reproduced with permission from Khalifa MA, Maksymov V and Roswell C (2009). *Virchows Arch.* 454:125-131.

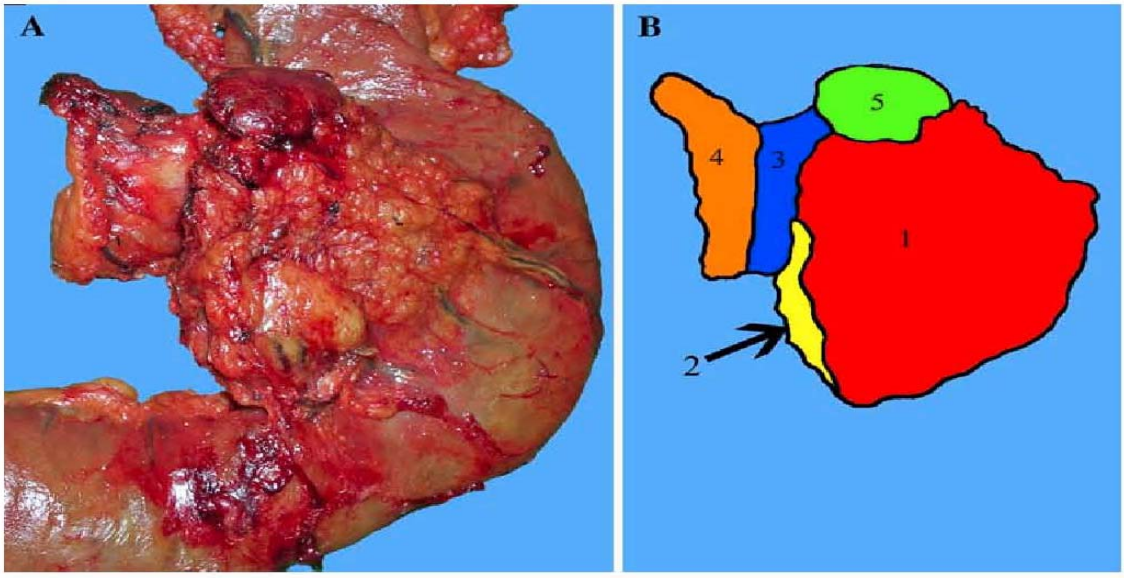


Fig SH2 A pancreaticoduodenectomy (Whipple's) specimen viewed from the medial aspect. The blue ink designates the pancreatic transection (neck) margin, the red ink marks the superior mesenteric vein/vascular groove margin and the green ink is on the superior mesenteric artery/uncinate margin. Reproduced with permission from Gill AJ et al Pathology 2009;41:161-72

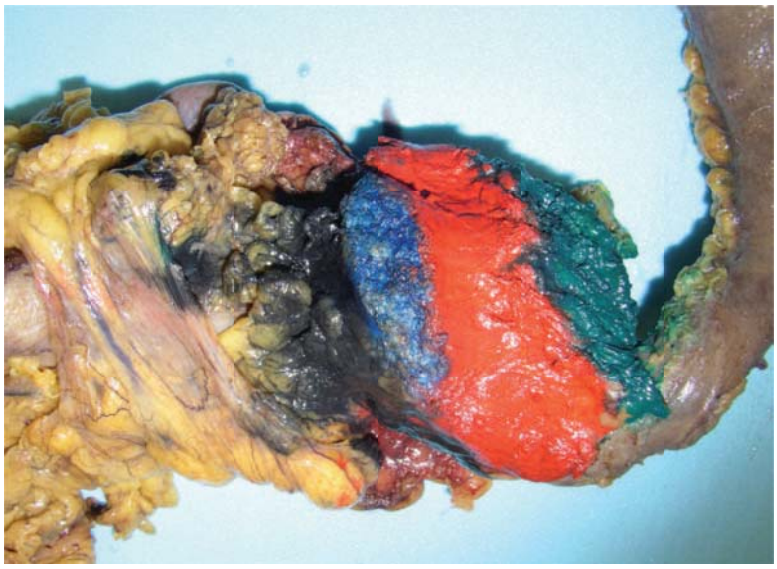
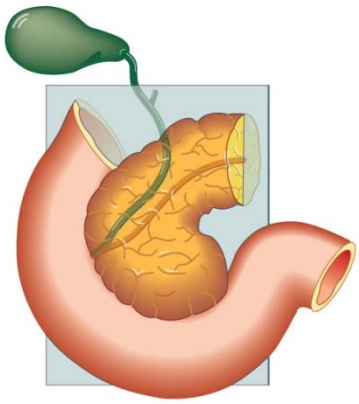


Fig SH3 Different methods of sectioning PD specimens (a) sectioning along the plane of the main pancreatic duct and common bile duct, (b) sectioning perpendicular to the main pancreatic duct, (c) sectioning in an axial plane, perpendicular to the duodenum, (d) sectioning perpendicular to the common bile duct followed by sectioning along the ampullary duct.

A.



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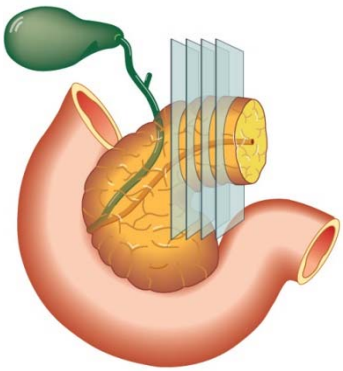
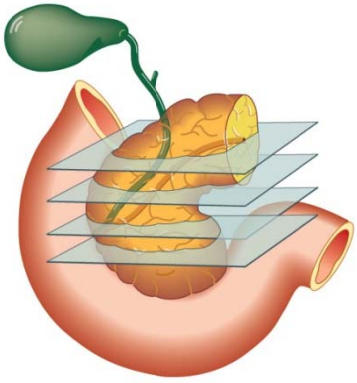
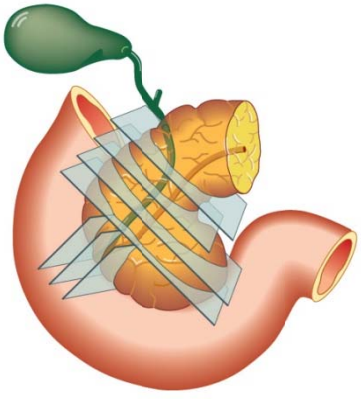


C.



D.



Macroscopic findings

S2.01 Record specimen labelling.

S2.02 The anatomical structures included in the specimen and dimensions of each structure in mm must be recorded.

CS2.02a Choose from one or more of the following structures:

- Pancreas (include portion(s) of pancreas included i.e. head, neck, body and/or tail) – measure in 3 dimensions
- Duodenum – length and maximum diameter
- Stomach – length along lesser and greater curvature
- Common bile duct – length and maximum diameter
- Gallbladder – length and maximum diameter
- Spleen – measure in 3 dimensions
- Adjacent large vessels – measure in 3 dimensions if tangential resection of the vessel has been performed or measure length and diameter if the whole circumference of the vessel is present,
    - Portal vein
    - Superior mesenteric vein
    - Other large vessel (specify)
- Other (specify)

CS2.02b Any separately submitted specimens such as lymph nodes or omentum must be recorded.

G2.01 The presence or absence of a stent should be recorded.

CG2.01a If present the location of the stent should be recorded.

S2.03 The macroscopic tumour site must be recorded.

CS2.03a Choose from one or more of the following locations based on assessment of tumour bulk:

- Head of pancreas
- Neck of pancreas
- Body of pancreas
- Tail of pancreas

- Uncinate process
- Ampulla of Vater
- Common bile duct (extrapancreatic or intrapancreatic)
- Duodenum
- Other (specify)

CS2.03b Tumours of the head of the pancreas are those arising to the right of the left border of the superior mesenteric vein. The uncinate process is the prolongation of the head that extends inferiorly and to the left. Tumours of the body of the pancreas are those arising between the left border of the superior mesenteric vein and the left border of the aorta. Tumours of the tail are those arising between the left border of the aorta and the hilum of the spleen.[9]

Tumours arising from the neck of the pancreas may be difficult to recognise macroscopically, however preoperative imaging and intraoperative information may indicate that this is the tumour site. Although infrequent, enucleation or partial resection of a tumour in the neck region may be undertaken and therefore this has been included as an option for tumour location.

CS2.03c Final tumour site is a synthesis of macroscopic and microscopic assessment of tumour bulk as tumour can often infiltrate beyond the confines of the macroscopic abnormality.[31] The finding of a preinvasive lesion is another factor that needs to be considered in the overall assessment of tumour site.[11,32]

Difficulties in assigning tumour site arise due to several factors including:

- the ability of periampullary cancers to colonise epithelial surfaces thereby mimicking preinvasive lesions,
- the relative large size of invasive cancers that obliterate pre-existing structures and/or lesions, and
- the high prevalence of low-grade pancreatic intraepithelial neoplasia, which may complicate assessment of the relative significance of any preinvasive lesions present.[10]

Nevertheless, detailed macroscopic and microscopic assessment combined with any radiological information obtained will often allow accurate determination of tumour site.[11]

S2.04 The maximum tumour diameter must be recorded.

CS2.04a For multiple tumours the diameter of the each focus should be recorded.

S2.05 A macroscopic tumour description must be provided.

CS2.05a The presence of an exophytic, cystic or mucinous component to the tumour should be described. These findings provide information

regarding the nature of either a coexisting preinvasive lesion or the invasive component itself.

For ampullary tumours, a description of whether the tumour is intra-ampullary, mixed intra-ampullary and peri-ampullary (for tumours growing toward the duodenal lumen) or entirely peri-ampullary is recommended.[9,31] In addition, whether the ampullary tumour is 'flat' or 'polypoid' should be recorded as there is increasing recognition that 'ampullary' carcinomas comprise a histologically heterogeneous group of cancers that display not only differences in macroscopic appearance, but also immunophenotype and behaviour.[32,33]

S2.06 The macroscopic distance of tumour to the margins/surfaces must be recorded.

CS2.06a The distance of tumour to each of the following margins/surfaces should be recorded:

- Pancreatic transection
- Superior mesenteric artery
- Posterior pancreatic
- Superior mesenteric vein/vascular groove
- Anterior pancreatic
- Bile duct
- Proximal intestinal/gastric
- Distal intestinal
- Other (specify)

G2.02 Macroscopic evidence of any other abnormality or co-existing pathology should be recorded.

CG2.02a Examples include cystic lesions, calculi or chronic pancreatitis.

G2.03 Whether or not a tissue block has been taken for research or tissue banking should be recorded.

CG2.03a Pathologists may be asked to provide tissue samples from fresh specimens for tissue banking or research purposes. The decision to provide tissue should only be made when Human Research Ethics Committee approval for the process has been obtained and the pathologist is sure that the diagnostic process including the measurement of maximum extent of invasion and other important parameters that influence patient prognosis and management will not be compromised. As a safeguard, research use of the specimen may be put on hold until the diagnostic process is complete so that the specimen can be retrieved. If for any reason, Ethics approval or patient consent is not obtained, the research sample can be discarded or processed for diagnostic use.

G2.04 The availability of any photographs taken during the cut-up process should be noted.

CG2.04a A specimen photograph is particularly useful if the person performing the cut up is not the pathologist reporting the specimen. Specimen photographs are also helpful in communicating with the surgeon, at tumour board meetings and for case presentations and reports.

S2.07 The nature and sites of all blocks must be recorded.

G2.05 A descriptive or narrative field should be provided to record any macroscopic information that is not recorded in the above standards and guidelines, and that would normally form part of the macroscopic description.

CG2.05a The traditional macroscopic narrative recorded at the time of specimen dissection is often reported separately from the cancer dataset. Although this remains an option, it is recommended that macroscopic information be recorded within the overall structure of this protocol.

CG2.05b Much of the information recorded in a traditional macroscopic narrative is covered in the standards and guidelines above and in many cases, no further description is required.

3 Microscopic findings

Microscopic findings relate to purely histological or morphological assessment. Information derived from more than one type of investigation (e.g. clinical, macroscopic and microscopic findings), are described in Chapter 5.

S3.01 The WHO histological tumour type must be recorded.

CS3.01a The histological type of the tumour should be recorded based on the current WHO classification[17] (refer to Appendices 4-7).

S3.02 The histological grade must be recorded.

CS3.02a The tumour should be graded according to the TNM/AJCC system, which assesses the degree of gland formation[a]:

- Grade X: Cannot be assessed
- Grade 1: Well differentiated (greater than 95% of tumour composed of glands)
- Grade 2: Moderately differentiated (50% to 95% of tumour composed of glands)
- Grade 3: Poorly differentiated (49% or less of tumour composed of glands)
- Grade 4: Undifferentiated (5% or less of tumour composed of glands)

High histological grade (grades 3 and 4) has been shown to be an adverse prognostic factor in some series.[34-36]

Other methods of grading pancreatic ductal adenocarcinoma such as the Klöppel and Adsay systems are in use.[36,37] The Klöppel system takes into account gland formation, nuclear changes, mitotic count and mucin production by the tumour. The system proposed by Adsay and colleges is based on patterns of infiltration akin to Gleason scoring for prostate carcinoma and has been shown to have prognostic value but is currently not widely adopted.[36] No difference in predictive value has been shown between the TNM and Klöppel grading system.[37]

S3.03 The microscopic tumour site must be recorded.

