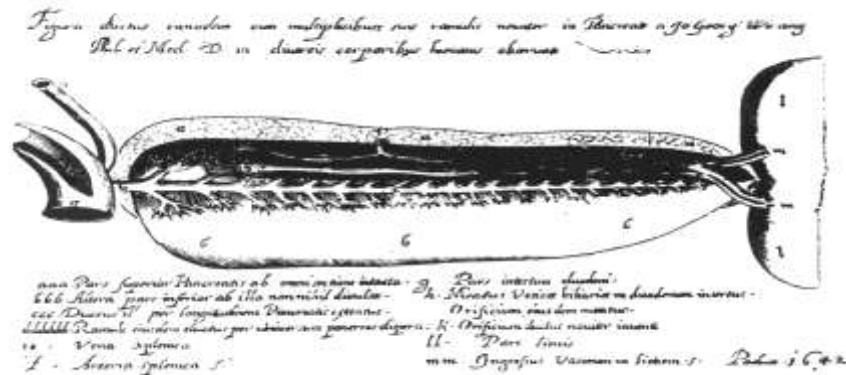


Upper Gastrointestinal Cancer – Seminar
Diagnostic and Treatment anno 2010
Copenhagen, 4. November 2010

**Histological evaluation of pancreatic
resection margins: R0- versus R1-resection**



CS Verbeke
St James's University Hospital Leeds

R1 rate and survival

	n	R1	Median survival R0	Median survival R1
Raut 2007	360	17 %	28	22
Neoptolemos 2001	111	19 %	17	11
Benassai 2000	75	20 %	17	9
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Willett 1993	72	51 %	20	12
Jamieson 2010	1848	74 %	26	15
Esposito 2008	111	76 %	-	-
Campbell 2009	163	79 %	25	15
Menon 2009	27	82 %	> 55	14
Verbeke 2006	26	85 %	37	11

Resection margins – Current controversies

- which surfaces?
- terminology?

Resection margins – terminology

“Among 109 free text reports, 28 different names were used to describe various margins of the resection specimen”

Gill AJ et al. Pathology 2009;42:161.

Terminology according to the UK Royal College of Pathologists guidelines (May 2010):

- **Transection margins:**

- pancreatic neck
- common bile duct
- proximal duodenum/stomach
- distal duodenum

