



Belgian Section for Hepato-Biliary and
Pancreatic Surgery (BSHBPS)
of the
Royal Belgian Society for Surgery
(RBSS) asbl-vzw

XIXth POST-GRADUATE COURSE

Primary liver tumors

Friday, 18th October 2019

Lamot Congress Center
Van Beethovenstraat 8-10
2800 Mechelen

President :

E. Vibert (Villejuif, F)

Course coordination:

A. Dili, B. Van den Bossche, A. Vanlander

Accreditation requested

The official language of the PGC is English.
Simultaneous translation is not provided



Hôpital
Erasme



ULB

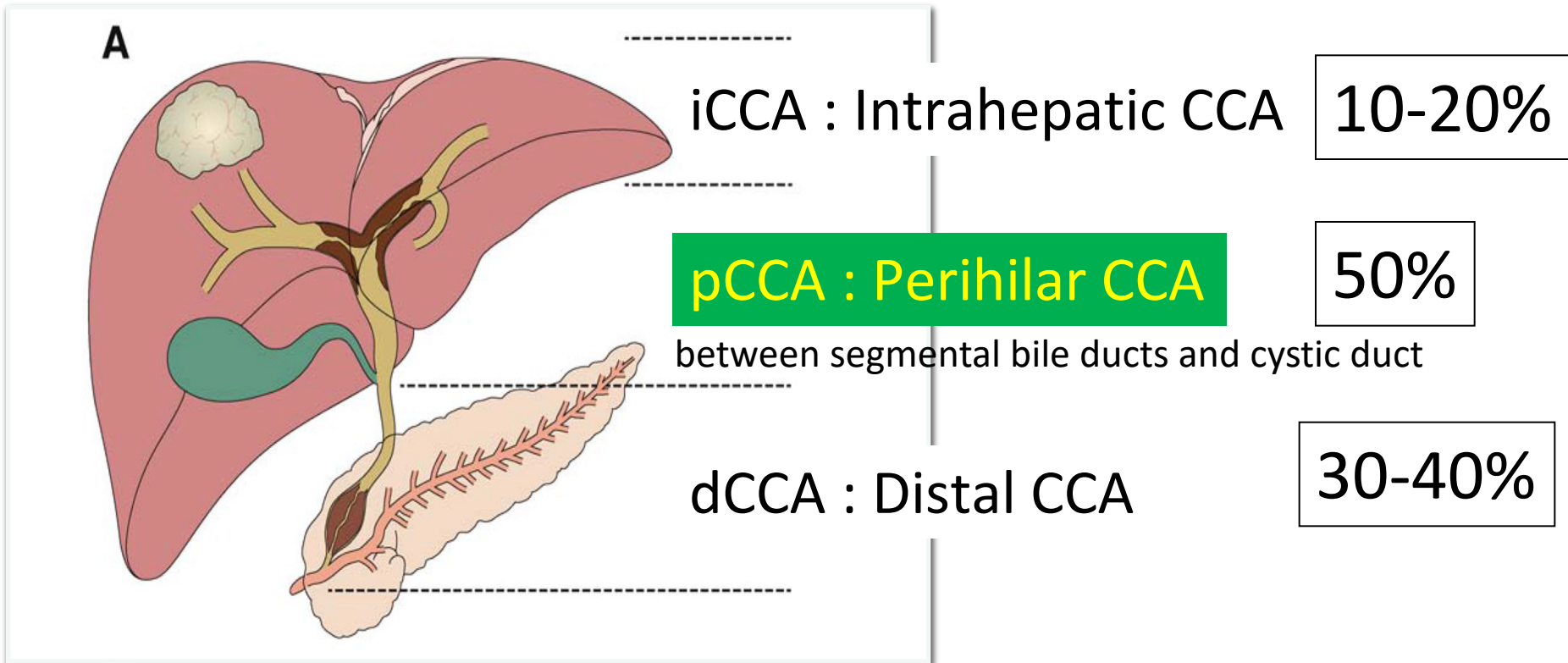
What is a Perihilar Cholangiocarcinoma (Klatskin tumor) & how to do the diagnosis?

Dr Valerio LUCIDI

Erasme-ULB University Hospital –
Brussels (Belgium)

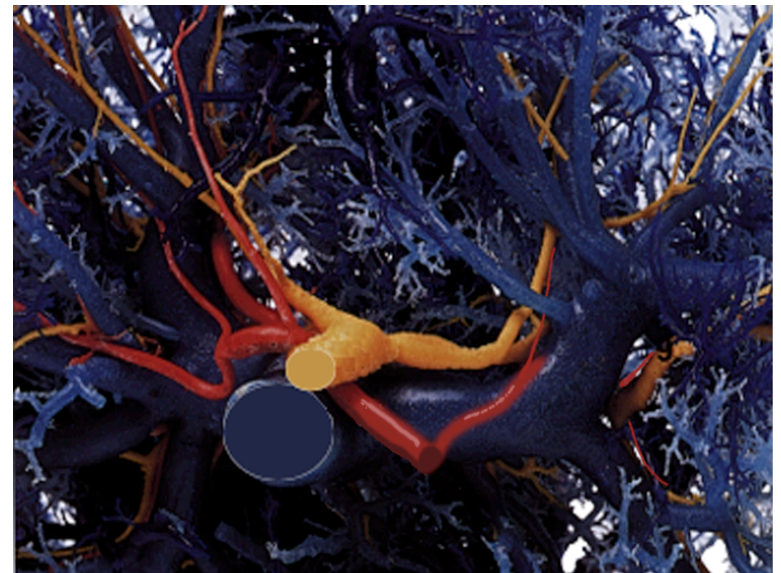
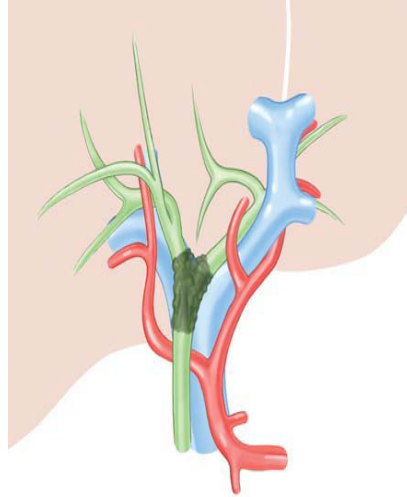
HBPS – PGC 2019

Malignant tumor rising from bile duct epithelial cells

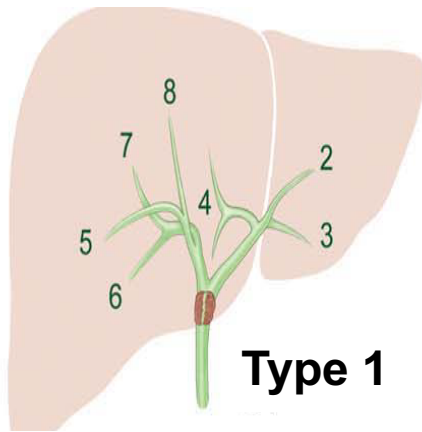


... terms of *Klatskin* tumor and *Extrahepatic CCA* should be *avoided*

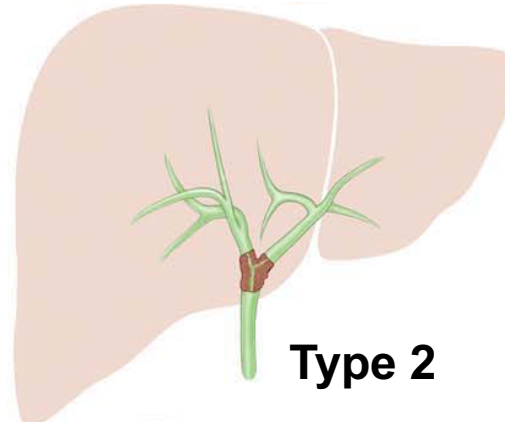
- Size
- Location
- Proximity with vessels
- Diagnosis



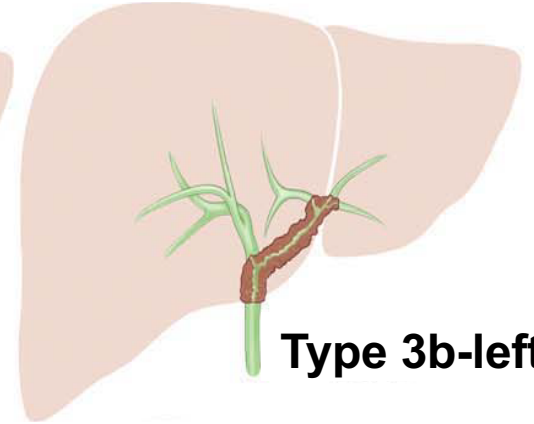
Classification of pCCA: Bismuth-Corlette



