

WELCOME TO AK LIVER DISEASE ECHO



ALASKA NATIVE
TRIBAL HEALTH
CONSORTIUM



NPAIHB

Indian Leadership for Indian Health

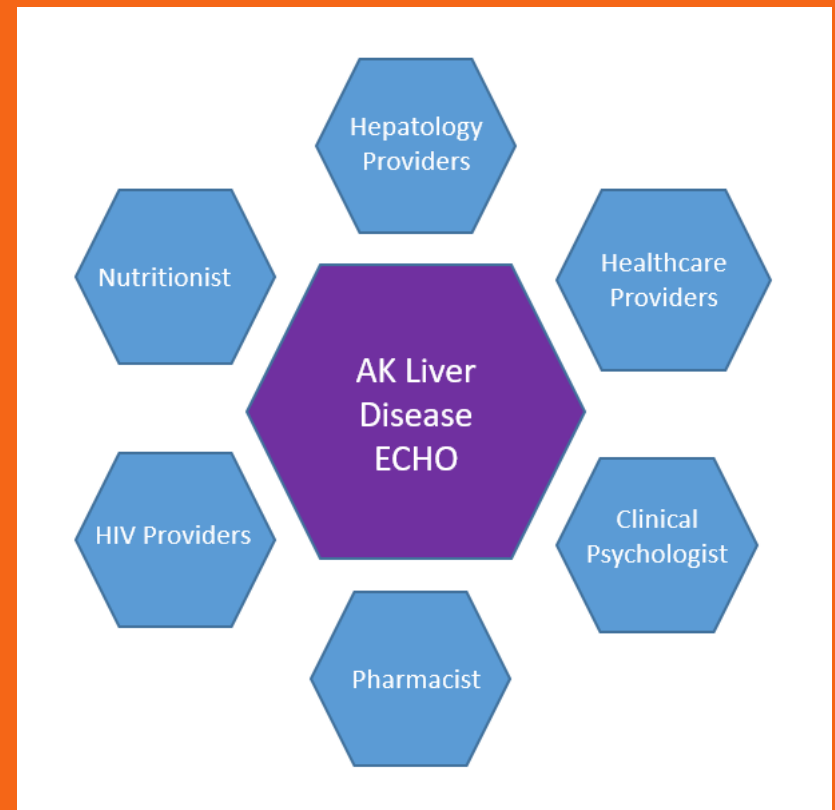
This project is supported by a grant from the Northwest Portland Area Indian Health Board and funding is provided from the HHS Secretary's Minority HIV/AIDS Fund.

WHAT WE DO

- Didactic Presentations pertaining to ECHO topics
- We're accepting **case presentations and questions pertaining to:**
 - Elevated Liver Function Tests
 - Cirrhosis
 - Managing Complications of Decompensated Cirrhosis – Ascites, encephalopathy, esophageal varices
 - Alcohol-related liver disease, including Alcohol Hepatitis
 - Autoimmune liver disease – Autoimmune Hepatitis, Primary Biliary Cholangitis, Overlap
 - Nonalcoholic fatty liver disease/Nonalcoholic steatohepatitis
 - Hepatocellular carcinoma
- Provide Expert Panelists

CONSULTANT TEAM

- Brian McMahon, MD Hepatologist
- Youssef Barbour, MD Hepatologist
- Lisa Townshend, ANP Hepatology Provider
- Annette Hewitt, ANP Hepatology Provider
- Leah Besh, PA-C HIV/Hepatology Provider
- Anne Fleetwood, MS, RDN, NDN
- Brittany Keener, PharmD, MPH, BCPS
- Lucia Neander, PhD Clinical Psychologist



Welcome to Alaska Liver Disease ECHO

Approved Provider Statements:

Alaska Native Tribal Health Consortium (ANTHC) is accredited by the Washington State Medical Association to provide continuing medical education for physicians. ANTHC is approved as a provider of nursing continuing professional development by the Montana Nurses Association, an accredited approver with distinction by the American Nurses Credentialing Center's Commission on Accreditation.

☒ The Alaska Pharmacists Association (AKPhA) in cooperation with ANTHC is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

Contact Hours:

ANTHC designates this live activity for a maximum 12 AMA PRA Category 1 Credit(s)™ for the entire series. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

ANTHC designates this activity as meeting the criteria for one nursing contact hour credit for each hour of participation up to a maximum 12 hour(s), including 3 total pharmacotherapeutics (Rx) contact hours for the entire series.