CS3.03a Tumour site is a synthesis of macroscopic and microscopic findings. The assessment is based on tumour bulk in relation to normal structures and the presence/absence of an associated preinvasive

[a] Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer Science and Business Media LLC, www.springerlink.com.

lesion.[11]

Any imaging information provided/obtained can also be amalgamated in the final assessment. The labelling of tumour site has important consequences for staging, therapy and prognosis.[1,2,4-9] Although immunohistochemistry may be used to determine whether an ampullary adenocarcinoma is of pancreaticobiliary or intestinal phenotype, there are currently no markers to assist in the separation of ampullary, distal bile duct and pancreatic adenocarcinomas.[38-40]

S3.04 The maximum extent of tumour invasion must be recorded.

CS3.04a Choose one or more of the following options:

- Pancreas
- Celiac axis
- Superior mesenteric artery
- Ampulla of Vater
- Sphincter of Oddi
- Duodenal wall
- Peripancreatic soft tissues
- Bile duct
- Gallbladder
- Other adjacent organs or structures (specify)

CS3.04b Determination of peripancreatic soft tissue invasion can be difficult as the pancreas lacks a true capsule separating the parenchyma from surrounding connective tissue. The frequent co-occurrence of chronic pancreatitis results in atrophy and distortion of the parenchyma, rendering interpretation of peripancreatic invasion even more difficult in some cases. Not infrequently the peripancreatic adipose tissue dips into the pancreatic parenchyma and invasion of this compartment should not be interpreted as peripancreatic invasion.

Identification of invasive glands beyond the contour/confines of any benign glandular tissue delineated on low magnification can assist in defining peripancreatic soft tissue invasion.

S3.05 The maximal dimension of tumour must be recorded.

CS3.05a A final estimate of the maximum dimension of the tumour should be given based on both the macroscopic and microscopic findings.

Head of pancreas carcinomas can have a highly dispersed pattern of growth. At the invasive front of the tumour it is not uncommon to identify small clusters of or single tumour cells widely separated

from the main tumour mass.[41] These microscopic foci should be incorporated into the final measurement of maximum tumour dimension.

S3.06 The presence or absence of lymphovascular invasion must be recorded.

CS3.06a Lymphovascular invasion must be recorded as not identified, suspicious or present, and if present, the type of vessel, "artery, vein or small vessel" should be recorded.

It may be difficult if not impossible to separate lymphatics from capillaries and small veins and therefore these are often grouped together as 'small vessel' invasion. Small veins may have a variable amount of recognisable muscular media and in larger veins, elastic tissue is present. The use of an elastic stain such as Verhoff Van Geisen (VVG) or immunohistochemistry for h-caldesmon may assist in the identification of venous invasion in a similar fashion to cases of colorectal carcinoma and may be especially useful to detect a form of vascular invasion that mimics pancreatic intraepithelial neoplasia.[42,43]

CS3.06b Lymphovascular invasion has been shown to be an adverse prognostic factor in periampullary carcinomas.[42,44-46]

CS3.06c Extended pancreatic resection with en bloc vascular resection (portal vein, superior mesenteric vein, hepatic artery or superior mesenteric artery) is been practiced with increasing frequency in many centres worldwide.[47]

Several studies have suggested that prognosis after pancreatic and portal vein resections is related to the depth of invasion into the vessel wall.[48,49] Survival of patients with invasion up to the tunica adventitia is almost similar to survival of patients without portal vein resection and of those without portal vein wall invasion. However, survival of patients with invasion into tunica media or tunica intima is almost similar to that of patients undergoing a non-curative resection.[23]

S3.07 The presence or absence of perineural invasion must be recorded.

CS3.07a Perineural invasion must be recorded as not identified, suspicious or present.

CS3.07b Perineural invasion has been shown to be an adverse prognostic factor for periampullary carcinoma.[45,50-52]

G3.01 Perineural invasion of the superior mesenteric artery margin neural plexus should be recorded.

CG3.01a Perineural invasion must be recorded as neural plexus not received, not identified, suspicious or present.

CG3.01b The superior mesenteric nerve plexus is present in the connective tissue surrounding the superior mesenteric artery and is usually resected as part of this margin (otherwise known as the uncinate margin). The surgeon needs to divide the connective tissue

adjacent to the uncinate process as close to the superior mesenteric artery as possible to gain clearance in this region, thereby in most instances incorporating the neural plexus.

CG3.01c Invasion of the extrapancreatic neural plexus in the region of the SMA margin is often associated with involved margins and therefore local recurrence.[53]

G3.02 The regression grade should be recorded for cases which have received preoperative chemotherapy or radiotherapy.

CG3.02a Responses will include: not known, no prior treatment or a Grade 0-3.

CG3.02b The following grading schema, though based on a study originally applied to rectal cancer, is recommended by the College of American Pathologists since it is simple and similar to that used in other organs. More specialised pancreatic cancer specific grading systems have been published, such as that of Breslin *et al.*[54], however these are too complex for routine use and are more suited to the research setting.

Tumour regression grade	**Description**
0 (complete response)	No viable cancer cells
1 (moderate response)	Single cells or small groups of cancer cells
2 (minimal response)	Residual cancer outgrown by fibrosis
3 (poor response)	Minimal or no tumour kill; extensive residual cancer

G3.03 The presence or absence of a preinvasive lesion should be recorded.

CG3.03a The nomenclature of preinvasive lesions of the periampullary region should follow the current WHO classification system[17]

Preinvasive lesions of the pancreas include:

1. Pancreatic intraepithelial neoplasia (PanIN)
2. Intraductal papillary mucinous neoplasms (IPMN)
3. Intraductal tubulopapillary neoplasm (ITPN)
4. Mucinous cystic neoplasms (MCN)

PanIN by definition is a microscopic lesion, which usually involves ducts <5mm in diameter (measured from basement membrane to basement membrane) and are classified as follows[55]:

1. PanIN-1A: Flat mucinous epithelium without dysplasia

2. PanIN-1B: Papillary mucinous epithelium without dysplasia

3. PanIN-2: Flat or papillary mucinous epithelium with mild-to-moderate dysplasia (mild-to-moderate nuclear irregularity, hyperchromasia, and loss of polarity)

4. PanIN-3: Flat or papillary mucinous epithelium with severe dysplasia (marked nuclear irregularity, hyperchromasia and loss of polarity), often with cribriforming and intraluminal blebbing.

If present the highest grade of PanIN should be recorded.

It may be difficult or impossible in some circumstances to separate PanIN from IPMN and there may be overlap in the calibre of ducts involved. In contrast to PanIN, IPMN is usually a grossly visible lesion involving the main pancreatic duct or branch ducts associated with duct dilatation, usually producing a lesion >1cm.[55]

IPMN and MCN are categorised as low, intermediate or high grade based on the highest degree of architectural and cytological atypia of the lining epithelium. ITPN by definition, show high grade dysplasia.

Preinvasive lesions of the distal common bile duct share similarities to those arising in the pancreas and are termed:

1. Biliary intra-epithelial neoplasia (BilIN)

2. Intraductal papillary neoplasm (IPN)

BilINs are categorized into BilIN-1, BilIN-2 and BilIN-3 according to the degree of architectural and cytological atypia. In a similar fashion to IPMN and MCN, IPNs of the biliary tree are divisible into low, intermediate and high grade, again according to the highest degree of epithelial atypia.

Preinvasive lesions common to the ampullary of Vater and duodenum include:

1. Intestinal-type adenoma (tubular, tubulovillous, villous)

2. Flat intraepithelial neoplasia (dysplasia)

In addition, there is a preinvasive neoplasm with pancreaticobiliary features that is recognised in the ampulla and currently labeled as 'non-invasive pancreatobiliary papillary neoplasm'. These preinvasive lesions of the ampulla of Vater are divisible into low and high grade according to the degree of epithelial atypia present.

A recent proposal to introduce the term 'intra-ampullary papillary-tubular neoplasm' for mass forming preinvasive neoplasms of the ampulla akin to intraductal lesions of the pancreas and biliary tree has the advantage of providing uniform terminology for these lesions, which show some immunophenotypic and morphological similarities.[56] Nevertheless, this terminology remains investigational

and is not yet in wide use.

S3.08 The status of all margins and surfaces must be assessed and recorded.

CS3.08a For pancreaticoduodenectomy specimens, the status of each of the following margins/surfaces should be recorded:

- Pancreatic transection margin
- Superior mesenteric artery (uncinate) margin
- Superior mesenteric vein (vascular groove margin)
- Posterior margin
- Anterior surface
- Bile duct margin
- Proximal margin (gastric/duodenal)
- Distal margin (distal duodenal/jejunal)

The nomenclature and definitions of PD resection specimen margins has undergone re-evaluation in the last few years following studies demonstrating that pathological assessment of margins is poorly standardised and inconsistently reported.[15,26,27,57] This has significant implications for assessments of patient prognosis, surgical and radiological feedback and quality assurance, as well as for clinical trials, hampering comparisons between cohorts from different centres and countries.

Routine sampling of the bile duct, proximal, distal and pancreatic transection margins is straightforward, however, the anatomical relationships of the pancreas to retroperitoneal structures is more complex and these margins are often inconsistently reported. Recent literature has defined these in a more standardised form as follows (see Fig SH1 and Fig SH2[57,58])

- The *superior mesenteric artery (SMA) margin*, also known variously as the uncinate, uncinate process, mesenteric or retroperitoneal margin, is the plane of abutment of the uncinate process on the SMA. It is the cut surface produced by the surgeon in dissecting the uncinate process from the SMA and tends to be irregular or granular, often with a small amount of attached adipose tissue.

- The *superior mesenteric vein margin/surface*, also known as the vascular groove or medial margin, is the concavity where the SMV/portal vein abuts on the posterior/retroperitoneal surface of the pancreas. It also serves as a landmark to separate the uncinate process from the rest of the pancreatic head.

- The *posterior margin/surface* is the non-peritonealised posterior surface of the uncinate process, not including the SMA margin. This margin tends to be smoother and more

regular than the SMA margin.

The anterior surface of the pancreas is generally not a surgical margin, as it borders on the peritoneal cavity and the surgeon does not have to resect/dissect it from other structures, however, in some cases it is adherent to other structures, such as the mesocolon, and requires en bloc resection. For this reason and the nature of the tumour involvement, i.e. serosa versus true resection margin, of the anterior surface should be recorded.

Inking of the resection margins in different colours before macroscopic dissection facilitates microscopic assessment (see Fig SH2).

If there is a portion of SMV/portal vein attached to the vascular groove the ends of the segment represent true resection margins. Likewise, if only a portion of the circumference of the vessel is included (tangential resection), the sides are also resection margins (see Fig SH4). However, when the tumour infiltrates through the vessel wall to the endothelium of attached SMV/portal vein this should be reported as a surface involvement rather than a resection margin, as the tumour would be bordering on a vascular space rather than directly on retroperitoneal soft tissue (see Fig S3.08). Recording of the depth of portal vein invasion also provides useful feedback to surgeons (see CS3.06c).

CS3.08b For distal pancreatectomy specimens the status of each of the following margins must be recorded:

- Pancreatic transection (body/neck) margin
- Posterior margin
- Anterior surface

For ampullectomy specimens the status of each of the following margins must be recorded:

- Intestinal margin
- Deep margin
- Ampullary duct margin

CS3.08c A resection margin is considered involved if tumour is less than 1mm from it. Various cut off points for designating a margin as positive in pancreatectomy specimens have been proposed, including 0, 1.0, and 1.5mm.[9,26,27,31,59] Currently, most European studies and trials utilise a cut off point of 1mm; an approach supported by a study showing cases with clearances of <1mm have a similar prognosis and local recurrence rate to those with transected (0mm tumour clearance) margins.[59] Another investigation also supported this point of view by demonstrating that pancreatic cancer is more dispersed than other cancers, such as colorectal cancer, with small clusters of tumour cells scattered more widely in the tumour stroma.[41] Conversely, in a series where an involved margin was defined as tumour touching the inked

surgical margin, the outcome for patients with involved margins so defined was not significantly different from the remaining patients (possibly reflecting the inclusion of patients with tumour within 1mm of the margin in the group defined as having "negative" margins).[60]

It should also be noted that the 1mm cut off point applies only to true resection margins and not to the anterior surface where it is covered by serosa; in this case only direct serosal surface involvement should be considered significant.

CS3.08d The presence of high grade pancreatic intraepithelial neoplasia (PanIN-3, carcinoma *in situ*) at a resection margin (usually the pancreatic transection margin) should be recorded. If the PanIN-3 is not transected but extends to within <1mm of the margin the distance between the lesion and resection margin should be stated. Low grade PanIN (PanIN-1 & 2) should not be reported as its clinical significance is currently unclear.[61]

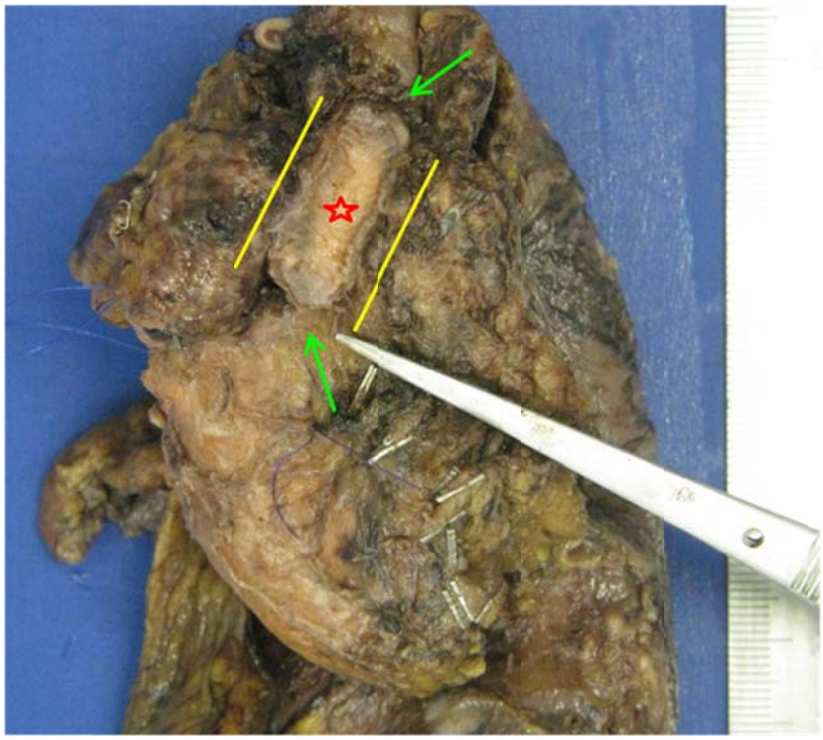
CS3.08e If present, the grade of dysplasia at the bile duct or mucosal margin should be recorded.

