KARNATAKA RADIOLOGY EDUCATION PROGRAM

LIVER Anatomy and applied [clinical]radiology -6

Liver biopsy (percutaneous)

Percutaneous liver biopsy, utilizing either ultrasound or CT guidance, allows for an accurate and reliable method of acquiring hepatic tissue for histopathological assessment. It is divided into two types:

- **non-focal or non-targeted liver biopsy (used in the assessment and staging of the parenchymal liver disease, e.g. MASH)**
- **focal or targeted liver biopsy (i.e. directed to a focal parenchymal lesion)**

Ultrasound is the modality of choice for imaging guidance in the vast majority of cases, with CT nowadays mostly reserved for a conjoined assessment together with the US in focal/targeted biopsies of lesions not sonographically demonstrated.

An alternative option for percutaneous CT/US guidance, particularly used in patients with coagulopathy and ascites, is the transjugular liver biopsy.

Indications

- **non-focal or non-targeted liver biopsy**
  - **staging of known parenchymal disease**
    cirrhosis
    metabolic dysfunction-associated steatotic liver disease (MASLD)
    metabolic dysfunction–associated steatohepatitis (MASH)
    primary biliary cirrhosis (PBC)
  - **abnormal liver function tests of unknown etiology**
  - **hepatic storage disorders**
    Wilson disease
    hemochromatosis
  - **assessment of liver transplant rejection**
- **focal or targeted liver biopsy**
  - **undetermined liver lesion**
  - **liver metastasis of unknown origin**

Contraindications

The contraindications must be considered individually in each case. Overall, the most important contraindications are:

- **uncooperative patient**
- **uncorrectable bleeding diathesis (abnormal coagulation indices)**
- **ascites**
  - **relative contraindication that can be usually tapped before the biopsy**
- **extrahepatic biliary obstruction**

Procedure

Laboratory parameters for a safe procedure

Interventional procedures like liver biopsy require special attention to coagulation indices. There are widely divergent opinions about the safe values of these indices for percutaneous biopsies [ref]. The values suggested below were considered based on literature review, whose references are cited below:

- **complete (full) blood count**
  - **platelets >50,000/mm^3 (some institutions determine other values between 50,000-100,000/mm^3)**
- **coagulation profile**
  - **some studies showed that having a normal INR or prothrombin time is no reassurance that the patient will not bleed after the procedure**
    - **international normalized ratio (INR) ≤1.5**
    - **normal prothrombin time (PT) / partial thromboplastin time (PTT)**

Pre-procedure preparation

- **written informed consent**
- **assessment of patient's cooperation for the procedure**

Especially explaining the procedure, time taken and advantages to be explained in patient in understandable knowledge