- **Circumferential resection margins/surfaces:**

- anterior
- posterior
- facing SMV
- facing SMA

Resection margins – Current controversies

- which surfaces?
- terminology?
- **dissection and sampling technique?**



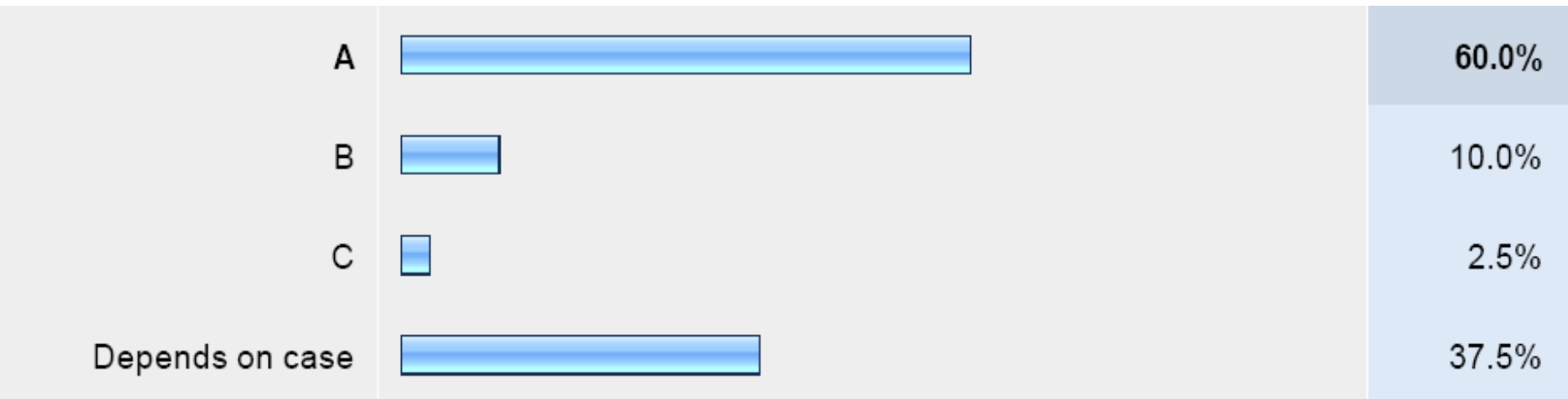
BRITISH SOCIETY OF
GASTROENTEROLOGY

National Audit

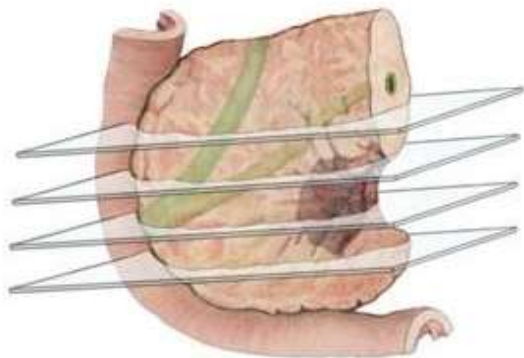
UK pathologists' approach to pancreatoduodenectomy specimens for pancreatic, ampullary and distal bile duct cancer

R Feakins
F Campbell
C Verbeke
2008

8. Which plane of section do you use to slice the pancreas?



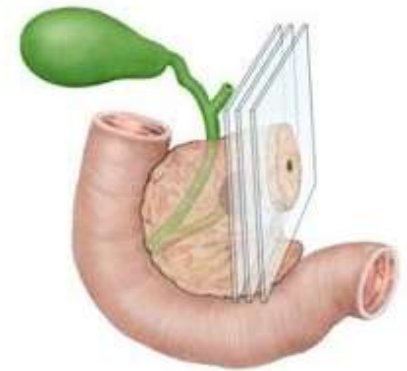
A. Axial
slicing



B. Bi- or
multivalve slicing



C. Bread loafing
(perpendicular slicing)





The Royal College of **Pathologists**

Pathology: the science behind the cure

Standards and datasets for reporting cancers

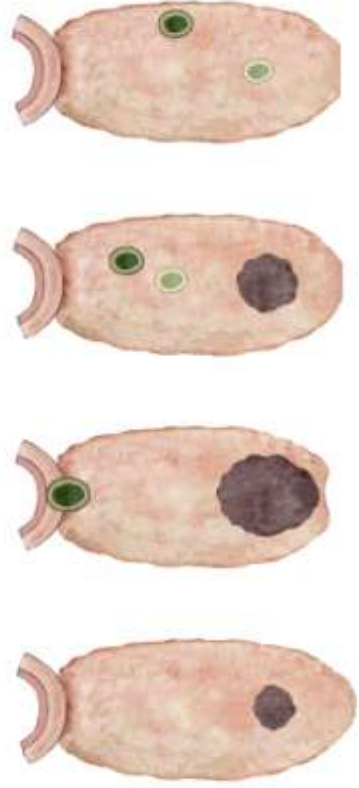
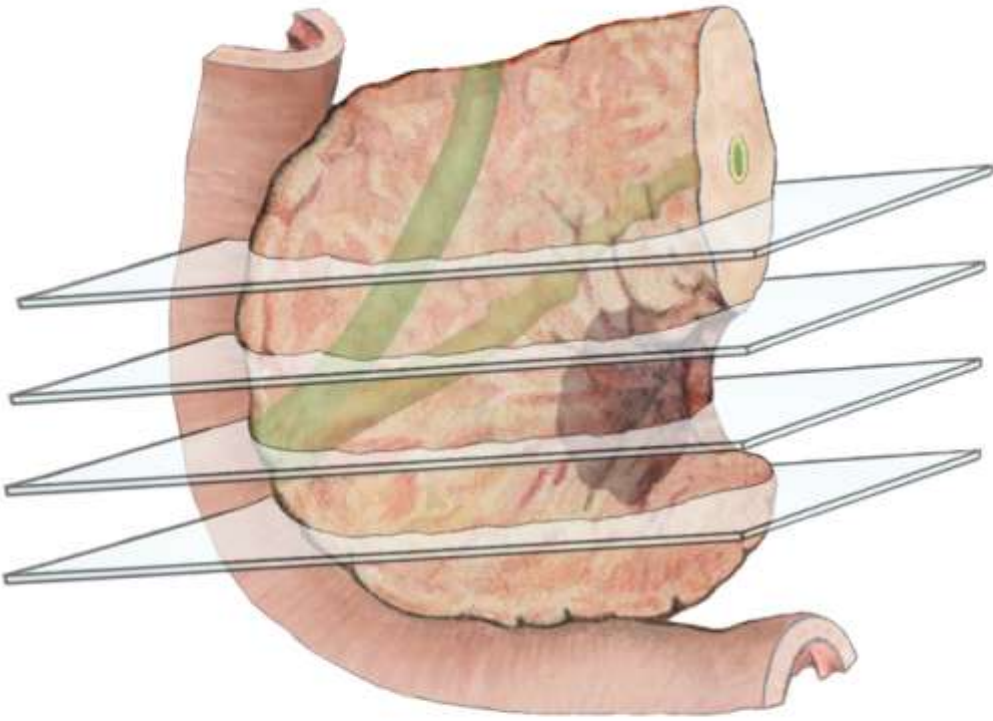
Dataset for the histopathological reporting of carcinomas of the pancreas, ampulla of Vater and common bile duct