CS3.08f There is currently no data on the risk of recurrence in the situation where intranodal, intravascular or intraneural tumour deposits are transected or within 1mm of the resection margin. A recent survey on pathology reporting of head of pancreas carcinomas conducted in the United Kingdom revealed that the majority (up to 83%) of respondents considered tumour in these areas to represent microscopic involvement of a margin (R1).[62]

In this scenario, like the analogous situation in colorectal carcinoma, it is recommended that until specific information is available the margin should be recorded as positive with the nodal, intravascular or intraneural nature of the involvement noted.[63]

CS3.08g If there are no involved resection margins the distance between the tumour and the nearest margin must be recorded in millimetres.

Fig S3.08 Segment of superior mesenteric vein/portal vein attached to vascular groove. The resection margins of the vein are either end of the segment (green arrows) and the two sides (yellow lines), as only a portion of the vein circumference was resected. The intimal surface of the vessel (red ☆) is not a resection margin.



S3.09 The number of lymph nodes involved and the total number received must be recorded.

CS3.09a Record the number of lymph nodes from the main resection specimen. Any separately labelled lymph nodes should be recorded and reported as submitted.

Involvement of lymph nodes either through direct invasion or lymphatic spread are recorded as nodal disease according to the AJCC 7th edition.

CS3.09b Lymph nodes involvement has been shown in multiple studies to be an independent adverse prognostic factor in periampullary carcinomas.[44,64-71]

Some studies indicate that the ratio of the number of lymph nodes with metastatic cancer to the total number of lymph nodes (lymph node ratio) is a more powerful prognostic marker than the overall nodal status in pancreatic and ampullary cancer.[72,73]

G3.04 The presence of any coexisting pancreatic/ductal/small intestinal pathology should be recorded.

S3.10 The presence or absence of histologically confirmed metastatic sites

must be recorded.

G3.05 Any other findings in other resected organs should be recorded.

CG3.05a Specifically this should include findings in the

- Gallbladder
- Omentum
- Spleen

G3.06 Any additional relevant information should be recorded.

4 Ancillary studies findings

Ancillary studies are being increasingly used as prognostic biomarkers or to indicate the likelihood of patient response to specific biologic therapies.

G4.01 Any ancillary testing performed should be noted and the results recorded in the pathology report.

CG4.01a Ancillary investigations with either immunohistochemical or molecular markers are not recommended routinely in pancreatic carcinoma and should be considered investigational.

The main areas in which ancillary investigations have been applied are in immunophenotyping IPMNs and periampullary carcinomas to assist in the distinction between intestinal, gastric, oncocytic and pancreatobiliary phenotypes; measurement of HER2 overexpression on the basis of case reports of response by pancreatcobiliary cancers to targeted treatment, genomic analysis for druggable targets and genetic testing for hereditary disease.

1. **Immunophenotyping periampullary carcinoma with CDX2 and MUC1.**

   The distinction between ampullary carcinoma and pancreatic carcinoma arising in the periampullary area is currently made anatomically. Chang et al[40] suggested that cancers which expressed the pancreatic mucin MUC1 and not the intestinal marker CDX2 demonstrate a significantly worse prognosis particularly in the absence of lymph node metastasis. The separation of periampullary carcinomas into intestinal and pancreatobiliary phenotypes may also be important for defining adjuvant chemotherapy and radiotherapy in the future.[5,74]

2. **Immunophenotyping IMPNs with mucin glycoproteins.**

   Based on morphological features and mucin glycoprotein expression, IPMNs can be subclassified into 4 types: gastric, intestinal, pancreatobiliary and oncocytic.[75,76] In the context of IPMN with invasive carcinoma, colloid and oncocytic carcinomas have been shown to arise only from intestinal and oncocytic IPMNs respectively, whereas tubular carcinomas arise predominantly from gastric type IPMNs. Patients with IPMN associated tubular carcinomas show worse overall survival compared with the oncocytic and colloid subtypes.[77]

3. **HER 2 expression**

   Trastuzumab is licensed for the treatment of breast and gastric cancer but is not licensed for treatment of pancreatic carcinoma. There have been case reports of

successful response of pancreatic carcinomas to trastuzumab and preclinical studies have supported its potential efficacy.[78-81] However, clinical trials have been hampered by non-standardised assays and a consequent lack of focus on appropriate subgroups. Chou et al[82] found Her2 amplification by in-situ hybridization in 2% of 469 pancreatobiliary carcinomas examined and suggested that HER2 amplified pancreatic carcinoma may commonly show lung and brain metastases but are less frequently associated with liver metastasis. The authors suggested that immunohistochemistry for HER2 could be used to screen for amplification. Using a scheme based on the gastric HER2 scoring protocol, the authors suggested that amplification could be considered excluded in all cases showing 0 or 1+ staining.

4. Genomic Analysis

Genomic analysis of pancreatic carcinoma is in its infancy. Biankin et al[83] have demonstrated that pancreatic carcinomas show considerable molecular heterogeneity and that some of the activated pathways are potentially targetable with drugs which are either under development or currently approved for other tumours.

5. Hereditary pancreatic carcinoma

Familial pancreatic cancer (FPC) describes families with at least two first-degree relatives with confirmed exocrine pancreatic cancer that do not fulfil the criteria of other inherited tumour syndromes with increased risks of pancreatic cancer, such as Peutz–Jeghers syndrome, hereditary pancreatitis, and hereditary breast and ovarian cancer.[84] There are currently no firm guidelines for which patients with pancreatic carcinoma with a family history of pancreatic carcinoma or other tumours should be offered genetic testing however in the appropriate clinical setting there may be a role for formal genetic testing for BRCA2, PALB2 and ATM in some FPC families.

5 Synthesis and overview

Information that is synthesized from multiple modalities and therefore cannot reside solely in any one of the preceding chapters is described here. For example, tumour stage is synthesized from multiple classes of information – clinical, macroscopic and microscopic. An overarching case comment is synthesis in narrative form. Although it may not necessarily be required in any given report, the facility for overarching commentary in a cancer report is essential.

By definition, synthetic elements are inferential rather than observational, often representing high-level information that is likely to form part of the 'Diagnostic summary' section in the final formatted report (see G5.01).

S5.01 The tumour stage must be recorded, incorporating clinical and pathological data, based on the TNM staging system of the AJCC Cancer Staging Manual (7th Edition).[9] (See Appendix 8)

S5.02 The year of publication and edition of the cancer staging system used in S5.01 must be included in the report.

G5.01 The 'Diagnostic summary' section of the final formatted report should include:

a. Operative procedure

b. Tumour location(s)

c. Tumour type

d. Tumour size

e. Tumour grade

f. Tumour stage

g. Lymph nodes status

h. Margin status

S5.03 A field for free text or narrative in which the reporting pathologist can give overarching case comment must be provided.

CS5.03a This field may be used, for example, to:

- list any relevant ancillary tests
- document any noteworthy adverse gross and/or histological features
- express any diagnostic subtlety or nuance that is beyond synoptic capture
- document further consultation or results still pending.

CS5.03b Use of this field is at the discretion of the reporting pathologist.

6 Structured checklist

The following checklist includes the standards and guidelines for this protocol which must be considered when reporting, in the simplest possible form. The summation of all 'standards' is equivalent to the 'minimum dataset' for colorectal cancer. For emphasis, standards (mandatory elements) are formatted in bold font.

S6.01 The structured checklist provided may be modified as required but with the following restrictions:

a. All standards and their respective naming conventions, definitions and value lists must be adhered to.

b. Guidelines are not mandatory but are recommendations and where used, must follow the naming conventions, definitions and value lists given in the protocol.

G6.01 The order of information and design of the checklist may be varied according to the laboratory information system (LIS) capabilities and as described in *Functional Requirements for Structured Pathology Reporting of Cancer* Protocols.[85]

CG6.01a Where the LIS allows dissociation between data entry and report format, the structured checklist is usually best formatted to follow pathologist workflow. In this situation, the elements of synthesis or conclusions are necessarily at the end. The report format is then optimised independently by the LIS.

CG6.01b Where the LIS does not allow dissociation between data entry and report format, (for example where only a single text field is provided for the report), pathologists may elect to create a checklist in the format of the final report. In this situation, communication with the clinician takes precedence and the checklist design is according to principles given in Chapter 7.

G6.02 Where the checklist is used as a report template (see G6.01), the principles in Chapter 7 and Appendix 2 apply.

CG6.02a All extraneous information, tick boxes and unused values should be deleted.

G6.03 Additional comment may be added to an individual response where necessary to describe any uncertainty or nuance in the selection of a prescribed response in the checklist. Additional comment is not required where the prescribed response is adequate.

Values in italics are conditional on previous responses.

Values in all caps are headings with sub values.

S/G	Item description	Response type	Conditional
Pre-analytic			
S1.01	**Demographic information provided**		
S1.02	**Clinical information provided on request form**	**Text** OR **Structured entry as below:**	
	Type of operation	**Single selection value list:** • Pancreaticoduodenectomy (Whipple resection), partial pancreatectomy • Pancreaticoduodenectomy (Whipple resection), total pancreatectomy • Pancreaticoduodenectomy (pylorus preserving), partial pancreatectomy • Pancreaticoduodenectomy (pylorus preserving), total pancreatectomy • Partial pancreatectomy, pancreatic neck • Partial pancreatectomy, pancreatic body • Partial pancreatectomy, pancreatic tail • Enucleation • Ampullectomy • Segmental resection of bile duct(s)	

S/G	Item description	Response type	Conditional
		• Other (specify)	
	Superior mesenteric vein/Portal vein resection	**Single selection value list:** • Not performed • Performed	**If performed, describe the type of vascular resection**
	Type of vascular resection	**Single selection value list:** • Tangential • Segmental	
	Additional specimens	**Multi select value list (select all that apply):** • Liver biopsy • Peritoneal nodules • Peritoneal cytology • Omentum • Gallbladder • Spleen • Other (specify)	***If peritoneal cytology record peritoneal cytology result.***
	Peritoneal cytology result	***Text***	
	Tumour location/site	**Single selection value list:** • Pancreatic head • Pancreatic neck • Pancreatic body • Pancreatic tail • Bile duct • Ampulla of Vater	

S/G	Item description	Response type	Conditional
		• Duodenum • Other (specify)	
	Preoperative therapy	**Single selection value list:** • Not administered • Preoperative chemotherapy • Preoperative radiotherapy • Preoperative chemoradiotherapy	
	Local residual cancer postsurgery	**Text**	
	Involvement of adjacent organs	**Text**	
	New primary cancer or recurrence	**Single selection value list:** • New primary • Regional (local) recurrence • Distant metastases	**If regional (local) recurrence or distant metastasis describe.**
	Describe	***Text***	
	Relevant patient or family history	**Text**	
	Pre-operative diagnosis	**Text**	
	Relevant issues noted during the procedure	**Text**	

S/G	Item description	Response type	Conditional
S1.03	**Pathology accession number**	**Alpha-numeric**	
G1.01	Other relevant details	**Text**	
Macroscopic findings			
S2.01	**Specimen labelled as**	**Text**	
S2.02	**ANATOMICAL STRUCTURES**		
	Pancreas	**Single selection value list:** • Not present • Present	**If present, record which portions of the pancreas and dimensions**
	Portions of the pancreas	**Multi select value list (select all that apply):** • Head • Neck • Body • Tail	
	Dimensions	***Numeric: __x__x__mm***	
	Duodenum	**Single selection value list:** • Not present • Present	**If present, record length and maximum diameter**
	Length	***Numeric: __mm***	
	Maximum diameter	***Numeric: __mm***	
	Stomach	**Single selection value list:** • Not present • Present	**If present, record length of lesser and greater curvature**
	Length of lesser curvature	***Numeric: __mm***	
	Length of greater curvature	***Numeric: __mm***	

S/G	Item description	Response type	Conditional
	Common bile duct	**Single selection value list:** • Not present • Present	**If present, record length and maximum diameter.**
	Length	***Numeric: __mm***	
	Maximum diameter	***Numeric: __mm***	
	Gallbladder	**Single selection value list:** • Not present • Present	**If present, record length and maximum diameter**
	Length	***Numeric: __mm***	
	Maximum diameter	***Numeric: __mm***	
	Spleen	**Single selection value list:** • Not present • Present	**If present, record dimensions**
	Dimensions	***Numeric: __x__x__mm***	
	Portal vein	**Single selection value list:** • Not present • Present	**If present, record dimensions**
	Dimensions	***Numeric: __x__x__mm***	
	Superior mesenteric vein	**Single selection value list:** • Not present • Present	**If present, record dimensions**
	Dimensions	***Numeric: __x__x__mm***	
	Other large vessel	**Single selection value list:** • Not present • Present	**If present, record the other vessel and dimensions**

