Liver Pathology Datasets and Pathways

– where have we got to?

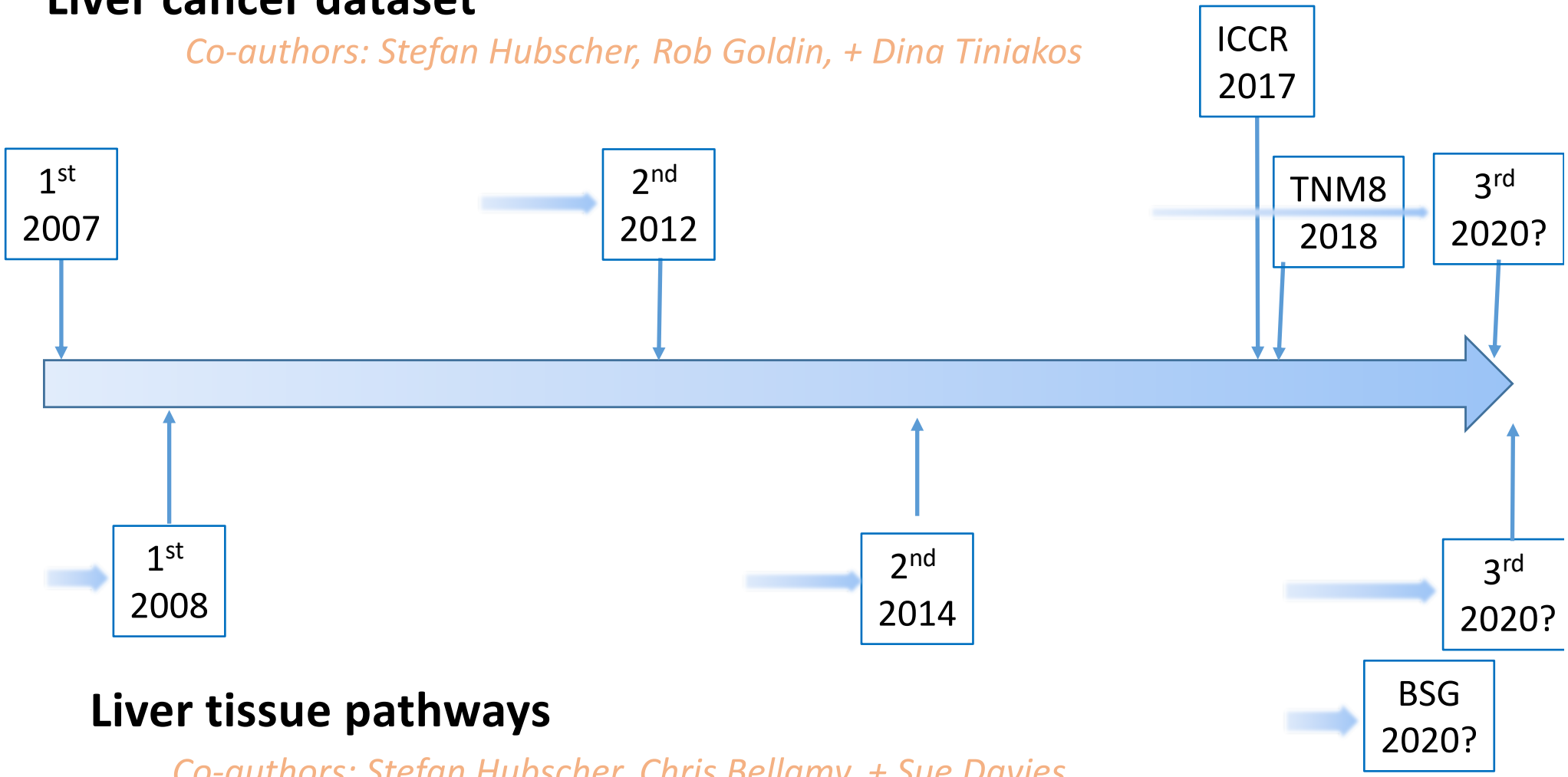
Judy Wyatt

Leeds, UK

Time lines

Liver cancer dataset

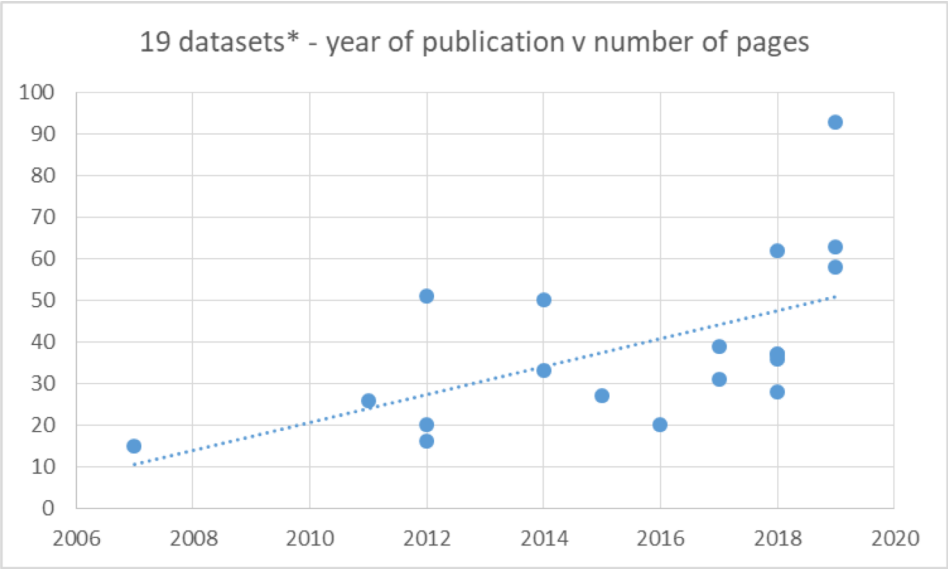
Co-authors: Stefan Hubscher, Rob Goldin, + Dina Tiniakos



Liver tissue pathways

Co-authors: Stefan Hubscher, Chris Bellamy, + Sue Davies

Hours of life……



- 47 datasets and
- 16 tissue pathways on RCPath website

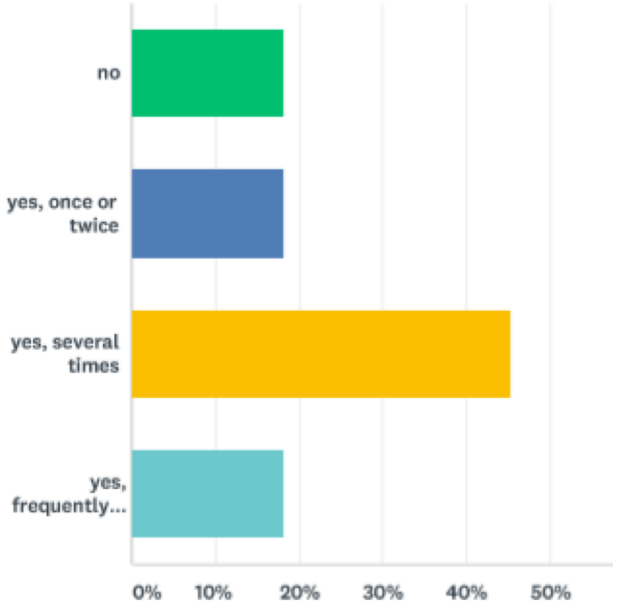
- Assuming no overlap, how many authors?

