



TURNING CANCER DATA  
INTO DISCOVERY

# Gross examination of Biliary Cancers

Jon Wagner, MHS, PA(ASCP)

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# Course summary:

- An introduction to pathologists' assistants and our role in pathology.
  - How does the gross examination connect with other medical specialties and what is our role in determining stage?
  - How are pathologists' assistants helping the practice of pathology to mature?
  - What is the gross Description?
- Biliary cancers:
  - Incidence, mortality rates
  - Anatomic challenges
- Biliary Cancers at the gross bench.
  - Determining primary site
  - Helping to establish an accurate diagnosis
  - Helping to establish an accurate stage and extent of disease
- Questions.



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# Who are pathologists' assistants and what is our role in pathology?

- Pathologists' assistants were introduced in the 1970s.
- Prior to pathologists' assistants, pathologists performed the gross tissue examinations.
- Evolution:
  - Pathologists' assistants perform the gross examination and handle pre-analytic processes.
  - Pathologists, supervise pathologists' assistants, perform microscopic assessment and oversee molecular studies.



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## Sidebar...

### NCCN guidelines: biliary cancers

- Biliary tract cancers are known to harbor clinically relevant molecular alterations that are differentially expressed in gallbladder cancers, and intrahepatic and extrahepatic (perihilar and distal) cholangiocarcinoma... for which specific treatments are now available.
  - FGFR2
  - NTRK
  - IDH1
  - BRAF...



Submitted in formalin, labeled with the patient's name, medical record number and "bile duct excision" is a bile duct resection having overall dimensions of 10.5 x 8.2 x 2.7 cm. The en bloc resection consists of a 4.2 x 3.7 x 3.6 cm portion of liver that gives rise to the right hepatic duct (1.5 cm) and left hepatic duct (1.6 cm) that converge to form a 1.5 cm segment of common hepatic duct which converges with the cystic duct (measuring 1.8 cm in length) that has been resected with the gallbladder (7.5 x 2.7 x 2.5). Finally, the distal extend of the resection consists of a segment of common bile duct measuring 2.2 cm in length. There is a small amount of attached fat focally. The specimen is intact and free of significant surgical defects. External examination is remarkable for dilatation that begins just proximal to the convergence of the cystic duct, with the common hepatic duct, effecting the proximal common hepatic duct, as well as the right and left hepatic ducts. The dilated area reaches a maximum diameter of 1.6 cm, and no sites of rupture are seen. Upon opening, the dilatation is caused by an obstructing tumor that is located at the common hepatic duct. The surface of the tumor is grey white and lobulated. The tumor has surface dimensions of 2.6 x 1.4 cm, centered at the common hepatic duct and occupying the full circumference of the common hepatic duct, causing marked stenosis/occlusion. On sectioning, the tumor has firm, grey white cut surfaces, measures up to 0.6 cm and is confined to the bile duct wall, approaching but not reaching the adventitial surface. The adventitial margin is free by less than 0.1 cm and this margin is inked black. The tumor is located approximately 5.3 cm from the liver parenchymal and intraparenchymal bile duct and vascular margins and 2.7 cm from the common bile duct margin. The remaining surfaces of the ducts are smooth to gently lobulated and no additional tumors are seen. There is a 1.6 cm cystic duct lymph node candidate that has tan pink, soft cut surfaces showing no obvious areas of involvement by tumor. Within the small amount of attached fat, there is a 1.6 cm cystic duct lymph node candidate. The candidate has tan-grey, soft cut surfaces.

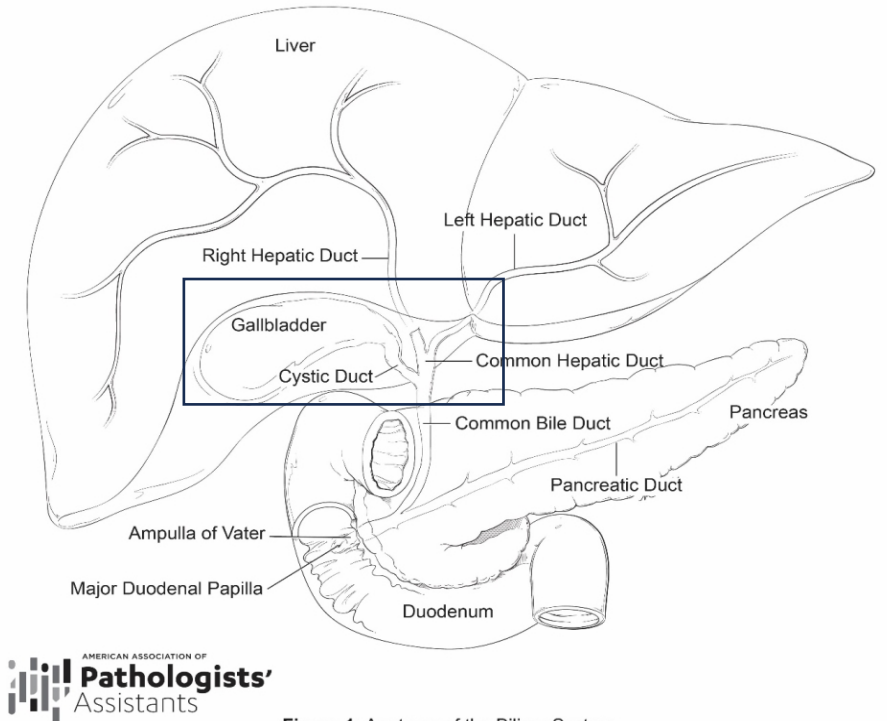
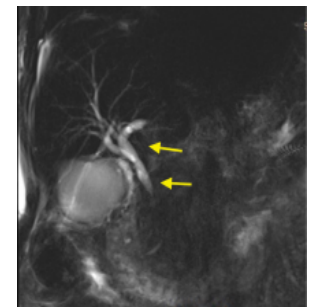


Figure 1: Anatomy of the Biliary System

A good gross description will, when appropriate correlate with other medical specialties, clinical features, offer important staging information, and often represents an important facet of an institutional quality system.

