Approach to cut up: Upper GI

Marco Novelli



Overview

- General points
- Oesophagus
 - Oesophagectomy specimens
 - EMRs + ESDs
- Stomach
 - Specimen handling
 - Recent changes in clinical practice
 - TNM
 - OGJ tumours
- Gastrointestinal Stromal Tumours

- Check name, numbers, specimen labelling.
- Check in bottom of specimen pot.
 - Donuts, extra margin etc.
- Description.
 - Does specimen match clinical details?
 - Can you orientate specimen?

- Check name, numbers, specimen labelling.
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- Description.
 - Does specimen match clinical details?
 - Can you orientate specimen?

→ IF NOT DO NOT CUT SPECIMEN

- No single "correct" way to cut a specimen
- RCPath datasets are very useful
 - Diagrams
 - Sampling guidelines
 - Read guideline BEFORE cutting specimen.
- Photograph resection specimens

Specimen dissection:

- Block order

- Margins
- Lymph nodes
- Tumour (3+ blocks, ? 1 large block)

– Margins

- Cut ends (full face)
- Ducts, vessels etc
- Circumferential margins

- Record block key in macroscopic report

Mega blocks:



- Pros
 - Good macro-micro correlation
 - Useful for tumour mapping (e.g. prostates)
 - Useful for photographs/talks
- Cons
 - Relatively labour intensive
 - Difficult to store
 - Difficult to stain (immunocytochemistry)

 \rightarrow Check with lab staff before using

Oesophagus





Riddell, A. M. et al. Am. J. Roentgenol. 2007;188:W37-W43



--Cadaver of 86-year-old woman



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Figure 1. Drawings illustrate transthoracic esophagectomy through a right thoracotomy.



Kim S H et al. Radiographics 2001;21:1119-1137





Oesophagectomy





Oesophagectomy

- Longterm morbidity
 - Dysphagia
 - -Reflux oesophagitis
 - Delayed gastric emptying
 - Dumping
 - -Nausea
 - Diarrhoea
 - -Vocal cord paralysis.

Oesophageal resections

- Vast majority are oesophagectomies/ oesophagogastrectomies for adenocarcinoma.
- SCC oesophagus primarily treated by radical chemoradiotherapy.
- Increasing number of EMR specimens.

Oesophagectomy specimens



- Oesophagus shrinks
 25% on removal from patient
- On fixation
 oesophagus may be
 33% of original length

Oesophagectomy specimens



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→ Pin specimen fresh if you can • Open gastric end (cut along staples) + pin on cork board



• Suboptimally pinned specimen



• Non-pinned specimen



Proximal margin assessment in non-pinned specimens



Proximal margin assessment in non-pinned specimens



• Ink circumferential margin





Circumferential margins



- Almost entire length of oesophagus.
 (≈ 1cm intra-abdominal peritonealised)
- At OGJ for gastric tumours.



Systematic review and meta-analysis of the influence of circumferential resection margin involvement on survival in patients with operable oesophageal cancer. Chan DS, Reid TD, Howell I, Lewis WG. Br J Surg. 2013 Mar;100(4):456-64.

- Meta-analysis 5 year mortality
- The College of American Pathologists (Tumour at CRM)

- OR 4.02, 95% CI - 2.25 to 7.20; P < 0.001.

• The Royal College of Pathologists (Tumour <1mm from CRM)

- OR 2.52, 95% CI - 1.96 to 3.25; P < 0.001.

CRM positivity rates

Histopathology	RCPath CRM status	
Histopathology 2013, 62 , 752–763. DOI: 10.1111/his.12078	RO	50 (26)
Prognostic value of added stratification of circumferential	R1	145 (74)
Jawad Ahmad, ^{1.} * Maurice B Loughrey, ^{1.2.} * David Donnelly, ³ Lisa Ranaghan, ³ Rajeev Shah, ¹ Giulio Napolitano ³ & Andrew J Kennedv ¹	CAP CRM status R0	137 (70)
¹ Royal Victoria Hospital/Belfast Health and Social Care Trust, Belfast, ² Northern Ireland Molecular Pathology Laboratory, Centre for Cancer Research and Cell Biology, Queens University Belfast, Belfast, and ³ Centre for Public Health, Mulhouse Building, Belfast, UK	R1	58 (30)