average 3 – around 190

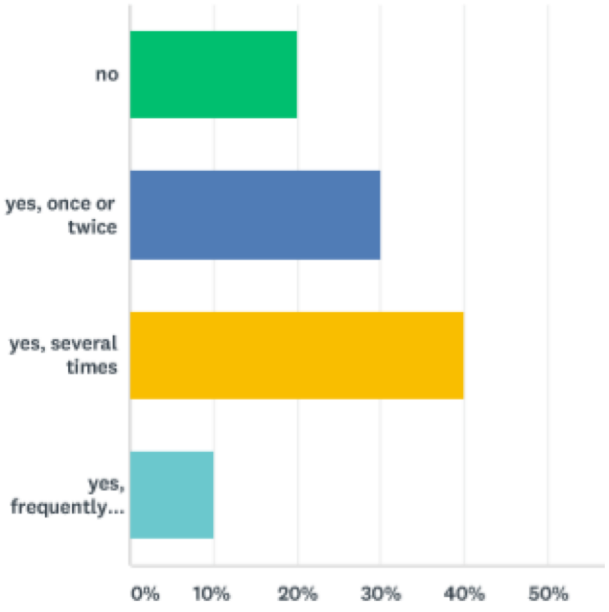
* GI, gynae, endocrine, musculoskeletal

Recent UKLPG questionnaire:

Have you referred to the RCPath dataset for liver tumours in the last few years?



Have you referred to the RCPath TIssue Pathways for liver biopsies in the last few years?



‘Several times per year’

Who is in the audience?

A	Consultant, Liver EQA member
B	Consultant, not in Liver EQA, Been to one of these annual liver update meetings before
C	Consultant, not a Liver EQA member, not been to one of these annual liver update meetings before
D	Trainee

Have you referred to any of the the RCPath datasets in the last year?

A	No
B	Yes, once or twice
C	Yes, several times
D	Frequently (several times per year)

Have you referred to the RCPath dataset for liver tumours in the last few years?

A	No
B	Yes, once or twice
C	Yes, several times
D	Frequently (several times per year)

Have you referred to the any RCPath Tissue Pathways in the last year?

A	No
B	Yes, once or twice
C	Yes, several times
D	Frequently (several times per year)

Have you referred to the RCPath
Tissue Pathways for liver biopsies in the last few years?

A	No
B	Yes, once or twice
C	Yes, several times
D	Frequently (several times per year)

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

Tissue pathways for liver biopsies for the investigation of medical disease and for focal lesions

March 2014

Details on laboratory handling and reporting of liver biopsies

Ideally would be integrated with clinical guidelines on the indications, method and risks of liver biopsy -

BSG guidelines "Guidelines on the use of Liver Biopsy in Clinical Practice" – 2004 – indications, methods, complications etc.
but not quality of biopsy or what to do with it, no pathologist.

Updating BSG guidelines during 2018-9, with RCR and also with RCPath – aiming for quick turnaround.

- **Therefore Tissue Pathways being updated in parallel with this – the 'test' component, with the BSG document as the 'pre-test'**

Wish list:

What would be really useful for Tissue Pathways?

Two things

- A good sized biopsy every time for medical liver biopsies

- Clinician and Pathologist know how the biopsy can help in the clinical management of the patient
  - Clinical information sufficient, clear,
  - Pathology report answers the question

RCPath has 16 tissue pathways, 2013-2019

- Most focus on the lab work – everything you do with the specimen up to it being reported

- Headings include ‘report content’ sometimes brief:

  ‘The report should contain a summary of the gross and histological findings and the diagnosis’

For liver – patterns of disease acute and chronic, fibrosis,

- Clinicians have ‘Non-Invasive Liver Screen’ results,
  and request a biopsy when cause or stage is unclear.

- ‘Personalised medicine’ – non-invasive tests are a statistical probability,

  A biopsy lets you actually see what’s actually happening
  in this patient’s liver
  at the time of the biopsy

BSG Clinical Guidelines

– current draft v 12 13 authors

CONTENTS

Emphasises importance of biopsy quality, and good clinical communication

BSG guidelines on the use of liver biopsy in clinical practice

Friday, 01, October, 2004

October 2004

In preparation: Joint clinical guidelines with RCR and RCPath

Recommendations (BSG draft 2019)

- The clinical indication for liver biopsy should be clearly communicated to the reporting pathologist by the requesting clinician (Grade C, IV).
- It must be clearly indicated if the biopsy is targeted at a focal lesion ('tumour biopsy') or taken for investigation of diffuse parenchymal disease ('medical liver biopsy'). (Grade C, IV)
- For percutaneous medical liver biopsy – the specimen should be obtained with a 16G needle and measure >20mm in order to provide adequate tissue. Consider a second pass if a smaller specimen is obtained, especially for investigation of fibrosis stage or possible biliary disease. (Grade A, I)
- For targeted biopsy from focal lesion, an 18G needle is recommended; an additional biopsy of non-lesional tissue (not adjacent to the lesion) should be considered to evaluate background liver disease and can be done using the same needle (Grade B, II).
- Transjugular biopsies require multiple passes as routine (at least 2-3), since the biopsy needle is narrower (Grade A, III).
- The biopsy report should clearly address the clinical indication for the biopsy and conclude with a concise diagnostic summary (Grade C, IV)
- For biopsies obtained outside a specialist liver centre, the reporting pathologist should have access to second opinion from a liver centre (Grade C, IV).

A good sample is an essential starting point for a good biopsy report.

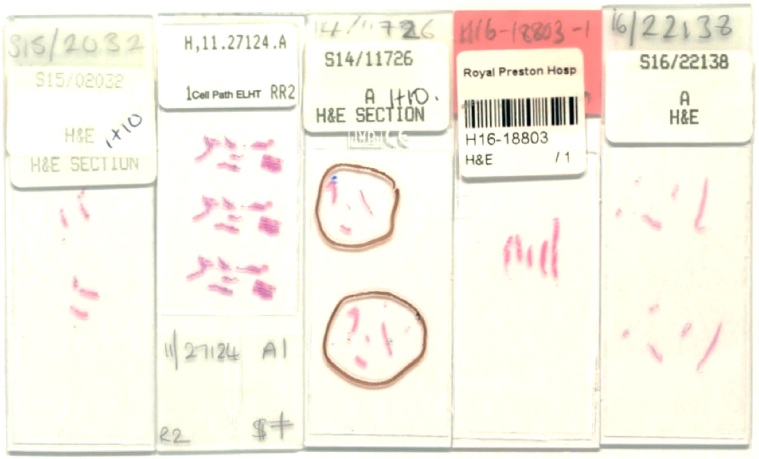
Size of biopsy*

- 16G needle,
- aim for core >20mm long

Why?