To receive CPE credit, participants must complete an Evaluation/Attendance Form for each session attended. You will be required to enter your NABP e-profile ID number, & birthdate (mm/dd). CPE credit will be posted to the online CPE Monitor system within 60 days after completion of each activity. No credit will be reported to CPE Monitor for CEs that do not have a completed evaluation. There is no charge to process CPE credit for ANTHC employees and AKPhA members, but a fee may apply to participants not affiliated with either organization.

Conflict of Interest Disclosures:

Youssef Barbour, MD & Lisa Townshend-Bulson, APRN / faculty for this educational event, are primary investigators in an ANTHC sponsored hepatitis C study funded in part by Gilead Sciences; Anne Fleetwood, faculty for this educational event, is a contractor with Tandem Diabetes Care. All of the relevant financial relationships listed for these individuals have been mitigated.

Requirements for Successful Completion:

To receive CE credit please make sure you have actively engaged in the entire activity, your attendance is recorded by the facilitator, and complete the course evaluation form found here: <https://forms.gle/R8vibUZgMbRcoScw9>.



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ALASKA NATIVE
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NON INVASIVE MARKERS OF LIVER FIBROSIS

Brian J McMahon, MD

Liver Disease and Hepatitis Program

Alaska Native Tribal Health Consortium

FINANCIAL DISCLOSURES

- None

PRE-DIDACTIC QUESTION

Choose the best answer...

A FibroScan can tell you:

- a. If the patient has fatty liver and fibrosis.
- b. If the patient has fatty liver.
- c. If the patient has liver fibrosis.
- d. If the patient has liver cancer.

WHY IS KNOWING THE STAGE OF LIVER FIBROSIS (SCARRING) IMPORTANT

- Persons with liver fibrosis may need careful follow-up and therapy for the underlying liver disease they have, whereas those who do not, may not need follow-up by liver specialists or further testing
- Persons with advanced fibrosis or cirrhosis will need surveillance for hepatocellular carcinoma (HCC) every 6 months with liver ultrasound and alpha-fetoprotein (AFP) to detect HCC when the tumor(s) are small enough to cure

GOALS OF THIS PRESENTATION

- To understand non-invasive markers of liver fibrosis
 - What are the markers
 - What is the sensitivity and specificity of each marker
 - How do I find the web-based calculators to determine the stage of liver fibrosis for my patient
 - What tests can I do in my clinic setting before referring for FibroScan or other tests
 - When I still have difficulty determining the degree of fibrosis, when should I refer a patient for a liver biopsy

LIST OF NON-INVASIVE MARKERS OF LIVER FIBROSIS

- APRI
- FIB-4
- NAFLD Fibrosis Score (NFS)
- FAST score
- Hepatic Steatosis Index (STI)
- Commercial liver fibrosis tests
- Incidental finding on US, CT or MRI
- Vibration-Controlled Transient Elastography (VCTE or FibroScan®)
- Acoustic radiation force impulse (ARFI) technology
- Magnetic Resonance Elastography (MRE)

STAGES OF LIVER FIBROSIS IN HEPATITIS: METAVIR

Stage of Fibrosis	Findings
Stage 0	No fibrosis
Stage 1	Mild: Only Portal Fibrosis
Stage 2	Moderate: Portal Fibrosis with extension
Stage 3	Severe: Bridging Fibrosis
Stage 4	Severe: Cirrhosis

DIAGNOSIS OF CIRRHOSIS

- Gold standard: Autopsy, laparotomy or stigma of cirrhosis on PE
- Liver biopsy: next best thing but sampling error occurs
 - Size of biopsy needs to be at least 2cm long and wide enough (16-gauge needle), and at least 6 portal tracts to have a 90% accuracy
 - Radiologists using a biopsy gun only get 2cm max
- Vibration Controlled Transient Elastography (VCTE FibroScan® or equivalent such as shear wave elastography), Magnetic Resonance Elastography (MRE)
- Fibrosis Markers: APRI, FIB₄, NAFLD fibrosis score
- Ultrasound findings:
 - Great if ascites, varices or flow study shows portal HTN
 - Often over read by radiologist based on liver contour



'Simple Scores' for Predicting Presence of Advanced (F3/4) Fibrosis

NAFLD Fibrosis Score

$$= -1.675 + 0.037 \times \text{Age} + 0.094 \times \text{BMI} + 1.13 \times \text{IFG/diabetes} + 0.99 \times \text{AST/ALT ratio} - 0.013 \times \text{Platelets} - 0.66 \times \text{Albumin.}$$

- A score of less than -1.455 excludes fibrosis (NPV 88-93%).
- A score of greater than 0.676 predicts fibrosis (PPV 82-90%).