May 2010

Axial specimen slicing

Advantages:

- simple to perform
- independent of pathology encountered
- all structures remain intact: pancreatic duct, cbd, ampulla, surfaces
- correlation with imaging
- many slices = good views
- easy sampling



Macroscopy of ductal adenocarcinoma of the pancreas:

Indistinct invasive tumour front

- due to:
 - concomitant 'obstructive pancreatitis'
 - dispersed and highly infiltrative growth pattern
- results in:
 - underestimation of tumour extent
 - tumour size / pT-stage
 - underestimation of margin involvement
- implications for (neo-adjuvant) treatment, epidemiology

R1 rate and survival

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Non-standardized pathology				
Raut 2007	360	17 %	28	22
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**“In contrast to common belief,
a high rate of R1 resections in pancreatic cancer
is not a marker of low-quality surgery but rather of high-quality pathology”**

Esposito et al. Ann Surg Oncol 2008;15:1651.

Unfavourable prognosis associated with K-ras gene mutation in pancreatic cancer surgical margins

J Kim, H A Reber, S M Dry, D Elashoff, S L Chen, N Umetani, M Kitago, O J Hines, K K Kazanjian, S Hiramatsu, A J Bilchik, S Yong, M Shoup, D S B Hoon

Gut 2006;55:1598–1605. doi: 10.1136/g

“Molecular” analysis of resection margins: K-ras mutation

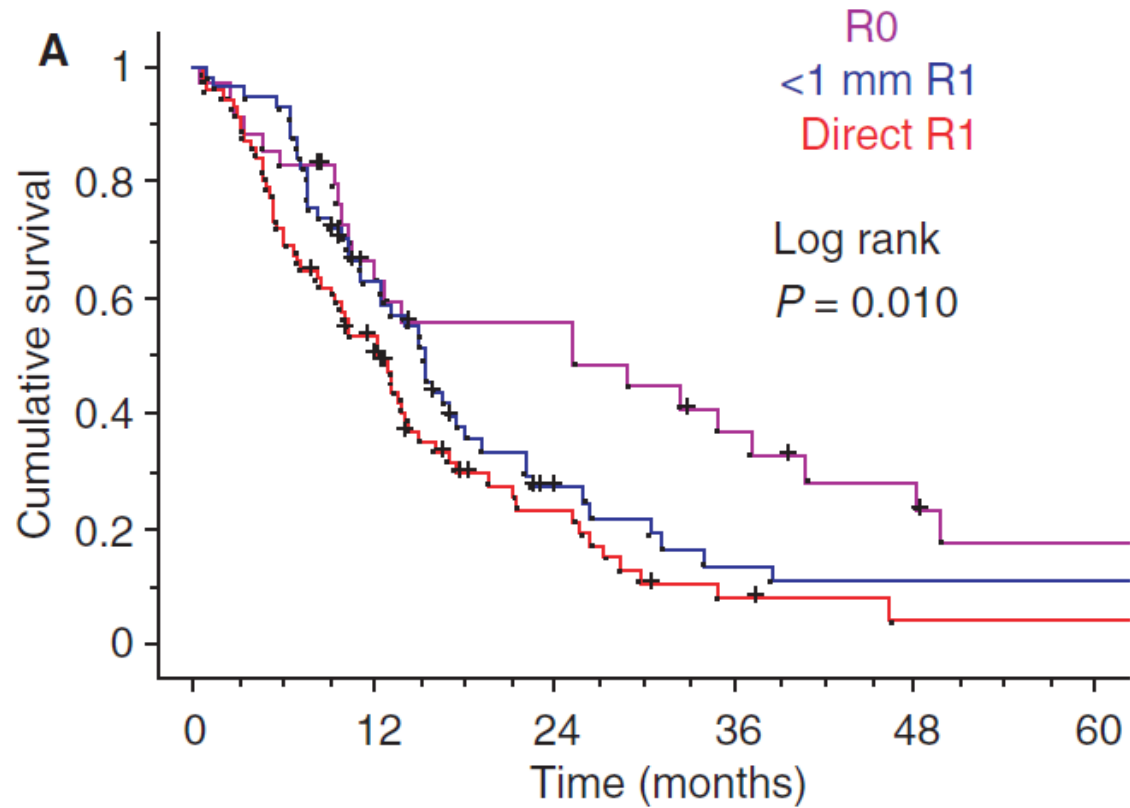
53% of cases R0 (histology) were in fact R1 (K-ras)