- Portal tracts and hepatic veins around 0.8mm apart
- Biopsy <10 portal tracts under-estimates disease stage and severity of inflammation

A: biopsies from elsewhere for review



B: biopsies from previous needle, inconsistently adequate

C: consistently good specimens from Biopince™

* Kleiner DE and Bedossa P
Gastroenterology 2015;149;1305-1308

One pass or two?

Risk of medical liver biopsy mortality <1 in 1,000.

Maybe < 1 in 10,000 – too small to count. Higher for targeted biopsy

No clear evidence for increased risk with two passes

- For biopsy <10mm, limited diagnostic value, second pass should be considered
- For biopsy 10 -20mm diagnosis may be compromised, consider second pass especially if staging fibrosis or investigation of biliary disease are the main indications for the biopsy

Trans-jugular biopsies – usually have 2-4 passes

FNAB under endoscopic ultrasound – patients with jaundice and pain – small fragmented specimen, limitations recognised.

Indications for liver biopsy – why?

Investigation of diffuse parenchymal liver disease

Persistent “abnormal LFTs”

- No clear diagnosis or >1 potential diagnosis
- Assess severity/stage of known disease,
- Monitor over time, atypical features

Proforma for clinical information? More than ‘abnormal LFTs’

(ALT, AST, ALP, bili, FBC, lipids, iron, copper, A1AT,
Immunoglobulins, autoantibodies, viral serology,
Alcohol, drugs, family history, travel,
Splenomegaly, hepatomegaly, features of chronic liver disease,
Ultrasound, fibroscan, biliary imaging, Doppler)

- or expect the clinicians to interpret these for us –
and tell us what they hope to find out from the biopsy
we answer the question they pose….

LIVER DISEASE

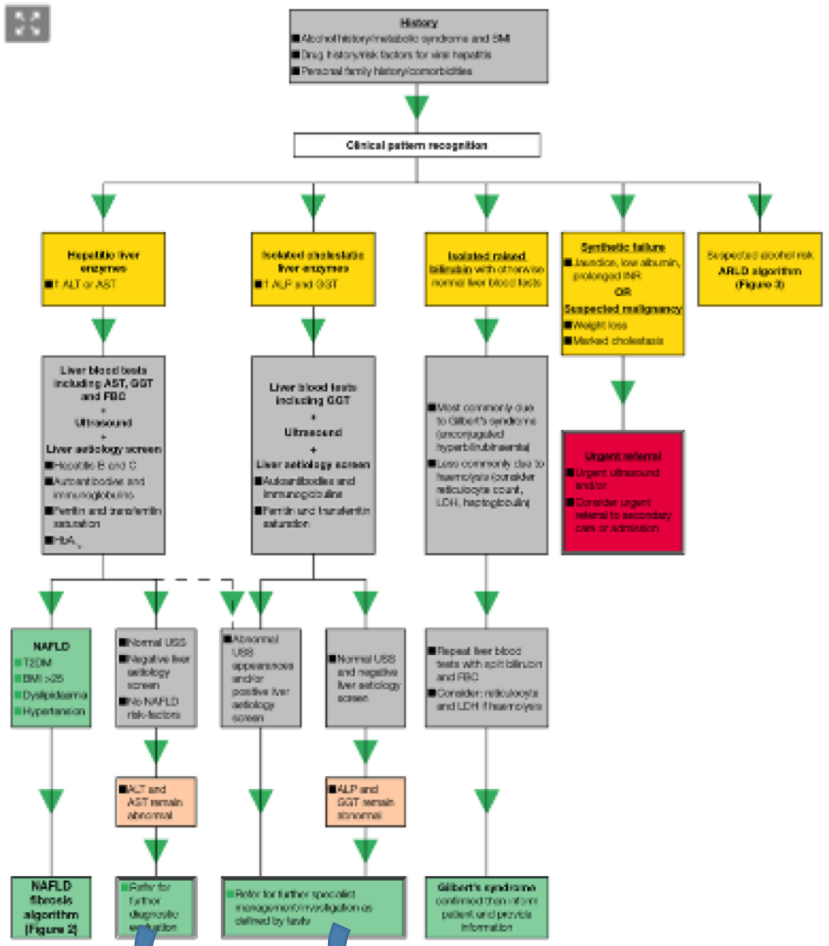
Guidelines on the management of abnormal liver blood tests

Guidelines Summarising clinical guidelines for primary care

By British Society of Gastroenterology | 9 April 2018

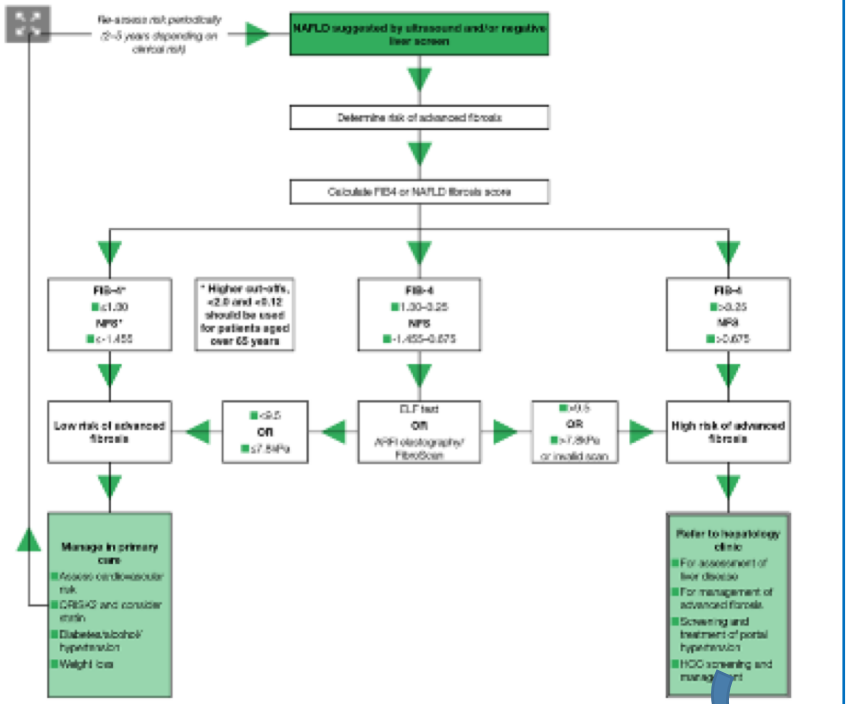
Refer to secondary care

Clinical pattern recognition for liver blood tests



Approach to common conditions

NAFLD



3.1.2 Medical staffing

Medical liver biopsies should be reported by pathologists who have sufficient knowledge of hepatology to formulate a report that addresses the clinical question posed by the clinician.