FIB-4 Score

$$= (\text{Age} * \text{AST}) / (\text{Platelets} * \text{Sqrt}(\text{ALT}))$$

- A score of less than 1.3 excludes fibrosis (NPV 95%)
- A score greater than 3.25 predicts fibrosis (PPV ~70%)



NAFLD FIBROSIS SCORE

NAFLD (Non-Alcoholic Fatty Liver Disease) Fibrosis Score ☆

Estimates amount of scarring in the liver based on several laboratory tests.

When to Use ▼ Pearls/Pitfalls ▼ Why Use ▼

Age years

BMI kg/m²

Impaired fasting glucose/diabetes ☒ No 0 ☐ Yes +1

[AST](#) U/L

[ALT](#) U/L

Platelet count × 10³/μL ↵

Albumin g/dL ↵

<https://www.mdcalc.com/nafl-d-non-alcoholic-fatty-liver-disease-fibrosis-score>

FAST SCORE: FOR NAFLD TO IDENTIFY PERSONS WITH NASH

- Uses AST plus VCTE scores for Liver Stiffness (LSM) and Steatosis (CAP)
- $FAST = e^{-1.65 + 1.07 \times \ln(LSM) + 2.66 \times 10^{-8} \times CAP - 63.3 \times AST - 11} + e^{-1.65 + 1.07 \times \ln(LSM) + 2.66 \times 10^{-8} \times CAP - 63.3 \times AST - 1}$
- Gives results as NAS score (NAFLD activity score) and advanced fibrosis score:
- Persons with a NAS score ≥ 4 and Fibrosis score ≥ 2 are at risk for progression of NASH
 - Sensitivity 0.90, specificity 0.67
 - PPV 0.83, NPV 0.85

COMMERCIAL SEROLOGIC MARKERS FOR LIVER FIBROSIS

- FibroTest/FibroSure, FibroSpect II, FibroMeter, Hepascore, OELF/ELF and others
- Most use a cutoff for $<\text{stage } 2$, $\geq \text{stage } 2$
- Cost: \$200 to \$300
- Accuracy: good at high and low ends, not so good in the middle
- Often not worth the high cost over FIB-4 and APRI

Indirect Serum Markers of Liver Fibrosis.

Indices	Individual components	Sensitivity (%)	Specificity (%)
AST/ALT ratio	Aspartate aminotransferase, Alanine aminotransferase	53	100
PGA	Prothrombin index, GGT, apolipoprotein A1	91	81
APRI	AST/platelet count	89	75
FibroSpect II	HA, TIMP-1, α 2-macroglobulin	83.5	66.7
FibroTest/FibroSure	γ 2 macroglobulin, γ 2 globulin, γ globulin, apolipoprotein A1, GGT, total bilirubin	75	85
FibroIndex	Platelet count, AST, GGT	78	74
FibroMeter	Platelet count, γ 2 macroglobulin, AST, age, prothrombin index, HA, blood urea nitrogen	81	84
Forns	Age, platelet count, GGT, cholesterol levels	94	51
Hepascore	Age, gender, bilirubin, GGT, HA, γ 2-macroglobulin	63	89
FIB-4	Platelet count, ALT, AST, platelet count, age	70	74
SHASTA Index	HA, AST, albumin	100	52
Simple test	age, hyperglycemia, BMI, platelet count, albumin, AST/ALT	78	58
OELF/ELF	age, HA, N-terminal propeptide of type III collagen, TIMP-1	90	41

GGT: γ glutamyl transferase, HA: hyaluronic acid, TIMP-1: Tissue inhibitors of matrix metalloproteinase- 1, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase

BMJ Gastro
2011;11:91
doi: [10.1186/
1471-230X-
11-91](https://doi.org/10.1186/1471-230X-11-91)

TRANSIENT ELASTOGRAPHY

- Allows painless and simultaneous measurement of two quantitative parameters:
 - Liver stiffness expressed in kPa
 - Correlated to liver fibrosis [1]
 - Controlled Attenuation Parameter (CAP™) expressed in dB/meter
 - Correlated to liver steatosis [2]
- Both quantitative parameters are assessed on the same volume of liver tissue
- 100 times bigger than liver biopsy