Resection margins – Current controversies

- which surfaces?
- terminology?
- dissection and sampling technique?
- **minimum clearance?**

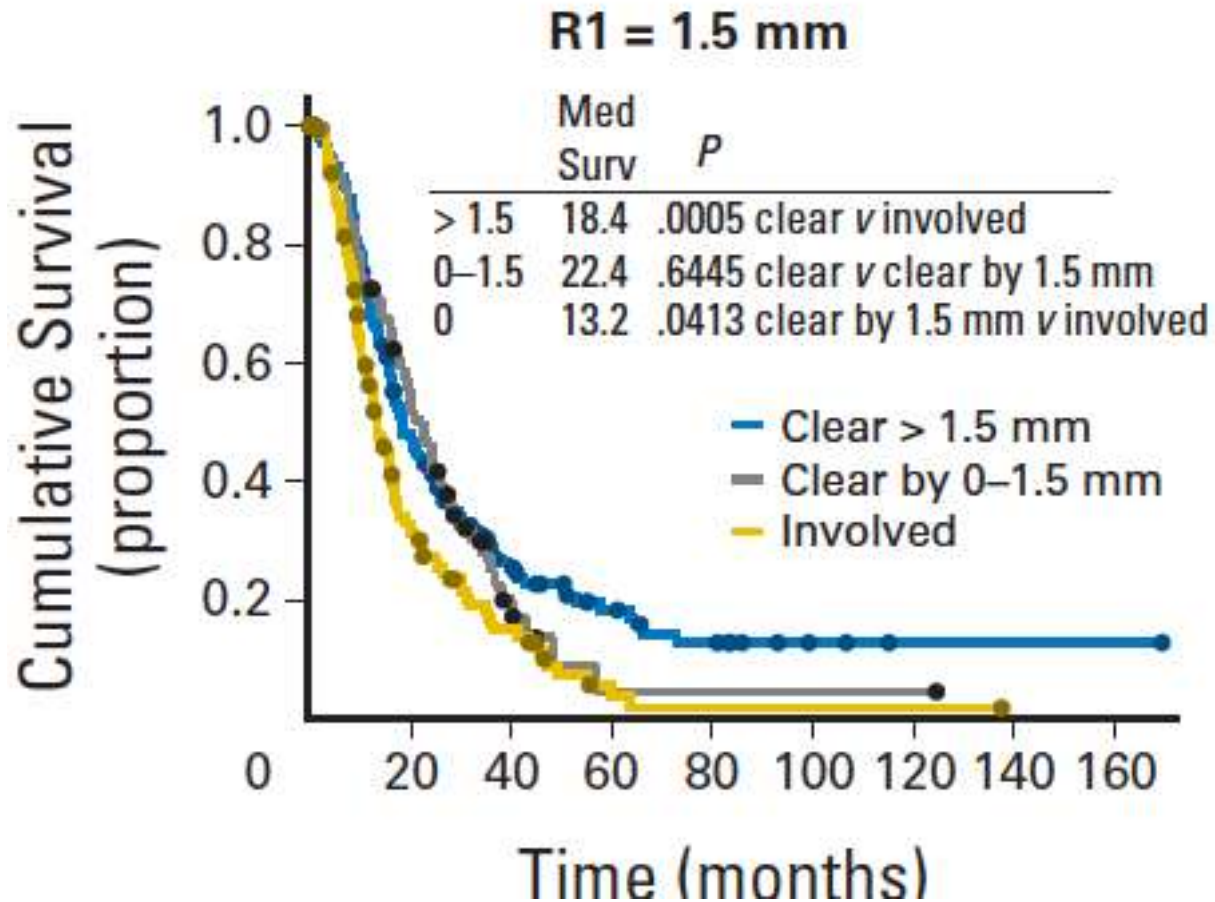
R1 = 0 mm or 1 mm?