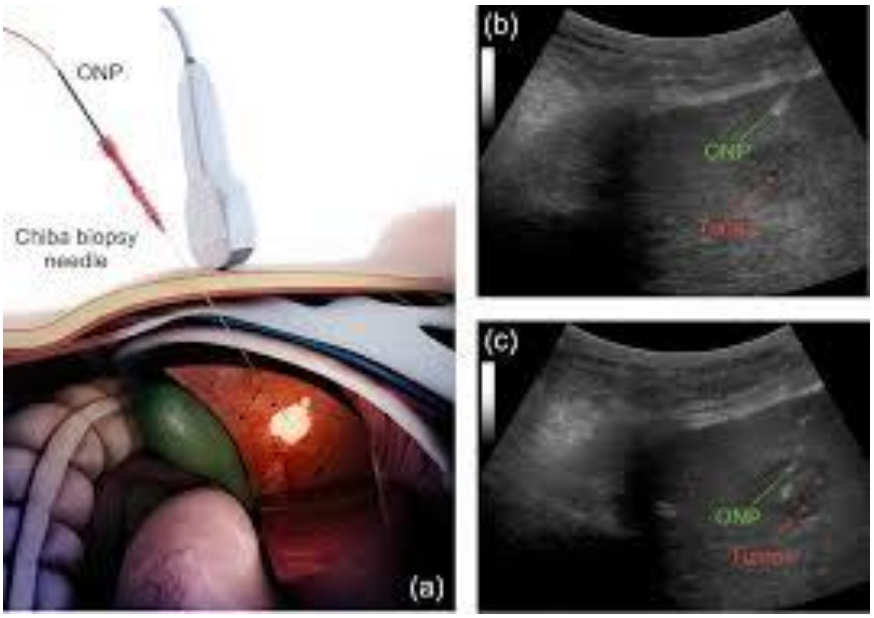
Equipment

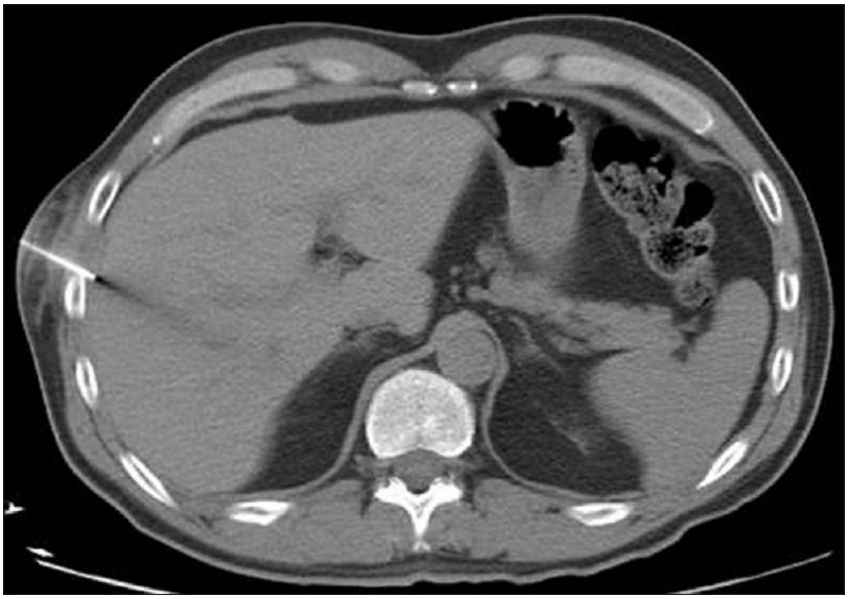
- **sterile procedure pack**
- **sterile gloves**
- **skin antiseptic**
- **scalpel**
- **single or co-axial needle set**
  - **calibers vary among institutional protocols and purpose of the biopsy, with commonly used core biopsy calibers being 14G, 16G, and 18G**
  - **16G core biopsy needle is recommended by many professional organizations [5]**
- **1% lidocaine**
- **midazolam (for sedation): its use varies according to different institutional guidelines, and should always be considered case-by-case**
- **histopathology department pot** .

Technique

As ultrasound is the most common imaging modality used to guide liver biopsy, that will be the technique approached in this article.

- **pre-procedure assessment of the liver with ultrasound should be performed for planning positioning and needle entrance point**
  - **supine, oblique, or total left lateral decubitus are the possible positioning of the patient - it is important to make sure that the patient is comfortable and can remain still in that position**
    - **wedge behind the patient's back helps for oblique positioning**
  - **assess if the procedure will be performed under breath held and practice this with the patient**
  - **marking of the entrance point on the skin is advised to aid the skin cleaning and dressing**
- **hemodynamic monitoring in place is recommended**
- **a time-out should be performed by this stage**
- **skin site is prepped and draped to ensure asepsis**
- **local anesthetic is infiltrated within the subcutaneous tissues, abdominal wall and down to the liver capsule**
- **entrance point is created with a scalpel (usually number 11 blade)**
- **using the freehand technique the needle is advanced under ultrasound guidance during the entire course of the biopsy**
  - **the needle tip must always cross the capsule prior to deploying the cutting device [1]**
  - **documentation of the needle positioning after firing is advised**
  - **usually only one pass is required if an adequate sample is obtained but this depends on the reason for biopsy [5]**
- **after the procedure, a brief ultrasound examination for perihepatic or intraparenchymal hemorrhage is usually performed .**





Post-procedure care

Bed-rest is advised as well as regular observations (pulse, blood pressure, and SpO2 in those receiving sedation) depending on risk factors, active questioning of the patient of any pain, and inspection of the biopsy site for bleeding every 30 minutes [5].

The observation period should allow an ample opportunity to identify and treat a potential complication in a timely manner to prevent a serious or catastrophic outcome, this varies with each institution's protocol but is between 3-8 hours [5]. Observations should be taken [5]:

- **every 15 minutes for the first hour**
- **every 30 minutes for the next two hours**
- **every hour for the remainder of the observation period**

The patient should only be discharged when there are stable observations with no evidence of hemodynamic instability or bleeding and new pain or shortness of breath .