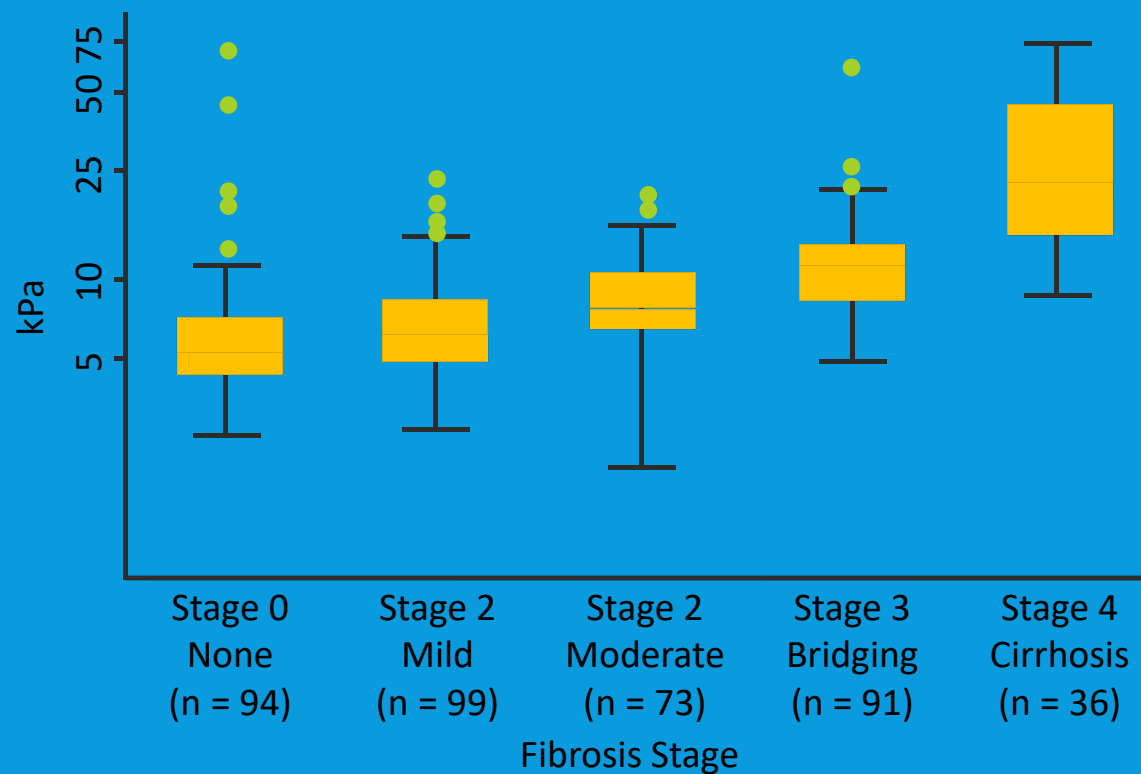


. Friedrich Rust, et al. *Gastroenterology*. 2008; 2. Sasso, et al. *Journal of Viral Hepatitis*. 2011.