No difference in survival



Campbell - Histopathology, 2009; 55: 277-283

Difference in survival only if R1 = 1.5 mm



Resection margins – Current controversies

- which surfaces?
- terminology?
- dissection and sampling technique?
- **minimum clearance? 0 mm? 1 mm? 1.5 mm? more?**

Resection margins – Current controversies

- which surfaces?
- terminology?
- dissection and sampling technique?
- minimum clearance? 0 mm? 1 mm? 1.5 mm? more?
- **direct invasion only?**

pR1 – what does it stand for?

- presence of residual tumour cells (AJCC/UICC) – where?
- risk of recurrence – where?
- quality of surgery?

Resection margins – Current controversies

- which surfaces?
- terminology?
- dissection and sampling technique?
- minimum clearance?
- direct invasion only?
- **prognostic significance?**

R1 rate and survival

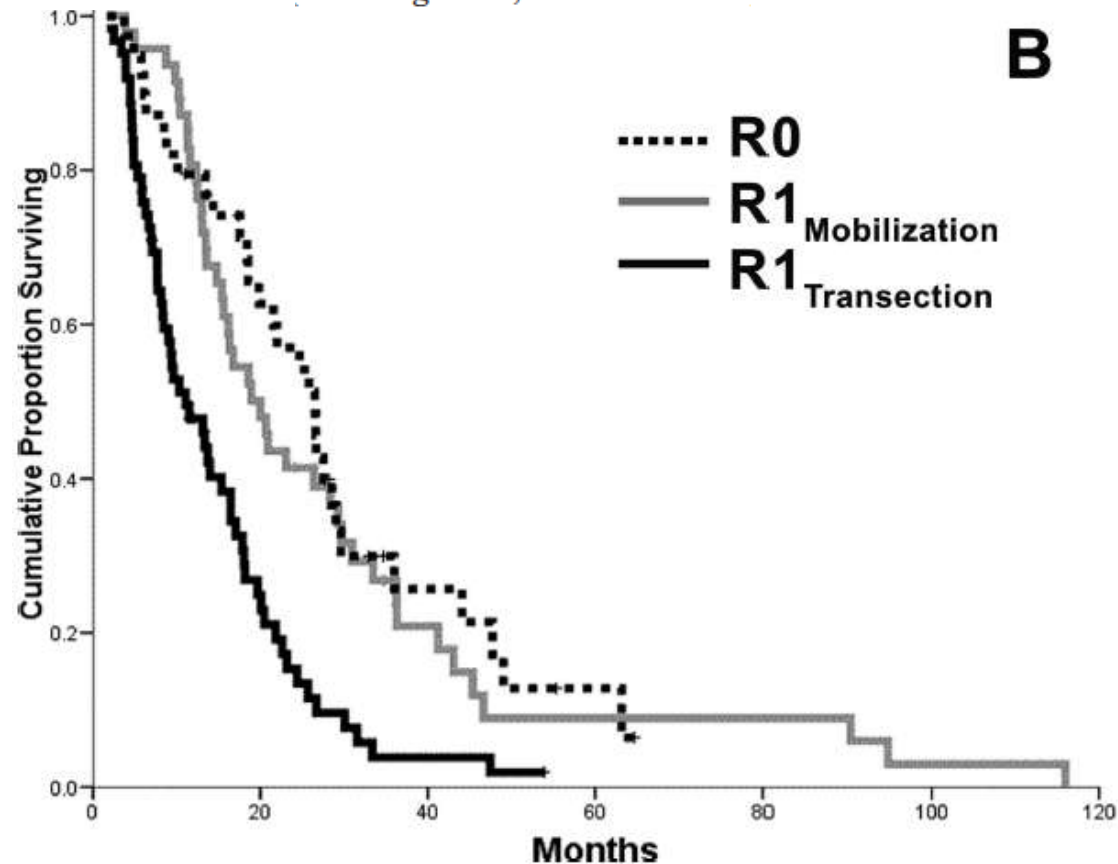
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Jamieson 2010	1848	74 %	26	15