- Submitted in formalin, labeled with the patient's name, medical record number and "bile duct excision" is a bile duct resection having overall dimensions of 10.5 x 8.2 x 2.7 cm. The en bloc resection consists of a 4.2 x 3.7 x 3.6 cm portion of liver that gives rise to the right hepatic duct (1.5 cm) and left hepatic duct (1.6 cm) that converge to form a 1.5 cm segment of common hepatic duct which converges with the cystic duct (measuring 1.8 cm in length) that has been resected with the gallbladder (7.5 x 2.7 x 2.5). Finally, the distal extent of the resection consists of a segment of common bile duct measuring 2.2 cm in length. There is a small amount of attached fat focally. **The specimen is intact and free of significant surgical defects.** External examination is remarkable for **dilatation that begins just proximal to the convergence of the cystic duct, with the common hepatic duct, effecting the proximal common hepatic duct, as well as the right and left hepatic ducts.** The dilated area reaches a maximum diameter of 1.6 cm, and no sites of rupture are seen. Upon opening, the dilatation is caused by an obstructing tumor that is located at the common hepatic duct. The surface of the tumor is grey white and lobulated. The tumor has surface dimensions of **2.6 x 1.4 cm**, centered at the common hepatic duct and occupying the full circumference of the common hepatic duct, causing marked stenosis/occlusion. **On sectioning, the tumor has firm, grey white cut surfaces, measures up to 0.6 cm and is confined to the bile duct wall, approaching but not reaching the adventitial surface.** The adventitial margin is free by less than 0.1 cm and this margin is inked black. The tumor is located approximately 5.3 cm from the liver parenchymal and intraparenchymal bile duct and vascular margins and 2.7 cm from the common bile duct margin. The remaining surfaces of the ducts are smooth to gently lobulated and no additional tumors are seen. There is a 1.6 cm cystic duct lymph node candidate that has tan pink, soft cut surfaces showing no obvious areas of involvement by tumor. Within the small amount of attached fat, there is a 1.6 cm cystic duct lymph node candidate. The candidate has tan-grey, soft cut surfaces.



# Bile duct cancer: incidence, mortality

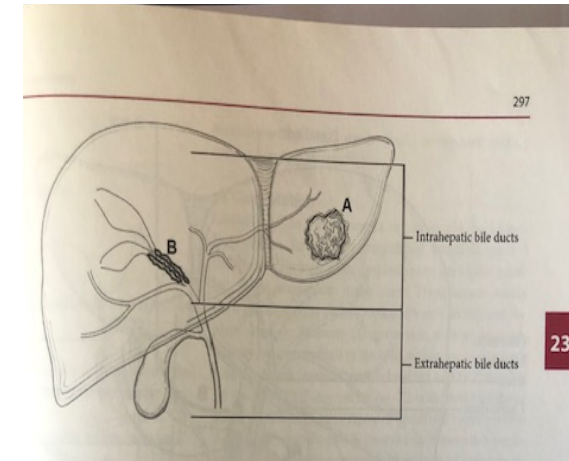
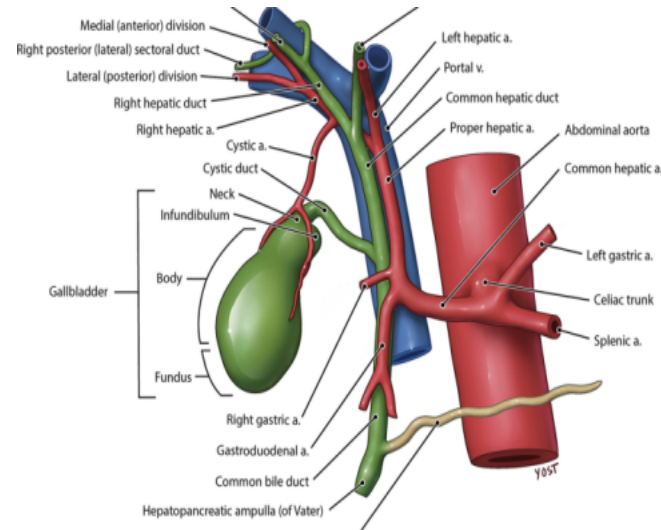
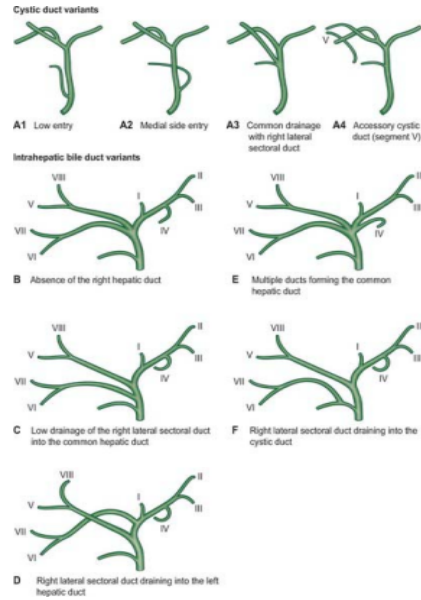
- Bile duct cancers are rare
  - About 8000 cases per year in US
  - breast is about 300,000 per year in US
- Bile duct cancers are lethal
  - 5 year survival:
    - 9% for intrahepatic
    - 11% for extrahepatic
    - 91% for breast