RCPath <1mm: 74%

Defining a positive circumferential resection margin in		
oesophageal cancer and its implications for adjuvant treatment	CRM (mm)	
J. R. O'Neill ¹ , N. A. Stephens ¹ , V. Save ² , H. M. Kamel ⁴ , H. A. Phillips ³ , P. J. Driscoll ⁵ and S. Paterson-Brown ^I Departments of ¹ General Surgery and ² Pathology, Royal Infirmary of Edinburgh, and ³ Department of Oncology, Western General Hospital, Edinburgh, ⁴ Department of Pathology, Wishaw General Hospital, Glasgow, and ⁵ Department of General Surgery, Victoria Hospital, Kirkealdy, UK <i>Correspondence to:</i> Mr J. R. O'Neill, Department of General Surgery, Royal Infirmary of Edinburgh, 51 Little France Crescent, Old Dalkeith Road, Edinburgh EH16 4SA, UK (e-mail: roneill1@staffmail.ed.ac.uk)	0	47 (20.8)
	0.1-0.9	83 (36.7)
	≥ 1	96 (42.5)

RCPath <1mm: 57.5%

Blocks

- Proximal and distal margins (full thickness).
- Circumferential margin.
- Lymph nodes.
- Tumour (4+).
- Background oesophagus, stomach etc

Handling and reporting EMRs

Endoscopic mucosal resection (EMR) + Endoscopic submucosal dissection (ESD)



Endoscopic mucosal resection (EMR)



- Resection not a biopsy.
- Treat like a cervical cone (do NOT bisect!).
- If received orientated ink margins.

Endoscopic mucosal resection (EMR)



- Often multiple with site range (e.g 32-36cm).
- Serially section, process all, ends in 1 cassette.
- Ideally no more than 2 sections a cassette.

Endoscopic mucosal resection (EMR)




Ideally only 2 sections a cassette to optimise orientation



ESDs



- Ink if orientated and large enough.
- Serially / cruciate section.



- Usually lots of diathermy artefact.
- Dysplasia often reaches circumferential margin.
- Diagnostic and "debulking" procedure!!

Pathological assessment of invasion



Colorectal adenocarcinoma with desmoplastic stroma





Benign glands in Barrett's often extend in between bundles of smooth muscle





Pseudo-invasion in high grade dysplasia





Early oesophageal adenocarcinoma often lacks a desmoplastic stroma



pT staging of adenocarcinoma

Oesophageal adenocarcinoma T staging, TNM7

Primary tumor (T)	
ТХ	Primary tumor cannot be assessed
ТО	No evidence of primary tumor
Tis	High-grade dysplasia
T1	Tumor invades lamina propria, muscularis mucosae, or submucosa
T1a	Tumor invades lamina propria or muscularis mucosae
T1b	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades adventitia
T4	Tumor invades adjacent structures
T4a	Resectable tumor invading pleura, pericardium, or diaphragm
T4b	Unresectable tumor invading other adjacent structures, such as the aorta, vertebral body, and trachea

Significance of the Depth of Tumor Invasion and Lymph Node Metastasis in Superficially Invasive (T1) Esophageal Adenocarcinoma



T1a – lamina propria. T1b – muscularis mucosae. T1c – superficial submucosa. T1d – deep submucosa.

Liu L et al. Am J Surg Pathol. 2005 Aug;29(8):1079-85.

Double Muscularis Mucosae in Barrett's Esophagus



Takubo *et al*. Hum Pathol. 1991 Nov;22(11):1158-61.

Double Muscularis Mucosae in Barrett's Esophagus



Takubo *et al*. Hum Pathol. 1991 Nov;22(11):1158-61.











- Stage invasive carcinoma.
 - Mostly pT1
 - Submucosal invasion?
 - May be difficult to assess as splaying/reduplication of muscularis mucosa)
- Measure depth of invasion beyond muscularis mucosae.
- Circumferential margins
- Deep resection margin



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- Desmin staining can be very helpful in delineating the lower border of the muscularis mucosae





Desmin staining



0.8mm invasion beyond muscularis mucosae \rightarrow pT1b, SM2

Staging of mucosal invasion I



Fig. 1. Subclassification of the depth of superficial esophageal cancer (number of patients). ep, carcinoma in situ; lpm, lamina propria mucosa, mm, muscularis mucosa; m, mucosa; sm, submucosa; mp, muscularis propria.

Shimada 2006 Am J Surg

Staging of EMRs

pT1a

- \bullet M1 Limited to the epithelial layer (HGD / IMC).
- •M2 Invades the lamina propria.
- \bullet M3 Invades into but not through the muscularis mucosa.

pT1b

- •SM1 Infiltrates submucosa <500 microns.
- •SM2 Infiltrates submucosa <1000 microns.
- •SM3 Infiltrates submucosa ≥ 1000 microns.

