How to Get the Most out of the Liver Biopsy: Technical Tips and Simple Algorithms

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Overview of the Lecture

- What you can do before you ever receive the sample (specimen adequacy)
- What you should do once you have the tissue

A scenario you have probably seen...

How big should a liver biopsy be?

Big enough to get the job done.

So, how big should a liver biopsy be?
The Anatomic Pathologist’s Mantra

What is it, and how bad is it?

The Mantra Applied to Liver Biopsy

What is it, and how bad is it?
- Abnormal “LFTs” of uncertain etiology
- Known HCV/HBV; anything else also present?
- Fever of unknown etiology
- Masses
- Portal hypertension - ? etiology
- Is it hemochromatosis ? (+/- iron quant)
- Is it Wilson’s? (often copper quant)

Grading and Staging

Biopsy Type and Recommended Sample Size Depend on The Problem at Hand

- What is the diagnosis?
  - Liver mass
  - Random liver/parenchymal disease
    - Iron and/or copper analysis needed?
- What is the grade and stage?

Major Biopsy Options

- Fine Needle Biopsy (> = 19 gauge needle)
  - Aspiration (Menghini, Jamshidi, or Klatskin style) or sheathed cutting needle (“trucut”)
- Large Bore Biopsy (< = 18 gauge needle)
  - Trucut

A brief guide:
- A big fat biopsy = 1.6 mm = 16 gauge
- An average biopsy = 1.4 mm = 18 gauge
- A skinny biopsy = 1 mm or less = 20 gauge or more
Major Complications of Liver Biopsy

- **Bleeding**
  - Some bleeding in all cases; usually trivial
  - Transfusion req’d 1 in 500
  - Risks:
    - Operator experience, needle diameter, # cores
    - Cutting possibly slightly greater risk than aspiration
- **Death:**
  - 1 in 10,000 overall
  - 9 in 10,000 for transjugular


You need to tell your radiologists, surgeons, and gastroenterologists your expectations.

*(If you fail to plan, you plan to fail.)*

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Sampling Liver Masses – The Big Picture

- Fine needle biopsy is generally sufficient
- A group in Belgium touts Fine Needle Tru-cut Biopsies (FNTCB) over Fine Needle Aspiration Biopsy (FNAB):*
  - Both in the 90-95% sensitivity and specificity ranges
  - Insufficient sampling rate may be lower with FNTCB (2.5%) vs FNAB (up to 15%) (not controlled)

*KPB Conclusion: Probably OK to let the fine needle operator use their preference.*

Aspirate without biopsy is the realm of cytopathology

Touch imprints can supplement cores

Two cell populations

Uniform, small, favor neuroendocrine (carcinoid, islet cell)
I prefer core biopsies to examine

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Parenchymal Liver Disease – Diagnosis Needed

- Little data on minimum required tissue for diagnosis
  - May depend considerably on the skill of the pathologist ("I can make that diagnosis in two portal tracts.")
  - Likely depends on the quality of clinical information that you receive
- In coaching clinicians, I presume that grading and staging is important and counsel them appropriately to get a liver biopsy that is optimal for grading and staging (see the next section)

Clinical: “Portal Hypertension”

Pretty good sample for the indication
Iron or Copper Disease – Quantitative Fe/Cu Analysis Needed

- Paraffin embedded samples are OK
- Review of histology first is advisable
- *Bare minimum required: 5 mm of 18 gauge needle not cut more than 50% through*
- In coaching clinicians, I counsel them to get a “usual” liver needle biopsy, tell us the clinical concern, and leave the rest to us (see the next section for optimal “usual” biopsy size)

Biopsy Type and Recommended Sample Size Depend on The Problem at Hand

- What is the diagnosis?
  - Liver mass
  - Random liver/parenchymal disease
- What is the grade and stage?

For tissue adequacy in grading and staging, literature largely focuses on chronic viral hepatitis

- Colloredo et al – 355 big biopsies; graded initially then regraded after masking portions of the biopsy to simulate smaller biopsies
- Rockey et al – exhaustive position paper by the AASLD on technical issues of liver biopsy

Chronic Viral Hepatitis: The Shorter the Sample the Milder the Disease

Chronic Viral Hepatitis: The Shorter and Thinner the Sample the Fewer the Portal Tracts

Grading and Staging Non-neoplastic Liver Disease – The AASLD Speaks*

- Portal tracts – 11 or more desirable
- Width:
  - 16 gauge recommended
  - 18 gauge OK
  - 20 gauge or greater (ie \(\leq 1\) mm) not recommended
- Length
  - 3 cm or greater recommended
  - 2-2.5 cm usually OK
  - <1.5 cm not recommended


This keeps the pathologist off the operator’s back, but is probably overkill

Anyone know a definition of “specialist liver pathologist”? 

After you have 11-15 portal tracts, no more staging/grading benefit from sampling more tissue, but morbidity/mortality go up.
Now you’ve got the biopsy. What are you going to do with it?

### Basic Grossing/Processing Issues in for Liver Biopsies
- Into cassette: avoid sponges*
- Fixation:
  - Neutral-buffered formalin remains the workhorse
  - 1 hour processing cycle acceptable
  - Microwave fixation is fine
- Sectioning:
  - Best to not go more than 50% through biopsy in case additional stains/studies needed
  - I get one slide and three levels for H&E but preferences vary

*Landas SK et al. Arch Pathol Lab Med. 1990 Dec;114(12):1285-7

### Stains – Let your conscience be your guide. Two approaches:
- Review H&E, then order stains
  - Most cost effective, but may delay case
- Preorder special stains
  - If stains done but not needed or reported, your costs may go up
  - If stains done but not needed yet reported anyway, patient is paying for a test of no value (perhaps to your financial benefit)

There is no absolute right or wrong answer.

### “Routine” Stains - My Approach
- H&E, Trichrome, Iron on “medical biopsies” up front
  - Trichrome to assess subtle pericellular fibrosis
  - Iron to assess subtle hepatocellular iron
- If portal hypertension without cirrhosis:
  - Low threshold for getting reticulin stain
- If degree of fibrosis appears premature:
  - PASd to evaluate for MZ/SZ A1AT