
Hepatitis C Choices in Care

Testing of Patients with Chronic Hepatitis C: What do I really need?

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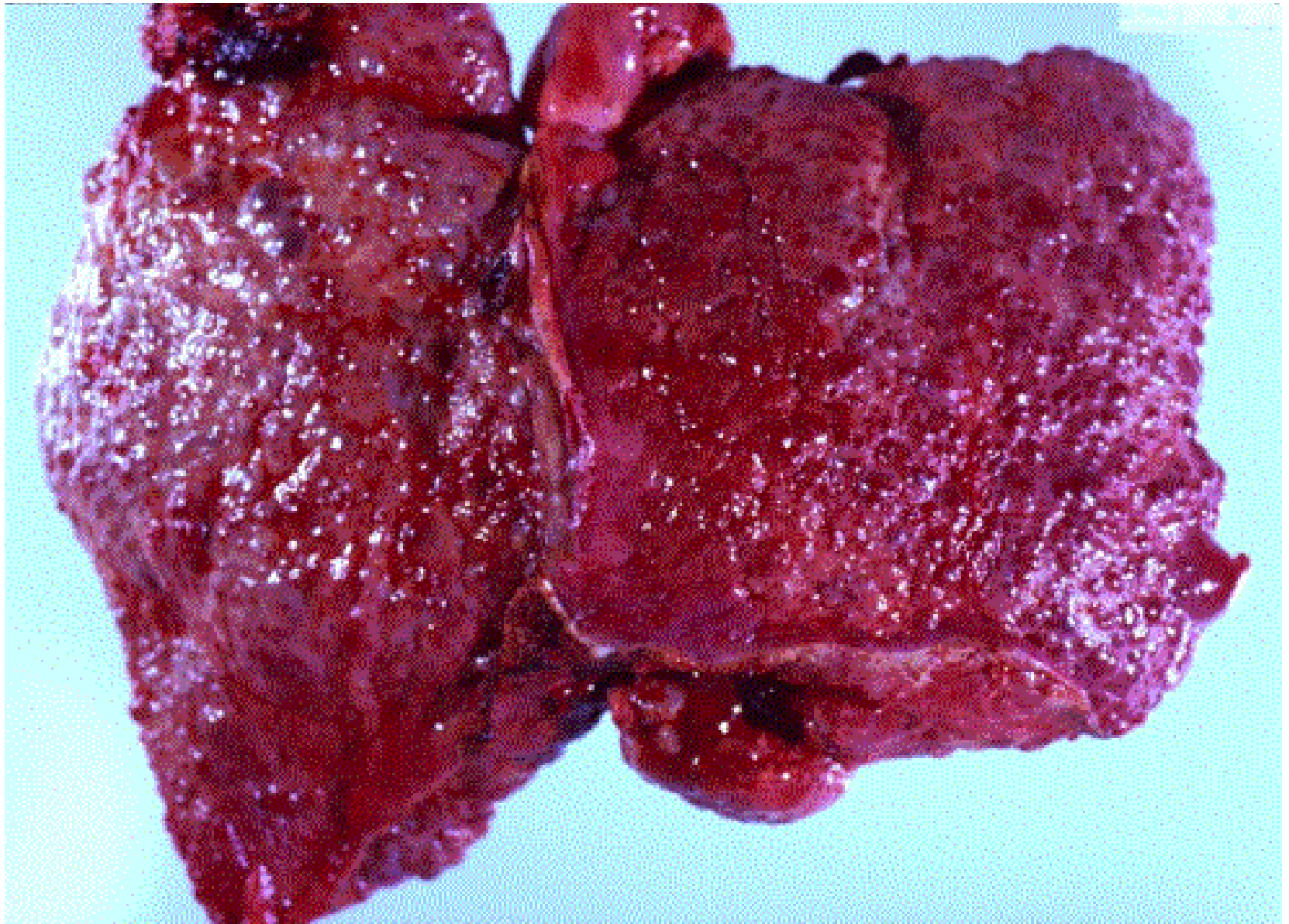
Main Reasons for Testing

- Defining disease severity
- Defining likelihood of response to antiviral therapy
- Screening for early stage hepatocellular carcinoma (HCC)

Defining Disease Severity



A Healthy Liver



A Cirrhotic Liver

Standard Clinical Evaluation

Standard Lab Tests Suggesting Cirrhosis

- AST:ALT ratio > 1
- Elevated total bilirubin > 2 mg/dL
- INR > 1.5
- Platelet count $< 125,000/\mu\text{L}$

Note: If the AST:ALT ratio > 2 , then alcohol-related liver injury is likely!

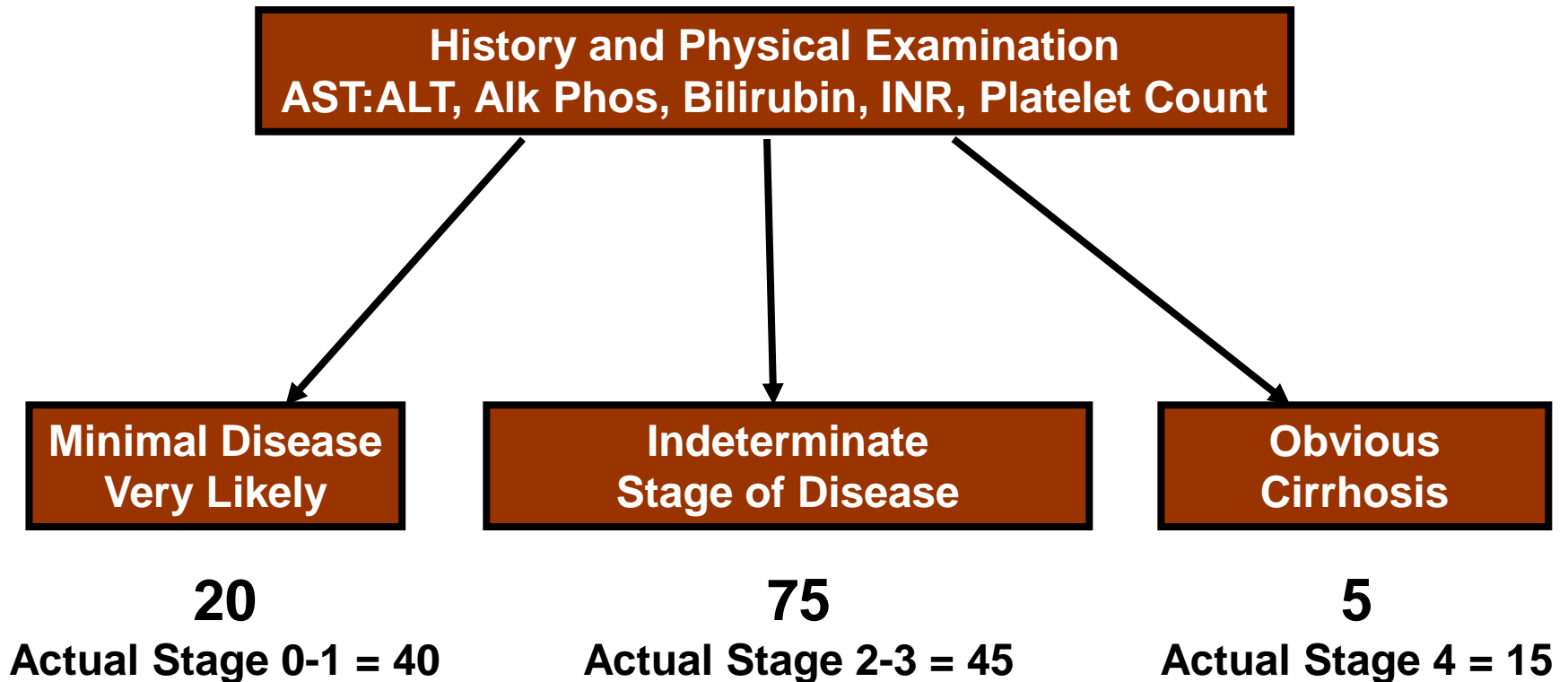
Liver Enzymes: AST & ALT

- Elevated blood levels of liver enzymes (AST, ALT) indicate ongoing liver injury – the membrane of the liver cells is damaged and liver enzymes leak into the blood stream
- The degree of elevation in liver enzymes in the blood correlates with the severity of liver cell injury.
- However, blood levels of liver enzymes do not correlate with the degree or severity of hepatic fibrosis. Patients with cirrhosis often have relatively lower enzyme elevations than patients with earlier stages of fibrosis.