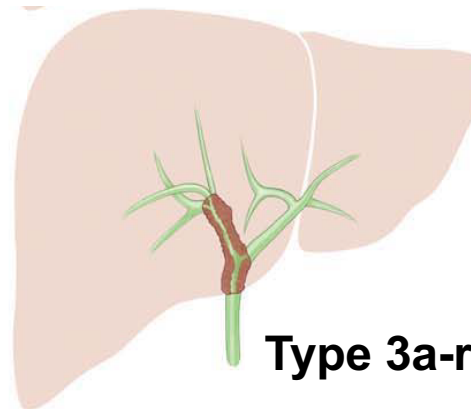
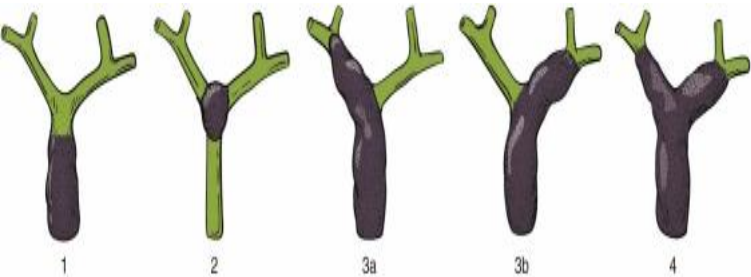
Type 1



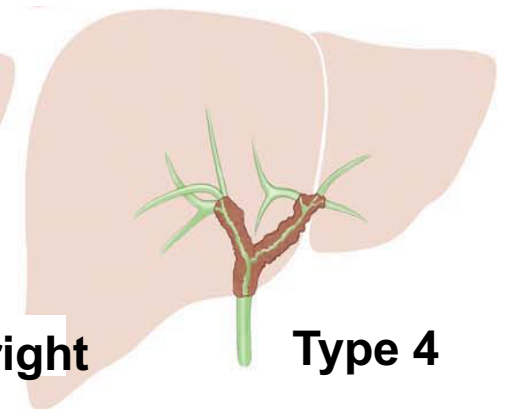
Type 2



Type 3b-left



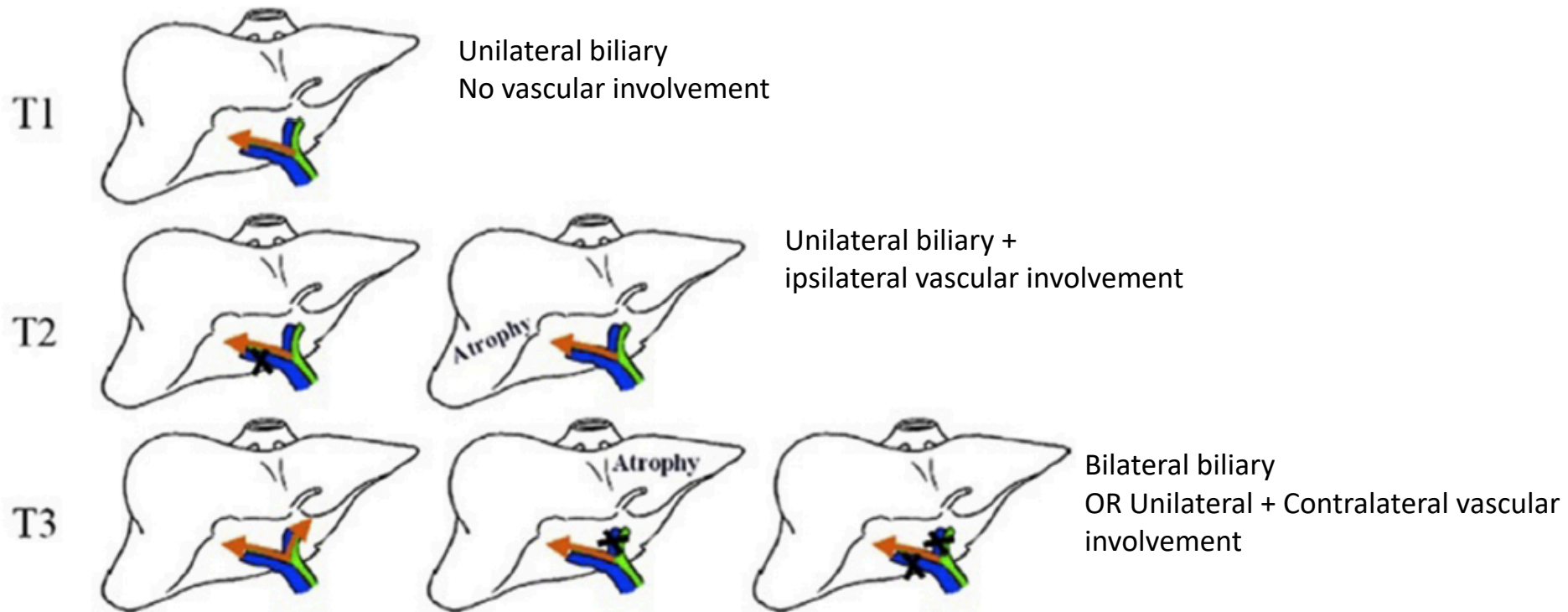
Type 3a-right



Type 4

Stratifies patients by **longitudinal** extension

- it ignores vascular involvement



Stratifies patients by **longitudinal** and **radial** extension

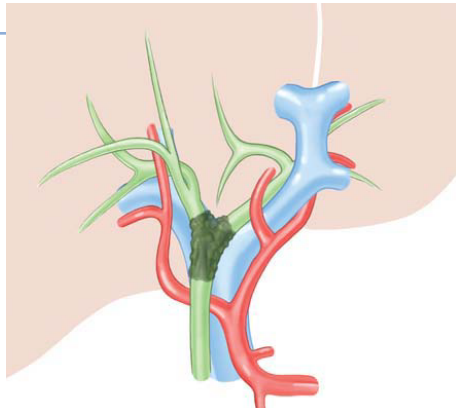
- extension of tumour in to the vascular structures
- surrogate indicators of radial tumour extension (atrophy)

Classification of pCCA: ... B-HA-PV-V

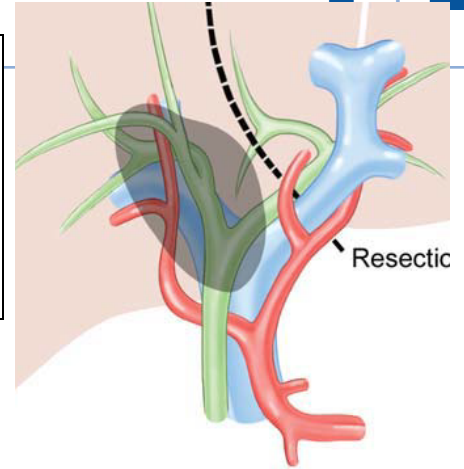
New Staging System and a Registry for Perihilar Cholangiocarcinoma

Michelle L. DeOliveira,¹ Richard D. Schulick,² Yuji Nimura,³ Charles Rosen,⁴ Gregory Gores,⁵ Peter Neuhaus,⁶ and Pierre-Alain Clavien¹