Complications

Percutaneous liver biopsy remains a safe procedure.

Complications include:

- **post-procedure pain: pain radiated to the right shoulder [3]**
- **severe hemorrhage: ~1% (range 0.35-1.7%) [1]**
- **death related to hemorrhage is uncommon and numbers in the literature are variable, with the most commonly quoted mortality rate being of ≤1 in 10,000 liver biopsies [4]**

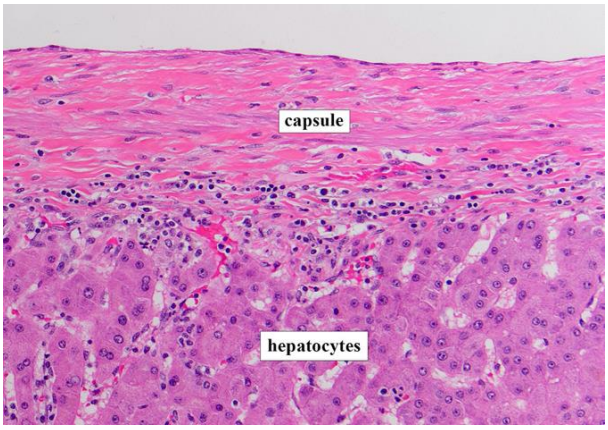
Liver Function Test Parameter	**Normal Range**
Alanine Transaminase (ALT)	7-56 U/L
Aspartate Transaminase (AST)	8-48 U/L
Alkaline Phosphatase (ALP)	44-147 U/L
Total Bilirubin	0.1-1.2 mg/dL
Albumin	3.5-5.0 g/dL
Total Protein	6.3-7.9 g/dL
Gamma-glutamyltransferase (GGT)	8-61 U/L
Lactate Dehydrogenase (LD)	122-222 U/L

Normal liver histology reveals a structure organized into hepatic lobules, with hepatocytes radiating from a central vein towards portal tracts containing branches of the hepatic artery, portal vein, and bile ducts.

Here's a more detailed breakdown of normal liver histology:

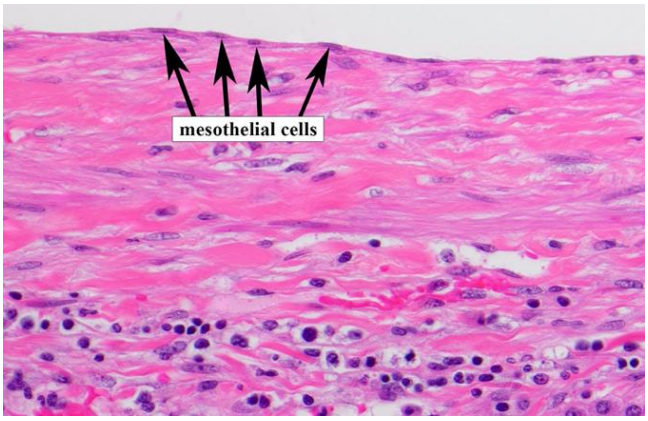
The Capsule

The outer surface of the liver is composed of a fibrous / connective tissue capsule .



Subcapsular liver biopsy showing the fibrous capsule surrounding hepatocytes.

The outermost surface is covered by a thin layer of mesothelial cells that arises from the peritoneum .



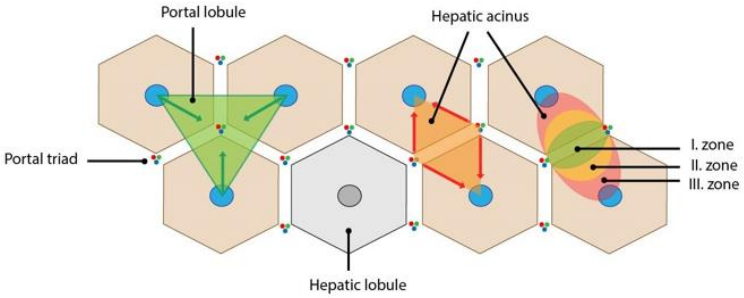
Subcapsular liver biopsy with mesothelial cells lining the outermost layer of the capsule.