**Local recurrence rate:
67- 86%**

Positive Mobilization Margins Alone Do Not Influence Survival Following Pancreatico-Duodenectomy for Pancreatic Ductal Adenocarcinoma

Nigel B. Jamieson, MRCs,† Alan K. Foulis, MD,‡ Karin A. Oien, PhD,†‡ James J. Going, PhD,†‡ Paul Glen, MD,* Euan J. Dickson, MD,* Clem W. Imrie, FRCS,* Colin J. McKay, MD,* and Ross Carter, MD**

Ann Surg 2010;251: 1003–1010



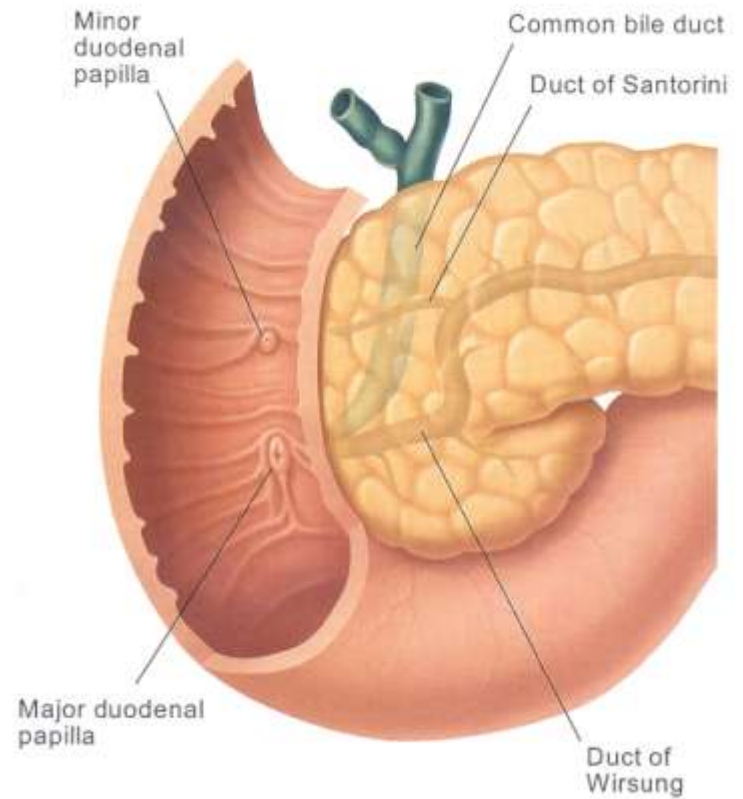
Resection margins – Issues to be resolved

- which surfaces?
- nomenclature?
- minimum clearance: 0 mm? 1 mm? 2 mm?
- direct invasion only?
- impact of dissection technique?
- prognostic significance?
- **R1 rate in pancreatic, ampullary and distal bile duct cancer?**

Pancreatic, ampullary or CBD cancer?

Difference in

- staging
- prognosis
- trials participation
- epidemiology



R1 & recurrence rate for pancreatic, ampullary and distal bile duct cancer

	R1		Recurrence rate
	Leeds	Literature	Literature
Pancreas	82%	17-78%	67-86%
Ampulla	25%	2-12%	25-27%
CBD	71%	7-30%	?

Which margins are involved?

	2009*	2006**
Posterior	57%	45%
SMV/SMA	52%	32%
Anterior	17%	18%
Pancreatic TM	13%	5%
Bile duct TM	-	-
Gastric/duodenal TM	-	-
Multiple	44%	45%

* HPB 2009;11:18

** Br J Surg 2006;93:1232

Conclusion

The problems:

- the current lack of consensus
- the risk of underestimation of R1 if pathology is not meticulous and standardized
- the incomparability of data from different centres

The solutions:

- reach an international consensus on a standardized approach
- ensure that gross examination is meticulous and gross findings are available for retrospective review
- implement systems for quality assurance