Standard Evaluation – Staging Disease

N = 100

Patients with Chronic Hepatitis C Presenting for Initial Evaluation



After standard evaluation, the stage of disease is indeterminate in 75%!

Noninvasive Tests and Models

Noninvasive Tests

- **Serum Fibrosis Tests - very low scores correlate with lack of significant fibrosis and very high scores, with cirrhosis**
 - Fibrosure, Fibrospect, Fibrotest, APRI
 - HALT-C model (standard labs)
 - Platelet count

HALT-C Model to Predict Cirrhosis

- log odds (predicting cirrhosis) =
 $-5.56 - 0.0089 \times \text{platelet (x10}^3/\text{mm}^3) + 1.26 \times \text{AST/ALT ratio} + 5.27 \times \text{INR}$.
- The formula to calculate predicted probability is $\exp(\text{logodds}) / (1 + \exp(\text{logodds}))$.
- Website: www.haltctrial.org/cirrhosis.html

Caution: May not be generalized to all patients with chronic hepatitis C!

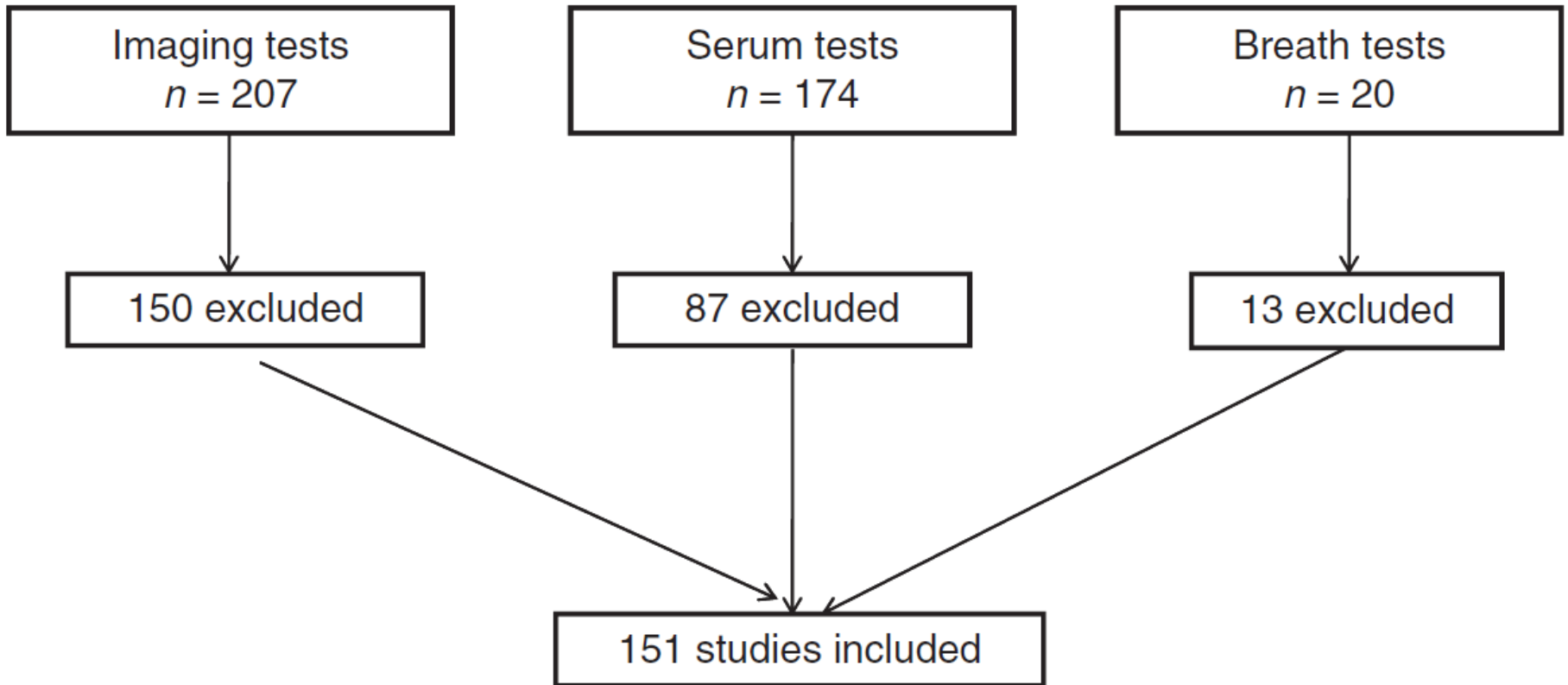
Noninvasive Tests

- **Elastography – measures liver stiffness**
 - Fibroscan - Validation studies ongoing
 - Gaining popularity due to marked ease of use
 - Probably best at the extremes of no fibrosis and cirrhosis
- **Radiologic Imaging – inaccurate for staging except for the most advanced disease**

Noninvasive Tests

- **Quantitative Liver Function Tests (QLFT's) - measure liver function**
 - Breath ID, metabolic tests
 - SPECT liver-spleen scans
 - Cholate Test (HepQuant-Dual and HepQuant-Oral)