De Oliveira et al. Hepatology 2011



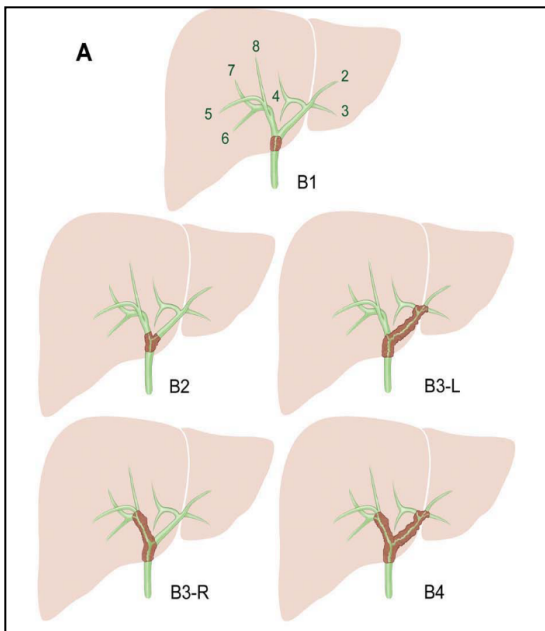
B2, PV0, HA0



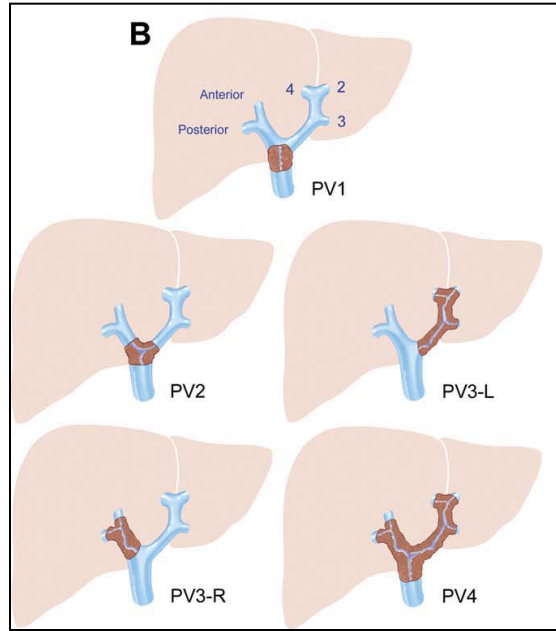
Resectic

B3-R, PV3-R, HA3-R

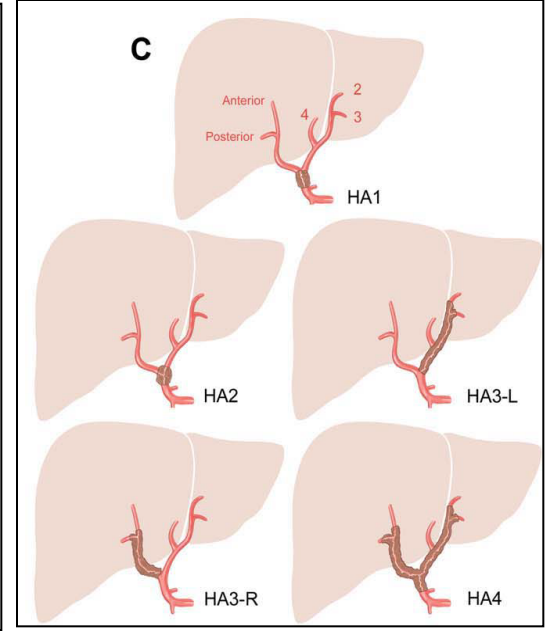
Longitudinal + Radial + Volume RL



Longitudinal Biliary extension

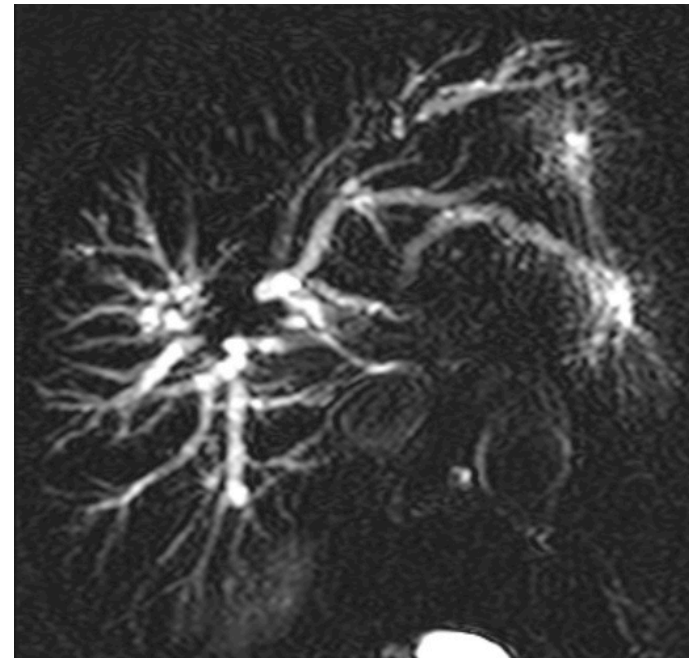
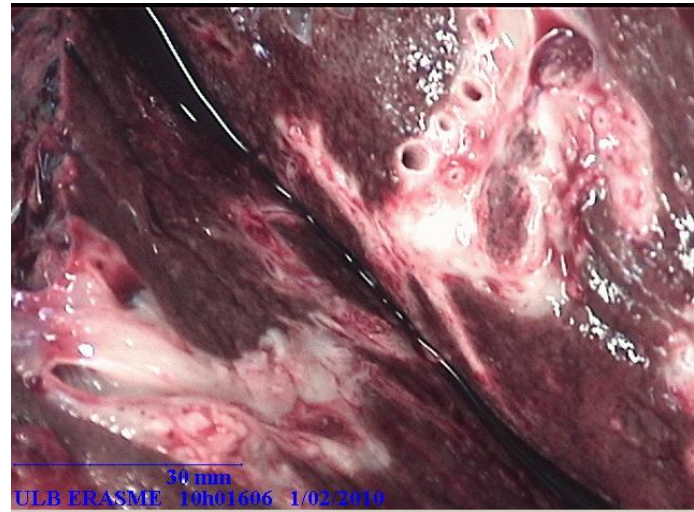


Radial Portal infiltration



Radial Arterial infiltration

- Differential diagnosis
 - Fibrotic & infiltrative tumor
- Invasive diagnostic exams:
consider surgical strategy



BENIGN

- PSC – Primary Sclerosing Cholangitis
- BDI – Bile Duct Injury post cholecystectomy (traumatic or ischemic)
- Mirizzi Syndrome
- IgG4 mediated inflammatory stenosis
 - Hilar stenosis without visible mass
 - 50% combined pancreatic anomaly
 - IgG4 positif Dosage in 60%
 - Test treatment by corticosteroids 1 month:
 - Decrease of IgG4 and CA19.9 levels
- Portal Biliopathy (Biliary compression due to portal cavernoma)

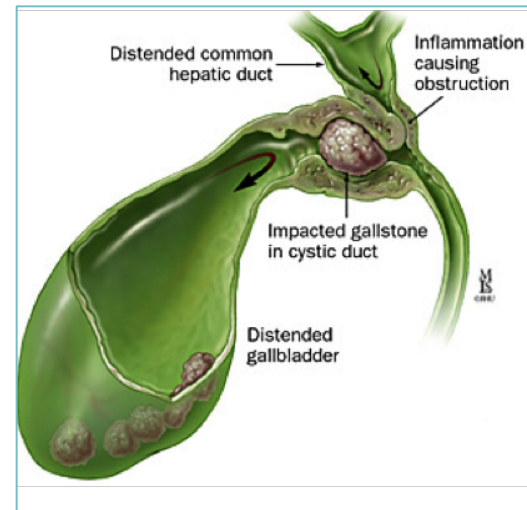
MALIGNANT

- Intrahepatic Cholangiocarcinoma infiltrating the hilum
- Gallbladder cancer infiltrating the hilum
- Metastatic infiltration of other cancer or peritoneal carcinomatosis

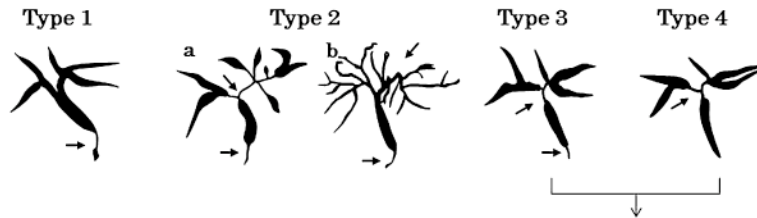
Traumatic BDI



Mirizzi Syndrome



IgG4-related cholangitis: differential diagnosis

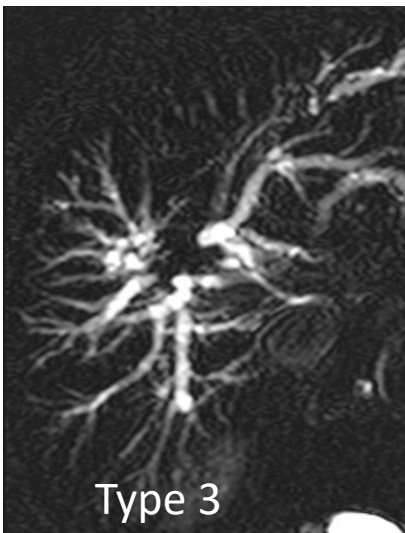


Differential diagnosis
 Pancreatic cancer
 Bile duct cancer
 Chronic pancreatitis

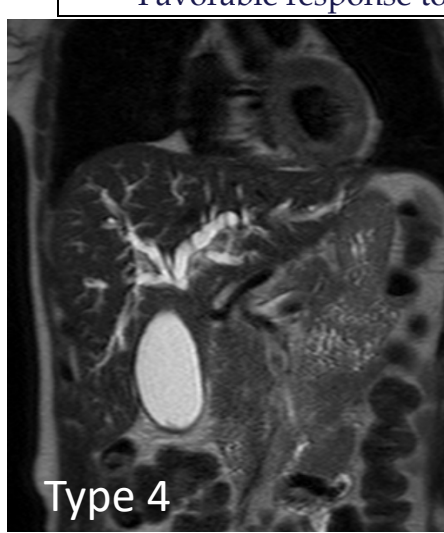
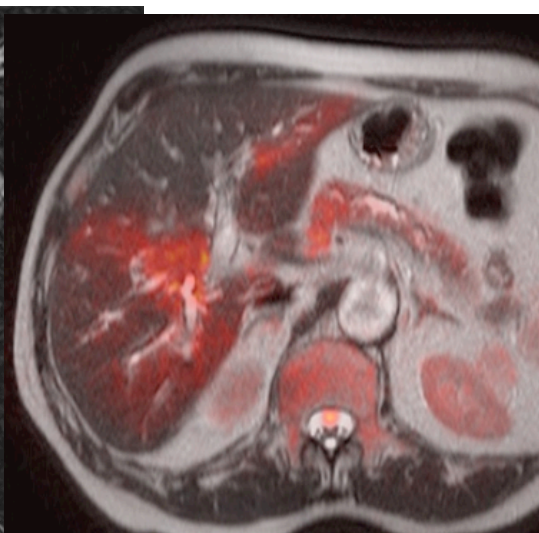
Primary sclerosing cholangitis