Organization: Lobules & Acini

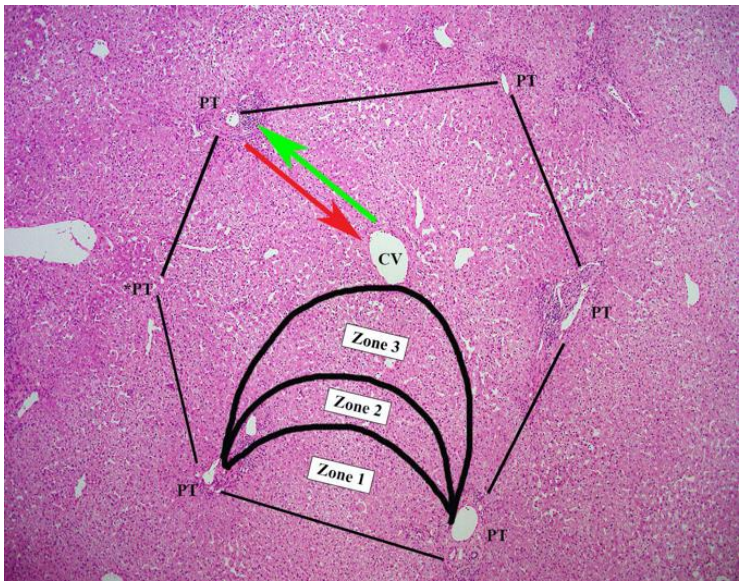
Microscopically, the organization of liver parenchyma can be represented by three different schematics: (1) the classic (hepatic) lobule, (2) the portal lobule, and (3) the hepatic acinus.

The Lobules

Classic (hepatic) lobules are based upon blood flow. They are organized as "hexagons," with the central vein (CV) in the center of the lobule and portal tracts (PTs) at the periphery of the lobule (corners of the hexagon) .



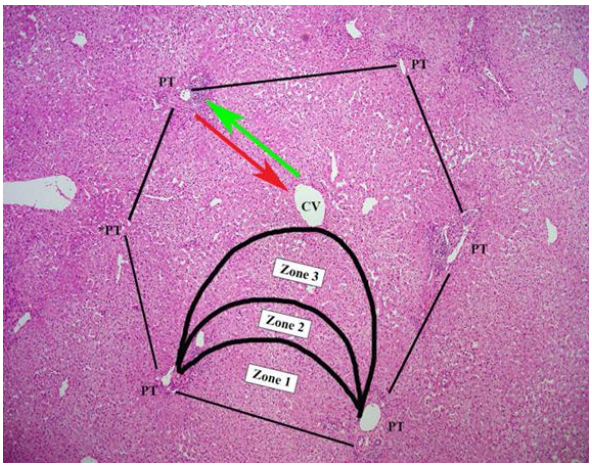
Organizational units of the liver including the (1) classic (hepatic) lobule (2) portal lobule and (3) hepatic acinus. [Fontana, Josef, et al. "Functions of Cells and Human Body: Multimedia Textbook." Liver and Biotransformation of Xenobiotics, http://fblt.cz/en/skripta/ix-travici-soustava/5-jatra-a-biotransformace-xenobiotik/



Classic (hepatic) lobule with PTs at the periphery of the lobule and CV in the center of the lobule. The PTs and CV are evenly spaced throughout the hepatic parenchyma. Blood flows from the PTs to the CV (red arrow), while bile flows in the opposite direction (green arrow). The acinus is represented by the thicker curved lines and is composed of zones 1-3. (H&E photo courtesy of Dr. Jennifer Findeis-Hosey, URMC)

The PT consists of the hepatic artery (HA), portal vein (PV), and bile duct (BD). Blood enters the liver via the PV and HA, drains into the CV, and exits the liver via the hepatic vein to the inferior vena cava.

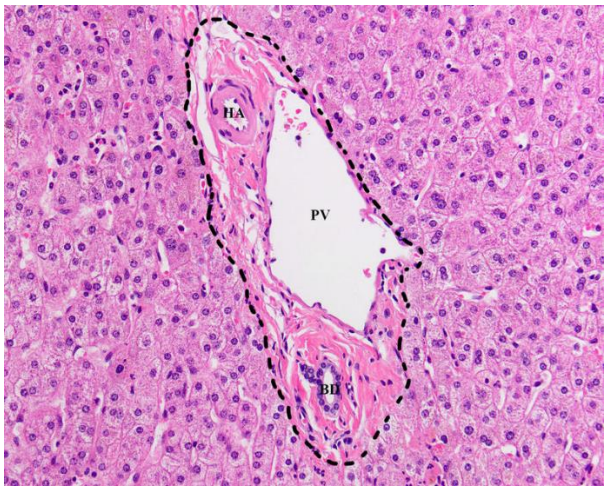
Portal lobules are based upon bile flow. They are organized as "triangles," with a PT at the center of the lobule and CVs at the periphery of the lobule (corners of the triangle) (Figure 3). Hepatocytes produce bile that drains from the bile canaliculi > canals of Hering > bile ductules > interlobular bile ducts > intrahepatic ducts > right and left hepatic ducts > common hepatic duct > joins with cystic duct to form the common bile duct > duodenum). The flow of bile is in the opposite direction of blood flow .