S/G	Item description	Response type	Conditional
	Other vessel	***Text***	
	Dimensions	***Numeric: __x__x__mm*** ***OR*** ***Length: Numeric:____mm*** ***AND*** ***Diameter: Numeric: ____mm*** ***<u>Note:</u>*** *Measure in 3 dimensions if tangential resection of the vessel has been performed or measure length and diameter if the whole circumference of the vessel is present.*	
	Other anatomical structure	**Single selection value list:** • Not present • Present	**If present, record the other structure and dimensions**
	Other structure	***Text***	
	Dimensions	***Numeric: __x__x__mm***	
	Separately submitted specimens	**Multi select value list (select all that apply):** • Lymph nodes • Omentum • Other (specify)	
G2.01	Stent	**Single selection value list:** • Not present • Present	**If present record location**
	Location	*Text*	
S2.03	**Macroscopic tumour site(s)**	**Multi select value list (select all that apply):**	

S/G	Item description	Response type	Conditional

		• Pancreas
		  o Head of pancreas
		  o Neck of pancreas
		  o Body of pancreas
		  o Tail of pancreas
		• Uncinate process
		• Ampulla of Vater
		• Common bile duct (extrapancreatic or intrapancreatic)
		• Duodenum
		• Other (describe)	

S2.04	**Maximum tumour diameter**	**Numeric: __mm** **Note:** For multiple tumours the diameter of each focus should be recorded.	
S2.05	**MACROSCOPIC TUMOUR DESCRIPTION**	**Note:** For multiple tumours the description of each focus should be recorded.	
	Description (eg exophytic or flat, solid and/or cystic, colour, texture, border)	**Text**	
	Type of ampullary tumour	**Single selection value list:** • intra-ampullary • mixed intra-ampullary and peri-ampullary • peri-ampullary	***Conditional on the tumour being located in the ampullary region***
S2.06	**MACROSCOPIC DISTANCE OF TUMOUR TO MARGINS/SURFACES**	**Note:** For multiple tumours the closest distance of *any* foci should be recorded.	

S/G	Item description	Response type	Conditional
	Pancreatic transection	**Not applicable** **OR** **Numeric: __mm**	
	Superior mesenteric artery	**Not applicable** **OR** **Numeric: __mm**	
	Posterior pancreatic	**Not applicable** **OR** **Numeric: __mm**	
	Superior mesenteric vein/vascular groove	**Not applicable** **OR** **Numeric: __mm**	
	Anterior pancreatic	**Not applicable** **OR** **Numeric: __mm**	
	Bile duct	**Not applicable** **OR** **Numeric: __mm**	
	Proximal intestinal/gastric	**Not applicable** **OR** **Numeric: __mm**	

S/G	Item description	Response type	Conditional
	Distal intestinal	**Not applicable** **OR** **Numeric: __mm**	
	Other margin/surface	**Not applicable** **OR** **Text:** description of margin /surface **AND** **Numeric: __mm**	
G2.02	Evidence of other abnormality or coexisting pathology	**Single selection value list:** • Not present • Present	**If present, describe the abnormality**
	Abnormality	***Multi select value list (select all that apply):*** • *Cystic lesion(s)* • *Calculi* • *Chronic pancreatitis* • *Other (describe)*	
G2.03	Tissue block for research or tissue bank	**Single selection value list:** • Not taken • Taken	
G2.04	Photographs	**Single selection value list:** • Not taken • Available	
S2.07	**Block identification key**	**Text**	
G2.05	Other macroscopic comment	**Text**	
Microscopic findings			

S/G	Item description	Response type	Conditional
S3.01	**Histological tumour type**	**Single selection value list from WHO Classification of Tumours. Pathology and Genetics of Tumours of the Digestive System (2010).**	
S3.02	**Histological grade**	**Single selection value list:** • Grade X: Cannot be assessed • Grade 1: Well differentiated (greater than 95% of tumour composed of glands) • Grade 2: Moderately differentiated (50% to 95% of tumour composed of glands) • Grade 3: Poorly differentiated (49% or less of tumour composed of glands) • Grade 4: Undifferentiated (5% or less of tumour composed of glands)	

S3.03	**Microscopic tumour site**	**Multi select value list (select all that apply):**
		• Pancreas
		  o Head of pancreas
		  o Neck of pancreas
		  o Body of pancreas
		  o Tail of pancreas
		• Uncinate process
		• Ampulla of Vater
		• Common bile duct (extrapancreatic or intrapancreatic)
		• Duodenum
		• Other (specify)	

S3.04	**Maximum extent of tumour invasion**	**Multi select value list (select all that apply):** • Pancreas • Celiac axis • Superior mesenteric artery	

S/G	Item description	Response type	Conditional
		• Ampulla of Vater • Sphincter of Oddi • Duodenal wall • Peripancreatic soft tissues • Bile duct • Gallbladder • Other adjacent organs or structures (specify)	
S3.05	**Maximum tumour diameter**	**Numeric: __mm** Note: Record for each tumour identified.	
S3.06	**Lymphovascular invasion**	**Single selection value list:** • Not identified • Suspicious • Present	**If present, record the type of vessel**
	Type of vessel	**Multi select value list (select all that apply):** • Artery • Vein • Small vessel	
S3.07	**Perineural invasion**	**Single selection value list:** • Not identified • Suspicious • Present	

S/G	Item description	Response type	Conditional
G3.01	Perineural invasion of the superior mesenteric artery margin neural plexus	**Single selection value list:** • Not received • Not identified • Suspicious • Present	
G3.02	Regression grade	**Single selection value list:** • Not known • No prior treatment • Grade 0 (complete response) • Grade 1 (moderate response) • Grade 2 (minimal response) • Grade 3 (poor response)	
G3.03	Preinvasive lesion	**Single selection value list:** • Not identified • Present	**If present, record the type(s)**
	Type(s)	**Multi select value list (select all that apply):** **Pancreas:** • Pancreatic intraepithelial neoplasia (PanIN) • Intraductal papillary mucinous neoplasms (IPMN) • Intraductal tubulopapillary neoplasm (ITPN) • Mucinous cystic neoplasms (MCN) **Distal common bile duct:** • Biliary intraepithelial neoplasia (BilIN)	

S/G	Item description	Response type	Conditional
		• Intraductal papillary neoplasm (IPN) **Ampullary of Vater and duodenum** • Intestinal-type adenoma (tubular, tubulovillous, villous) • Flat intraepithelial neoplasia (dysplasia) • Non-invasive pancreatobiliary papillary neoplasm	
	Highest grade PanIN	***Single selection value list:*** • *Grade 1a/1b* • *Grade 2* • *Grade 3*	***Conditional on PanIN being selected above.***
	Grade of intraepithelial neoplasia or dysplasia	**Single selection value list:** • Low-grade • Intermediate-grade • High-grade • Grade 1 • Grade 2 • Grade 3	
S3.08	**MARGIN/SURFACE STATUS**		**If no involved margins record the distances to the closest resection margin.**

S/G	Item description	Response type	Conditional
	Pancreatic transection margin	**Single selection value list:** • Not applicable • Not involved • Involved	**For pancreaticoduodenectomy (Whipple's) resection and distal pancreatectomy specimens** **If involved record the type of involvement.** **If not involved record the microscopic clearance.**
	Type of involvement	***Multi select value list (select all that apply):*** • *Involved by invasive tumour* • *Involved by preinvasive lesion*	***If involved by preinvasive lesion, record the type and grade***
	Type of preinvasive lesion at margin	***Text***	
	Grade of preinvasive lesion at margin	***Single selection value list:*** • *Low-grade* • *Intermediate-grade* • *High-grade*	
	Microscopic clearance	***Numeric: __mm***	
	Superior mesenteric artery margin	**Single selection value list:** • Not applicable • Not involved • Involved	**For pancreaticoduodenectomy (Whipple's) resection specimens** **If not involved record the microscopic clearance.**
	Microscopic clearance	***Numeric: __mm***	

S/G	Item description	Response type	Conditional
	Superior mesenteric vein/vascular groove margin	**Single selection value list:** • Not applicable • Not involved • Involved	**For pancreaticoduodenectomy (Whipple's) resection specimens** **If not involved record the microscopic clearance.**
	Microscopic clearance	***Numeric: __mm***	
	Posterior margin	**Single selection value list:** • Not applicable • Not involved • Involved	**For pancreaticoduodenectomy (Whipple's) resection and distal pancreatectomy specimens** **If not involved record the microscopic clearance.**
	Microscopic clearance	***Numeric: __mm***	
	Bile duct margin	**Single selection value list:** • Not applicable • Not involved • Involved	**For pancreaticoduodenectomy (Whipple's) resection specimens** **If involved, record type of involvement.** **If not involved record the microscopic clearance.**
	Type of involvement	***Multi select value list (select all that apply):*** • *Involved by invasive tumour* • *Involved by preinvasive lesion*	***If involved by preinvasive lesion, record the type and grade***
	Type of preinvasive lesion at margin	***Text***	
	Grade of preinvasive lesion at margin	***Single selection value list:*** • *Low-grade* • *Intermediate-grade* • *High-grade*	

S/G	Item description	Response type	Conditional
	Microscopic clearance	***Numeric: __mm***	
	Proximal gastric/duodenal margin	**Single selection value list:** • Not applicable • Not involved • Involved	**For pancreaticoduodenectomy (Whipple's) resection specimens** **If involved, record type of involvement** **If not involved record the microscopic clearance.**
	Type of involvement	***Multi select value list (select all that apply):*** • *Involved by invasive tumour* • *Involved by preinvasive lesion*	***If involved by preinvasive lesion, record the grade***
	Grade of preinvasive lesion at margin	***Single selection value list:*** • *Low grade* • *High grade*	
	Microscopic clearance	***Numeric: __mm***	
	Distal duodenal/jejunal margin	**Single selection value list:** • Not applicable • Not involved • Involved	**For pancreaticoduodenectomy (Whipple's) resection specimens** **If involved, record type of involvement** **If not involved record the microscopic clearance.**
	Type of involvement	***Multi select value list (select all that apply):*** • *Involved by invasive tumour* • *Involved by preinvasive lesion*	***If involved by preinvasive lesion, record the grade***

S/G	Item description	Response type	Conditional
	Grade of preinvasive lesion at margin	***Single selection value list:*** • *Low grade* • *High grade*	
	Microscopic clearance	***Numeric: __mm***	
	Other margin	**List margin: Text** **AND** **Single selection value list:** • Not applicable • Not involved • Involved <u>Note</u>: repeat for each other margin.	**Record only if applicable.** **If involved, record type of involvement** **If not involved record the microscopic clearance.**
	Type of involvement	***Multi select value list (select all that apply):*** • *Involved by invasive tumour* • *Involved by preinvasive lesion*	***If involved by preinvasive lesion, record the grade***
	Grade of dysplasia at margin	***Single selection value list:*** • *Grade 1* • *Grade 2* • *Grade 3* • *Low grade* • *High grade*	

S/G	Item description	Response type	Conditional
	Microscopic clearance	***Numeric: __mm***	
	Anterior surface	**Single selection value list:** • Not applicable • Not involved • Involved	**For pancreaticoduodenectomy (Whipple's) resection specimens** **If involved record the nature of surface.** **If not involved record the microscopic clearance.**
	Nature of surface/margin	***Single selection value list:*** • *Serosa* • *Resection margin*	
	Microscopic clearance	***Numeric: __mm***	
S3.09	**LYMPH NODE STATUS**		
	Lymph nodes from main resection specimen	***Single selection value list:*** • *None found* • *Nodes present*	***If nodes present, record the number of lymph nodes found and the number of positive nodes***
	Lymph nodes found	***Numeric:*** ___	
	Number of positive nodes	***Numeric:*** ___	
	Separately labelled lymph nodes (if applicable)		***Conditional on Lymph nodes being recorded as received in S2.03.***
	Lymph nodes found	***Numeric:*** ___	

S/G	Item description	Response type	Conditional
	Number of positive nodes	***Numeric:*** _____	
G3.04	Co-existing pancreatic/ductal/small intestinal pathology	**Text**	
S3.10	**Histologically confirmed metastatic sites**	**Text**	
G3.05	Findings in other resected organs	**Text**	
G3.06	Other microscopic information	**Text**	
Ancillary test findings			
G4.01	ANCILLARY TESTS		
	Performed	**Single selection value list:** • No • Yes • Pending	If yes or pending, record test type
	Test type eg IHC, molecular, etc	***Text*** *Note: Test result type, result and interpretive comment will need to repeat for each ancillary test performed.*	If IHC, record the antibodies
	Antibodies	***List (as applicable) all:*** • ***Positive antibodies*** • ***Negative antibodies*** • ***Equivocal antibodies***	

S/G	Item description	Response type	Conditional
	Result	***Text*** *<u>Note:</u> Test result type, result and interpretive comment will need to repeat for each other ancillary test performed.*	
	Interpretive comment	***Text*** *<u>Note:</u> Test result type, result and interpretive comment will need to repeat for each other ancillary test performed.*	
Synthesis and overview			
S5.01	**PATHOLOGICAL STAGING (AJCC)**		
	Primary tumour category (pT)	**<u>PANCREAS</u>** **Single selection value list:** **TX** Primary tumour cannot be assessed **T0** No evidence of primary tumour **Tis** Carcinoma in situ* **T1** Tumour limited to the pancreas, 2 cm or less in greatest dimension **T2** Tumour limited to the pancreas, more than 2 cm in greatest dimension **T3** Tumour extends beyond the pancreas but without involvement of the celiac axis or the superior mesenteric artery **T4** Tumour involves the celiac axis or the superior mesenteric artery (unresectable primary tumour) *This also includes "PanIn-III" classification **<u>AMPULLA OF VATER</u>**	