Bile duct cancer
 Gallbladder cancer

- IgG4-related disease:
 - pancreatitis (60%)
 - sialoadenitis (34%)
 - nephritis (23%)
 - dacryoadenitis (23%)
 - periaortitis (20%)
 - cholangitis (13%)
- M>F (4:1) middle aged or the elderly
- 80% have elevated serum IgG4 (> 135mg/dL)
- At imaging: may mimick other biliary disorders
- Lymphoplasmacytic infiltration, including abundant IgG4-bearing plasma cells in the bile duct lesions
- Favorable response to treatment (stenting, steroids)



Type 3

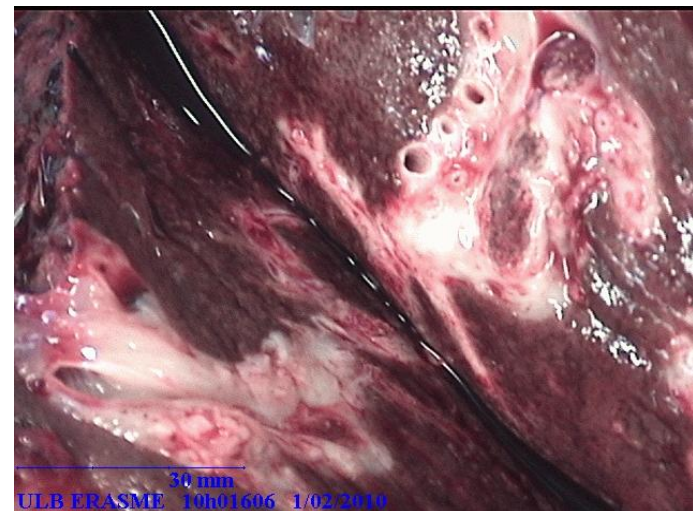
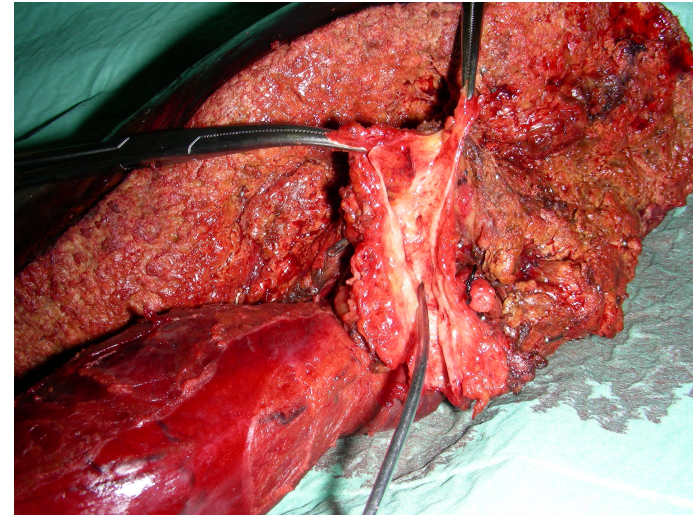


Type 4



Almost certain diagnosis of pCCA

- Jaundice or biological cholestasis
- Regular-shaped IHBD
- Small but visible hilar mass
- No previous cholecystectomy
- No portal cavernoma
- Normal pancreas

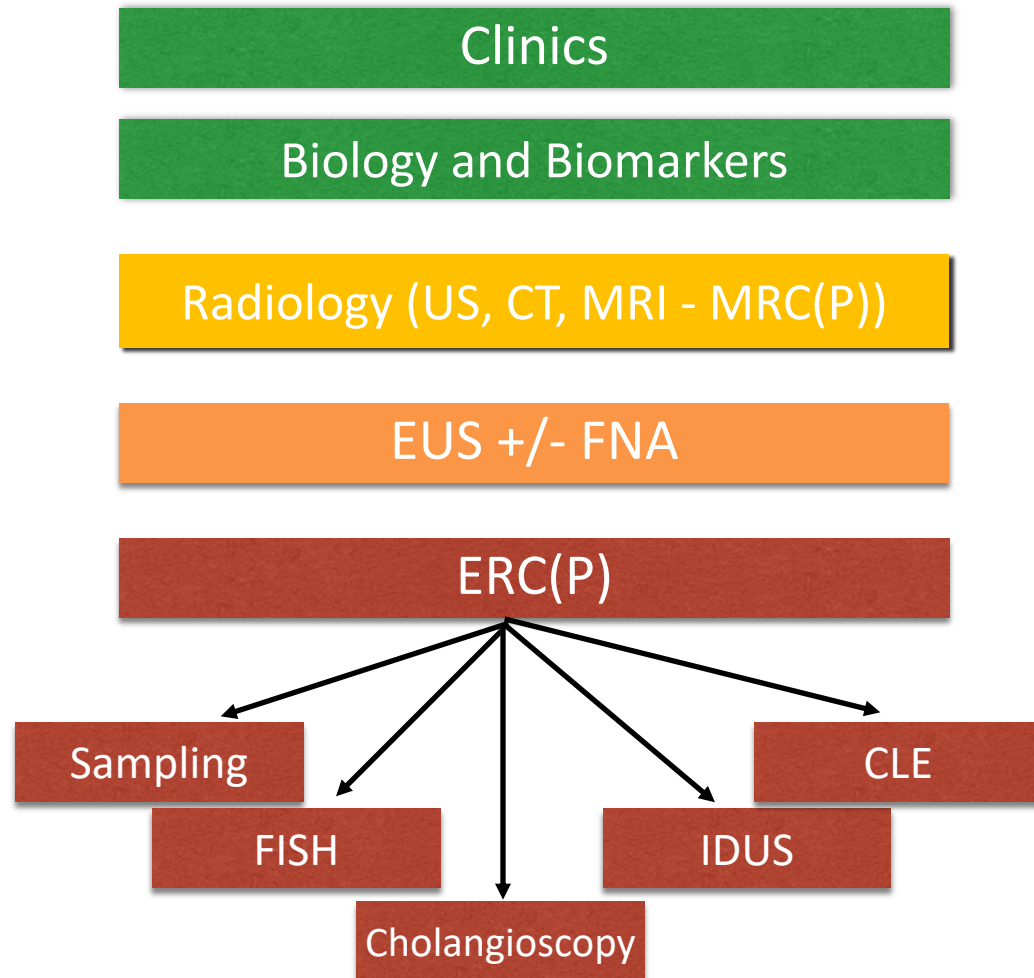


Hilar Cholangiocarcinoma
(80%)

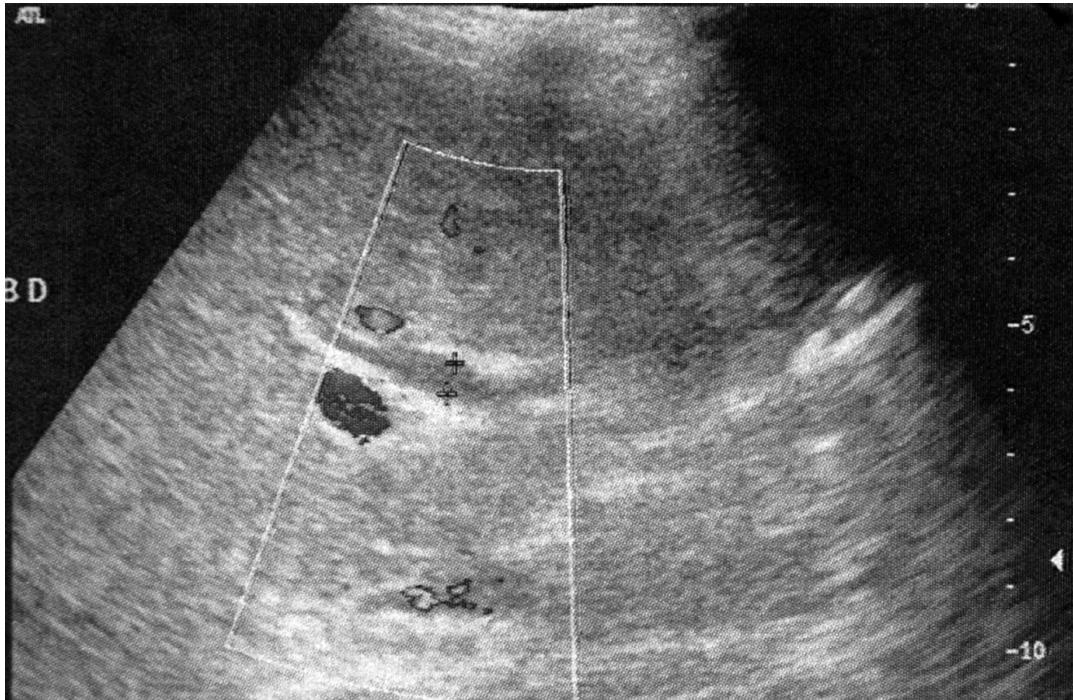
VS

- Benign stricture (post surgical)
- Lithiasis
- IgG4 cholangiopathy
- PSC
- Other tumor (benign or malignant)