Classic (hepatic) lobule with PTs at the periphery of the lobule and CV in the center of the lobule. The PTs and CV are evenly spaced throughout the hepatic parenchyma. Blood flows from the PTs to the CV (red arrow), while bile flows in the opposite direction (green arrow). The acinus is represented by the thicker curved lines and is composed of zones 1-3. (H&E photo courtesy of Dr. Jennifer Findeis-Hosey, URMC)

The Portal Tract

The PT consists of the HA, PV, and BD .

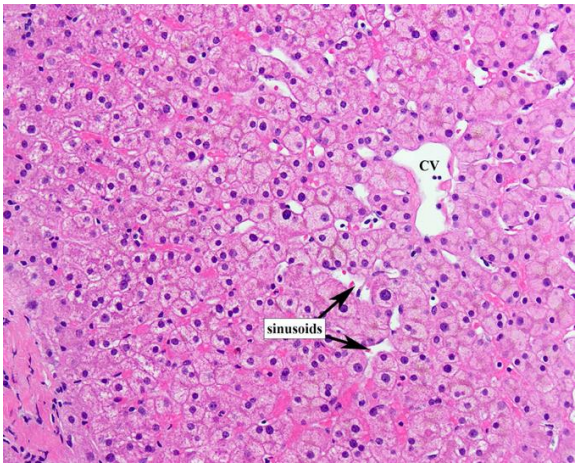


The portal tract consists of branches of the hepatic artery (HA), portal vein (PV), and bile duct (BD), which are surrounded by connective tissue (CT). The limiting plate (black dashed line) is delineated by the layer of hepatocytes immediately adjacent to the portal tract

The HA and PV are lined by endothelial cells. The HA is small with thick walls, while the PV is larger with thin walls. The BD is roughly the same size as the hepatic artery and is lined by a single layer of cuboidal (square-shaped) epithelium. Occasionally, lymphatic ducts may also be seen. The structures in the portal tract are surrounded by fibrous connective tissue. Although it is normal to see a few scattered inflammatory cells (ex. lymphocytes), no neutrophils or plasma cells should be present. The single layer of hepatocytes immediately adjacent to the portal tract delineates the limiting plate.

The Central Vein

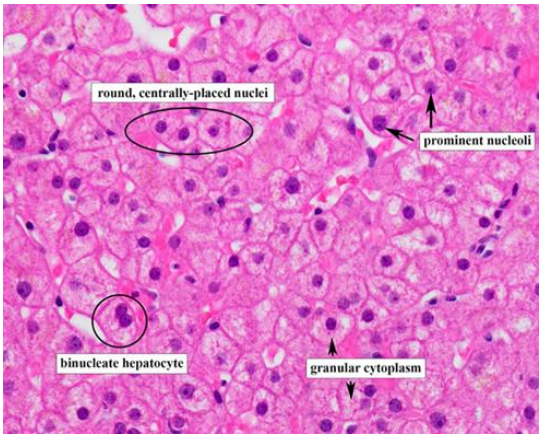
The CV is lined by a single layer of endothelial cells and drains blood coming from the PTs via sinusoids. Plates of hepatocytes radiate outward from the CV toward the PTs (Figure 6).



Plates of hepatocytes radiate out from the central vein (CV) toward the PTs. The CV drains blood coming from the PT via the sinusoids.