3.1.3 For pathologists working outside hepatology centres

- Local lead pathologists for liver should participate either in a liver EQA scheme or other regular CPD activity in liver pathology.

3.1.4 For pathologists working within hepatology centres

- All pathologists who work within hepatology centres should participate in a specialist liver EQA scheme.

Indications for referral of case for second opinion

- Patient is referred to hepatology centre for clinical management

- Patient managed locally, pathologist (or clinician) initiates referral

  - Include relevant clinical information/recent clinical letter

When to refer?? Depends on the circumstances and the pathologist – in general, based on evidence from reviews of referred biopsies:

"It is strongly suggested/advised, due to the difficulties in diagnosis and also management implications, that specialist review should be considered in:

***new diagnoses of auto-immune disease** (27),*
***problematic biliary disease**, including overlap entities (28)*
subtle vascular abnormalities

as a matter of routine."

Who looks at our reports?

Diagnosis, presentation and initial severity of autoimmune hepatitis in patients attending 28 hospitals in the UK

1267 patients

who met 1999 International AIH Group diagnostic criteria (92%) or treated for clinical diagnosis (8%).

96% had biopsy, report available in 92%.

Histological feature	IAIHG histology score (1999)	Of 1163 patients (%)
Interface hepatitis	3	88%
Lympho/plasma cell predominance	1	75%
Rosettes	1	19%
Emperipolesis	0	0.4%

31% who met 1999 IAIHG criteria did not meet 2008 'simplified criteria'

'**typical**' 2 points -
interface hepatitis -
emperipolesis -
rosettes

'**compatible**' – 1 point

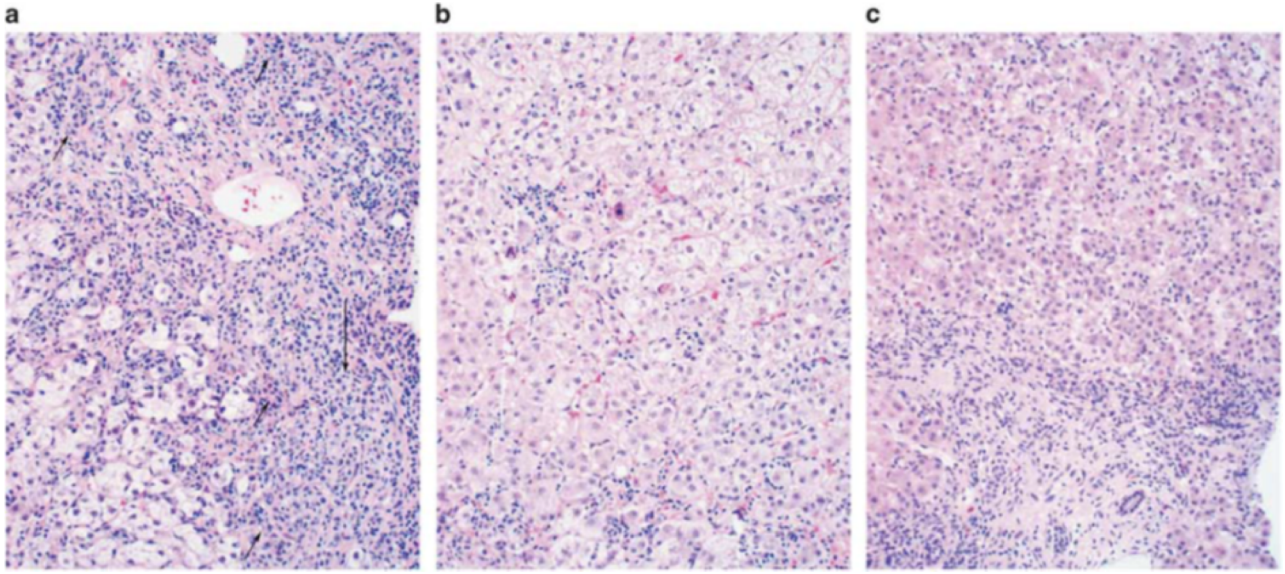
Gordon V *et al.* Liver International 2018:38:1686-1695

Autoimmune hepatitis: review of histologic features included in the simplified criteria proposed by the IAIHG and proposal for new histological criteria

Biopsy is required for AIH diagnosis

2008 IAHG simplified:

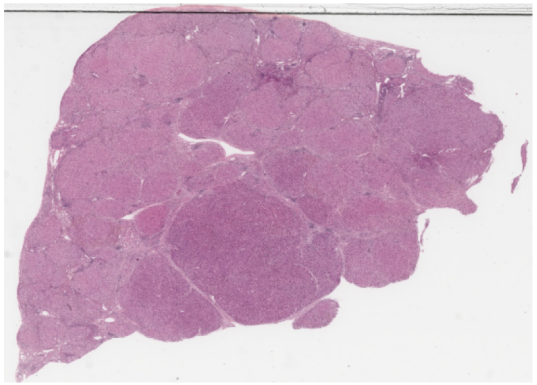
For 2 points – interface hepatitis, emperipolesis and rosettes – the latter two poorly reproducible and non-specific

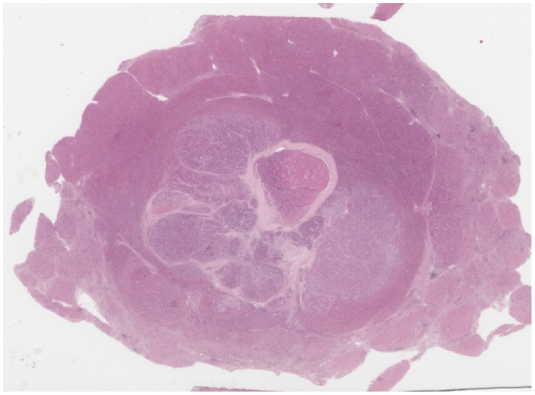


Proposed: **interface/lobular activity,**
number of plasma cells,
presence/absence of biliary features (copper and CK7 stain).