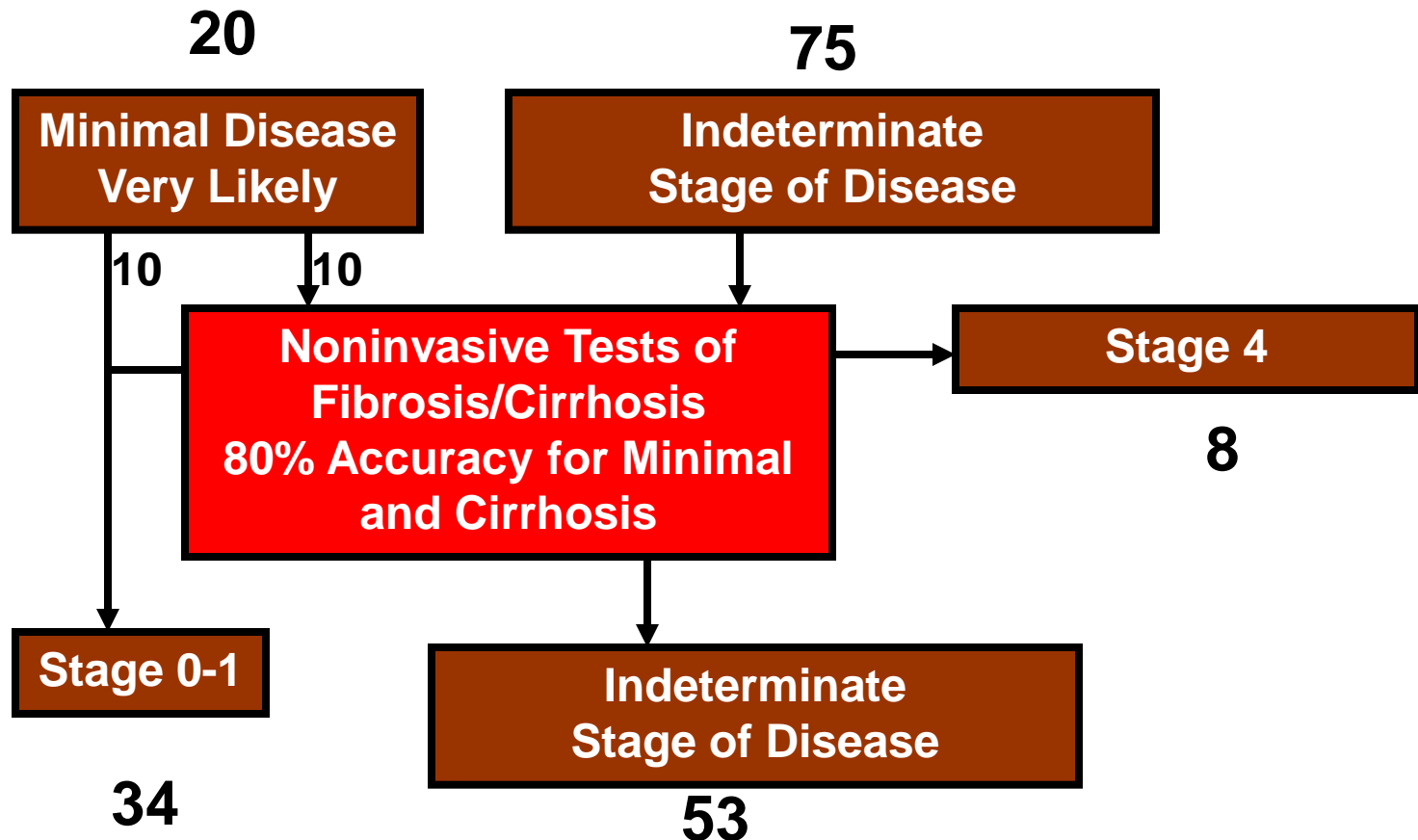
Noninvasive Tests of Fibrosis



Noninvasive Tests of Fibrosis

| Test | Fibrosis Stage | |
|--------------|----------------------------|--------------------|
| | Not significant (F0-F1/F2) | Significant (F2-4) |
| APRI | ≤ 0.5 | ≥ 1.5 |
| FIB-4 | ≤ 1.45 | ≥ 3.25 |
| Fibroindex | ≤ 1.25 | ≥ 2.25 |
| Forns | < 4.2 | > 6.9 |
| Elastography | ≤ 7 kPa | ≥ 8 kPa |