S/G	Item description	Response type	Conditional
		Single selection value list: **TX** Primary tumour cannot be assessed **T0** No evidence of primary tumour **Tis** Carcinoma in situ **T1** Tumour limited to ampulla of Vater or sphincter of Oddi **T2** Tumour invades duodenal wall **T3** Tumour invades pancreas **T4** Tumour invades peripancreatic soft tissues or other adjacent organs or structures other than pancreas **<u>COMMON BILE DUCT</u>** **Single selection value list:** **TX** Primary tumour cannot be assessed **T0** No evidence of primary tumour **Tis** Carcinoma in situ **T1** Tumour confined to the bile duct histologically **T2** Tumour invades beyond the wall of the bile duct **T3** Tumour invades the gallbladder, pancreas, duodenum, or other adjacent organs without involvement of the celiac axis, or the superior mesenteric artery **T4** Tumour involves the celiac axis, or the superior mesenteric artery	
	Regional lymph node category (pN)	**Single selection value list:** **NX** Regional lymph nodes cannot be assessed **N0** No regional lymph node metastasis **N1** Regional lymph node metastasis	

S/G	Item description	Response type	Conditional
	Distant metastasis category (pM)	**Single selection value list:** **M0** No distant metastases **M1** Distant metastasis	
S5.02	**Year and edition of staging system**	**Numeric:** year **AND** **Text:** Edition eg 1st, 2nd etc	
G5.01	Diagnostic summary Include: a. Operative procedure b. Tumour location(s) c. Tumour type d. Tumour size e. Tumour grade f. Tumour stage g. Lymph nodes status h. Margin status	**Text**	
S5.03	**Overarching comment**	**Text**	

7 Formatting of pathology reports

Good formatting of the pathology report is essential for optimising communication with the clinician, and will be an important contributor to the success of cancer reporting protocols. The report should be formatted to provide information clearly and unambiguously to the treating doctors, and should be organised with their use of the report in mind. In this sense, the report differs from the structured checklist, which is organised with the pathologists' workflow as a priority.

Uniformity in the format as well as in the data items of cancer reports between laboratories makes it easier for treating doctors to understand the reports; it is therefore seen as an important element of the systematic reporting of cancer. For guidance on formatting pathology reports, please refer to Appendix 2.

Appendix 1 Pathology request information and surgical handling procedures

This appendix describes the information that should be collected before the pathology test. Some of this information can be provided on generic pathology request forms; any additional information required specifically for the reporting of pancreatic cancer may be provided by the clinician on a separate request information sheet. An example request information sheet is included below. Elements which are in bold text are those which pathologists consider to be required information. Those in non-bold text are recommended.

Also included in this appendix are the procedures that are recommended before handover of specimens to the laboratory.

Patient information

- **Adequate demographic and request information should be provided with the specimen.**
  - Items relevant to cancer reporting protocols include:
    - patient name
    - date of birth
    - sex
    - identification and contact details of requesting doctor
    - date of request
  - The patient's ethnicity should be recorded, if known. In particular whether the patient is of aboriginal or Torres Strait islander origin. This is in support of a government initiative to monitor the health of indigenous Australians particularly in relation to cancer.
- The patient's health identifiers should be provided.
  - The patient's health identifiers may include the patient's Medical Record Number as well as a national health number such as a patient's Medicare number (Australia), Individual Healthcare Identifier (IHI) (Australia) or the National Healthcare Identifier (New Zealand).

Clinical Information

- **The type of operation or procedure should be recorded.**
  - Choose from one of the following:
    - Pancreaticoduodenectomy (Whipple resection), partial pancreatectomy

- Pancreaticoduodenectomy (Whipple resection), total pancreatectomy
- Pancreaticoduodenectomy (pylorus preserving), partial pancreatectomy
- Pancreaticoduodenectomy (pylorus preserving), total pancreatectomy
- Partial pancreatectomy, pancreatic neck
- Partial pancreatectomy, pancreatic body
- Partial pancreatectomy, pancreatic tail
- Enucleation
- Ampullectomy
- Segmental resection of bile duct(s)
- Other (specify)

- Indicate if superior mesenteric vein/portal vein resection has been performed and if so the type of vascular resection. Choose from one of the following:
  - Tangential
  - Segmental

➢ Additional specimens taken e.g. peritoneal nodules, liver biopsy, omentum, gallbladder, spleen, other etc should be labelled and recorded separately.

- The presence of positive peritoneal cytology is classified as metastatic disease. This information should be provided to the reporting pathologist, in part because the diagnosis may have been made at a different laboratory.

➢ **The tumour location/site should be recorded.**

- Choose from one of the following:
  - Pancreatic head
  - Pancreatic neck
  - Pancreatic body
  - Pancreatic Tail
  - Bile duct
  - Ampulla of Vater

- Duodenum

➢ **Any preoperative therapy that has been administered should be recorded.**

- Choose from one of the following:
  - Not administered
  - Preoperative chemotherapy
  - Preoperative radiotherapy
  - Preoperative chemoradiotherapy

➢ **The involvement of adjacent organs should be recorded.**

- Involvement of adjacent organs, either resected or not resected, is required for assessment of the tumour (T) stage of the tumour. Unless obvious, the area of involvement should be marked with a suture or other marker.

➢ **The Surgeon's opinion on the existence of local residual cancer following the operative procedure should be recorded.**

- This item relates to the overall completeness of resection of the tumour, including evidence of macroscopic residual disease at surgical margins or within regions in which resection has not been attempted (R2). It allows for residual tumour status (R) to be reported by the pathologist following microscopic assessment of the surgical margins. Residual microscopic disease is reported as R1.

➢ **Record if this is a new primary cancer or a recurrence of a previous cancer, if known.**

- The term recurrence defines the return, reappearance or metastasis of cancer (of the same histology) after a disease free period.

  Recurrence should be classified as distant metastases or regional (local) recurrence.

  Regional (local) recurrence refers to the recurrence of cancer cells at the same site as the original (primary) tumour or the regional lymph nodes.

  Distant metastasis refers to the spread of cancer of the same histologic type as the original (primary) tumour to distant organs or distant lymph nodes. The reporting of metastatic deposits, either resected or not resected, is required for assessment of the metastatic (M) stage of the tumour. The sites of such deposits should be stated.

- This information will provide an opportunity for previous reports to be reviewed during the reporting process, which may provide valuable information to the pathologist. This information also has

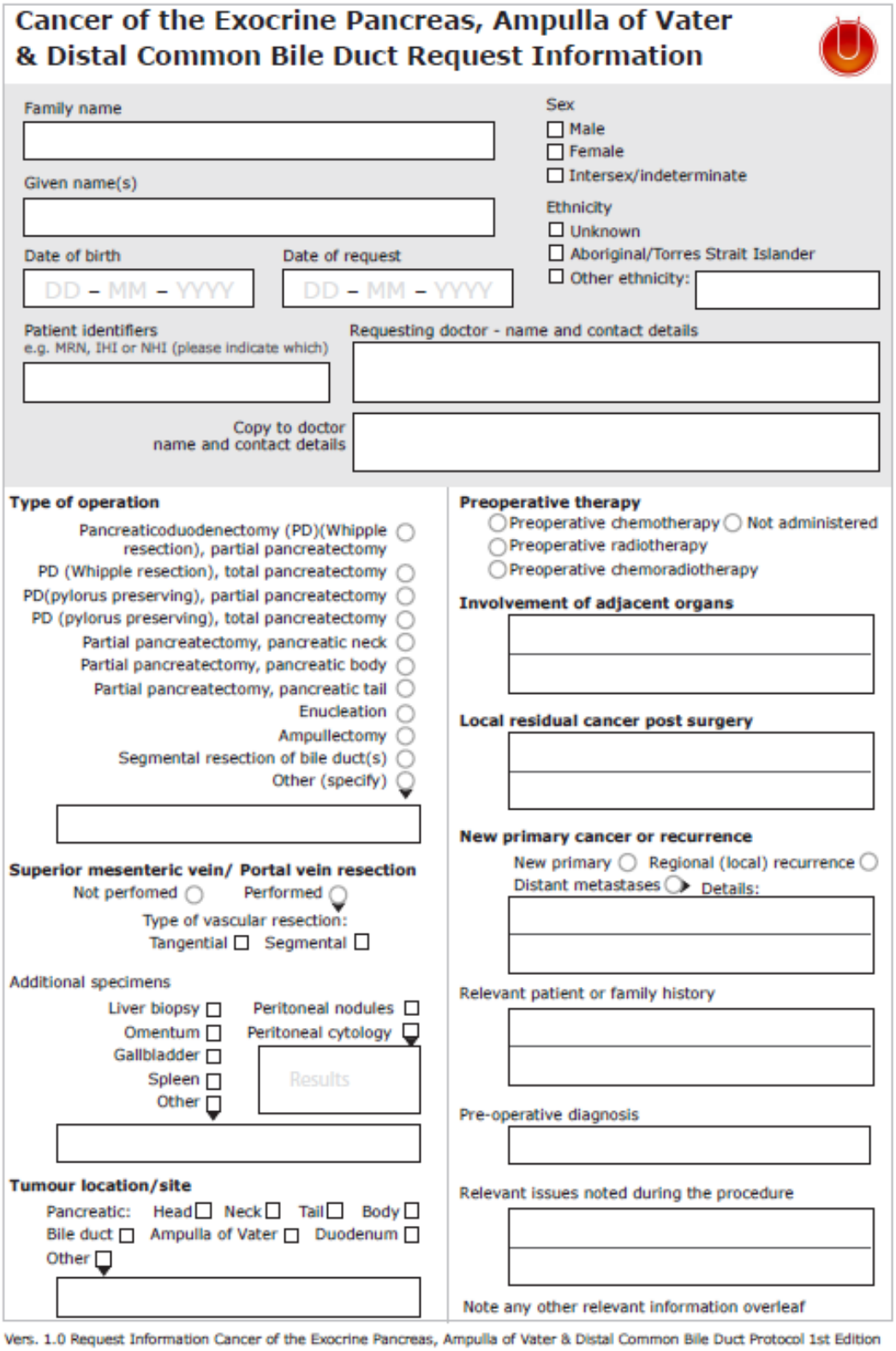
implications for recording cancer incidence and evidence based research.

- Any relevant patient or family history should be provided.
- Any pre-operative diagnosis should be provided.
- Any other relevant issues noted during the procedure.
- Any additional relevant information should be recorded.
    - A free text field should be completed by the referring doctor to communicate anything that is not addressed by the above points.

Surgical handling

- **The specimen must be capable of orientation if the status of specific surgical margins is critical in determining the need for, or extent of, further surgery.**
    - Where there are no anatomical landmarks, specimen orientation may be indicated with marking sutures or other techniques. If a specimen is orientated, the orientation should be indicated on the specimen request form (this may be facilitated by the use of a diagram). Relevant margins should be marked by the surgeon.
- The specimen should be sent to the laboratory in the fresh state without delay where possible.
    - The laboratory should be informed if the specimen is likely to be received outside normal working hours.
    - Where a specimen is unable to be received by the laboratory (e.g. outside normal working hours), it should be placed in an adequate volume of formalin based solution.
- The specimen should be sent to the laboratory intact where possible.
    - When a specimen needs to be opened e.g. to confirm adequate surgical margins or tumour localisation, e.g. bile duct or duodenum, the specimen should be opened by a single longitudinal incision and should avoid cutting through tumour if at all possible.
- Lymph nodes must be labelled clearly, identifying the site.
    - Lymph nodes taken separately from the main resection specimen must be labelled as to site.

Example Request Information Sheet



Cancer of the Exocrine Pancreas, Ampulla of Vater & Distal Common Bile Duct Request Information

Family name

Given name(s)

Date of birth DD – MM – YYYY

Date of request DD – MM – YYYY

Sex
- ☐ Male
- ☐ Female
- ☐ Intersex/indeterminate

Ethnicity
- ☐ Unknown
- ☐ Aboriginal/Torres Strait Islander
- ☐ Other ethnicity:

Patient identifiers
e.g. MRN, IHI or NHI (please indicate which)

Requesting doctor - name and contact details

Copy to doctor name and contact details

Type of operation
- Pancreaticoduodenectomy (PD)(Whipple resection), partial pancreatectomy ○
- PD (Whipple resection), total pancreatectomy ○
- PD(pylorus preserving), partial pancreatectomy ○
- PD (pylorus preserving), total pancreatectomy ○
- Partial pancreatectomy, pancreatic neck ○
- Partial pancreatectomy, pancreatic body ○
- Partial pancreatectomy, pancreatic tail ○
- Enucleation ○
- Ampullectomy ○
- Segmental resection of bile duct(s) ○
- Other (specify) ○

Superior mesenteric vein/ Portal vein resection

Not perfomed ○ Performed ○

Type of vascular resection:

Tangential ☐ Segmental ☐

Additional specimens
- Liver biopsy ☐
- Omentum ☐
- Gallbladder ☐
- Spleen ☐
- Other ☐
- Peritoneal nodules ☐
- Peritoneal cytology ☐

Results

Tumour location/site

Pancreatic: Head ☐ Neck ☐ Tail ☐ Body ☐

Bile duct ☐ Ampulla of Vater ☐ Duodenum ☐

Other ☐

Preoperative therapy
- ○ Preoperative chemotherapy ○ Not administered
- ○ Preoperative radiotherapy
- ○ Preoperative chemoradiotherapy

Involvement of adjacent organs

Local residual cancer post surgery

New primary cancer or recurrence

New primary ○ Regional (local) recurrence ○

Distant metastases ○ Details:

Relevant patient or family history

Pre-operative diagnosis

Relevant issues noted during the procedure

Note any other relevant information overleaf

Vers. 1.0 Request Information Cancer of the Exocrine Pancreas, Ampulla of Vater & Distal Common Bile Duct Protocol 1st Edition

The above Request Information Sheet is published to the RCPA website.