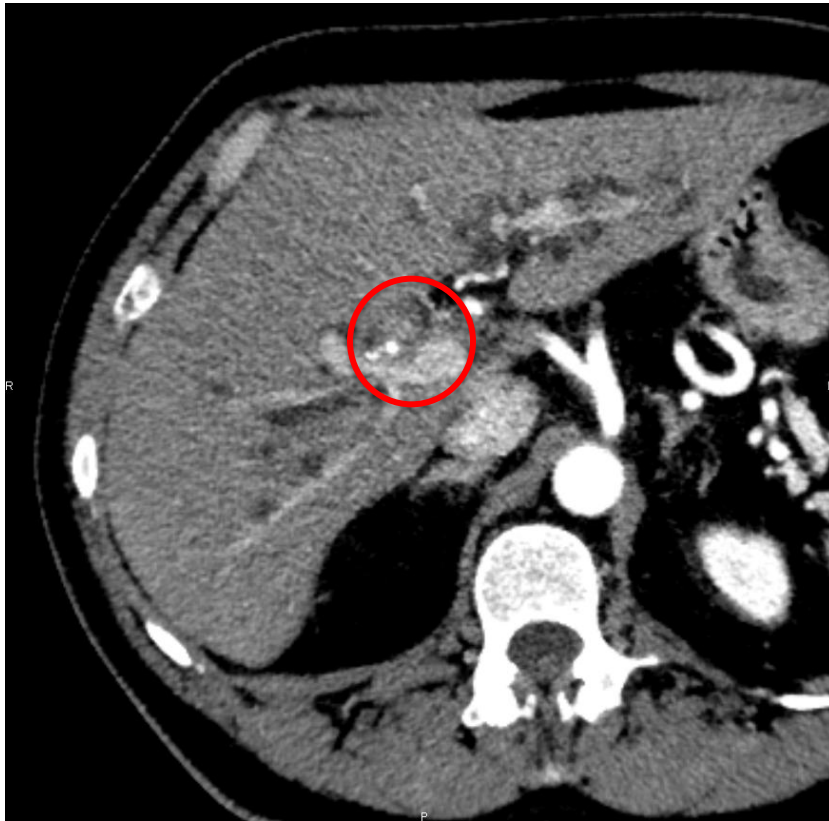
Are. Surgery. 2006



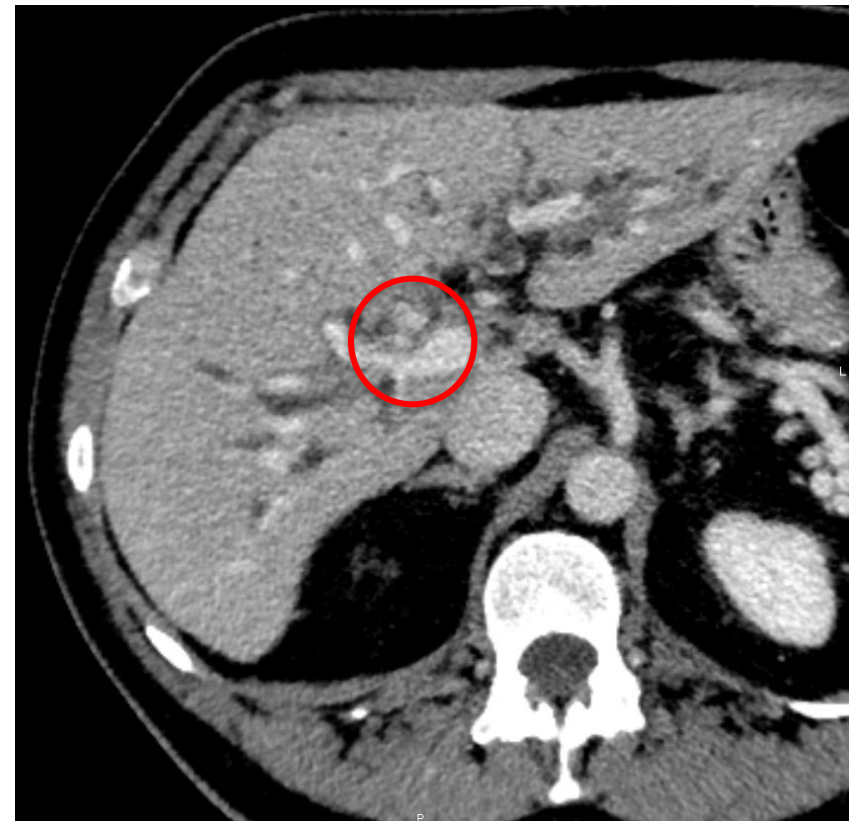
- **Biological cholestasis** (may be isolated)
- **Jaundice (70%)**
- **Dilatation of IHBD**
- **Non-dilated gallbladder**
- nonspecific symptoms including abdominal discomfort, cachexia, weight loss, and malaise typically consistent with biliary obstruction presenting with jaundice and less commonly cholangitis



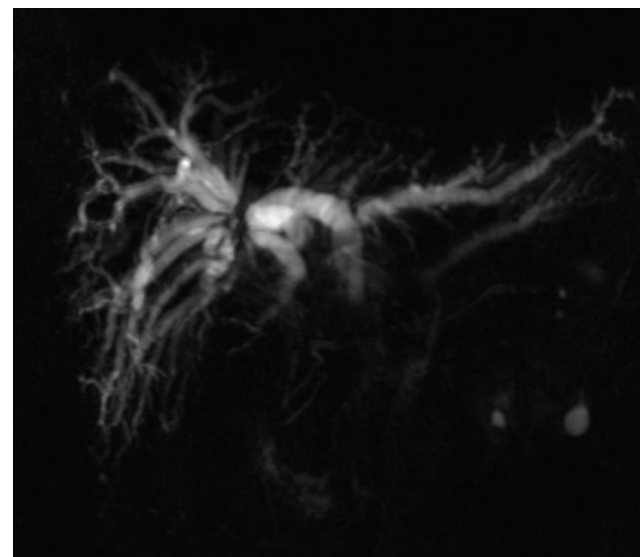
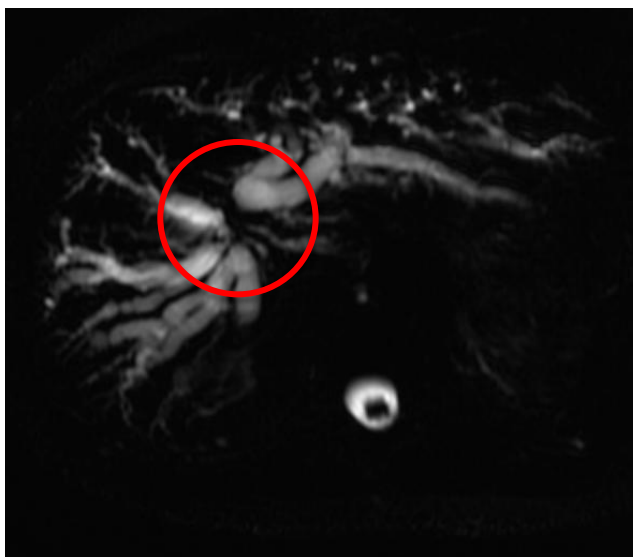
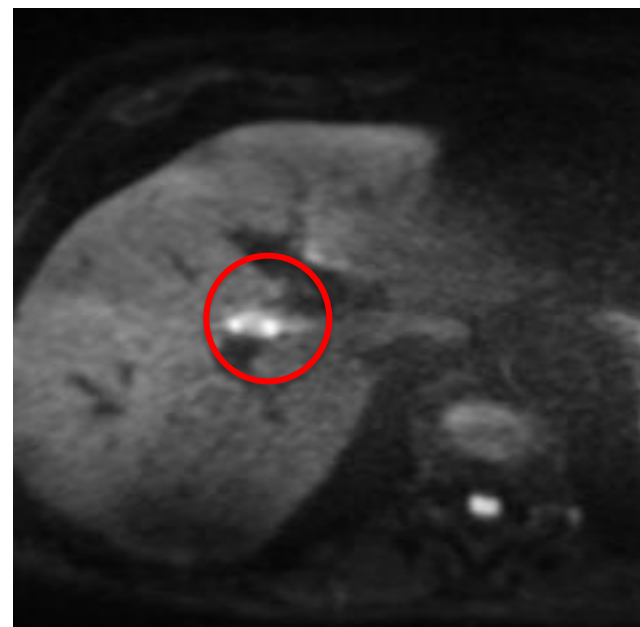
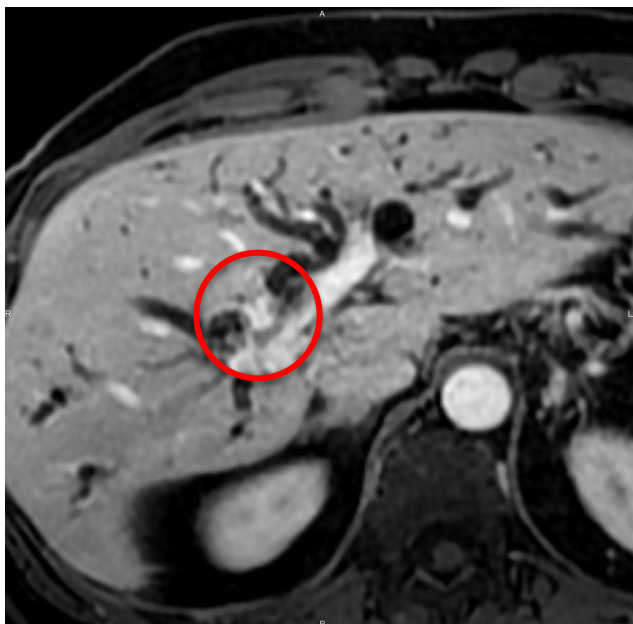
- Dilatation of Intra-Hepatic Bile Ducts
- Non distended gallbladder
- Hilar mass ?