TRANSIENT ELASTOGRAPHY

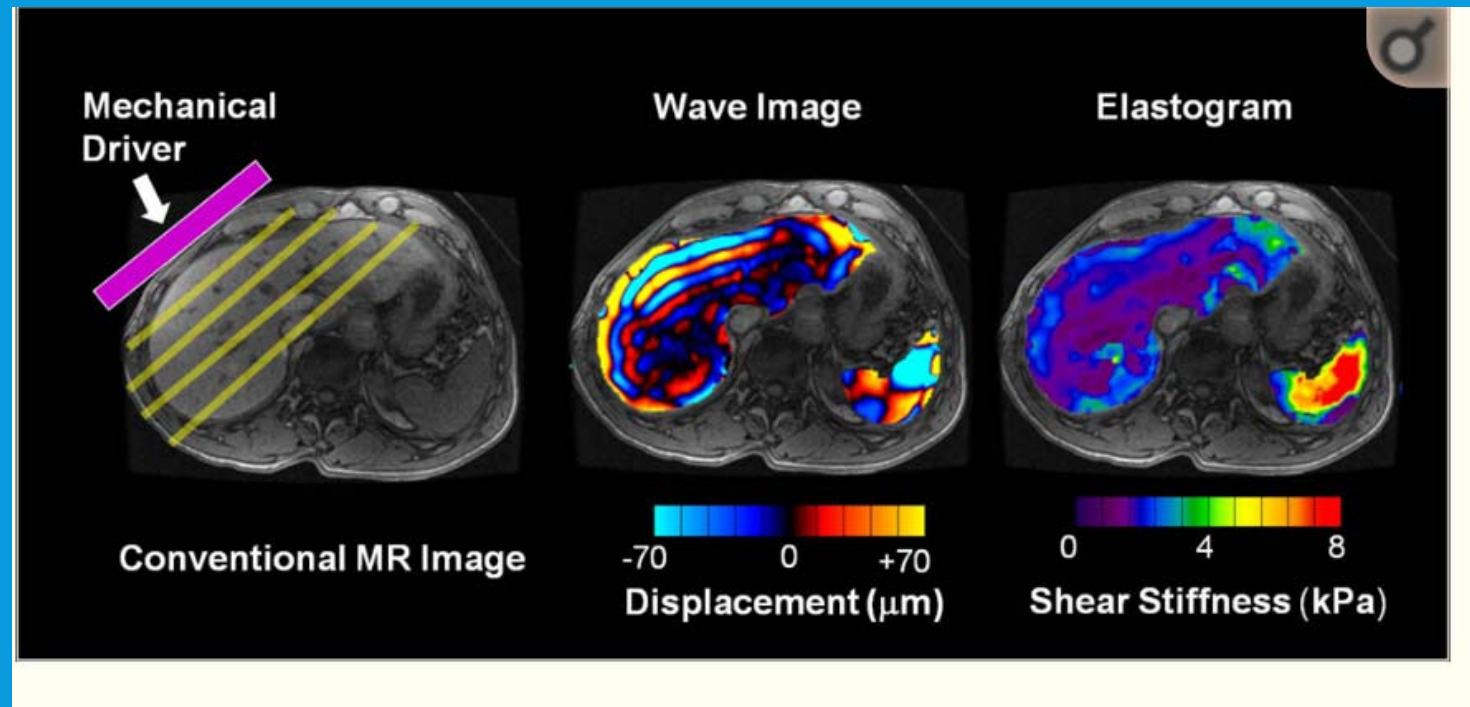
- Measures velocity of a low-frequency (50 Hz) elastic shear wave propagating through the liver
 - Normal liver: ~5.5 kPa: Reading below 7-8 kPa corresponds with no/minimal fibrosis
- Good performance for excluding advanced stage disease (stage 3-4)
- User-friendly, short procedure time
- Problems still with severe obesity, ascites, operator experience
 - CAP software may help: it estimates amount of liver fat
- False positives: acute hepatitis, extrahepatic cholestasis and congestion
- Fibroscan VCTE, one method of TE, has an XL and pediatric probe:
- Good news for our THO partners. We have a portable FibroScan machine that we bring with us to Field Clinics