Bile duct  
cancers at the  
gross bench,  
determining  
primary site,  
accurate  
diagnosis and  
stage

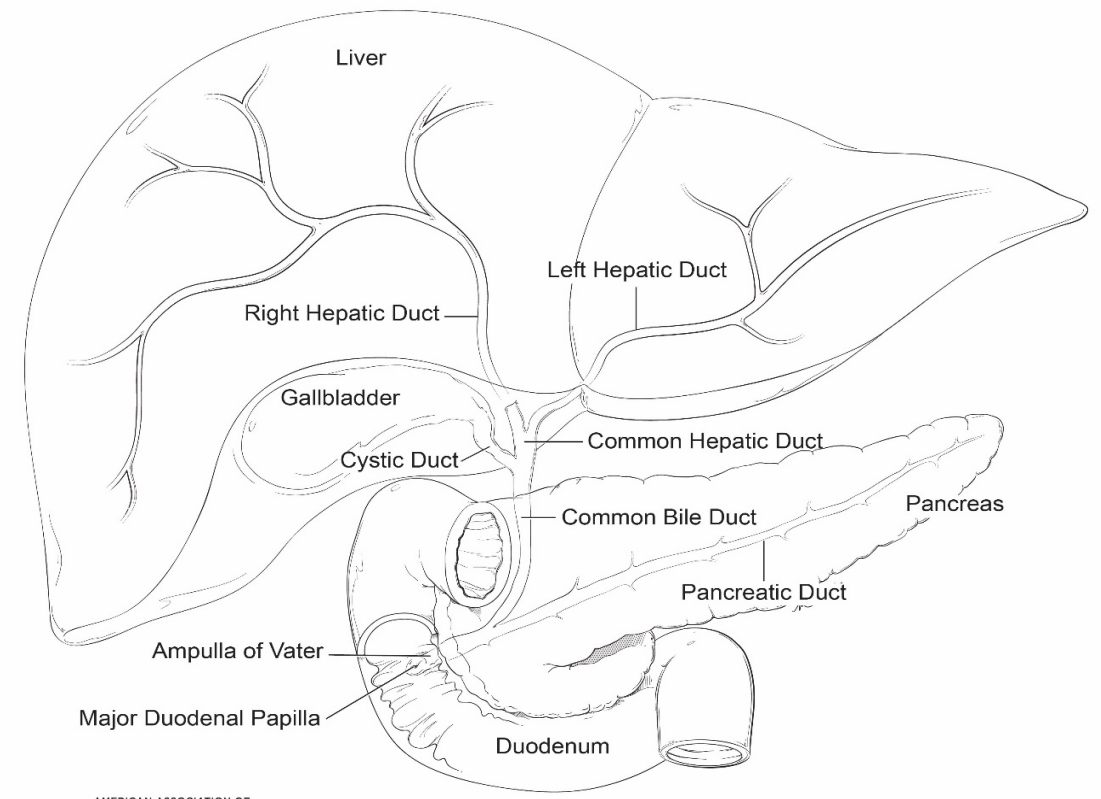
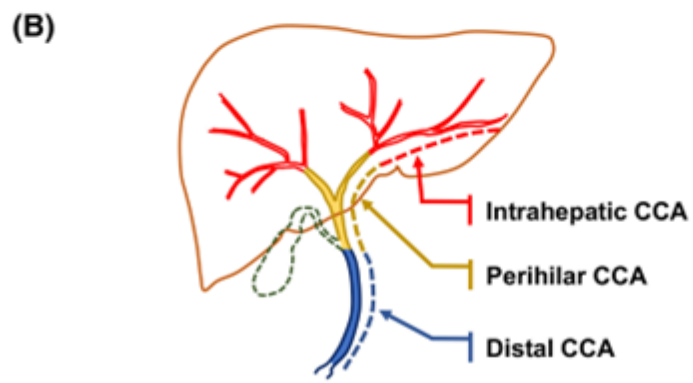
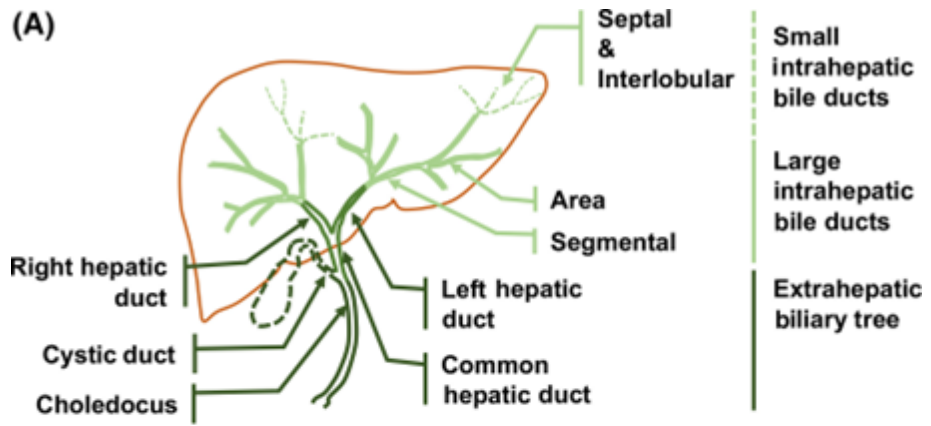
- What are the primary sites and how are they assigned “primary” in the College of American Pathologists (CAP) cancer checklists and American Association of Pathologists’ Assistants (AAPA) grossing guidelines?
  - Intrahepatic
  - Perihilar bile duct (50-67%)
  - Distal extrahepatic bile duct
  - Gall bladder (which includes the cystic duct)
  - Choledochal cysts