- Dilatation of Intra-Hepatic Bile Ducts
- Non distended gallbladder
- Hilar mass
- Vascular behaviour of mass

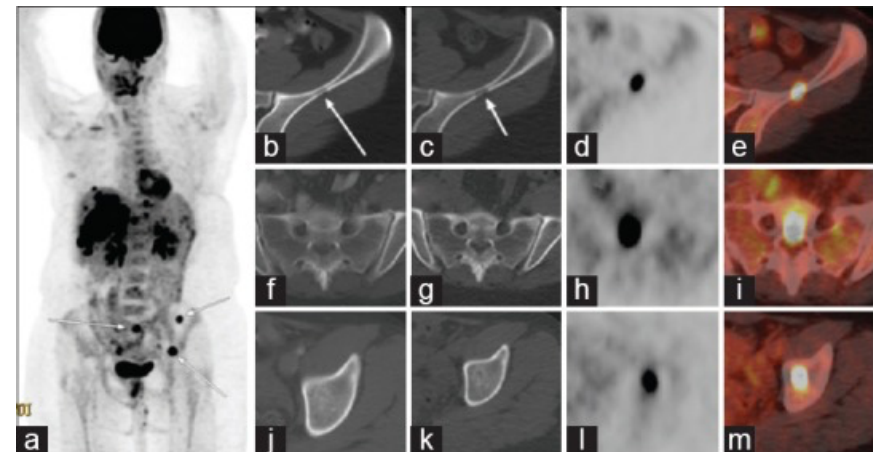
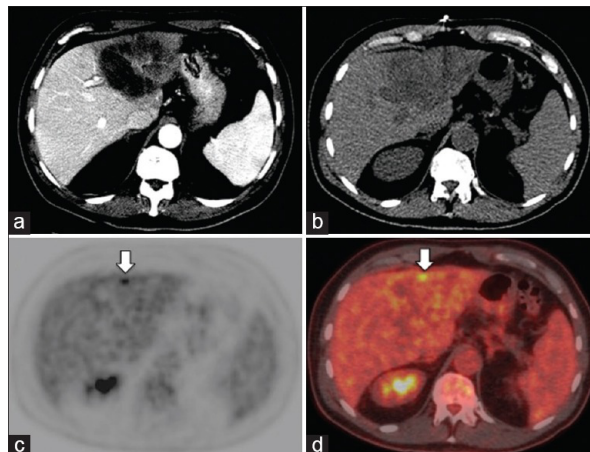


- Portal vein invasion ?
- Arterial branch invasion?
- Hilar & coeliac adenopathies ?
- Peritoneal seeding?



	FDG PET/CT	CECT	P
Sensitivity (%)	96.5 (91.61, 98.71)	62.2 (53.72, 70.09)	<0.0001
Specificity (%)	55.5 (22.65, 84.65)	66.7 (30.92, 90.96)	NS
PPV (%)	97.2 (92.50, 99.09)	96.7 (90.09, 99.15)	NS
NPV (%)	50.0 (23.66, 76.34)	10.0 (4.13, 21.17)	0.0064
Accuracy (%)	94.1 (88.72, 97.08)	62.5 (54.25, 70.11)	<0.0001

FDG PET/CT: Fluoro-D-glucose positron emission tomography/computer tomography; CECT: Contrast enhanced computed tomography; PPV: Positive predictive value, NPV: Negative predictive value, values in parenthesis are 95% confidence intervals



Pre-operative Histological proof ?

	NCCN 2016	SEOM 2015	Japanese 2014	Chinese 2014	EASL 2014	Asia-Pacif 2013
iCCA	no for non-cirrhotic	not always needed		is very important for planning a treatment	no for non-cirrhotic	
pCCA	no if the index of suspicion is high	not always needed	Should be obtain	is very important for planning a treatment		yes even by EUS FNA
dCCA	no if the index of suspicion is high	not always needed	Should be obtain	is very important for planning a treatment		

Benson 2009, Benavides 2015, Miyazaki 2015, Xiao-ping 2014, Bridgewater 2014, Rerknimitr 2013

Pre-operative Histological proof ?

	NCCN 2016	SEOM 2015	Japanese 2014	Chinese 2014	EASL 2014	Asia-Pacif 2013
<p>« based on radiologic imaging and ERCP, the rate of unnecessary surgical intervention for benign biliary lesions has been shown to be as high as 15%-25% »</p>						
pCCA	no if the index of suspicion is high	not always needed	Should be obtain	is very important for planning a treatment		yes even by EUS FNA
dCCA	no if the index of suspicion is high	not always needed	Should be obtain	is very important for planning a treatment		

Benson 2009, Benavides 2015, Miyazaki 2015, Xiao-ping 2014, Bridgewater 2014, Rerknimitr 2013

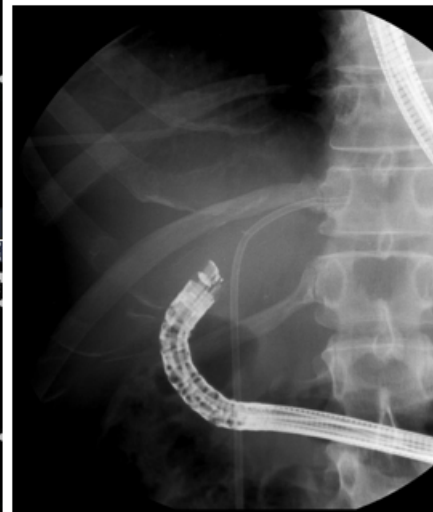
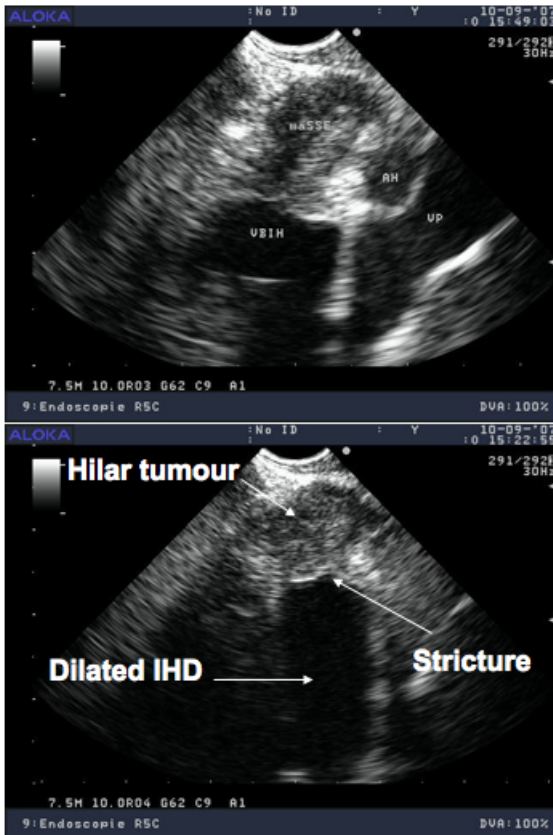


- NO ERCP before analysis of imaging work-up by specialized HB-surgical team !!!