Stomach

Gastric resections

- Variety of operations:
 - Oesophagogastrectomy
 - Proximal gastrectomy
 - Distal gastrectomy
 - Subtotal/total/extended gastrectomy
 - Sleeve gastrectomy

Gastric resections

- Open specimen and pin out where possible.
- Identify OGJ (if present).
- Lymph nodes (lesser curve, greater curve etc).
- Margins
 - Proximal
 - Distal
 - Circumferential (OGJ)
- Serosal involvement.



OG Junction





Mucosal aspect

Serosal aspect

Nodal stations of the stomach.



Figure 1. Diagram of the abdomen: gastro-oesophageal (black); hepatic artery (aqua); splenic (pink); gastro-omental (light purple); left gastric (blue); hepatoduodenal ligament (orange).



Figure 2. Diagram of the abdomen: left gastric (green); coeliac (yellow); diaphragmatic (red); paraoesophageal (blue); lesser curvature (aqua).

Morón FE, Szklaruk J. Br J Radiol. 2007 Oct;80(958):841-8.






- Margins:
 - Where possible sample entire margin.
- Nodes:
 - OGJ, proximal lesser curve, distal lesser curve, proximal greater curve, distal greater curve.



Measure tumour (3 dimensions)

• Bread-slice tumour, lay our slices and photograph

- 3+ blocks of tumour (+/- megablock).
- Sample:
 - Extension into perigastric connective tissue.
 - Circumferential margin at OGJ.
 - Serosal involvement.

Bariatric sleeve gastrectomy

- Open specimen with scissors.
- Wash and examine mucosa.
- Sample any focal lesions.
- 1-2 random blocks.

Changes in clinical practice

Morón FE, Szklaruk J. Br J Radiol. 2007 Oct;80(958):841-8.

Gastric cancer surgical resections

- D1 lymphadenectomy
 - Traditional nodal dissection taking nodes directly adjacent to stomach.
 - Used in palliative cases.
- D2 lymphadenectomy
 - Typical UK surgical practice (?).
 - Lymph nodes from coeliac axis, left gastric, common hepatic and splenic arteries.
- D3 lymphadenectomy
 - Radical nodal dissection commonly practiced in Far East.
 - Lymph nodes from hepatoduodenal ligament, SMV, aorta/vena cava to IMA and retropancreatic area.

Nodal dissection for patients with gastric cancer: a randomised controlled trial. Wu CW *et al*. Lancet Oncol. 2006;7(4):309-15.

- 221 patients randomised to D1 or D3 surgery.
- 5.9% 5-year survival advantage for D3 surgery.

MAGIC study: peri-operative Epirubicin, cisplatin and infused 5-FU (ECF).

• 5 year survival: 23% surgery vs 36% surgery + neoadjuvent chemo.

D. Cunningham *et al*, for the MAGIC Trial Participants. Perioperative Chemotherapy versus Surgery Alone for Resectable Gastroesophageal Cancer. New Engl J Med 2006;355 (1):11-20.

TNM

International Union Against Gancer

TNM Classification of Malignant Tumours

Fifth Edition

UICC International Union Against Cancer

TNM Classification of Malignant Tumours

Sixth Edition

1997

UICC International Union Against Cancer

TNM Classification of Malignant Tumours

SEVENTH EDITION

EDITED BY LESLIE SOBIN MARY GOSPODAROWICZ CHRISTIAN WITTEKIND

- Published Nov 2009
- Becoming widely utilised but TNM5 recommended for colorectal tumours.
- For oesophago-gastric tumours quote TNM used: ypT3 N1 (TNM7).

APPENDIX D

NATIONAL DATASET FOR

OESOPHAGEAL CARCINOMA HISTOPATHOLOGY REPORTS

Surname	Forenames	Date of birth
Hospital	Hospital no	NHS no
Date of receipt	Date of reporting	Report no
Pathologist	Surgeon	Sex

Shaded data items = 'non core' data

GROSS DESCRIPTION

Maximum length of specimen: mm	Tumour edge to nearest distal margin:	mm
Length of oesophagus: mm	Tumour edge to nearest proximal margin:	mm
Length of stomach:	Type of tumour Dolypoid	Other
Length of tumour mm	Pinned	Not pinned
Width of tumour:	Siewert tumour type (cardiac cancers only)	1 2

... mm)

Number positive.....