# Challenges to the anatomy and determining the primary site

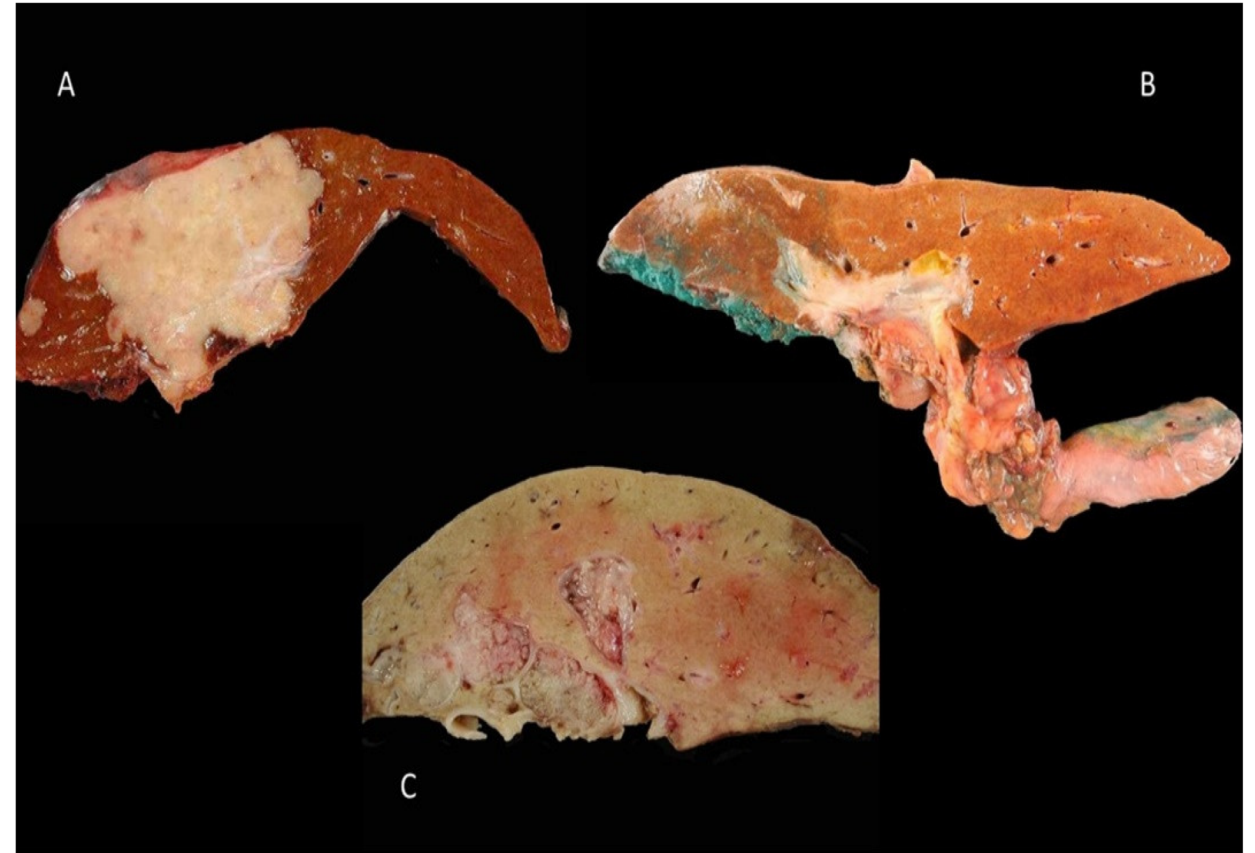
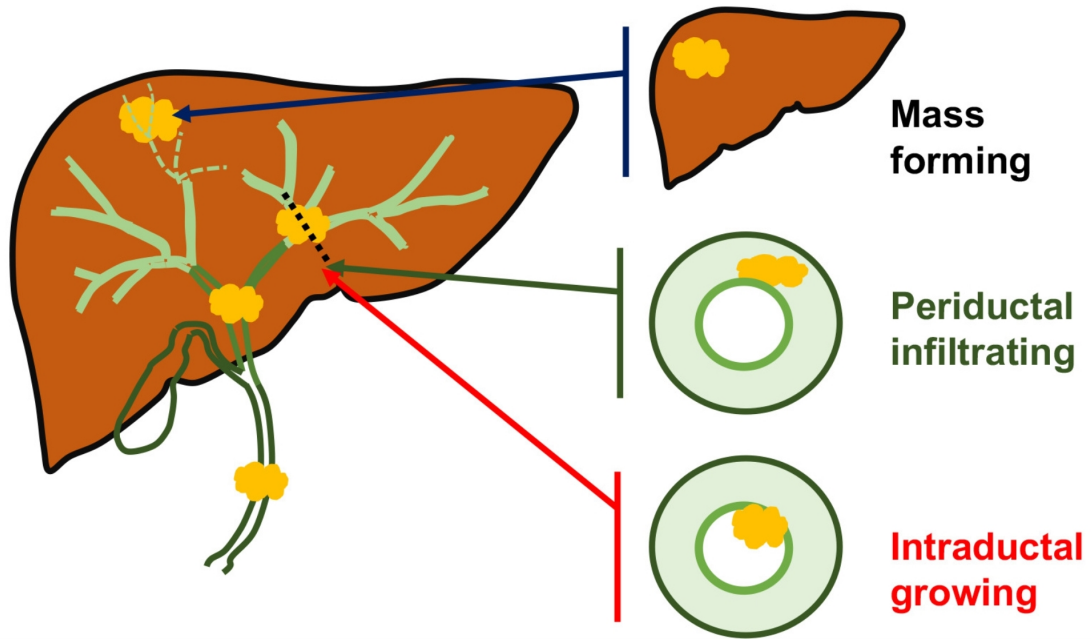
- Anatomic variants are common (perihilar/intrahepatic interface).
- Significant anatomic alterations occur over a small distance.
- Tumor overlap (a single tumor bridging over two anatomic primary sites).
  - Most resections are en bloc and include more than one primary site.
- Incorrect information
- Variation in growth patterns can lead to confusion.