Appendix 2 Guidelines for formatting of a pathology report

Layout

Headings and spaces should be used to indicate subsections of the report, and heading hierarchies should be used where the LIS allows it. Heading hierarchies may be defined by a combination of case, font size, style and, if necessary, indentation.

Grouping like data elements under headings and using 'white space' assists in rapid transfer of information.[86]

Descriptive titles and headings should be consistent across the protocol, checklist and report.

When reporting on different tumour types, similar layout of headings and blocks of data should be used, and this layout should be maintained over time.

Consistent positioning speeds data transfer and, over time, may reduce the need for field descriptions or headings, thus reducing unnecessary information or 'clutter'.

Within any given subsection, information density should be optimised to assist in data assimilation and recall. The following strategies should be used:

- Configure reports in such a way that data elements are 'chunked' into a single unit to help improve recall for the clinician.[86]
- Reduce 'clutter' to a minimum.[86] Thus, information that is not part of the protocol (eg billing information or Snomed codes) should not appear on the reports or should be minimised.
- Reduce the use of formatting elements (eg bold, underlining or use of footnotes) because these increase clutter and may distract the reader from the key information.
- Where a structured report checklist is used as a template for the actual report, any values provided in the checklist but not applying to the case in question must be deleted from the formatted report.

Reports should be formatted with an understanding of the potential for the information to 'mutate' or be degraded as the report is transferred from the LIS to other health information systems.

As a report is transferred between systems:

- text characteristics such as font type, size, bold, italics and colour are often lost
- tables are likely to be corrupted as vertical alignment of text is lost when fixed font widths of the LIS are rendered as proportional fonts on screen or in print
- spaces, tabs and blank lines may be stripped from the report, disrupting the formatting
- supplementary reports may merge into the initial report.

Appendix 3 Example of a pathology report

Citizen, George W.
C/O Paradise Close
Nar Nar Goon East, 3181
Tasmania

Male

DOB 1/7/1964
MRN FMC1096785

Lab Ref: **13/P28460**
Referred: 30/2/2013

Copy to: Dr G. Gleason
Rainforest Cancer Centre.
46 Smith Road,
Woop Woop, 3478

Referred by: Dr V. Smith
Suite 3, AJC Medical Centre,
Bunyip Crescent
Nar Nar Goon East, 3182

PANCREATIC CANCER STRUCTURED REPORT

Diagnostic Summary

Pancreaticoduodenectomy (Whipple resection) partial pancreatectomy:

Pancreas, ductal adenocarcinoma, 30mm, Grade 1
2/14 involved nodes,
Involved margins: <1mm from Superior mesenteric artery (SMA) margin,
pT3N1M0 Stage IIB (2010. AJCC 7th edition)

Supporting Information

CLINICAL

Type of operation:	Pancreaticoduodenectomy (Whipple resection) partial pancreatectomy
Tumour site:	Pancreas
Relevant patient hx:	Previous bx: EUS FNA, adenocarcinoma
Preoperative therapy:	None
Involvement of adjacent organs:	None noted
New primary or recurrence:	New primary
Completeness of resection:	Complete
Orientation:	Short tie, one clip, SMA margin, Medium tie, two clips, posterior margin, Long tie, three clips CBD margin.

MACROSCOPIC

Specimen labelled as:	A. Pancreaticoduodenectomy B. Gallbladder C: Omentum
Anatomical structures:	
Pancreas:	Present. Head and neck. 45 x 30 x 25mm
Duodenum:	Present. 220 x 32mm
Stomach:	Present. Greater curvature 60mm, lesser curvature 35mm
Common bile duct:	Present. 53 x 4mm
Gallbladder:	Present. 70 x 30mm
Spleen:	Not present
Portal Vein:	Not present
Superior mesenteric vein:	Not present
Other large vessel:	Not present
Other anatomical structure:	Cystic duct. 10 x 4mm
Separately submitted specimens:	Omentum. Fatty tissue measuring 220x110x50mm

Macroscopic tumour site: Pancreas
Maximum tumour diameter: 30mm
Macroscopic tumour description: Firm white to tan lesion with an irregular margin

Macroscopic distance of tumour to margins/ surfaces
- **Pancreatic transection:** 15mm
- **Superior mesenteric artery:** 0mm
- **Posterior pancreatic:** 5mm
- **Superior mesenteric vein/vascular groove:** 5mm
- **Anterior pancreatic:** 10mm
- **Bile duct:** 60mm
- **Proximal intestinal/gastric:** 160mm
- **Distal intestinal:** 120mm
- **Other margin/surface:** Not applicable

Photographs: Available

Block identification key: **Specimen A:** Block 1: CBD margin. Block 2: Pancreatic neck margin. Block 3 & 4: Tumour And SMA margin. Block 5 & 6: Tumour and SMV Margin. Block 7 & 8: Tumour and posterior Margin. Block 9: Anterior surface. Block 10: Gastric margin. Block 11: Duodenal margin. Block 12: Ampulla. Block 13: Periampullary Duodenum. Block 14-20: Lymph nodes
Specimen B: Block 1: Cystic duct and neck. Block 2: Body and fundus.
Specimen C:
Block 1-4: representative sections

MICROSCOPIC

Histological tumour type: Ductal adenocarcinoma
Histological grade: Grade 1: Well differentiated (greater than 95% of tumour composed of glands)
Microscopic tumour site: Pancreas
Maximum extent of tumour invasion: Peripancreatic soft tissues
Maximum tumour diameter: 30mm
Lymphovascular invasion: Present
- **Type of vessel:** Vein and small vessel, focal

Perineural invasion: Present
Perineural invasion of the
- **SMA margin neural plexus:** Present

Preinvasive lesion: Present
- **Type:** Pancreatic intraepithelial neoplasia (PanIN)
- **Highest grade PanIN:** Grade 3

Margin/surface status
- **Pancreatic transection:** Not involved. 15mm clearance
- **Superior mesenteric artery:** Involved.
- **Superior mesenteric vein:** Not involved. 3mm clearance
- **Posterior:** Not involved. 5mm clearance
- **Bile duct:** Not involved. 60mm clearance
- **Proximal gastric/duodenal:** Not involved. 160mm clearance
- **Distal duodenal/jejunal:** Not involved. 100m clearance
- **Anterior surface:** Not involved. 12mm clearance

Lymph node status
- **LN from main resection specimen:** Nodes present
  - **Lymph nodes found:** 14
  - **No. of positive nodes:** 2
- **Separately labelled LN:** Not submitted

Co-existing pathology:	Chronic pancreatitis
Histologically confirmed metastatic sites:	None
Findings in other resected organs:	**Gallbladder:** No histological abnormality identified. **Omentum:** Mature adipose tissue with abnormality.

ANCILLARY STUDIES

Test type:	Immunohistochemistry
Antibodies:	S100P Positive MUC1 Positive CEA Positive
Interpretive comment:	S100P highlights perineural invasion. Pancreaticobiliary phenotype.

Reported by Dr Robert Beckstein Authorised 4 /3/2013

Appendix 4 WHO Classification of Tumours of the pancreas[17]

Benign	
Acinar cell cystadenoma	8551/0
Serous cystadenoma	8441/0
Premalignant lesions	
Pancreatic intraepithelial neoplasia, grade 3 (PanIN-3)	8148/2
Intraductal papillary mucinous neoplasm with low- or intermediate-grade dysplasia	8453/0
Intraductal papillary mucinous neoplasm with high-grade dysplasia	8453/2
Intraductal tubulopapillary neoplasm	8503/2
Mucinous cystic neoplasm with low- or intermediate-grade dysplasia	8470/0
Mucinous cystic neoplasm with high- grade dysplasia	8470/2
Malignant	
Ductal adenocarcinoma	8500/3
Adenosquamous carcinoma	8560/3
Colloid carcinoma (mucinous noncystic carcinoma)	8480/3
Hepatoid carcinoma	8576/3
Medullary carcinoma	8510/3
Signet ring cell carcinoma	8490/3
Undifferentiated carcinoma	8020/3
Undifferentiated carcinoma with osteoclast-like giant cells	8035/3
Acinar cell carcinoma	8550/3
Acinar cell cystadenocarcinoma	8551/3
Intraductal papillary mucinous neoplasm with an associated invasive carcinoma	8453/3
Mixed acinar-ductal carcinoma	8552/3
Mixed acinar-neuroendocrine carcinoma	8154/3
Mixed acinar-neuroendocrine-ductal carcinoma	8154/3
Mucinous cystic neoplasm with an associated invasive carcinoma	8470/3
Pancreatoblastoma	8971/3
Serous cystadenocarcinoma	8441/3
Solid-pseudopapillary carcinoma	8452/3
Neuroendocrine neoplasms	
Mature teratoma	
Mesenchymal tumours	
Lymphomas	
Secondary tumours	

#Morphology code of the International Classification of Diseases for Oncology (ICD-O) and the Systematized Nomenclature of Medicine (http://snomed.org). Behaviour is coded /0 for benign tumours, /1 for unspecified, borderline or uncertain behaviour, (/2 for in situ carcinomas) and /3 for malignant tumours.

Appendix 5 WHO Classification[a] of Tumours of the ampullary region[17]

Epithelial tumours

Premalignant lesions	
Intestinal-type adenoma	8144/0
Tubular adenoma	8211/0
Tubulovillous adenoma	8263/0
Villous adenoma	8261/0
Noninvasive pancreatobiliary papillary neoplasm with low-grade dysplasia (low grade intraepithelial neoplasia)	8163/0*
Noninvasive pancreatobiliary papillary neoplasm with high-grade dysplasia (high grade intraepithelial neoplasia)	8163/2*
Flat intraepithelial neoplasia (dysplasia), high grade	8148/2
Carcinoma	
Adenocarcinoma	8140/3
Invasive intestinal type	8144/3
Pancreatobiliary type	8163/3*
Adenosquamous carcinoma	8560/3
Clear cell carcinoma	8310/3
Hepatoid adenocarcinoma	8576/3
Invasive papillary adenocarcinoma	8260/3
Mucinous adenocarcinoma	8480/3
Signet ring cell carcinoma	8490/3
Squamous cell carcinoma	8070/3
Undifferentiated carcinoma	8020/3
Undifferentiated carcinoma with osteoclast-like giant cells	8035/3
Neuroendocrine neoplasms[b]	
Neuroendocrine tumour (NET)	
NET G1 (carcinoid)	8240/3
NET G2	8249/3
Neuroendocrine carcinoma (NEC)	8246/3
Large cell NEC	8013/3
Small cell NEC	8041/3
Mixed adenoneuroendocrine carcinoma	8244/3
EC cell, serotonin-producing NET	8241/3
Gangliocytic paraganglioma	8683/0
Somatostatin-producing NET	8156/3

Mesenchymal tumours

Secondary tumours

EC, enterochromaffin

a Morphology code of the International Classification of Diseases for Oncology (ICD-O). Behaviour is coded /0 for benign tumours, /1 for unspecified, borderline or uncertain behaviour, /2 for carcinoma *in situ* and grade III intraepithelial neoplasia, and /3 for malignant tumours.

b The classification is modified from the previous (third) edition of the WHO histological classification of tumours taking into account changes in our understanding of these lesions. In the case of neuroendocrine neoplasms, the

classification has been simplified to be of more practical utility in morphological classification.

* These new codes were improved by the IARC /WHO Committee for ICD-O at its meeting in March 2010.

Appendix 6 WHO Classification[a] of Tumours of the gallbladder and extrahepatic bile ducts[17]

Epithelial tumours

Premalignant lesions	
Adenoma	8140/0
Tubular	8211/0
Papillary	8260/0
Tubulopapillary	8263/0
Biliary intraepithelial neoplasia , grade 3 (BillN-3)	8148/2
Intracystic (gallbladder) or intraductal (bile ducts) papillary neoplasm with low- or intermediate-grade intraepithelial neoplasia	8503/0
Intracystic (gallbladder) or intraductal (bile ducts) papillary neoplasm with high-grade intraepithelial neoplasia	8503/2*
Mucinous cystic neoplasm with low- or intermediate-grade intraepithelial neoplasia	8470/0
Mucinous cystic neoplasm with high-grade intraepithelial neoplasia	8470/2
Carcinoma	
Adenocarcinoma	8140/3
Adenocarcinoma, biliary type	8140/3
Adenocarcinoma, gastric foveolar type	8140/3
Adenocarcinoma, intestinal type	8144/3
Clear cell adenocarcinoma	8310/3
Mucinous adenocarcinoma	8480/3
Signet ring cell carcinoma	8490/3
Adenosquamous carcinoma	8560/3
Intracystic (gallbladder) or intraductal (bile ducts) papillary neoplasm with an associated invasive carcinoma	8503/3*
Mucinous cystic neoplasm with an associated invasive carcinoma	8470/3*
Squamous cell carcinoma	8070/3
Undifferentiated carcinoma	8020/3
Neuroendocrine neoplasms[b]	
Neuroendocrine tumour (NET)	
NET G1 (carcinoid)	8240/3
NET G2	8249/3
Neuroendocrine carcinoma (NEC)	8246/3
Large cell NEC	8013/3
Small cell NEC	8041/3
Mixed adenoneuroendocrine carcinoma	8244/3
Goblet cell carcinoid	8243/3
Tubular carcinoid	8245/1

Mesenchymal tumours

Granular cell tumour	9580/0
Leiomyoma	8890/0
Karposi sarcoma	9140/3

Leiomyosarcoma	8890/3
Rhabdomyosarcoma	8900/3

Lymphomas

Secondary tumours

a The morphology codes are from the International Classification of Diseases for Oncology (ICD-O). Behaviour is coded /0 for benign tumours, /1 for unspecified, borderline or uncertain behaviour, /2 for carcinoma *in situ* and grade III intraepithelial neoplasia, and /3 for malignant tumours.

b The classification is modified from the previous WHO histological classification of tumours taking into account changes in our understanding of these lesions. In the case of neuroendocrine neoplasms, the classification has been simplified to be of more practical utility in morphological classification.