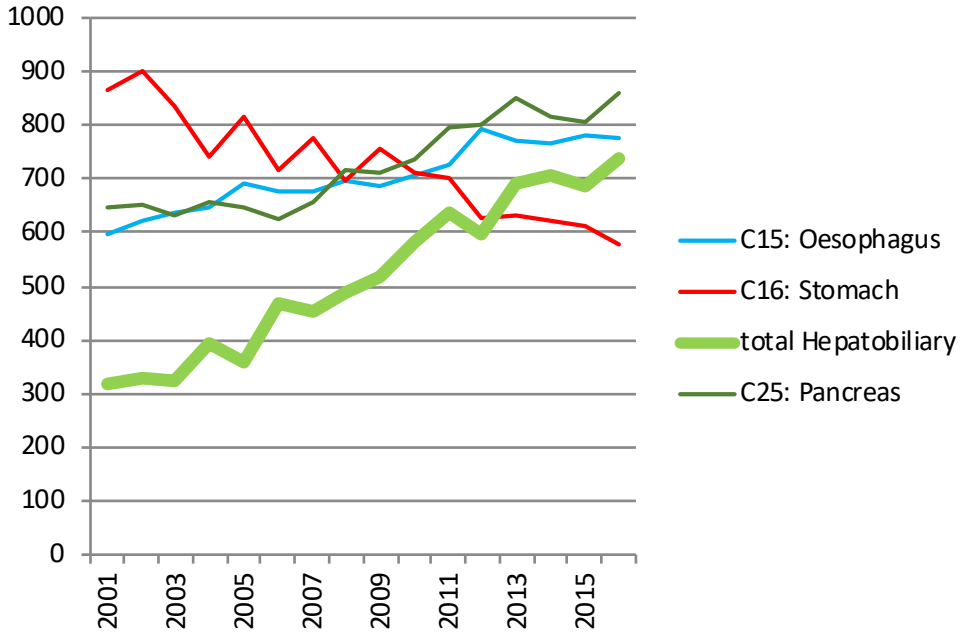
Increased sensitivity for AIH especially in acute presentation.

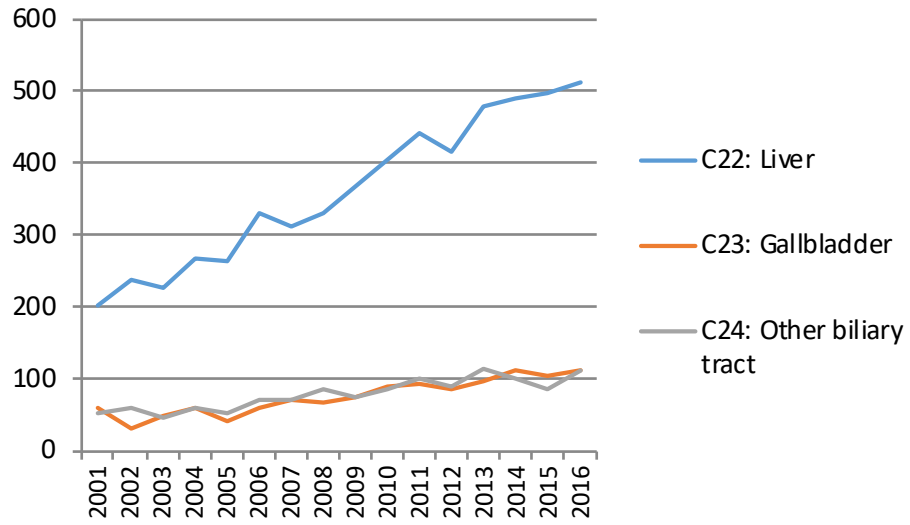
Balitzer D et al, (san Francisco) Modern Pathology 2017;30;773-783





Upper GI malignancy: Yorkshire 2001-2016





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June 2012

Standards and datasets for reporting cancers

Dataset for histopathology reporting of liver resection specimens (including gall bladder) and liver biopsies for primary and metastatic carcinoma (2nd edition)

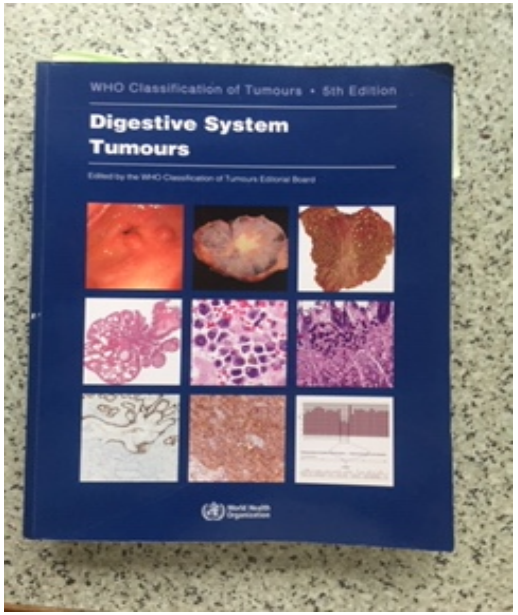
Updated Appendix A TNM classification of liver tumours
OCTOBER 2017

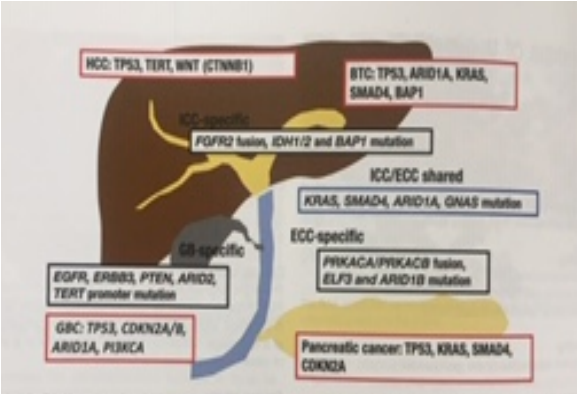
October 2017

Wait for ICCR:

Wait for TNM8:

Wait for WHO Blue Book – July 2019





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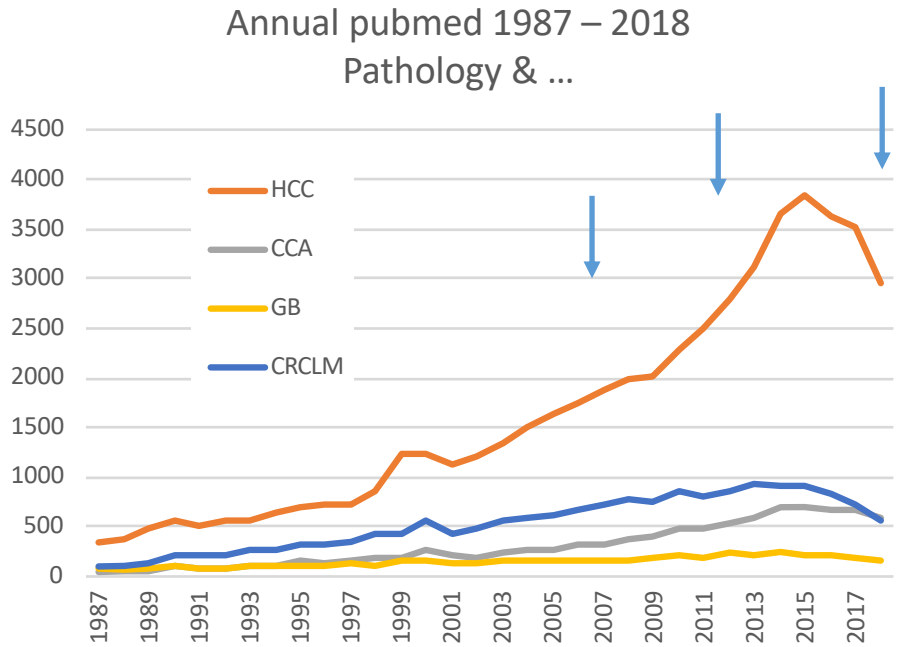
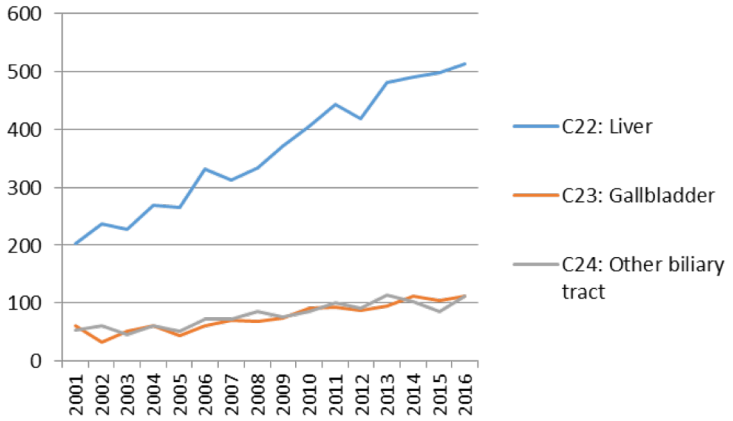


What is special about RCPath datasets?

-More practical information on dissection, block taking, aiming for pragmatic uniform practice in UK
– started off as ‘minimum dataset’ in 1990’s



Increasingly important:

- More liver cancer
- Surveillance for HCC in patients with cirrhosis
  – correlation with radiology
- More treatments for HCC

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

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CANCER DATASETS AND TISSUE PATHWAYS

The College's Datasets for Histopathological Reporting on Cancers have been written to help pathologists work towards a consistent approach for the reporting of the more common cancers and to define the range of acceptable practice in handling pathology specimens.

TNM 8 was implemented in many specialties from 1 January 2018. A full list of staging

USEFUL RESOURCES

- Working Group on Cancer Services
- Recommendations from the Working Group on Cancer Services

Liver 2012
3 authors

Appendix C1 Reporting proforma for liver resection: hepatocellular carcinoma

Surname: ..... Forenames: ..... Date of birth: .....
Sex: ..... CHI/NHS no: ..... Hospital: .....
Hospital no: ..... Date of receipt:..... Date of reporting: .....
Report no: ..... Pathologist: ..... Surgeon: .....

Gross description

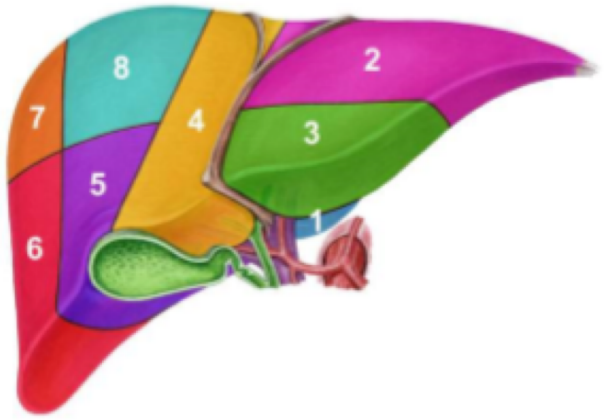
Type of specimen: Segmental resection ☐ List segments (if known): .....
Non-anatomic (wedge) resection ☐ Site/segment of origin: ..... Hepatectomy (at transplant) ☐
Specimen weight.....g
For segmental resections, specimen dimensions:
antero-posterior .....mm, medio-lateral .....mm, supero-inferior.....mm

Number of tumours present. ..... List maximum tumour diameters (up to largest 4): .....mm
Satellite tumour(s) present: Yes ☐ No ☐
Distance from nearest hepatic resection margin: .....mm

4 Preparation of the specimen before dissection

The segmental anatomy of the liver is shown in Figure 1. The boundaries of the eight segments represent the watershed between portions of liver perfused by main branches of the hepatic artery and portal vein, and form the basis of the various surgical options for major liver resection. Liver tumours are resected either by segmental resection[4] following the planes of whole liver segments defined by intra-operative ultrasound, or non-anatomical (wedge) resection for small, accessible, subcapsular lesions. The dataset should also be applied to total hepatectomy specimens from patients undergoing liver transplantation when tumour is present.

Segmentectomy procedures result in sizeable resection specimens. The surgeon should state which segments are included as this may not be clear from the topography of the specimen. The boundary of segments is defined by the course of intrahepatic vessels and cannot be inferred from surface landmarks. Wherever possible, the preoperative imaging report should be available to the pathologist at the time of specimen dissection.



INTERNATIONAL COLLABORATION ON CANCER REPORTING

LIVER - INTRAHEPATIC & PERIHILAR CHOLANGIOCARCINOMA & HEPATOCELLULAR CARCINOMA (TNM8)

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DATASETS

PUBLISHED DATASETS

FEMALE REPRODUCTIVE

SCOPE

This dataset has been developed for resection specimens of the liver with intrahepatic, and perihilar cholangiocarcinoma and hepatocellular carcinoma. It does not apply to neuroendocrine carcinomas, hepatoblastoma, carcinomas of the extrahepatic bile ducts, gall bladder and benign lesions such as adenomas.