AMERICAN ASSOCIATION OF  
**Pathologists'**  
Assistants

Figure 1: Anatomy of the Biliary System

# Anatomy of the primary site

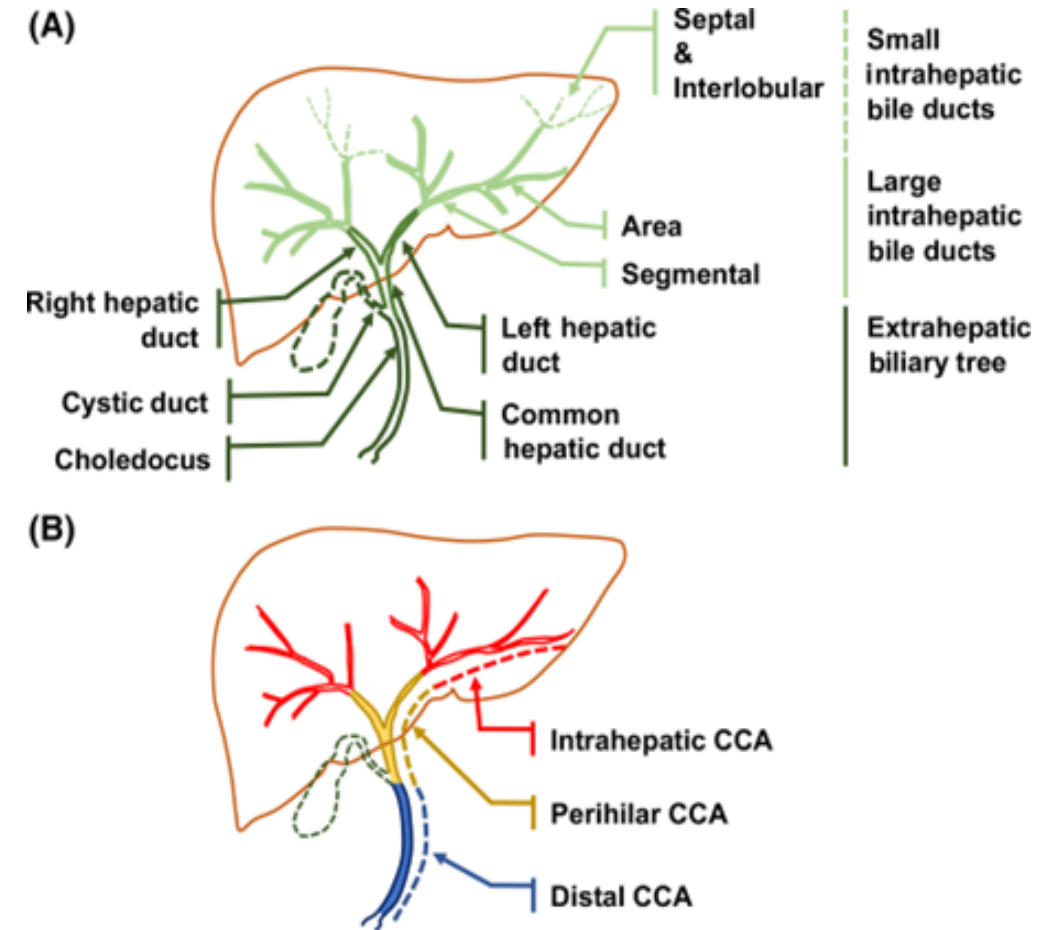


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# Growth patterns

# Determining the primary site at the gross bench

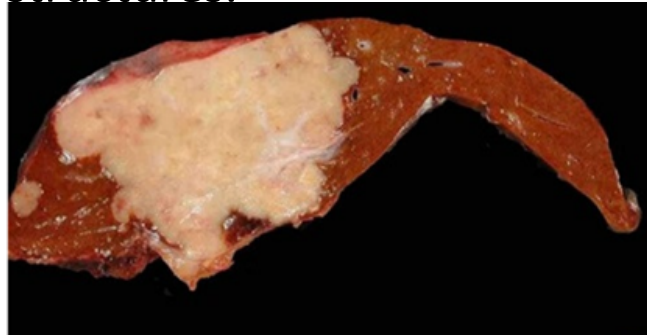
- Remember, these are often compound or en bloc excisions:
  - Where is the tumor epicenter?
  - Is the epicenter the area of the most advanced T category?
    - Have I accounted for the variation among T categories?
    - Have I taken the growth pattern into account?