Noninvasive Tests – Staging Disease

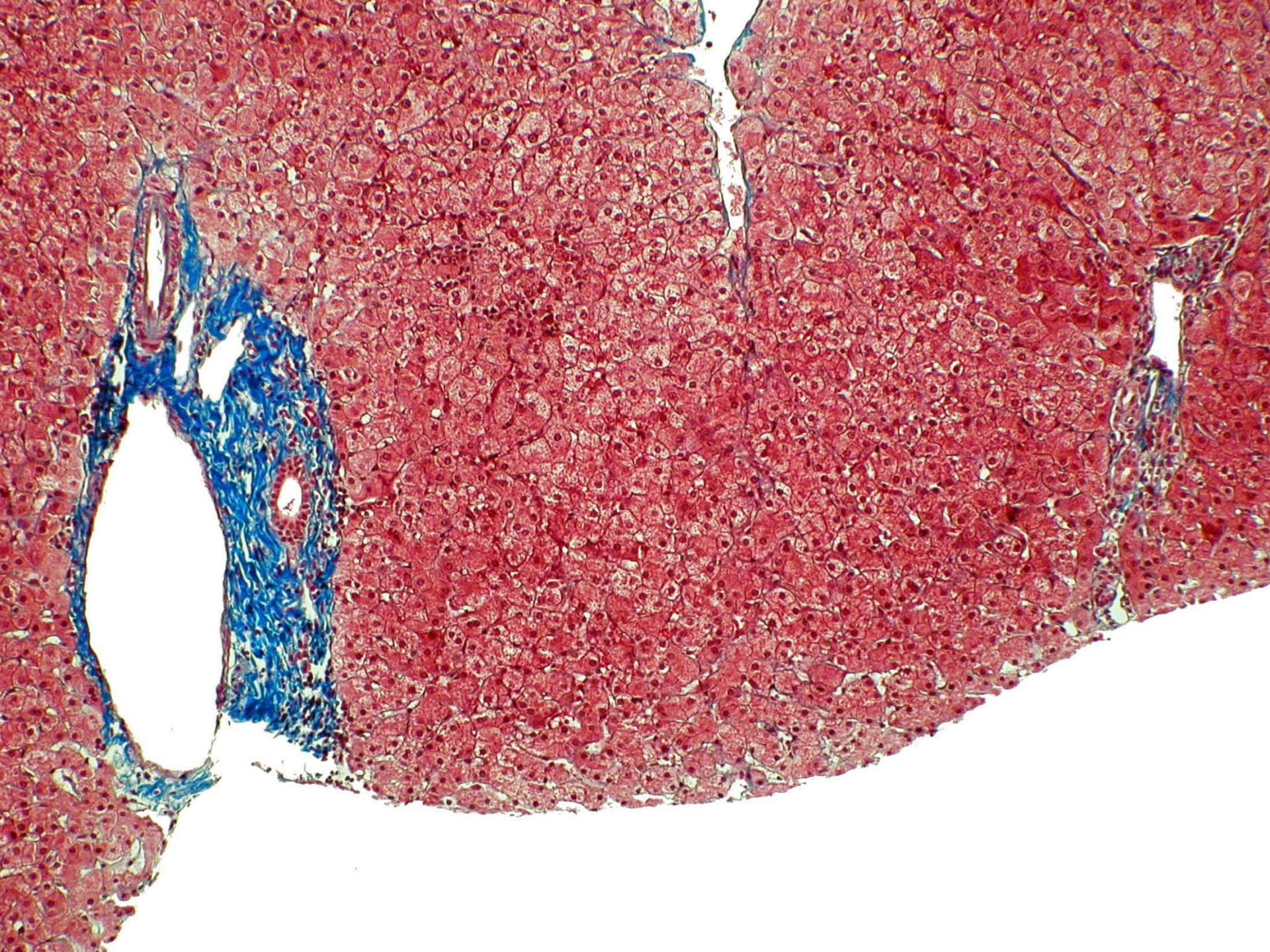


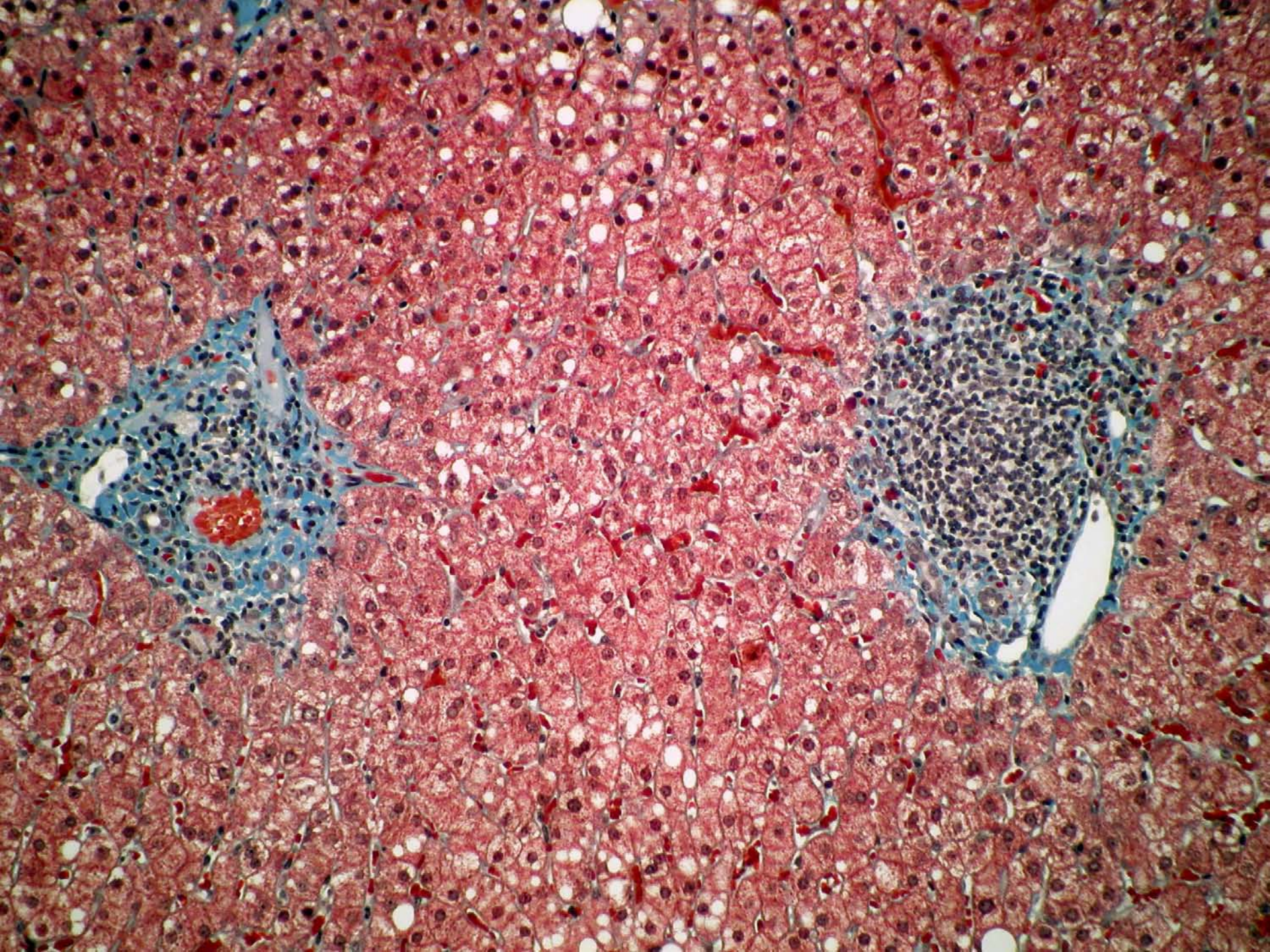
After noninvasive testing, the stage of disease is indeterminate in 53%!