ICCR Liver - Intrahepatic & Perihilar Cholangiocarcinoma & Hepatocellular Carcinoma Bookmarked guide - 1114 KB

ICCR

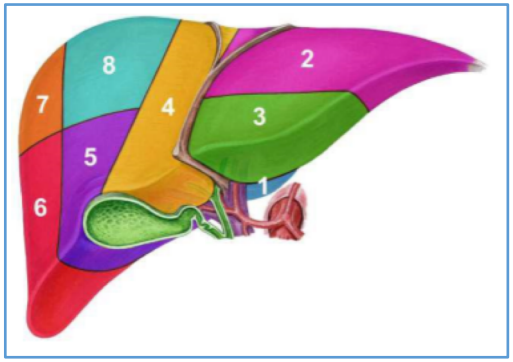
April 2017

13 Authors

Specimen(s) submitted (Required)

Reason/Evidentiary Support

In assessing macroscopic specimens which contain mali



Intrahepatic Cholangiocarcinoma, Perihilar Cholangiocarcinoma and Hepatocellular Carcinoma Histopathology Reporting Guide

Family/Last name

Given name(s)

Date of birth DD – MM – YYYY

Patient identifiers

Date of request DD – MM – YYYY

Accession/Laboratory number

Elements in **black text** are REQUIRED. Elements in grey text are RECOMMENDED. SCOPE OF REPORTING GUIDE

SPECIMEN(S) SUBMITTED (select all that apply)

- ○ Not specified ○ Indeterminate
- ☐ Liver
  - ☐ Total hepatectomy
  - ☐ Segmental resection (List segments or type of segmentectomy)

TUMOUR SITE AND NUMBER

- ○ No macroscopic residual tumour

Specify site / No./site (if possible)

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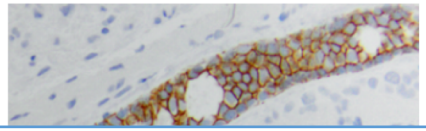
Home > Protocols and Guidelines > Cancer Protocol Templates

Cancer Protocol Templates

The College of American Pathologists September 2019 errata release includes 2 revised cancer protocols and 1 revised biomarker templates with typographical corrections to the Background Information.



Required Cancer Protocols - Revised
Breast, Invasive, Resection
Breast, DCIS, Resection

CAP

June 2017

9 authors

COLLEGE of AMERICAN PATHOLOGISTS

Protocol for the Examination of Specimens From Patients With Hepatocellular Carcinoma

ol Posting Date: June 2017
taging Manual

sed for the following procedures AND tumor types:

ignated hepatic resection, partial or complete
a and fibrolamellar carcinoma

ses for the following:

following presurgical therapy)

COLLEGE of AMERICAN PATHOLOGISTS

Protocol for the Examination of Specimens From Patients With Carcinoma of the Perihilar Bile Ducts

Version: PerihilarBileDuct 4.0.0.1 **Protocol Posting Date:** June 2017
Includes pTNM requirements from the 8th Edition, AJCC Staging Manual

For accreditation purposes, this protocol should be used for the following procedures AND tumor types:

Procedure	Description
Resection	Includes specimens designated bile duct resection, local or segmental, hilar resection with or without hepatic resection
Tumor Type	**Description**
Carcinoma	Invasive carcinomas including small cell and large cell (poorly differentiated) neuroendocrine carcinoma

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CANCER PROTOCOLS

PUBLISHED PROTOCOLS

The majority of the following RCPA Structured Reporting Protocols are based on the 2010 AJCC/UICC 7th edition Cancer Staging Manual. However, updates to the 2016 TNM 8th edition are underway, where applicable.

The guides, forms and request information sheets are provided for educational purposes and to support

GASTROINTESTINAL

cancer v1.0 (804 kB) Nov 2013
Protocol - liver cancer v1.0 (803 kB) Jun 2019

Guide - liver cancer v1 (248 kB) Jun 2019

cancer V1.0 (276 kB) Nov 2013
Proforma - liver cancer v1 (247 kB) Jun 2019

cancer V1.0 (192 kB) Nov 2013
Request - liver cancer v1 (159 kB) Jun 2019

pancreatic cancer V1.0 (36 kB) Nov 2013
Typist template - liver cancer v1 (21 kB) Jun 2019

STRUCTURED REPORTING PROTOCOL FOR

Intrahepatic Cholangiocarcinoma, Perihilar Cholangiocarcinoma and Hepatocellular Carcinoma

(1st Edition 2019)

Incorporating the:
International Collaboration on Cancer Reporting (ICCR)
Intrahepatic Cholangiocarcinoma, Perihilar Cholangiocarcinoma and Hepatocellular Carcinoma Dataset
www.ICCR-Cancer.org
Core Document versions:

A guide to Intrahepatic Cholangiocarcinoma, Perihilar Cholangiocarcinoma and Hepatocellular Carcinoma Histopathology Reporting

Includes the ICCR International Collaboration on Cancer reporting dataset denoted by *

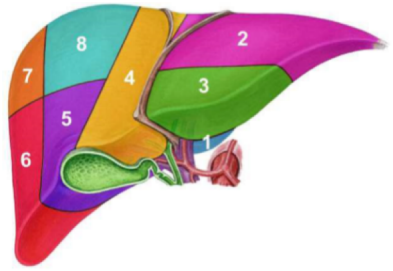
Clinical details		
S1.02	**Clinical info. on request form** (complete as narrative or use the structured format below)	Text
	New primary cancer or recurrence	New primary Recurrence-regional Recurrence-distant
	Radiological / imaging information	Text
	Operative procedure	Text
G1.01	Copy to doctor	Text
S1.03	**Pathology accession number**	Text
S1.04	**Principal clinician**	Text
G1.02	Other relevant details	Text

Macroscopic findings		
S2.01	**Specimen labelled as**	Text

Macroscopic findings (cont.)		
G2.07	Minimum distance of tumour to liver capsule (Applicable to intrahepatic tumour specimens)	__mm
G2.08	Distance of tumour to closest resection margin	__mm AND Text (margin, if possible)
G2.09	Macroscopic involvement of vessels (Applicable to intrahepatic tumour specimens)	Not identified Present, *specify vessel(s) involved*
G2.10	Extent of invasion into biliary tree (Applicable to hilar cholangiocarcinoma specimens)	Text
G2.11	Depth of invasion beyond biliary tree (Applicable to hilar cholangiocarcinoma	Text

11 authors, 40 stakeholders

Figure 1: Segmentectomy specimens[59]



Right hepatectomy, Segments 5–8
Right trisegmentectomy, Segments 4–8
Left lateral segmentectomy, Segments 2–3
Left hepatectomy, Segments 2–4
Left trisegmentectomy, Segments 1–5 and 8
Total hepatectomy, Segments 1–8

RCPath dataset for liver resections:

Introduction

The primary purpose of this document is twofold:

to define the set of data necessary for the uniform recording and staging of the core pathological features in liver cancer resection specimens

to describe its application in sufficient detail and clarity that reports from different departments will contain equivalent information, allowing comparison of clinical practice and outcomes. This will be of particular importance when the dataset is incorporated into the national cancer outcomes and services dataset (COSD).