## Intrahepatic bile duct CCA, accurate diagnosis and stage

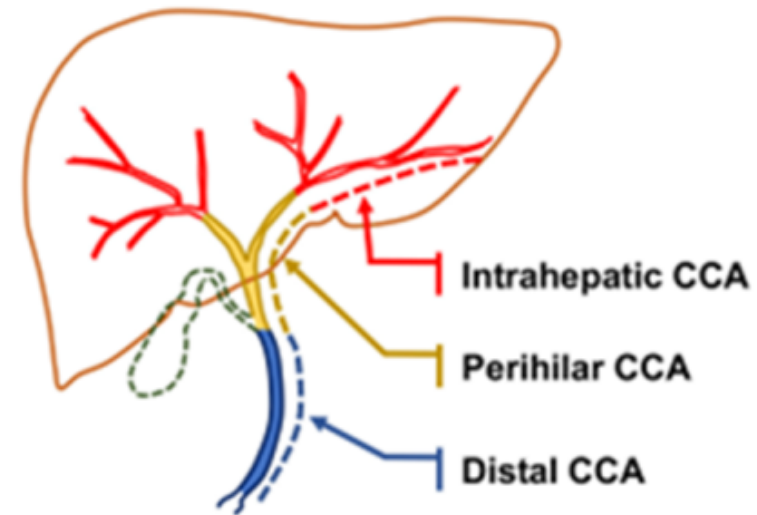
What is the size, are there multiple tumors or peritumoral vessels involved, has it stayed in in the liver or not?

- Review of imaging and surgeons preoperative report (surgical strategy).
- Establishing the growth pattern and tumor size:
  - Mass forming vs. periductal vs. intraductal.
  - Solitary tumor, is it less than 5 cm (T1a) or greater than 5 cm (T1b)?
- Establishing vascular involvement and the presence of additional tumors:
  - T2: **intrahepatic** vascular involvement or additional tumors in the liver (T4 **Retro hepatic** vena cava).
- Establishing relationship to the visceral peritoneum and adjacent structures:
  - T3 tumor is penetrating the visceral peritoneum (liver capsule) without direct invasion of adjacent organs and structures.
  - T4 tumor is directly invading adjacent organs and structures.



# Perihilar bile duct CCA

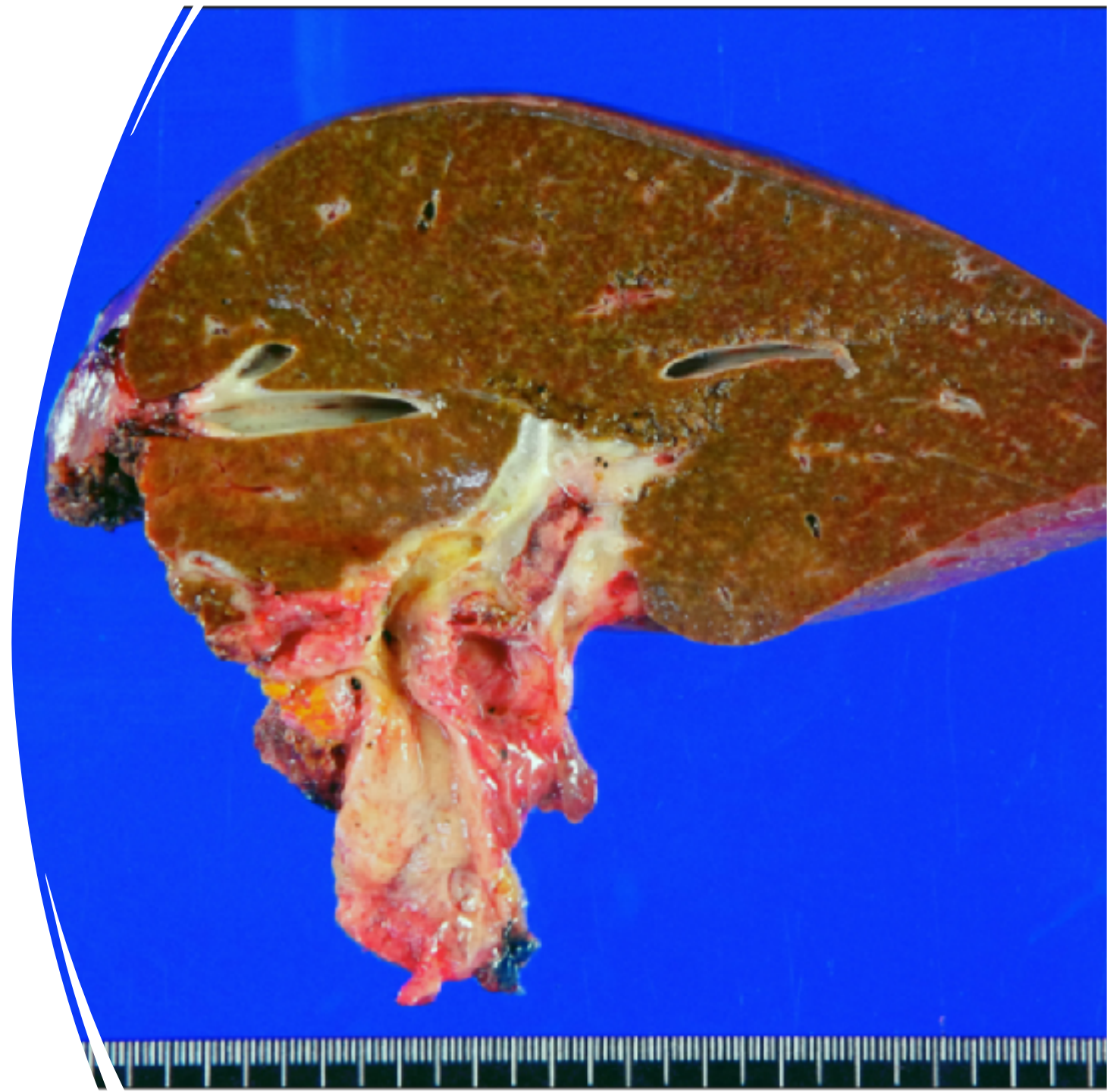
- AJCC 8<sup>th</sup> edition:  
Perihilar bile duct CCA is defined as arising predominantly in the main lobar extrahepatic bile ducts distal to segmental bile ducts and proximal to the cystic duct.