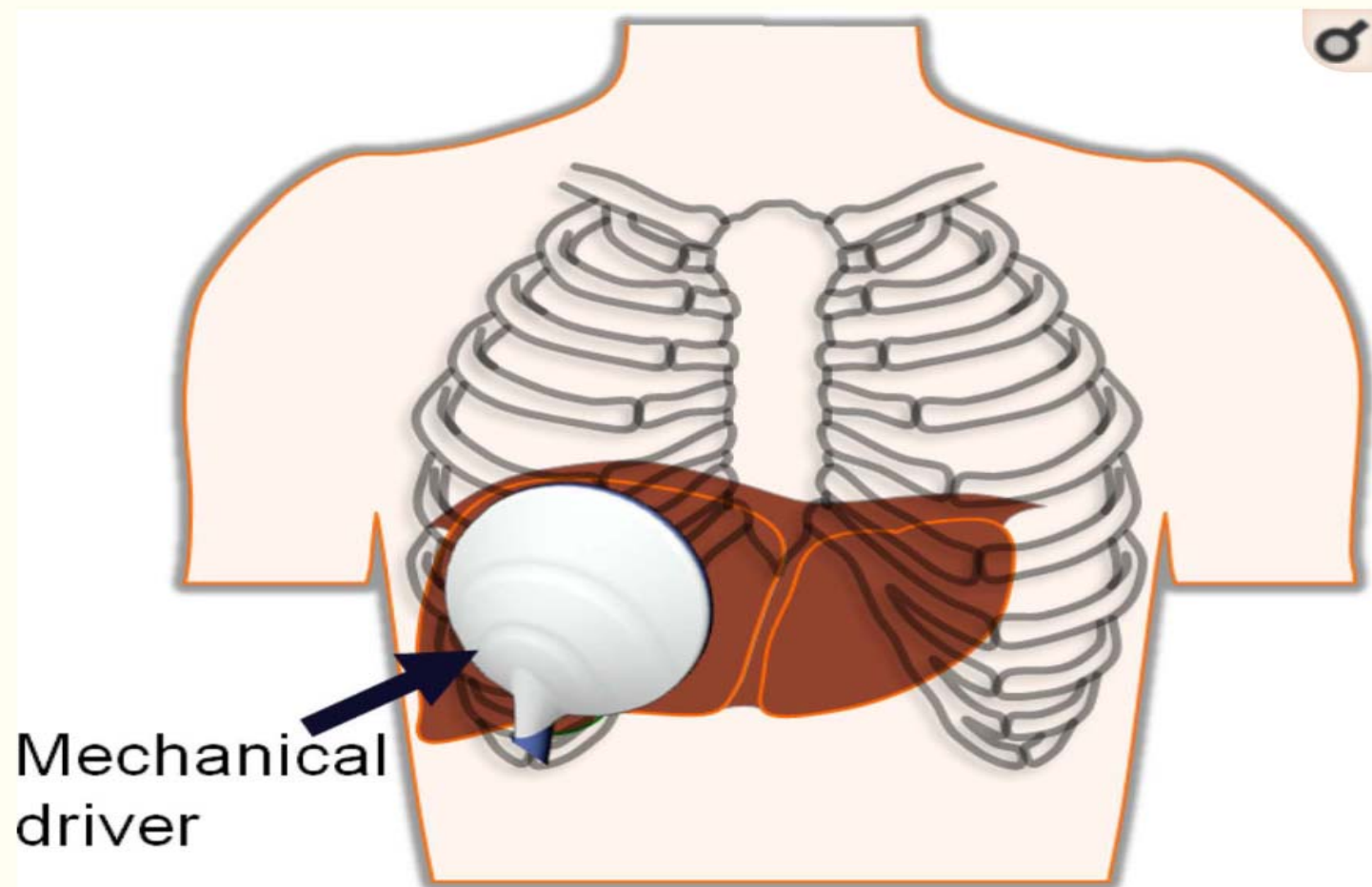
DETECTING LIVER FIBROSIS WITH *FIBROSCAN*