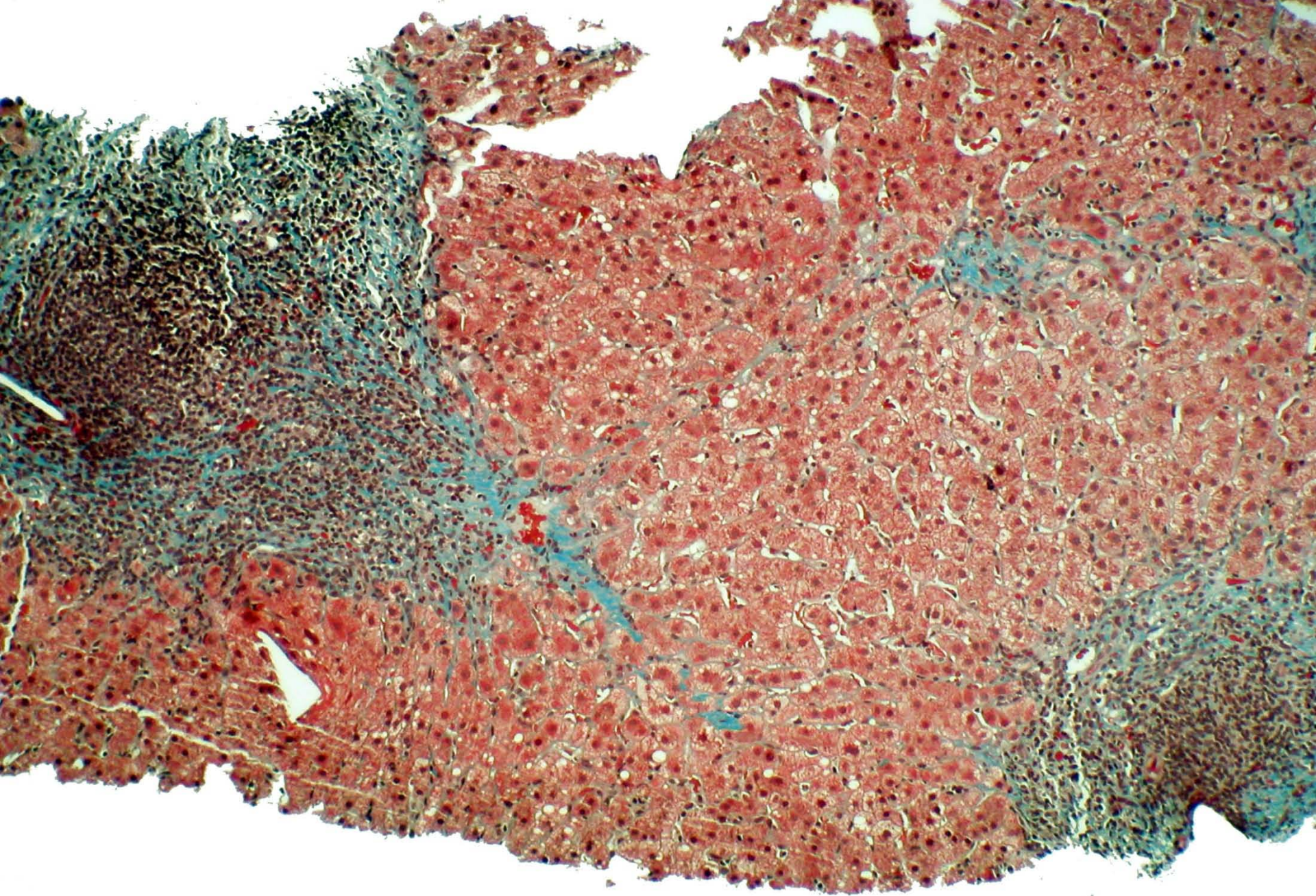
Liver Biopsy

Staging of Disease Severity by Liver Biopsy

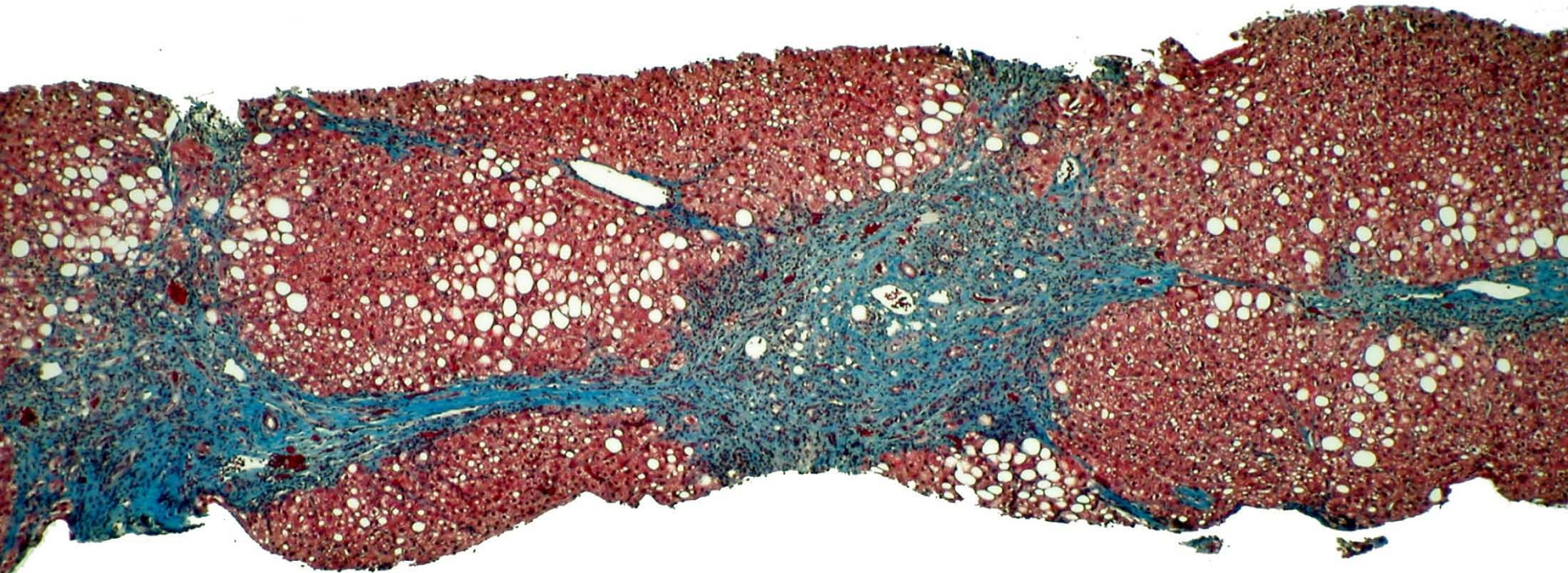
- Grading degree of Inflammation
- Staging degree of fibrosis
- Define risk for future decompensation
- Identify patients at risk for HCC



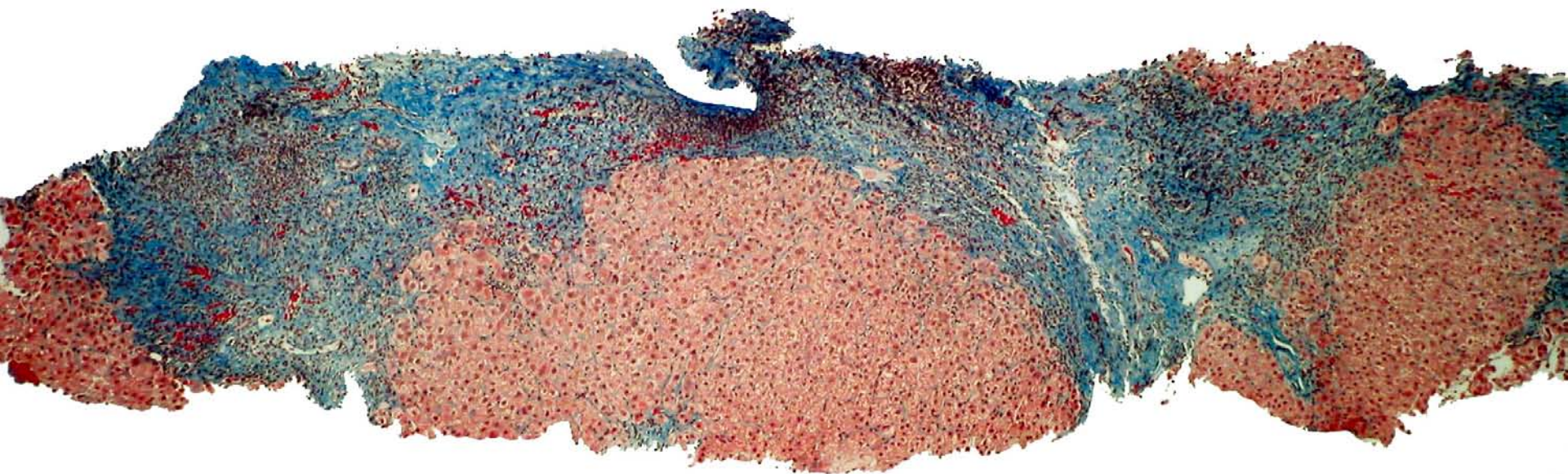




Stage 2



Stage 3



Stage 4

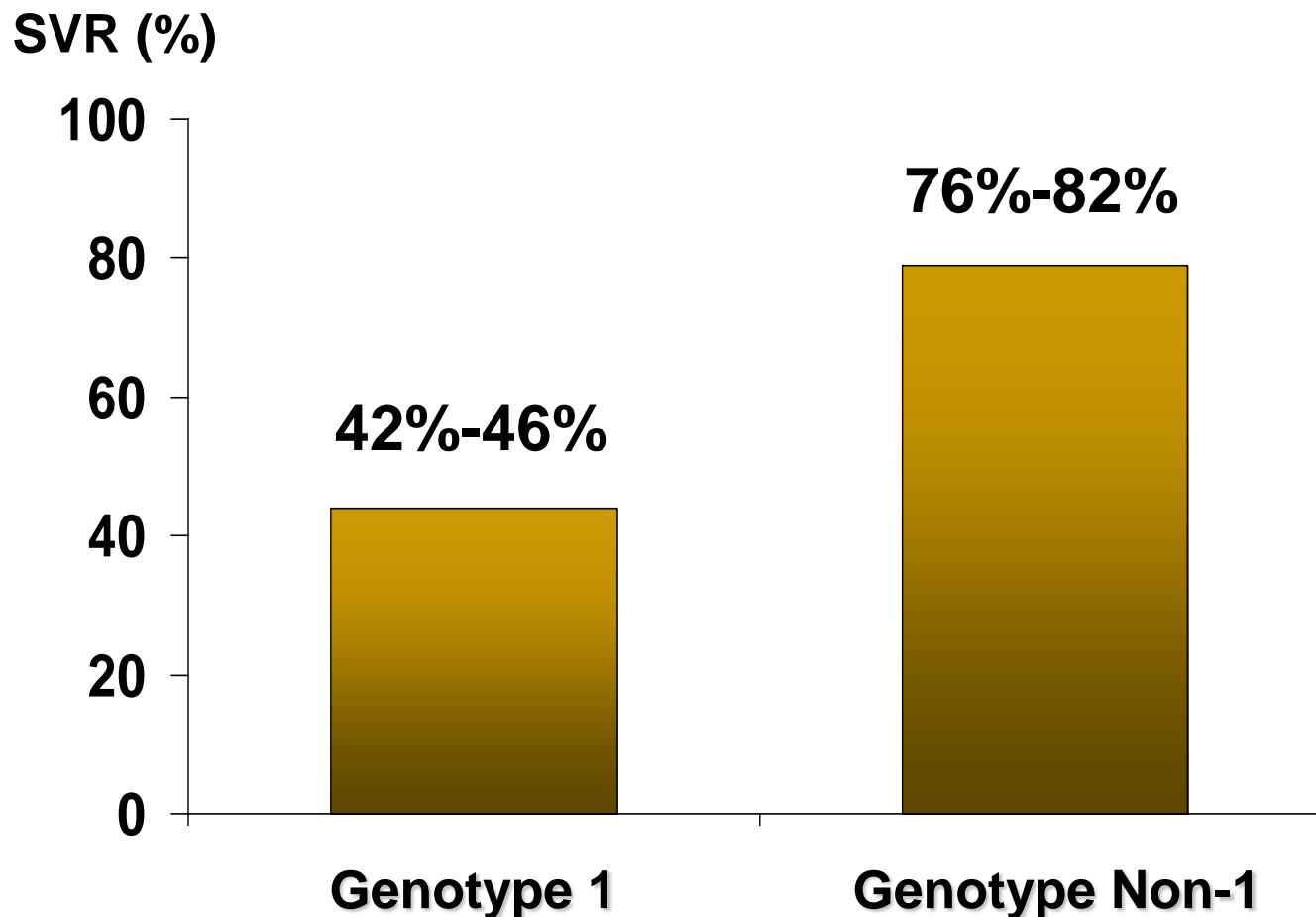
Defining Likelihood of Response to Antiviral Therapy