# Perihilar bile duct CCA, accurate diagnosis and stage

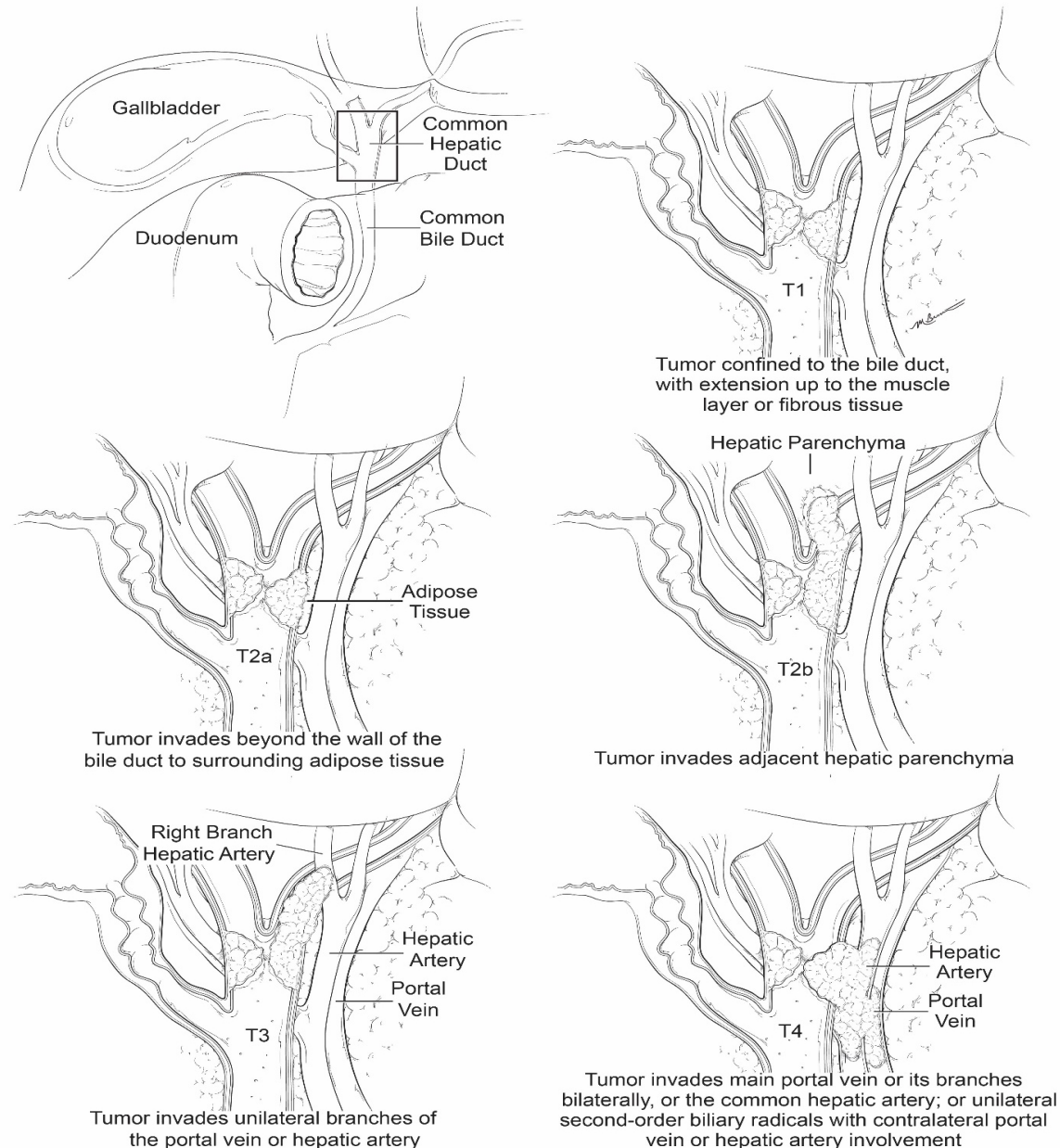
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- Review of the imaging and preoperative surgeons report (surgical strategy).
- Perihilar resections generally include liver (be careful when determining a primary site)