Trend test $P < .0001$

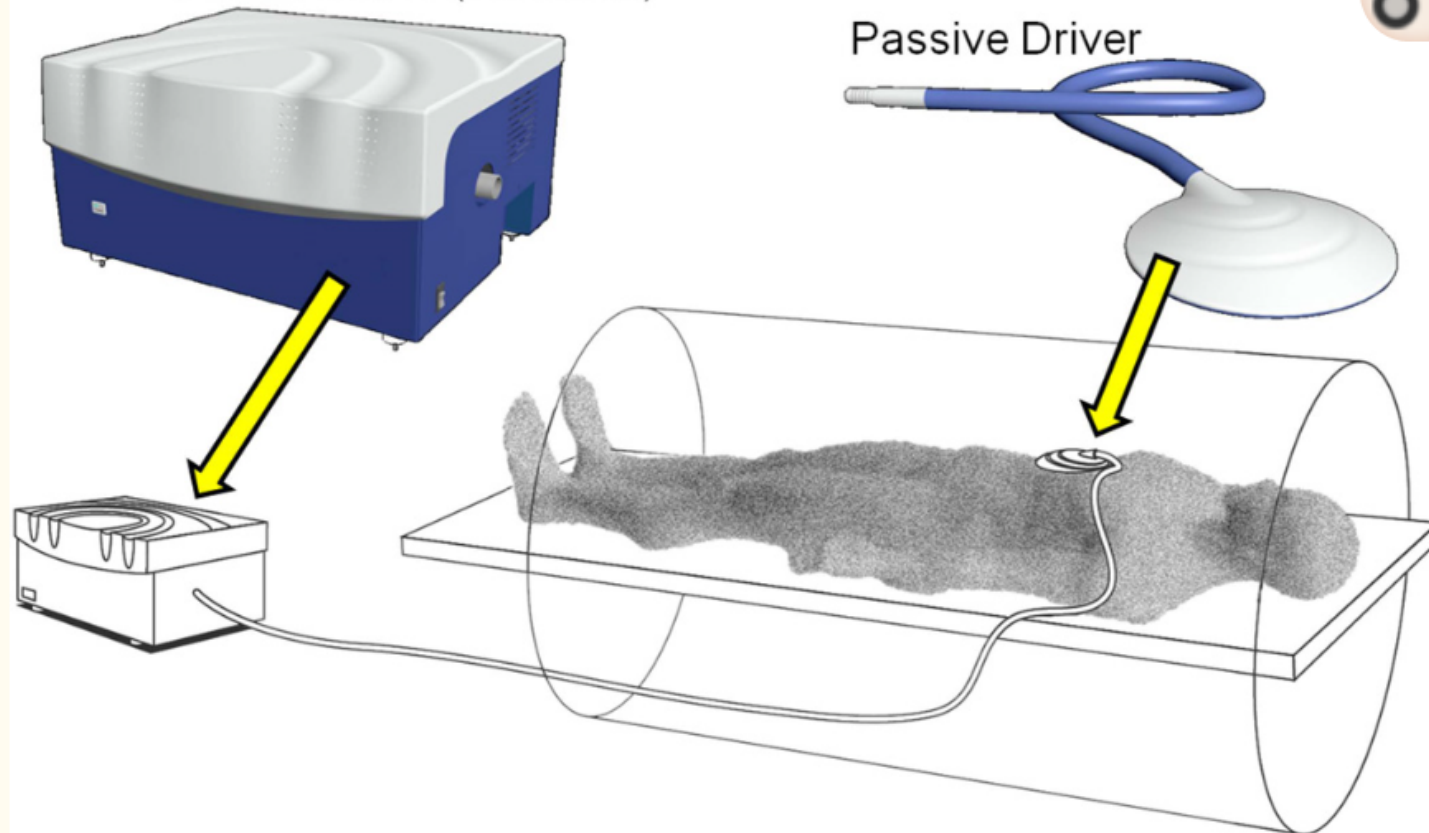
Magnetic Resonance Elastography (MRE)