Role of EUS for preoperative evaluation of cholangiocarcinoma: a large single-center experience

Mehdi Mohamadnejad, MD, John M. DeWitt, MD, Stuart Sherman, MD, Julia K. LeBlanc, MD, Henry A. Pitt, MD, Michael G. House, MD, Kelly J. Jones, MD, Evan L. Fogel, MD, Lee McHenry, MD, James L. Watkins, MD, Gregory A. Cote, MD, Glen A. Lehman, MD, Mohammad A. Al-Haddad, MD

Indianapolis, Indiana, USA; Tehran, Iran



- High level of tumor detection *
 - compare to CT and MRI
- EUS increase the detection of unresectable lesion *
 - vascular invasion
 - liver M+
 - Coeliac and distant LN
- Sensitivity of EUS-FNA is significantly higher in distal than in proximal CCA.

Mohamadnejad et al. GIE 2011 *

Weilert et al. GIE 2014 **

Moura et al. Endoscopy International Open 2018 **

ORIGINAL ARTICLE

Trans-peritoneal fine needle aspiration biopsy of hilar cholangiocarcinoma is associated with disease dissemination

Julie K. Heimbach, William Sanchez, Charles B. Rosen & Gregory J. Gores

William J von Liebig Transplant Center, Mayo Clinic College of Medicine, Rochester, MN, USA

« Transperitoneal biopsy of hilar cholangiocarcinoma is associated with a higher rate of peritoneal metastases, and it **should not be performed if a curative approach is available** »

Table 2 Incidence of peritoneal metastasis in patients who underwent a diagnostic transperitoneal fine needle aspiration (FNA) biopsy of hilar cholangiocarcinoma (CCA)

	No biopsy	Positive transperitoneal biopsy	Negative transperitoneal biopsy
Peritoneal metastasis	14/175 (8%)	5/6 (83%) ^a	0/9
at staging	14/175 (8%)	5/15 (33%) ^b	

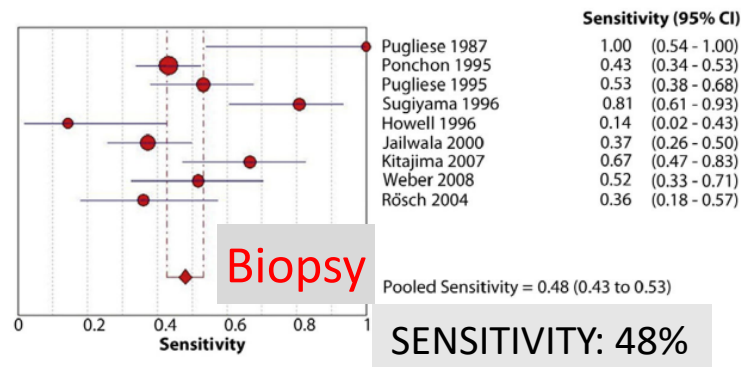
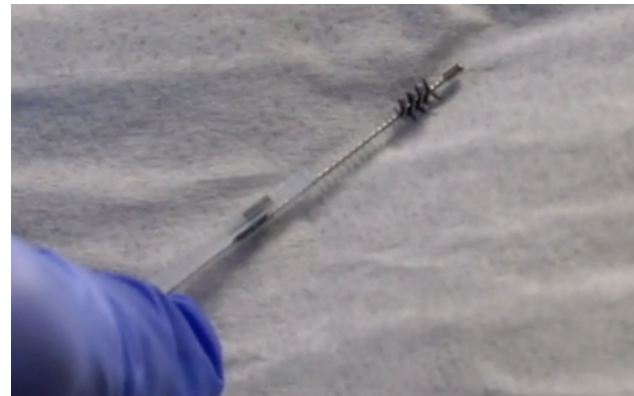
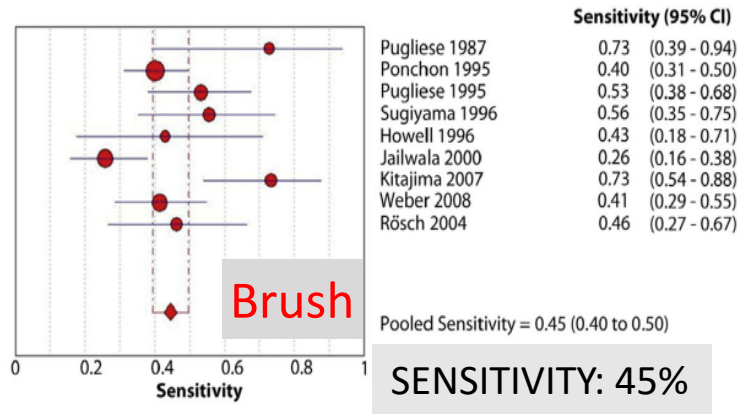
^a*P* = 0.0001 using Fisher's exact test.

- YES for local US evaluation of pCCA
- YES for Lymph-nodes biopsies
- NO for direct hilar mass biopsy

Comparative effectiveness of biliary brush cytology and intraductal biopsy for detection of malignant biliary strictures: a systematic review and meta-analysis

Udayakumar Navaneethan, MD^{1,2}, Basile Njei, MD, MPH³, Vennisvasanth Lourdasamy, MD¹,

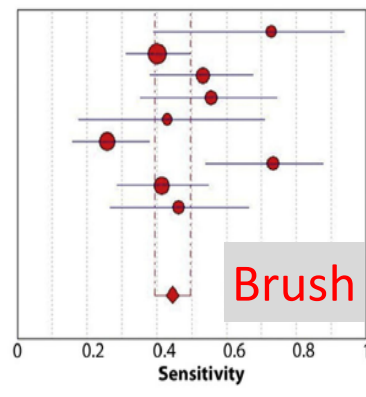
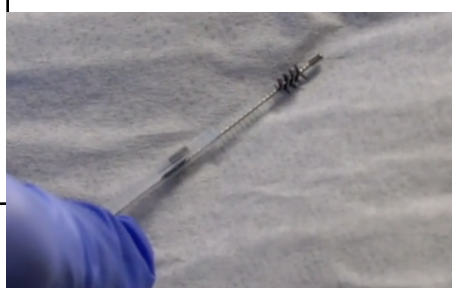
Navaneethan GIE 2015



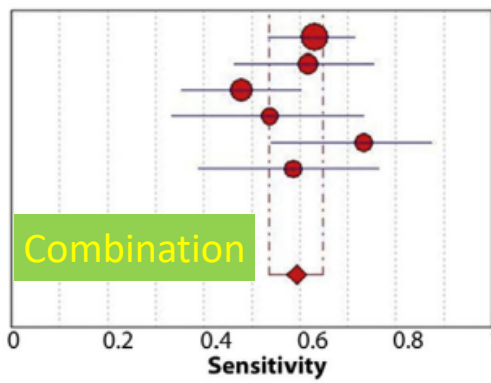
Comparative effectiveness of biliary brush cytology and intraductal biopsy for detection of malignant biliary strictures: a systematic review and meta-analysis

Udayakumar Navaneethan, MD^{1,2}, Basile Njei, MD, MPH³, Vennisvasanth Lourdasamy, MD¹,

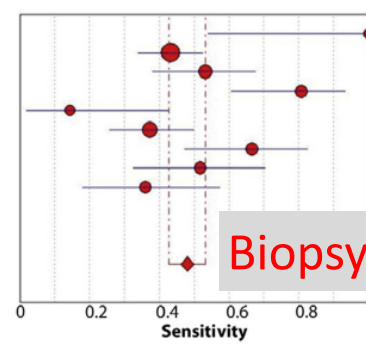
Navaneethan GIE 2015



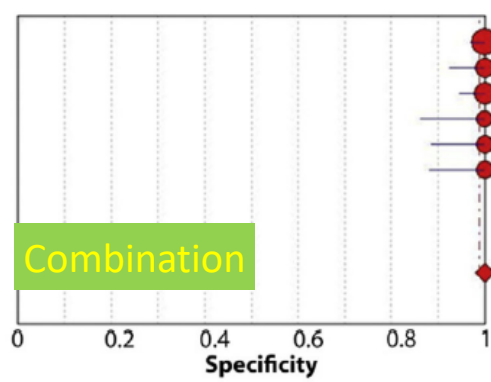
Study	Sensitivity (95% CI)
Pugliese 1987	0.73 (0.39 - 0.94)
Ponchon 1995	0.40 (0.31 - 0.50)
Pugliese 1995	0.53 (0.38 - 0.68)
Sugiyama 1996	0.56 (0.35 - 0.75)
Howell 1996	0.43 (0.18 - 0.71)
Jailwala 2000	0.26 (0.16 - 0.38)
Kitajima 2007	0.73 (0.54 - 0.88)
Weber 2008	0.41 (0.29 - 0.55)
Rösch 2004	0.46 (0.27 - 0.67)