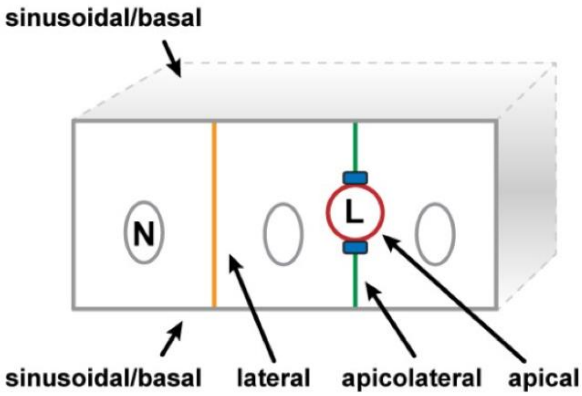
Parenchyma - Hepatocytes

Hepatocytes are polygonal cells (20-30µm) with abundant granular eosinophilic (pink) cytoplasm, centrally placed round to ovoid nuclei, and prominent nucleoli .



Hepatocytes with abundant granular, eosinophilic cytoplasm and centrally placed, round nuclei with prominent nucleoli. Occasional binucleate forms are present.

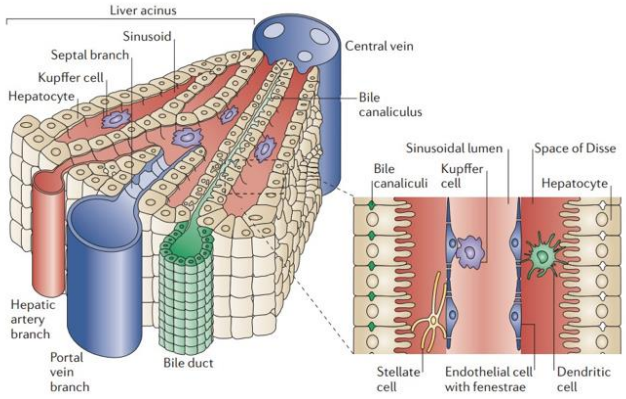
Normal hepatocytes can also show binucleation and pleomorphism (differences in size). Hepatocytes are arranged in plates that are 1 cell thick. Hepatocyte plasma membranes are separated into sinusoidal, canalicular, and apicolateral domains. The sinusoidal (basal) domain contains microvilli and faces the space of Disse, while the canalicular (apical) domain forms the bile canaliculus. The apicolateral domain is between the sinusoidal and canalicular domains .



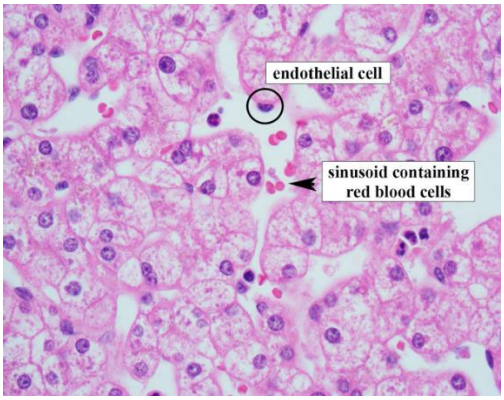
Hepatocytes are separated into sinusoidal (basal), canalicular (apical), and apicolateral domains. Tight junctions (blue rectangles) separate the canalicular domain from the apicolateral domain. L = lumen, N = nucleus. [C. L. Slim et al., "Par1b Induces Asymmetric Inheritance of Plasma Membrane Domains via LGN-Dependent Mitotic Spindle Orientation in Proliferating Hepatocytes," PLoS Biol., 2013, doi: 10.1371/journal.pbio.1001739.]

Sinusoids

Hepatocytes are separated by sinusoids , which are spaces lined by fenestrated endothelial cells that transport blood from the PTs to the CVs. Sinusoids contain macrophages called Kupffer cells.



Hepatocytes are separated by sinusoids, which are lined by fenestrated endothelial cells. The space of Disse lies between the endothelial cells and hepatocytes. [D. H. Adams and B. Eksteen, "Aberrant homing of mucosal T cells and extra-intestinal manifestations of inflammatory bowel disease," Nature Reviews Immunology. 2006, doi: 10.1038/nri1784.]



Sinusoids are lined by a single layer of endothelial cells and transport blood from the PT to the CV. (H&E photo courtesy of Dr. Jennifer Findeis-Hosey, URMC)

Space of Disse

The space of Disse (SoD) is the space between the endothelium and the hepatocytes , which transports lymphatic fluid to lymphatic capillaries in the portal tract and contains reticulin fibers. The SoD also contains stellate (Ito) cells that store lipids (vitamin A) and are involved in fibrinogenesis.

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Ref;

https://www.aasld.org/liver-fellow-network/authors/phoenix-bell

https://radiopaedia.org/articles/liver-biopsy-percutaneous