HCV Genotype

HCV Genotype

- **What is genotype and why should I be tested?**
 - Genotypes are genetic subclasses of HCV – there are 6 common genotypes, 1 through 6.
 - The greatest predictor of response to PEG(IFN)/RBV therapy is genotype. Geno 1 is least responsive, but still has 40 - 50% chance for SVR. Geno 2 is most responsive, 80 – 90% SVR.
 - Genotype does not predict rate of progression, severity of liver disease, or risk for HCC.

SVR Rates with Peg-IFN/RBV: According to Genotype



Adapted from Strader DB et al. Hepatology. 2004;39:1147-1171.



Virologic Response during Antiviral Therapy

“Viral-response Guided Treatment”

HCV RNA Blood Level (“Viral Load”)

- **What is “viral load” and why should I be tested?**
 - HCV RNA blood level, commonly called “viral load”, is monitored throughout the course of treatment – early virologic response to interferon-based treatment is associated with greatest chance for SVR and cure. The main purpose of measuring viral load is monitoring response to treatment.
 - In patients with Geno 1 infection, low viral load, particularly less than 400,000 IU/ml, is associated with greatest chance for SVR with interferon-based therapy. In patients with Geno 3 infection, high viral load may identify patients who might benefit from prolongation of treatment beyond 24 weeks.
 - Viral load does not predict rate of progression or severity of liver disease.

Virologic Response to Antiviral Therapy

■ Rapid Virologic Response (RVR)

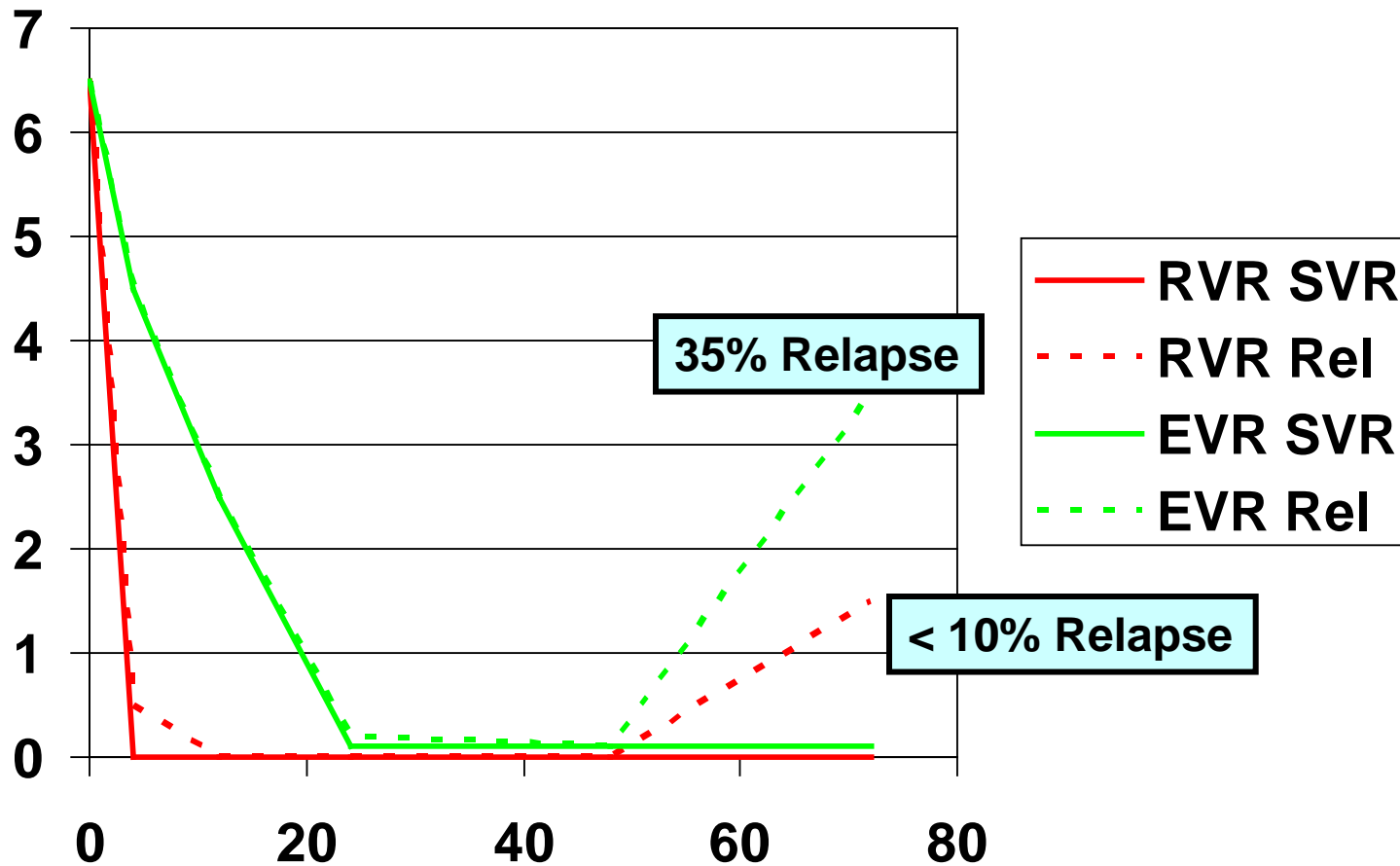
- Definition: HCV RNA negative by pcr at week 4 of treatment
- Implications:
 - RVR identifies patients with highest likelihood of achieving SVR
 - RVR may also identify patients who can be treated with shorter courses of therapy

■ Early Virologic Response (EVR)

- Definition: HCV RNA has dropped 2 logs (100 fold) or more from baseline at week 12 of treatment
- Implications:
 - EVR identifies responders - excellent chance of achieving SVR
 - Stop Guideline – patients without EVR have only 2% chance of SVR with continued treatment. Generally, treatment is stopped in those patients who fail to achieve EVR.