* These new codes were improved by the IARC /WHO Committee for ICD-O at its meeting in March 2010.

Appendix 7 WHO Classification[a] of Tumours of the small intestine[17]

Epithelial tumours	
Premalignant lesions	
Adenoma	8140/0
Tubular	8211/0
Villous	8261/0
Tubulovillous	8263/0
Dysplasia (intraepithelial neoplasia), low grade	8148/0*
Dysplasia (intraepithelial neoplasia), high grade	8148/2
Hamartomas	
Juvenile polyps	
Peutz-Jeghers polyp	
Carcinoma	
Adenocarcinoma	8140/3
Mucinous adenocarcinoma	8480/3
Signet ring cell carcinoma	8490/3
Adenosquamous carcinoma	8560/3
Medullary carcinoma	8510/3
Squamous cell carcinoma	8070/3
Undifferentiated carcinoma	8020/3
Neuroendocrine neoplasms[b]	
Neuroendocrine tumor (NET)	
NET G1 (Carcinoid)	8240/3
NET G2	8249/3
Neuroendocrine carcinoma (NEC)	8246/3
Large cell NEC	8013/3
Small cell NEC	8041/3
Mixed adenoneuroendocrine carcinoma	8244/3
EC cell, serotonin-producing NET	8241/3
Gangliocytic paraganglioma	8683/0
Gastrinoma	8153/3
L cell, Glucagon-like peptide-producing and PP/PYY-producing NETs	8152/1*
Somatostatin-producing NET	8156/3
Mesenchymal tumors	
Leiomyoma	8890/0
Lipoma	8850/0
Angiosarcoma	9120/3
Gastrointestinal stromal tumor	8936/3
Kaposi sarcoma	9140/3
Leiomyosarcoma	8890/3
Lymphomas	
Secondary tumours	

a The morphology codes are from the International Classification of Diseases for Oncology (ICD-O). Behaviour is coded /0 for benign tumours, /1 for unspecified,

borderline or uncertain behaviour, /2 for carcinoma *in situ* and grade III intraepithelial neoplasia, and /3 for malignant tumours.

b The classification is modified from the previous (third) edition of the WHO histological classification of tumours taking into account changes in our understanding of these lesions. In the case of neuroendocrine neoplasms, the classification has been simplified to be of more practical utility in morphological classification.

* These new codes were improved by the IARC /WHO Committee for ICD-O at its meeting in March 2010.

Appendix 8 AJCC Pathological Staging

pT Primary tumour definitions

Pancreas

Category	Description
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ*
T1	Tumour limited to the pancreas, 2 cm or less in greatest dimension
T2	Tumour limited to the pancreas, more than 2 cm in greatest dimension
T3	Tumour extends beyond the pancreas but without involvement of the celiac axis or the superior mesenteric artery
T4	Tumour involves the celiac axis or the superior mesenteric artery (unresectable primary tumour)

*This also includes "PanIn-III" classification

Ampulla of Vater

Category	Description
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ
T1	Tumour limited to ampulla of Vater or sphincter of Oddi
T2	Tumour invades duodenal wall
T3	Tumour invades pancreas
T4	Tumour invades peripancreatic soft tissues or other adjacent organs or structures other than pancreas

Common Bile duct

Category	Description
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ
T1	Tumour confined to the bile duct histologically
T2	Tumour invades beyond the wall of the bile duct
T3	Tumour invades the gallbladder, pancreas, duodenum, or other adjacent organs without involvement of the celiac axis, or the superior mesenteric artery

T4	Tumour involves the celiac axis, or the superior mesenteric artery

pN Regional lymph nodes definitions

Category	Description
NX	Cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis

pM Distant metastasis definitions

Category	Description
M0	No distant metastasis
M1	Distant metastasis

References

1 Yeo CJ, Cameron JL and Sohn TA et al (1997). Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: pathology, complications and outcomes. *Ann Surg* 226(3):248-260.

2 Riall TS, Cameron JL, Lillemoe KD, Winter JM, Campbell KA and al. HRe (2006). Resected periampullary adenocarcinoma: 5-year survivors and their 6- to 10-year follow-up. *Surgery* 140(5):764-772.

3 Michelassi F, Erroi F, Dawson PJ, Pietrabissa A, Noda S, Handcock M and Block GE (1989). Experience with 647 consecutive tumors of the duodenum, ampulla, head of the pancreas, and distal common bile duct. *Ann Surg.* 10(4):544-554.

4 Kim K and Chie E et al (2012). Prognostic significance of tumour location after adjuvant chemoradiotherapy for periampullary adenocarcinoma. *Clinical & translational oncology* 14(5):391-395.

5 Kim R, Chabot J and Saif MW (2011). Adjuvant treatment for ampullary cancer. Highlights from the "2011 ASCO annual meeting". Chicago IL, USA. *JOP* 12(4):362-363.

6 Schmidt CM, Powell ES, Yiannoutsos CT, Howard TJ, Wiebke E and Wiesenauer CA et al (2004). Pancreaticoduodenectomy: a 20-year experience in 516 patients. *Arch Surg* 139(7):718-725.

7 Winter JM, Cameron JL and Campbell KA et al (2006). 1423 pancreaticoduodenectomies for pancreatic cancer: a single institution experience. *J Gastrointest Surg* 10(9):1199-1210.

8 Balachandran P, Sikora SS and Kapoor S et al (2006). Long-term survival and recurrence patterns in ampullary cancer. *Pancreas* 32(4):390-395.

9 Edge SE, Byrd DR, Compton CC, Fritz AG, Greene FL and Trotti A (eds) (2010). *AJCC Cancer Staging Manual 7th ed.*, New York, NY.: Springer.

10 Polydorides AD, Shia J, Tang LH and Klimstra DS (2008). An immunohistochemical panel distinguishes colonization by pancreatic ductal adenocarcinoma from adenomas of ampullary and duodenal mucosa. *Mod Pathol.* 21(1s):132A.

11 Verbeke CS and Gladhaug IP (2012). Resection margin involvement and tumour origin and pancreatic head cancer. *Br J Surg* 99(8):1036-1049.

12 Cross SS, Feeley KM and Angel CA (1998). The effect of four interventions on the informational content of histopathology reports of resected colorectal carcinomas. *J Clin Oncol* 51(6):481–482.

13 Mathers M, Shrimankar J, Scott D, Charlton F, Griffith C and Angus B (2001). The use of a standard proforma in breast cancer reporting. *J Clin Pathol* 54(10):809–811.

14 Srigley JR, McGowan T, MacLean A, Raby M, Ross J, Kramer S and Sawka C (2009). Standardized synoptic cancer pathology reporting: A population-based approach. *J Surg Oncol* 99(8):517–524.

15 Gill AJ, Johns AL, Eckstein R, Samra JS, Kaufman A, Chang DK, Merrett ND, Cosman PH, Smith RC, Biankin AV and Kench JG (2009). Synoptic reporting improves histopathological assessment of pancreatic resection specimens. *Pathology* 41(2):161–167.

16 RCP (Royal College of Pathologists) (2007). *Standards and Datasets for Reporting Cancers — Dataset for Colorectal Cancer*. RCP, London.

17 WHO (World Health Organization) (2010). *Classification of Tumours. Pathology and Genetics of Tumours of the Digestive System (4th edition)*. Bosman FT, Carneiro F, Hruban RH and Theise ND. IARC Press, Lyon.

18 RCPA (Royal College of Pathologists of Australasia (2009). *Guidelines for Authors of Structured Cancer Pathology Reporting Protocols*. RCPA, Surry Hills NSW.

19 RCPA (Royal College of Pathologists of Australasia) (2004). *Chain of Information Custody for the Pathology Request-Test-Report Cycle — Guidelines for Requesters and Pathology Providers*. RCPA, Surry Hills, NSW.

20 Winter JM, Cameron JL and Olino K et al (2010). Clinicopathologic analysis of ampullary neoplasms in 450 patients: implications for surgical strategy and long-term prognosis. *J Gastrointest Surg* 14:379-387.

21 Yoon YS, Kim SW and Park SJ et al (2005). Clinicopathologic analysis of early ampullary cancers with a focus on the feasibility of ampullectomy. *Ann Surg* 242(1):92-100.

22 Zhong J, Palta M and Willett CG et al (2013). The role of local excision in invasive adenocarcinoma of the ampulla of Vater. *J Gastrointest Oncol* 4(1):8-13.

23 Fukuda S, Oussoultzoglou E, Bachellier P, Rosso E, Nakano H, Audet M and Jaeck D (2007). Significance of the depth of portal vein wall invasion after curative resection for pancreatic adenocarcinoma. *Arch Surg* 142(2):172-179.

24 Menon KV, Gomez D, Smith AM, Anthoney A and Verbeke CS (2009). Impact of margin status on survival following pancreaticoduodenectomy for cancer: the Leeds Pathology Protocol (LEEPP). *HPB* 11(1):18-24.

25 Verbeke CS (2008). Resection margins and R1 rates in pancreatic cancer – are we there yet? *Histopathology* 52:787-796.

26 Verbeke CS, Leitch D, Menon KV, McMahon MJ, Guillou PJ and Anthoney A (2006). Redefining the R1 resection in pancreatic cancer. *Br J Surg.* 93:1232-1237.

27 Esposito I, Kleeff J and Bergmann F et al (2008). Most pancreatic resections are R1 resections. *Ann Surg Oncol* 15:1651-1660.

28 Westgaard A, Clausen OPF and Gladhaug IP (2011). Survival estimates after pancreatoduodenectomy skewed by non-standardized histopathology reports. *APMIS* 119(10):689-700.

29 Han SS, Jang JY, Kim SW, Kim WH, Lee KU and Park YH (2006). Analysis of long-term survivors after surgical resection for pancreatic cancer. *Pancreas* 32:271−275.

30 Sierzega M, Popiela T, Kulig J and Nowak K (2006). The ratio of metastatic/resected lymph nodes is an independent prognostic factor in patients with node-positive pancreatic head cancer. *Pancreas* 33:240−245.

31 College of American Pathologists (2012). Protocol for examination of specimens from patients with carcinoma of the exocrine pancreas.

32 Klöppel G, Hruban RH and Longnecker DS et al (eds) (2000). *Pathology and Genetics of Tumours of the Digestive System*, IARC press Lyon, France.

33 Adsay V, Ohike N, Tajiri T, Kim GE, Krasinskas A, Balci S, Bagci P, Basturk O, Bandyopadhyay S, Jang KT, Kooby DA, Maithel SK, Sarmiento J, Staley CA, Gonzalez RS, Kong SY and Goodman M (2012). Ampullary region carcinomas: definition and site specific classification with delineation of four clinicopathologically and prognostically distinct subsets in an analysis of 249 cases. *Am J Surg Pathol.* 36(11):1592-1608.

34 Shimizu Y, Kimura F and Shimizu H et al (2008). The morbidity, mortality, and prognostic factors for ampullary carcinoma and distal cholangiocarcinoma. *Hepatogastroenterology* 55:699-703.

35 Sellner FJ, Riegler FM and Machacek E (1999). Implications of histological grade of tumour for the prognosis of radically resected periampullary adenocarcinoma. *Eur J Surg* 165(9):865-870.

36 Adsay NV, Basturk O and Bonnett M et al (2005). Proposal for a new and more practical grading system for pancreatic ductal adenocarcinoma. *Am J Surg Pathol* 29:724-733.

37 Giulianotti PC, Boggi U, Fornaciari G, Bruno J, Rossi G, Giardino D, Di Candio G and Mosca F (1995). Prognostic value of histological grading in ductal adenocarcinoma of the pancreas. Klöppel vs TNM grading. *Int J Pancreatol.* 17(3):279-289.

38 Chu PG, Schwarz RE, Lau SK, Yen Y and Weiss LM (2005). Immunohistochemical staining in the diagnosis of pancreatobiliary and ampulla of Vater adenocarcinoma: application of CDX2, CK17, MUC1, and MUC2. *Am J Surg Pathol* 29(3):359-367.

39 Moriya T, Kimura W, Hirai I, Takasu N and Mizutani M (2011). Expression of MUC1 and MUC2 in ampullary cancer. *Int J Surg Pathol.* 19(4):441-447.

40 Chang DK, Jamieson NB and Johns AL et al (2013). Histomolecular phenotypes and outcome in adenocarcinoma of the ampulla of vater. *J Clin Oncol.* 31(10):1348-1356.