Study	Sensitivity (95% CI)
Ponchon 1995	0.63 (0.53 - 0.72)
Pugliese 1995	0.62 (0.46 - 0.75)
Jailwala 2000	0.48 (0.35 - 0.60)
Rösch 2004	0.54 (0.33 - 0.73)
Kitajima 2007	0.73 (0.54 - 0.88)
Weber 2008	0.59 (0.39 - 0.76)

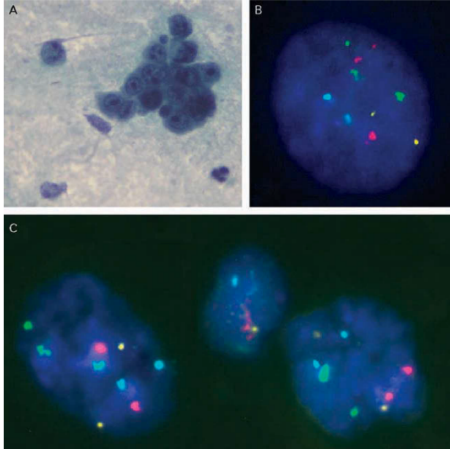


Study	Sensitivity (95% CI)
Pugliese 1987	1.00 (0.54 - 1.00)
Ponchon 1995	0.43 (0.34 - 0.53)
Pugliese 1995	0.53 (0.38 - 0.68)
Sugiyama 1996	0.81 (0.61 - 0.93)
Howell 1996	0.14 (0.02 - 0.43)
Jailwala 2000	0.37 (0.26 - 0.50)
Kitajima 2007	0.67 (0.47 - 0.83)
Weber 2008	0.52 (0.33 - 0.71)
Rösch 2004	0.36 (0.18 - 0.57)



Study	Specificity (95% CI)
Ponchon 1995	1.00 (0.97 - 1.00)
Pugliese 1995	1.00 (0.92 - 1.00)
Jailwala 2000	1.00 (0.95 - 1.00)
Rösch 2004	1.00 (0.86 - 1.00)
Kitajima 2007	1.00 (0.88 - 1.00)
Weber 2008	1.00 (0.88 - 1.00)

FISH : Fluorescence *in situ* hybridization



SENSITIVITY: 50-80%
SPECIFICITY: ... up to 100%

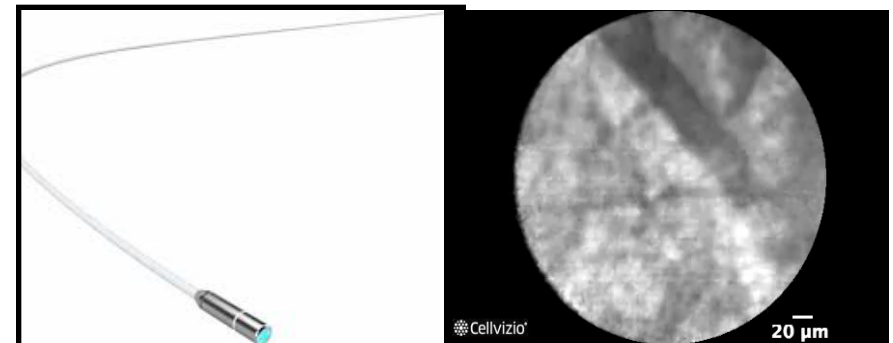
Spyglass



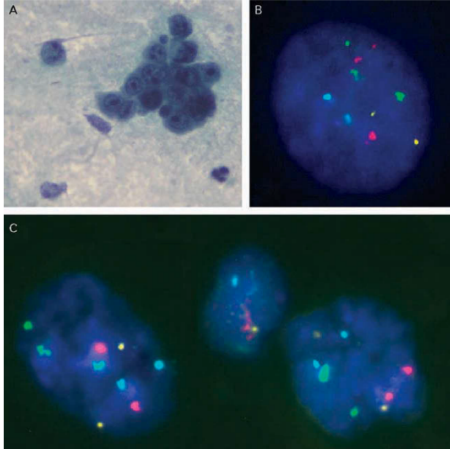
Intraductal US



Confocal Laser Endomicroscopy



FISH : Fluorescence *in situ* hybridization



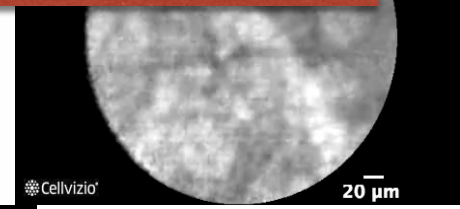
SENSITIVITY: 50-80%
SPECIFICITY: ... up to 100%

Spyglass

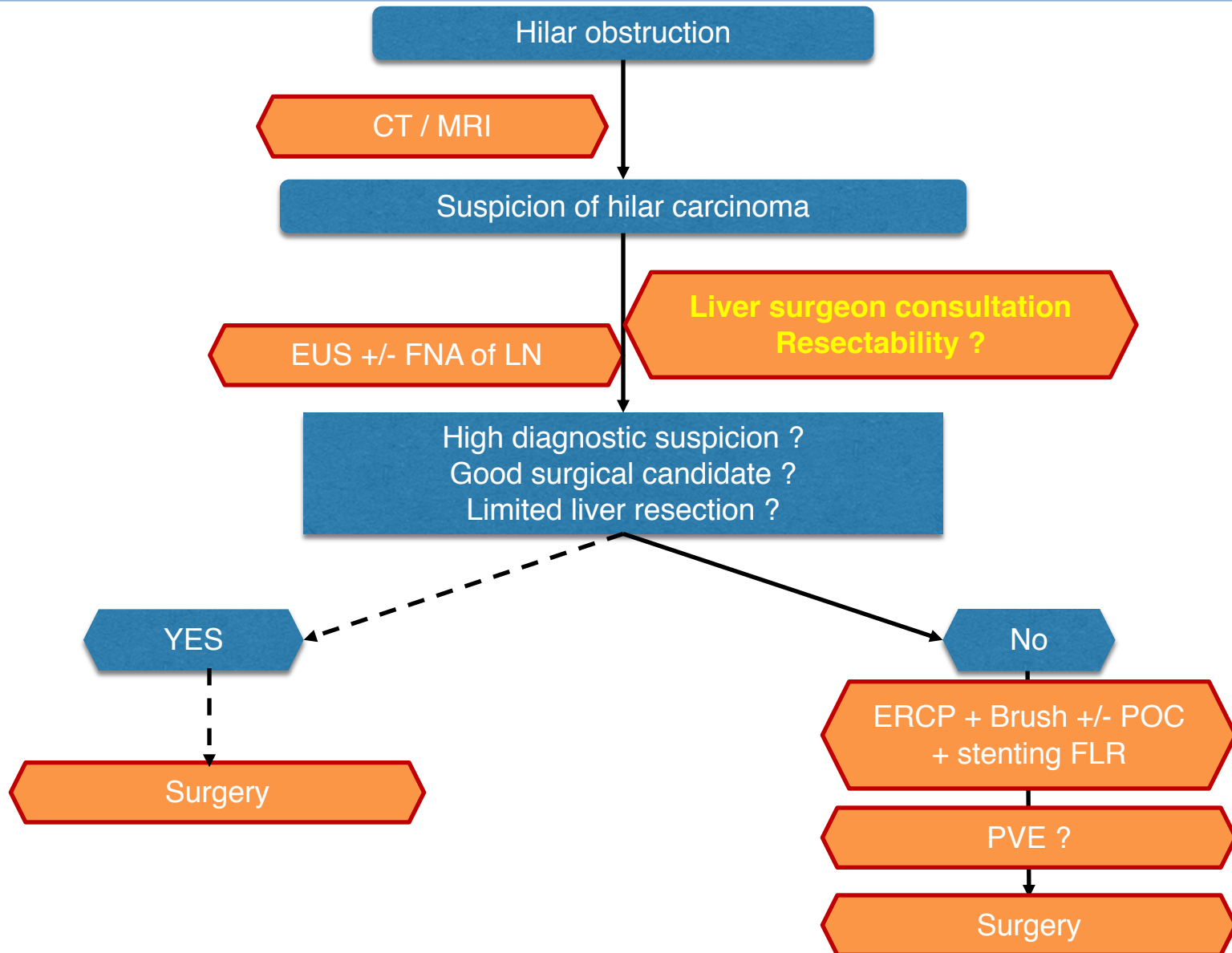


Drawbacks :

- Expert center / hands
- Cost +++
- Complication rate around 7.1% (most common cholangitis)



Work-up for pCCA diagnosis



- Hepato-Biliary Surgeon has to determine resectability at initial diagnosis : he decides on necessity of invasive exams
- Histological proof not indispensable to go to surgery
- Transperitoneal puncture of the lesion to be avoided!!!
- Exclude metastatic sites: MRI / AngioCT / EUS+/-FNA ADP / PET / CT Thorax
- Biliary drainage often needed after ERCP : type of drainage depending on established surgical strategy
 - Future liver remnant drainage