Geographic variation in primary liver and gallbladder cancer

NCIN Data Briefing

NCIN national cancer intelligence network

Background

Cancers of the liver and gallbladder are rare in the UK. Primary liver

KEY MESSAGE:

The incidence of liver cancer varies between cancer networks in England with the highest incidence evident in

ncras
National Cancer Registration and Analysis Service

SEARCH

About NCRAS | Events | Collecting & Using Data | Publications | Cancer Information Tools | Cancer Type & Topic Specific Work | Local Intelligence

PUBLICATIONS

- Reports
- Data Briefings
- Guidance Documents
  - Local Awareness and Early

Geographic variation in primary liver and gallbladder cancer

Background

KEY MESSAGE:

The incidence of liver cancer varies between cancer

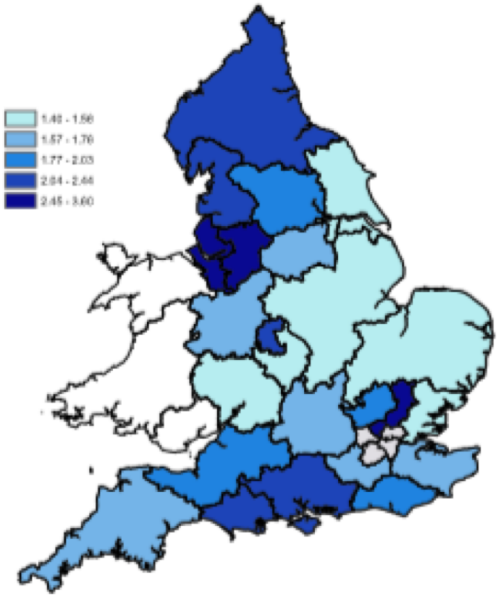


Figure 1: Map of age-standardised incidence rates of liver cancer (per 100,000 European standard population, ASR(E)) by cancer network, males and females, England, 1998-2006

TNM staging for Hepatocellular Carcinoma

	TNM6 2002	TNM7 2010	TNM8 2018
pT1	Single, no vascular inv.	Single, no vascular inv.	pT1a single, <2cm +/- vascular invasion
			pT1b single, >2cm, no vascular invasion
pT2	Single with vascular inv. Or multiple <5cm	single with vascular invasion or multiple, none >5cm	single >2cm with vasc. inv. or multiple, none >5cm
pT3	Multiple >5cm or involves major branch of portal or hepatic vein	pT3a multiple tumours any more than 5cm	multiple tumours any more than 5cm
		pT3b tumour involving major branch of portal or hepatic vein	
pT4	Direct invasion of adjacent organs other than GB or perforates visceral peritoneum		Involves major branch of portal or hepatic vein, or direct invasion of adjacent organs (except GB) or perforates visceral peritoneum.
pN1	Regional nodes +ve		Sample ≥3 nodes

TNM staging for Intrahepatic Cholangiocarcinoma

	TNM6 2002 = hepatocellular carcinoma	TNM7 2010 ICC now has separate TNM	TNM8 2018
pTis		Carcinoma in situ	Inc. BilIN3
pT1	Single, no vascular inv.	Single, no vascular inv.	Single, no vasc. inv. pT1a <5cm pT1b >5cm
pT2	Single with vascular inv. Or multiple <5cm	pT2a single with vasc. inv.	Single with vasc. Inv. or multiple +/- vascular invasion
		pT2b multiple +/- vascular invasion	
pT3	Multiple >5cm or involves major branch of portal or hepatic vein	Perforates visceral peritoneum or invades local extra-hepatic structures	Perforates visceral peritoneum
pT4	Direct invasion of adjacent organs other than GB or perforates visceral peritoneum	Tumour with periductal growth pattern	Invades local extra-hepatic structures
pN1	Regional nodes +ve Sample ≥3 nodes		Sample ≥6 nodes

TNM staging for Perihilar Cholangiocarcinoma

	TNM6 2002 = extrahepatic ducts	TNM7 2010	TNM8 2018
pTis	Carcinoma in situ		Inc. BilIN3
pT1	Ductal wall	Confined to wall	
pT2	Beyond ductal wall	pT2a into surrounding adipose tissue	
		pT2b into adjacent hepatic parenchyma	
pT3	Liver, GB, pancreas or unilateral vessels	Unilateral branch of PV or HA	
pT4	Other adjacent organs or main vessels	Main PV or bilateral branches, or common HA or second order biliary radicals with contralateral PV or HA	
pN1	Regional nodes +ve	Regional nodes +ve	pN1 1-3 nodes +ve pN2 >3 nodes +ve Sample 15 nodes

TNM staging for Gall Bladder Carcinoma

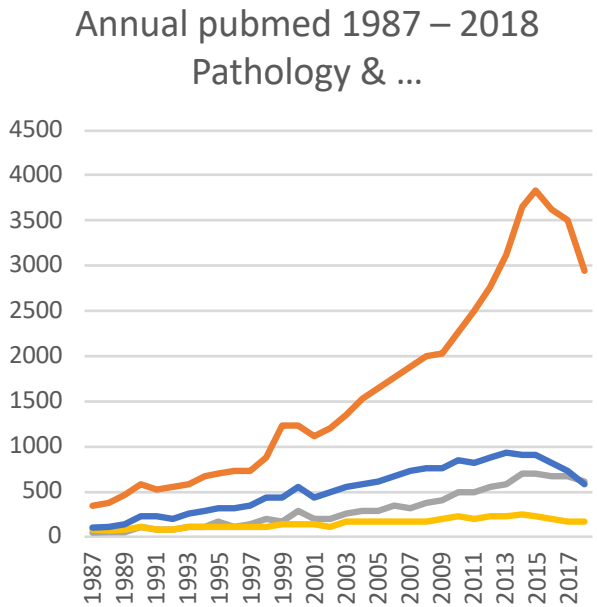
United Kingdom Liver Pathology Group

TNM8 for hepatobiliary cancers PDF
Summary of changes

	TNM6 2002 = hepatocellular carcinoma	TNM7 201
pTis	Carcinoma in situ	
pT1	pT1a invades lamina propria pT1b invades muscle	
pT2	Invades perimuscular connective tissue – no extension beyond visceral peritoneum or into liver	Invades perimuscular connective tissue – no extension beyond visceral peritoneum or into liver
		pT2a peritoneal side pT2b hepatic side
pT3	Perforates visceral peritoneum and/or invades liver and/or one other adjacent organ	
pT4	Invades main portal vein or hepatic artery or ≥2 extrahepatic organs	
pN1	Regional nodes +ve Sample ≥3 nodes	Sample ≥6 nodes

For Liver Dataset v3:

- TNM 8 and the changes since TNM7
- Includes hepatocellular adenoma, and combined HCC-CCA
- Liver targeted tumour biopsy in both dataset and pathway
- Matches 2019 WHO ‘Blue Book’
- Concentrates on consistent staging
  Don’t worry too much about references
  – well taken care of in other publications,



Liver Pathology Datasets and Pathways

– where have we got to?

A long journey

Are we nearly there yet? – yes

and it will be worth it……