41 Verbeke CS, Knapp J and Gladhaug IP (2011). Tumour growth is more dispersed in pancreatic head cancers than in rectal cancer: implications for resection margin assessment. *Histopathology* 59:1111-1121.

42 Hong SM, Goggins M, Wolfgang CL, Schulick RD, Edil BH, Cameron JL, Handra-Luca A, Herman JM and Hruban RH (2012). Vascular invasion in infiltrating ductal adenocarcinoma of the pancreas can mimic pancreatic intraepithelial neoplasia: a histopathologic study of 209 cases. *Am J Surg Pathol.* 36(2):235-241.

43 Kirsch R, Messenger DE, Riddell RH, Pollett A, Cook M, Al-Haddad S, Streutker CJ, Divaris DX, Pandit R, Newell KJ, Liu J, Price RG, Smith S, Parfitt JR and Driman DK (2013). Venous invasion in colorectal cancer: impact of an elastin stain on detection and interobserver agreement among gastrointestinal and nongastrointestinal pathologists. *Am J Surg Pathol* 37(2):200-210.

44 Garcea G, Dennison AR, Ong SL, Pattenden CJ, Neal CP, Sutton CD, Mann CD and Berry DP (2007). Tumour characteristics predictive of survival following resection for ductal adenocarcinoma of the head of pancreas. *Eur J Surg Oncol.* 33(7):892-897.

45 Inoue Y, Hayashi M, Hirokawa F, Egashira Y and Tanigawa N (2012). Clinicopathological and operative factors for prognosis of carcinoma of the ampulla of vater. *Hepatogastroenterology* 59(117):1573-1576.

46 Chatterjee D, Rashid A, Wang H, Katz MH, Wolff RA, Varadhachary GR, Lee JE, Pisters PW, Gomez HF, Abbruzzese JL, Fleming JB and Wang H (2012). Tumor invasion of muscular vessels predicts poor prognosis in patients with pancreatic ductal adenocarcinoma who have received neoadjuvant therapy and pancreaticoduodenectomy. *Am J Surg Pathol* 36(4):552-559.

47 Yekebas EF, Bogoevski D, Cataldegirmen G, Kunze C, Marx A, Vashist YK, Schurr PG, Liebl L, Thieltges S, Gawad KA, Schneider C and Izbicki JR (2008). En bloc vascular resection for locally advanced pancreatic malignancies infiltrating major

blood vessels: perioperative outcome and long-term survival in 136 patients. *Ann Surg* 247(2):300-309.

48 Nakagohri T, Kinoshita T, Konishi M, Inoue K and Takahashi S (2003). Survival benefits of portal vein resection for pancreatic cancer. *Am J Surg* 186(2):149-153.

49 Shibata C, Kobari M, Tsuchiya T, Arai K, Anzai R, Takahashi M, Uzuki M, Sawai T and Yamazaki T (2001). Pancreatectomy combined with superior mesenteric-portal vein resection for adenocarcinoma in pancreas. *World J Surg* 25(8):1002-1005.

50 Ozaki H, Hiraoka T, Mizumoto R, Matsuno S, Matsumoto Y, Nakayama T, Tsunoda T, Suzuki T, Monden M, Saitoh Y, Yamauchi H and Ogata Y (1999). The prognostic significance of lymph node metastasis and intrapancreatic perineural invasion in pancreatic cancer after curative resection. *Surg Today* 29(1):16-22.

51 Bouvet M, Gamagami RA, Gilpin EA, Romeo O, Sasson A, Easter DW and Moossa AR (2000). Factors influencing survival after resection for periampullary neoplasms. *Am J Surg* 180(1):13-17.

52 Wagner M, Redaelli C, Lietz M, Seiler CA, Friess H and Büchler MW (2004). Curative resection is the single most important factor determining outcome in patients with pancreatic adenocarcinoma. *Br J Surg* 91(5):586-594.

53 Noto M, Miwa K, Kitagawa H, Kayahara M, Takamura H, Shimizu K and Ohta T (2005). Pancreas head carcinoma: frequency of invasion to soft tissue adherent to the superior mesenteric artery. *Am J Surg Pathol* 29(8):1056-1061.

54 Breslin TM, Hess KR, Harbison DB, Jean ME, Cleary KR, Dackiw AP, Wolff RA, Abbruzzese JL, Janjan NA, Crane CH, Vauthey JN, Lee JE, Pisters PW and Evans DB (2001). Neoadjuvant chemoradiotherapy for adenocarcinoma of the pancreas: treatment variables and survival duration. *Ann Surg Oncol.* 8(2):123-132.

55 Hruban RH, Takaori K and Klimstra D et al (2004). An Illustrated Consensus on the Classification of Pancreatic Intraepithelial Neoplasia and Intraductal Papillary Mucinous Neoplasms. *Am J Surg Pathol* 28:977-987.

56 Ohike N, Kim GE and Tajiri T et al (2010). Intra-ampullary Papillary-Tubular Neoplasm (IAON): Characterisation of Tumoral Intraepithelial Neoplasia Occurring Within the Ampulla. A clinicopathologic Analysis of 82 Cases. *Am J Surg Pathol* 34:1731-1748.

57 Evans DB, Farnell MB and Lillemoe KD et al (2009). Surgical treatment of resectable and borderline resectable pancreas cancer: expert consensus statement. *Ann Surg Oncol* 16:1736-1744.

58 Khalifa MA, Maksymov V and Roswell C (2009). Retroperitoneal margin of the pancreaticoduodenectomy specimen: anatomic mapping for the surgical pathologist. *Virchows Arch.* 454:125-131.

59 Chang DK, Johns AL and Merrett ND et al (2009). Margin clearance and outcome in rejected pancreatic cancer. *J Clin Oncol* 27:2855-2862.

60 Raut CP, Tseng JF and Sun CC et al (2007). Impact of resection status on pattern of failure survival after pancreaticoduodenectomy for pancreatic adenocarcinoma. *Ann Surg* 246:52-60.

61 Matthaei H, Hong SM, Mayo SC, dal Molin M, Olino K, Venkat R, Goggins M, Herman JM, Edil BH, Wolfgang CL, Cameron JL, Schulick RD, Maitra A and Hruban RH (2011). Presence of pancreatic intraepithelial neoplasia in the pancreatic transection margin does not influence outcome in patients with R0 resected pancreatic cancer. *Ann Surg Oncol* 18(12):3493-3499.

62 Feakins R, Campbell F and Verbeke CS (2013). Survey of UK histopathologists' approach to the reporting of resection specimens for carcinomas of the pancreatic head. *J Clin Pathol.* 66(8):715-717.

63 Quirke P and Morris E (2007). Reporting colorectal cancer. *Histopathology* 50(1):555–556.

64 Lim JE, Chien MW and Earle CC (2003). Prognostic factors following curative resection for pancreatic adenocarcinoma: a population-based, linked database analysis of 396 patients. *Ann Surg* 237(1):74-85.

65 House MG, Gönen M, Jarnagin WR, D'Angelica M, DeMatteo RP, Fong Y, Brennan MF and Allen PJ (2007). Prognostic significance of pathologic nodal status in patients with resected pancreatic cancer. *J Gastrointest Surg* 11(11):1549-1555.

66 Shimada K, Sakamoto Y, Sano T and Kosuge T (2006). Prognostic factors after distal pancreatectomy with extended lymphadenectomy for invasive pancreatic adenocarcinoma of the body and tail. *Surgery* 139(3):288-295.

67 Brown KM, Tompkins AJ, Yong S, Aranha GV and Shoup M (2005). Pancreaticoduodenectomy is curative in the majority of patients with node-negative ampullary cancer. *Arch Surg* 140(6):529-532.

68 Falconi M, Crippa S, Domínguez I, Barugola G, Capelli P, Marcucci S, Beghelli S, Scarpa A, Bassi C and Pederzoli P (2008). Prognostic relevance of lymph node ratio and number of resected nodes after curative resection of ampulla of Vater carcinoma. *Ann Surg Oncol* 15(11):3178-3186.

69 Hong SM, Cho H, Lee OJ and Ro JY (2005). The number of metastatic lymph nodes in extrahepatic bile duct carcinoma as a prognostic factor. *Am J Surg Pathol* 29(9):1177-1183.

70 Gomez D, Menon KV, Smith AM and Verbeke CS (2008). Tumour location and number of positive lymph nodes are independent prognostic factors in distal bile duct cancer. *HPB (Oxford)* 10(Suppl. 1):227.

71 Qiao QL, Zhao YG, Ye ML, Yang YM, Zhao JX, Huang YT and Wan YL (2007). Carcinoma of the ampulla of Vater: factors influencing long-term survival of 127 patients with resection. *World J Surg* 31(1):137-143.

72 Robinson SM, Rahman A, Haugk B, French JJ, Manas DM, Jaques BC, Charnley RM and White SA (2012). Metastatic lymph node ratio as an important prognostic factor in pancreatic ductal adenocarcinoma. *Eur J Surg Oncol* 38(4):333-339.

73 La Torre M, Cavallini M, Ramacciato G, Cosenza G, Rossi Del Monte S, Nigri G, Ferri M, Mercantini P and Ziparo V (2011). Role of the lymph node ratio in pancreatic ductal adenocarcinoma. Impact on patient stratification and prognosis. *J Surg Oncol* 104(6):629-633.

74 Marsh R, Talamonti MS and Ji Y (2013). Effect of adjuvant chemotherapy with fluorouracil plus folinic acid or gemcitabine vs. observation on survival in patients with resected periampullary adenocarcinoma. *Transl Gastrointest Cancer* 2(3):157-159.

75 Basturk O, Khayyata S, Klimstra DS, Hruban RH, Zamboni G, Coban I and Adsay NV (2010). Preferential expression of MUC6 in oncocytic and pancreatobiliary types of intraductal papillary neoplasms highlights a pyloropancreatic pathway, distinct from the intestinal pathway, in pancreatic carcinogenesis. *Am J Surg Pathol* 34(3):364-370.

76 Adsay NV, Merati K, Andea A, Sarkar F, Hruban RH, Wilentz RE, Goggins M, Iocobuzio-Donahue C, Longnecker DS and Klimstra DS (2002). The dichotomy in the preinvasive neoplasia to invasive carcinoma sequence in the pancreas: differential expression of MUC1 and MUC2 supports the existence of two separate pathways of carcinogenesis. *Mod Pathol.* 15(10):1087-1095.

77 Mino-Kenudson M, Fernández-del Castillo C, Baba Y, Valsangkar NP, Liss AS, Hsu M, Correa-Gallego C, Ingkakul T, Perez Johnston R, Turner BG, Androutsopoulos V, Deshpande V, McGrath D, Sahani DV, Brugge WR, Ogino S, Pitman MB, Warshaw AL and Thayer SP (2011). Prognosis of invasive intraductal papillary mucinous neoplasm depends on histological and precursor epithelial subtypes. *Gut* 60(12):1712-1720.

78 Larbouret C, Robert B, Bascoul-Mollevi C, Penault-Llorca F, Ho-Pun-Cheung A, Morisseau S, Navarro-Teulon I, Mach JP, Pèlegrin A and Azria D (2010). Combined cetuximab and trastuzumab are superior to gemcitabine in the treatment of human pancreatic carcinoma xenografts. *Ann Oncol.* 21(1):98-103.

79 Larbouret C, Robert B, Navarro-Teulon I, Thèzenas S, Ladjemi MZ, Morisseau S, Campigna E, Bibeau F, Mach JP, Pèlegrin A and Azria D (2007). In vivo therapeutic synergism of anti-epidermal growth factor receptor and anti-HER2 monoclonal antibodies against pancreatic carcinomas. *Clin Cancer Res.* 13(11):3356-3362.

80 Law LY (2012). Dramatic response to trastuzumab and paclitaxel in a patient with human epidermal growth factor receptor 2-positive metastatic cholangiocarcinoma. *J Clin Oncol.* 30(27):e271-273.

81 Chou A, Waddell N, Cowley MJ, Gill AJ, Chang DK, Patch AM, Nones K, Wu J, Pinese M, Johns AL, Miller DK, Kassahn KS, Nagrial AM, Wasan H, Goldstein D, Toon CW, Chin V, Chantrill L, Humphris J, Mead RS, Rooman I, Samra JS, Pajic M, Musgrove EA, Pearson JV, Morey AL, Grimmond SM and Biankin AV (2013).

Clinical and molecular characterization of HER2 amplified-pancreatic cancer. *Genome Medicine. In print* 5(8):78.

82 Chou A, Waddell N and Cowley MJ et al (2013). Clinical features of HER2 amplified pancreatic cancer *Genome Medicine. In print*.

83 Biankin AV, Waddell N, Kassahn KS and Gingras MC et al (2012). Pancreatic cancer genomes reveal aberrations in axon guidance pathway genes. *Nature* 491(7424):399-405 doi: 310.1038/nature11547. Epub 12012 Oct 11524.

84 Bartsch DK, Gress TM and Langer P (2012). Familial pancreatic cancer—current knowledge. *Nature Reviews Gastroenterology and Hepatology* 9:445-453.

85 Royal College of Pathologists of Australasia (2011). Functional Requirements for Laboratory Information Systems to support Structured Pathology Reporting of Cancer Protocols http://www.rcpa.edu.au/Publications/StructuredReporting/LISFunctionalRequirements.htm.

86 Valenstein PN (2008). Formatting pathology reports: applying four design principles to improve communication and patient safety. *Arch Path Lab Med.* 132(1):84–94.