RVR and EVR: Geno 1, 48 wks Rx

Log HCV RNA



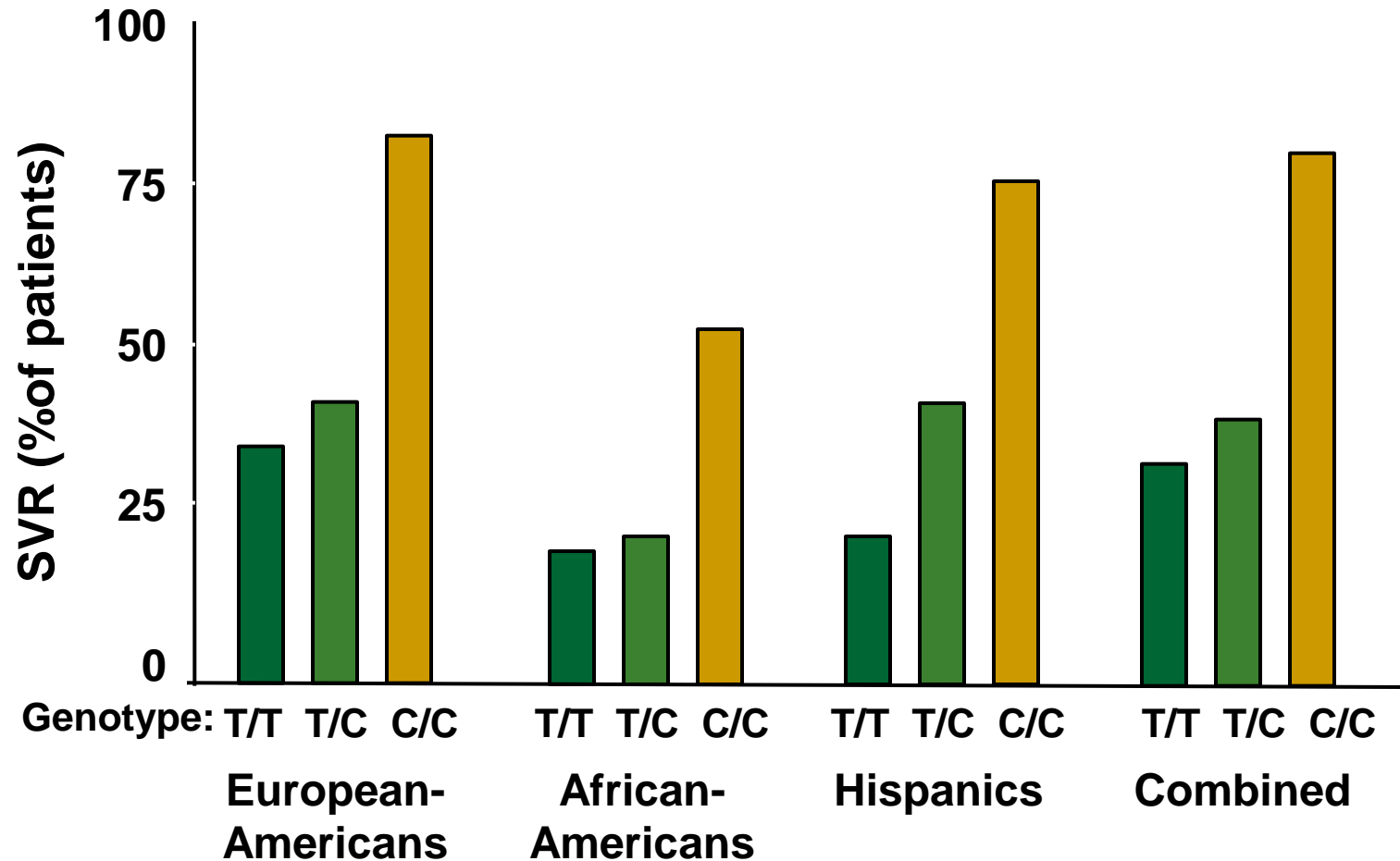
IL28b Polymorphism

**Role in Assessing Patients for
Treatment is under study**

***IL28B* Genetic Variation and Genotype 1 Response**

- 1137 patients from the IDEAL trial
- IL28B polymorphisms:
 - C/C
 - C/T
 - T/T

Percentage of SVR by Genotypes of rs12979860



Screening for Early-Stage Liver Cancer (Hepatoma, HCC)

Blood Tests for HCC

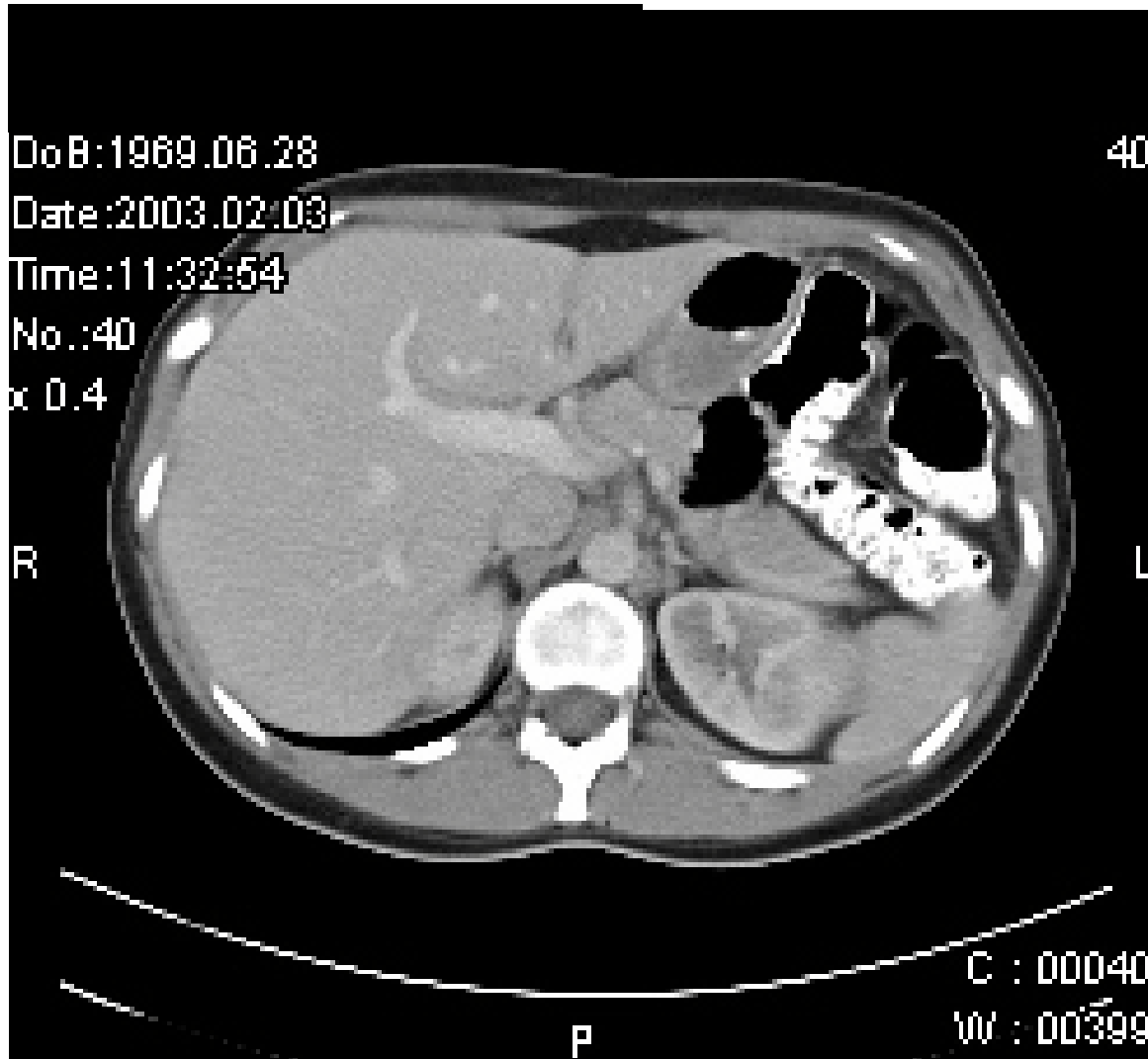
■ Alpha-fetoprotein (AFP)

- ❑ Insensitive – elevated in only 1/3 of cases of HCC
- ❑ Nonspecific – may be elevated due to HCV
- ❑ One AFP subtype, AFP-L3, may be more specific
- ❑ Other tests (DCP, proteome/genome)
- ❑ If used, measure q 3 – 6 months