HISTOLOGY

COMMENTS

Type of tumour	Circumferential margin
Squamous Adenocarcinoma	Involvement (<1 mm): Yes No N/A
Other (specify)	(If no: distance of carcinoma to nearest circumferential
Differentiation by worst area:	margin mm
Well Moderately Poorly differentiated	Other features
Depth of invasion	Vascular invasion Yes No
Tis high-grade dysplasia	Barrett's metaplasia 🗌 Yes 🗌 No
T1 invasion of lamina propria/submucosa	adjacent to tumour
T2 invasion of muscularis propria	Lymph nodes
T3 invasion beyond muscularis propria	Number examined Number positive
T4 invasion of adjacent structures	(N0 if no nodes positive, otherwise N1)
Yes No – serosal involvement:	Distant metastases
Proximal margin	Coeliac axis node positive Yes No
Normal Dysplasia Carcinoma Barrett's	(M1a if lower thoracic carcinoma, otherwise M1b)
Distal margin	Cervical node positive Yes No
🗌 Normal 🔲 Dysplasia 🔲 Carcinoma	(M1a if upper thoracic carcinoma, otherwise M1b)
	Other distant metastasis (M1b) Yes No

Complete resection \Box Yes(R0) \Box No(R1 or R2)	(v) pT pN	рМ	TNM 5 th edition
	(v) pT $pN (i +/-)$	рМ	TNM 6 th edition
	(y) pT pN(i +/-)	pM	TNM 6 th editi

The Royal College of Pathologists Pathology: the science behind the cure

Standards and Datasets for Reporting Cancers

Dataset for the histopathological reporting of oesophageal carcinoma (2nd edition)

February 2007

Coordinator: Dr Nicholas P Mapstone, Royal Lancaster Infirmary

APPENDIX C Reporting proforma

NATIONAL DATASET FOR GASTRIC CARCINOMA HISTOPATHOLOGY REPORTS

Surname	Forenames	Date of birth
Hospital	Hospital no	NHS no
Date of receipt	Date of reporting	Report no
Pathologist	Surgeon	Sex

Specimen dimensions

Length of stomach - greater curve mm Length of stomach - lesser curve mm

Length of oesophagus mm Length of duodenum mm Site of tumour Maximum tumour diametermm Distance of tumour to nearest margin (cut end)

.....mm

GROSS DESCRIPTION

Type of specimen		
Oesophago-gastrectomy	Distal gastrectomy	
Total gastrectomy	Local resection	
Type of tumour		
Polypoid, ulcerating or fungatin	g 🗌	
Diffusely infiltrating		

HISTOLOGY

Type of tumour	Proximal margin involved Yes No
Adenocarcinoma	Distal margin involved Yes No
Lauren classification Intestinal Diffuse/mixed D Differentiation by worst area Well/moderately Poorly D	Circumferential margin lower oesophagus Involvement (< 1 mm): Yes No N/A (If no, distance of tumour to nearest circumferential margin mm)
Local invasion	Lymphatic/vascular invasion Yes No
T0 No tumour identified	Lymph nodes Number examined Number positive N0 (0 nodes) N2 (7–15 nodes) N1 (1–6 nodes) N3 (>15 nodes) Distant metastases Unknown (MX) Yes (M1)
PATHOLOGICAL STAGING Complete resection Yes (R0) No (R1 or R2) History of neoadjuvant therapy (y) Yes No	TNM (y) $pT \square N \square M \square$
Signature/	/ SNOMED codes T/M/M.

The Royal College of Pathologists *Pathology: the science behind the cure*

Standards and Datasets for Reporting Cancers

Dataset for the histopathological reporting of

gastric carcinoma (2nd edition)

Coordinator: Professor Marco R Novelli, University College London

January 2007

Current RCPath datasets for oesophagus and stomach (2nd Edition).

OGJ tumours

- Siewert classification
- Gastric versus oesophageal dataset?

Siewert classification

Leading article

Classification of adenocarcinoma of the J. R. Siewert oesophagogastric junction H. J. Stein

We have defined and described adenocarcinomas of the oesophagogastric junction as tumours that have their centre within 5 cm proximal and distal of the anatomical cardia and have differentiated the following three distinct tumour entities within this area^{1,3}:

Type I tumour	Adenocarcinoma of the distal oesophagus which usually arises from an area with specialized intestinal metaplasia of the oesophagus (i.e. Barrett's oesophagus) and which may infiltrate the oesophagogastric junction from above.
Type II tumour	True carcinoma of the cardia arising from the cardiac epithelium or short segments with intestinal metaplasia at the oesophagogastric junction; this entity is also often referred to as 'junctional carcinoma'.
Type III tumour	Subcardial gastric carcinoma which infiltrates the oesophago- gastric junction and distal oesophagus from below.