# Assessing the tumor

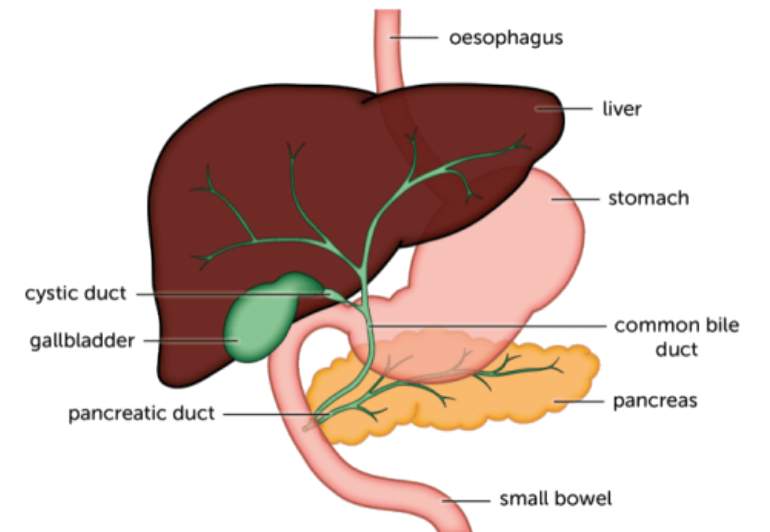
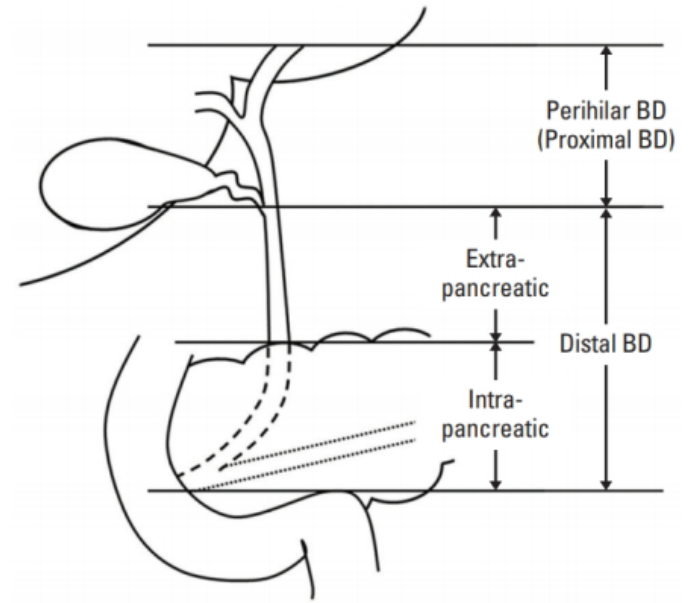
In the wall, through the wall, or invading adjacent structures?





# Distal bile duct CCA, accurate diagnosis and stage

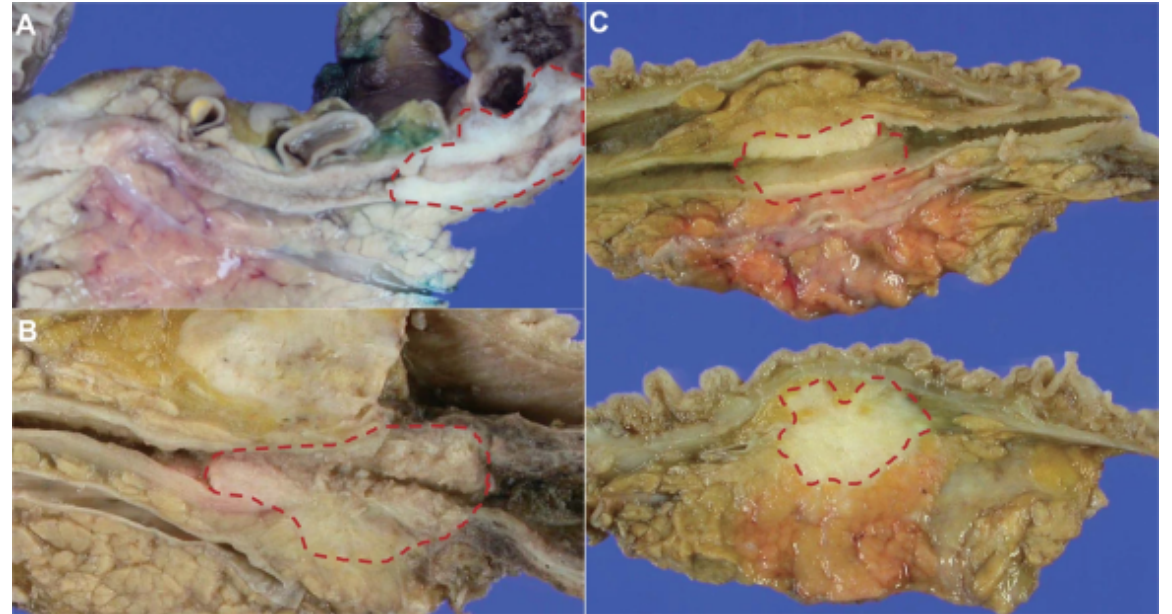
- Review of the imaging and preoperative surgeons report (surgical strategy).
- Distal resections often include additional primary sites (including the pancreas).



# Assessing the tumor

SECTION CAREFULLY. How thick is the tumor (stents can influence this), has it invaded beyond the local environment?

- 8<sup>th</sup> edition change: T1, T2, T3 have been revised based on measured depth of invasion as this is a better predictor of patient outcomes.
- T1: Tumor invades the bile duct wall with a depth of less than 5mm.
- T2: Tumor invades the bile duct wall with a depth of 5-12 mm.
- T3: Tumor invades the bile duct wall with a depth greater than 12mm.
- T4: Tumor involves the celiac axis, superior mesenteric artery, and /or common hepatic artery.



# What about lymph nodes for extent of disease?

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- Intrahepatic CCA: any regional node involvement results in N1 which is the highest N category.
- Perihilar CCA and Distal Bile Duct CCA:
  - N1: metastasis in 1-3 regional lymph nodes
  - N2: metastasis in 4 or more regional lymph nodes.





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# Thank you!