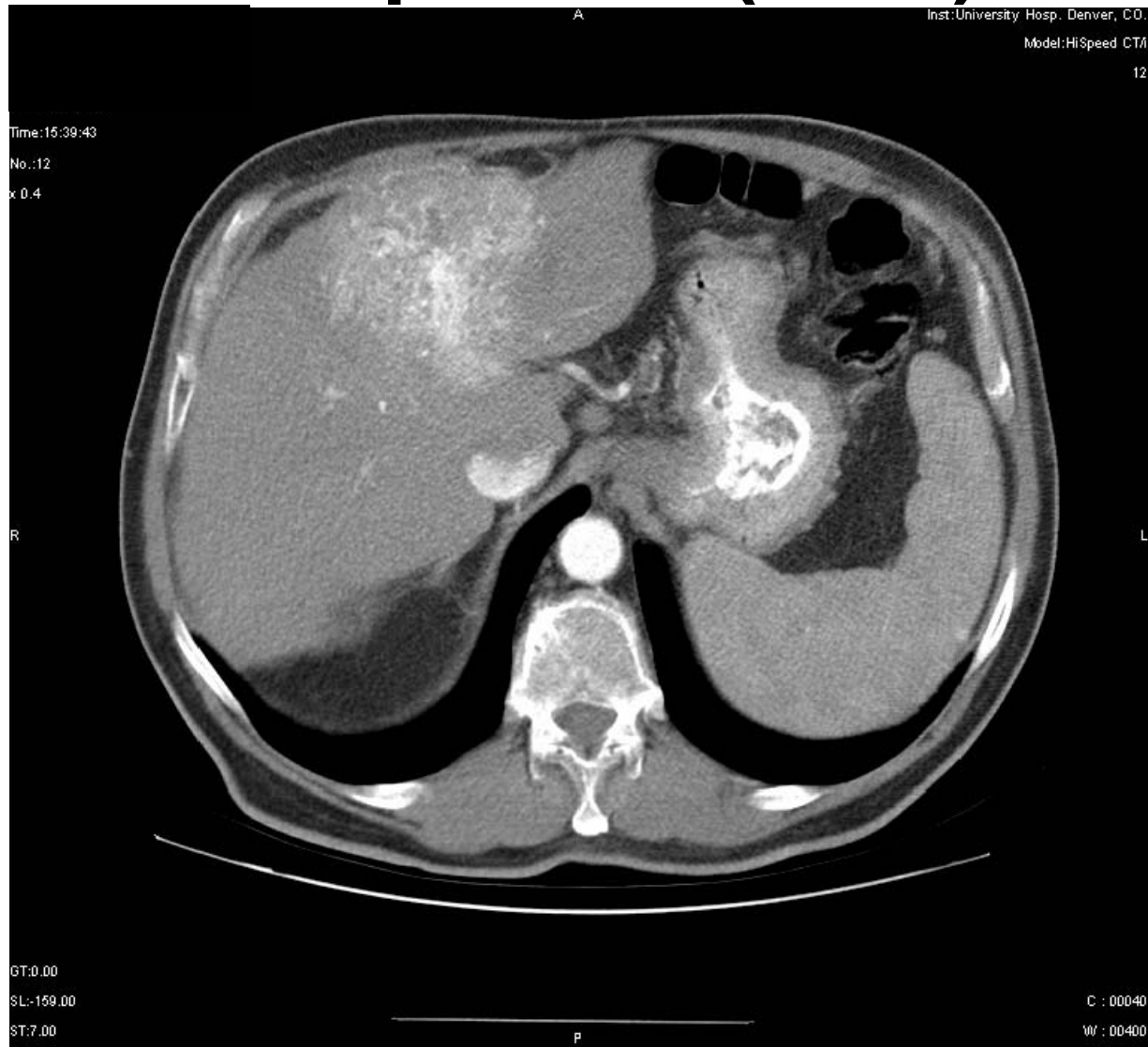
Radiologic Imaging

- **Most reliable method for screening**
 - Candidates for radiologic screening for HCC should have bridging fibrosis or cirrhosis on liver biopsy – and, they should be candidates for treatment (chemoembolization, RFA, chemotherapy, liver resection, or transplantation) if HCC diagnosed.
 - Based on cost, US is preferred over CT. Based on imaging, CT is favored over US.
 - Frequency of imaging – US/CT every 6 months
 - Cirrhotic/bridging fibrotic patients should be screened in long-term followup, even after SVR

CT Scan of Normal Healthy Liver



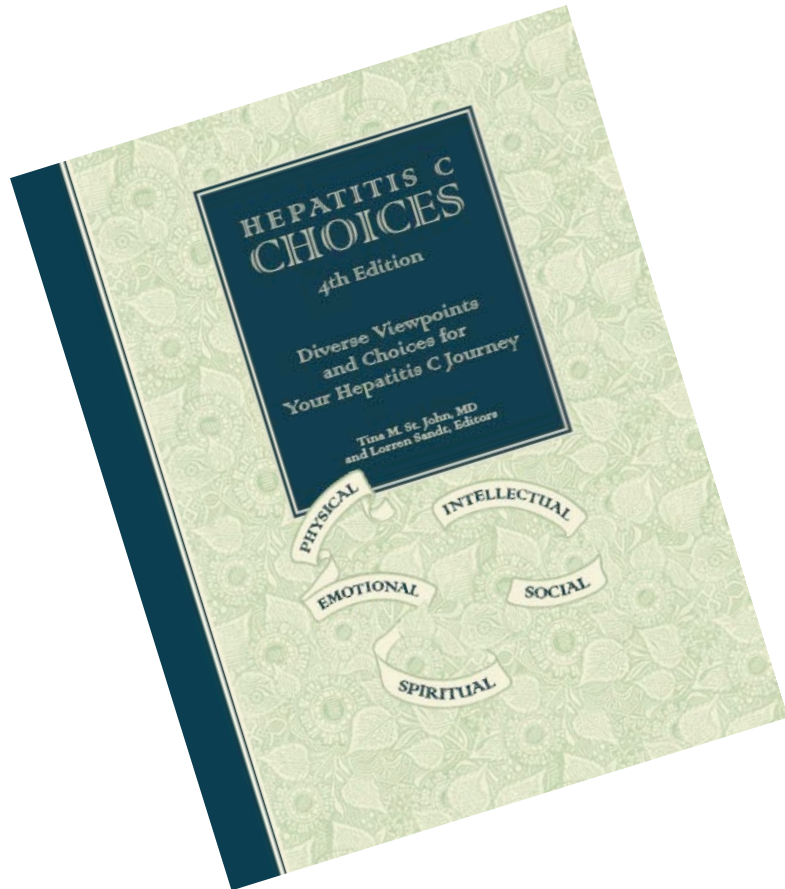
CT Scan of Hepatoma (HCC)



Summary - Testing

- **For defining disease severity**
 - Standard clinical and laboratory evaluation
 - Noninvasive Testing – Fibrotest, Fibroscan, QLFT
 - Liver biopsy – for indeterminate cases
- **Defining likelihood of response to antiviral therapy**
 - HCV Genotype
 - HCV RNA blood level prior to treatment
 - HCV RNA response during treatment (RVR, EVR)
 - IL28b polymorphism?
- **Screening for Hepatoma (HCC)**
 - Radiologic imaging – q 6 to 12 mo for advanced fibrosis/cirrhosis

For more information



Chapter 6: Laboratory Tests and Procedures

http://www.hepcchallenge.org/choices/pdf/Chapter_06_OL.pdf

Visit us on line at www.HepCChallenge.org