British Journal of Surgery 1998, 85, 1457-1459

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Siewert Classification of OGJ Tumours

SIEWERT TYPE	I	п	ш
Mediastinal stations			
1. Paratracheal	4%	0%	
2. Carinal	10%	0%	
Left bronchial	15%	0%	
4. Right bronchial	19%	0%	-
5. Para-aortic	20%	2%	-
6. Middle and			
7. lower paraoesophageal	55%	5%	3%
Abdominal stations			
8. Right paracardial	41%	46%	
9. Left paracardial	32%	50%	-
10. Left gastric	60%	65%	24%
11. Lesser curve	14%	65%	41%
12. Common hepatic	3%	16%	17%
13. Splenic artery	6%	30%	28%
14. Coeliac axis	5%	30%	

Gastric versus oesophageal dataset?

OG Junction

Mucosal aspect

Serosal aspect

Oesophageal dataset

Gastric dataset

Siewert type 2 tumours (50:50)

international union against cancer

TNM-7 Oesophagogastric junction tumours

A tumour the epicenter of which is within 5 cm of the esophagogastric junction and also extends into the oesophagus is classified and staged according to the **oesophageal** scheme

All other tumours with an epicenter in the stomach greater than 5 cm from the oesophagogastric junction or those within 5 cm of the EGJ *without* extension into the oesophagus are staged using the **gastric** carcinoma scheme

WWW.UICC.OFg

international union against cancer

TNM-7 Oesophagogastric junction tumours

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→ Most tumours which involve the OGJ will be classified under oesophageal dataset

Future for RCPath OG datasets

- Oesophageal and gastric datasets will be merged.
- Gastric and oesophageal datasets will adopt TNM8.

Comparison with colorectal dataset (resection specimens).

- Tumour grading
 - Oesophagus/stomach \rightarrow Worst area of tumour
 - Colorectal \rightarrow Predominant differentiation of tumour
- Vascular/lymphatic invasion
 - Oesophagus/stomach \rightarrow Lymphatic/vascular invasion
 - Colorectal \rightarrow Venous invasion
- Response to treatment (chemoradiotherapy)
 - Colorectal assessed
 - Oesophagogastric not assessed (yet!)

TNM Classification: extra codes

- y Symbol
 - classification during or following multimodality therapy (e.g. neoadjuvant chemotherapy).
 - ypT3 N0 Mx

- **R** codes residual tumour (after treatment)
 - Rx Presence of tumour cannot be assessed
 - R0 No residual tumour
 - R1 Microscopic residual tumour
 - R2 Macroscopic residual tumour

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Gastrointestinal stromal tumour (GIST) resections

- Sleeve resections full gastrectomies.
- Resection margins.
- Absence/presence of serosal involvement.
- 1 tumour block per cm diameter
- Lymph nodes NOT so important

(<2% GISTs have LN metastases)



Gastrointestinal stromal tumours



Standards and datasets for reporting cancers

Dataset for gastrointestinal stromal tumours (GISTs)

February 2011

Coordinators: Dr Elaine MacDuff, Western Infirmary Glasgow Dr Shaun Walsh, Ninewells Hospital Dundee Dr Robin Reid, Western Infirmary Glasgow

Unique document number	G103
Document name	Dataset for gastrointestinal stromal tumours (GISTs)
Version number	1
Produced by	Dr Elaine MacDuff, Dr Shaun Walsh and Dr Robin Reid, on behalf of the College's Cancer Services Working Group
Date active	February 2011
Date for review	February 2014
Comments	In accordance with the College's pre-publications policy, this document was put on The Royal College of Pathologists' website for consultation from 23 August to 17 September 2010. Twenty-six items of feedback were received and the authors considered them and amended the document as appropriate.
	Please email publications@rcpath.org if you wish to see the responses and comments.
	Dr Peter Cowling Director of Communications

The Royal College of Pathologists 2 Carlton House Terrace, London, SW1Y 5AF Tel: 020 7451 6700 Fax: 020 7451 6701 Web: www.rcpath.org Registered charity in England and Wales, no. 261035

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PUB 140211

V6 Final INVESTOR IN PEOPLE

National Guidelines for Gastrointestinal Stromal Tumour Reporting