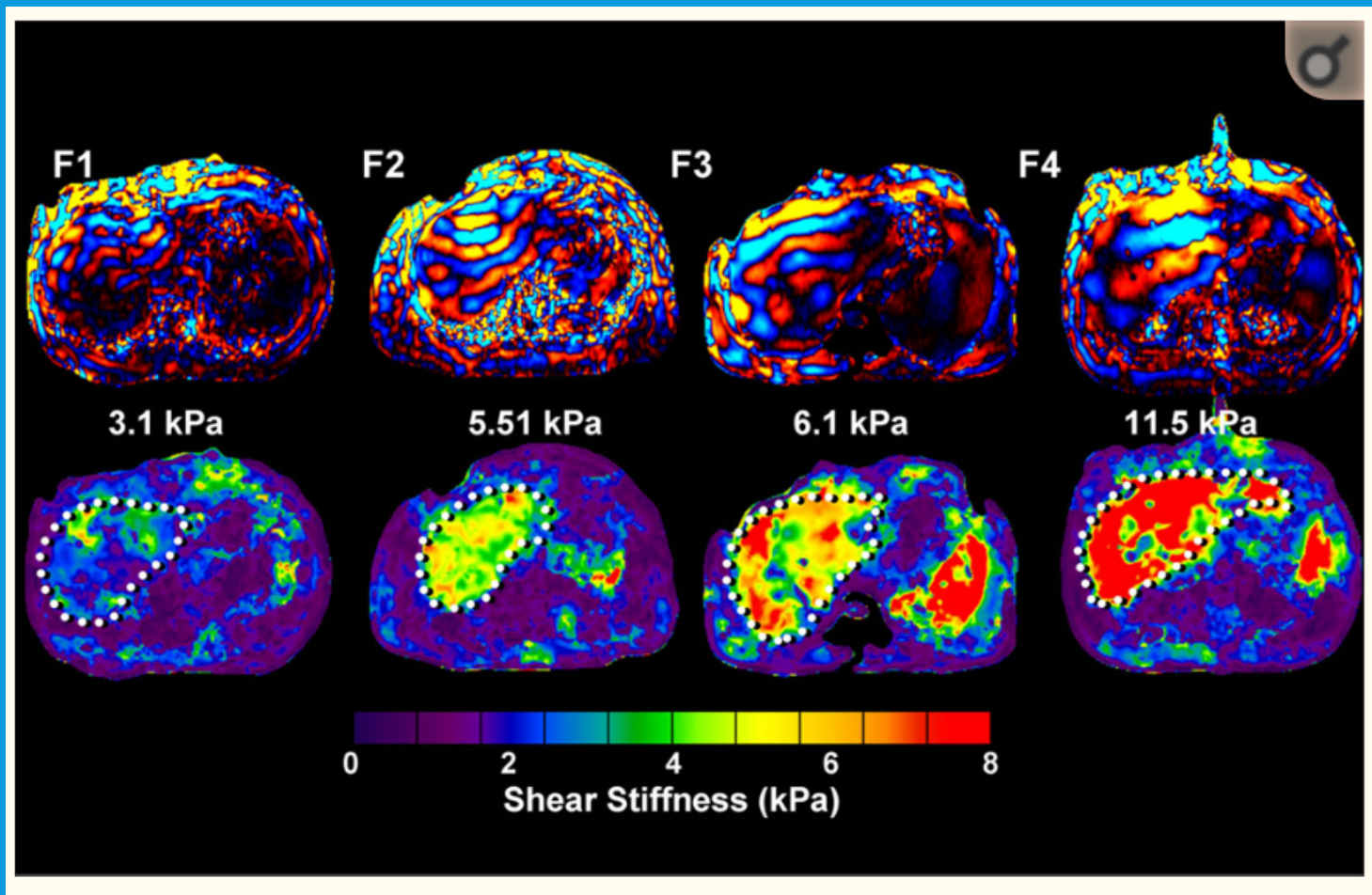




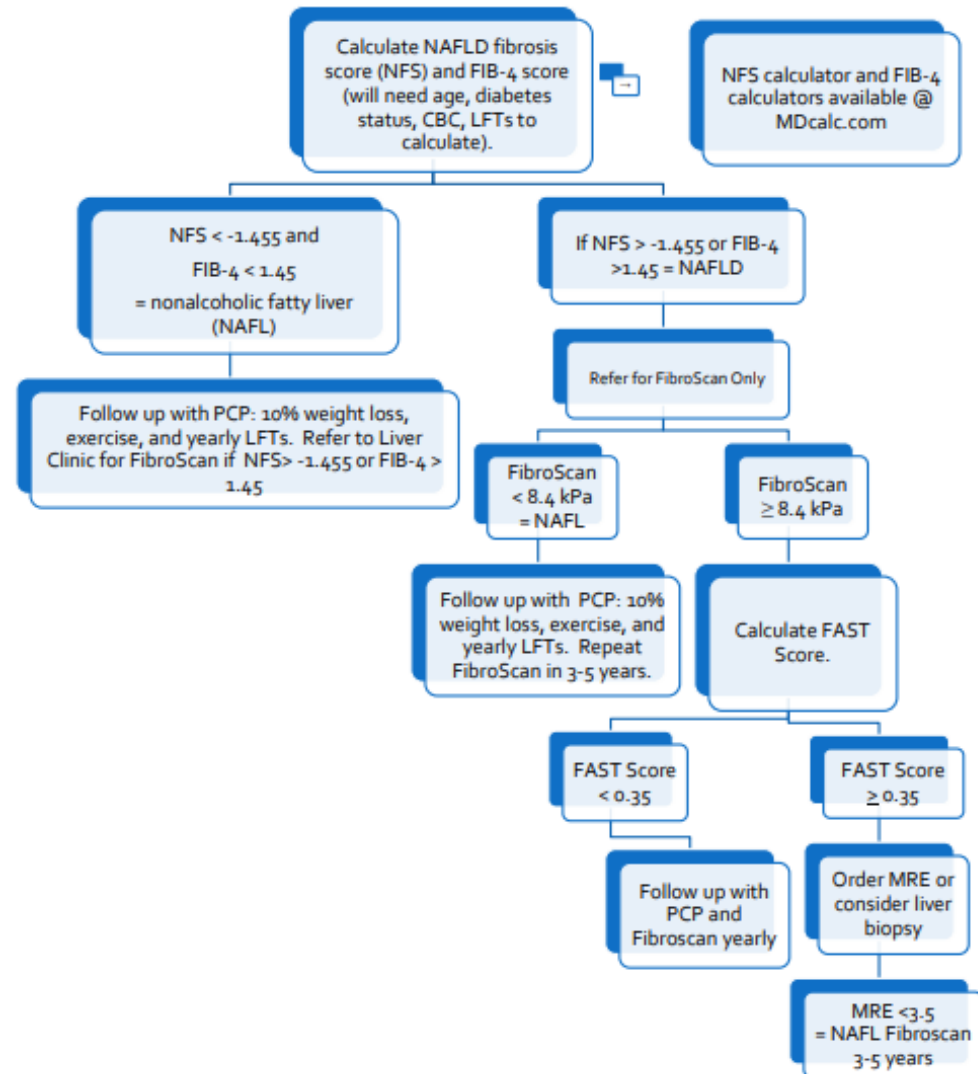
Active Driver (Acoustic)

Passive Driver





FIBROSIS ASSESSMENT IN NAFLD



EVALUATING LIVER FIBROSIS: A PRACTICAL PATH

- Do APRI and FIB-4 first: If both tests show no fibrosis, you can stop and assume that further tests are unnecessary and follow APRI and FIB-4 for future visits
 - If the patient has risk factors, also calculate NAFLD Fibrosis marker
- If APRI and/or FIB-4 indeterminate or high, FibroScan next
- If FibroScan < 8.4 kPa, stop, repeat in 3-5 years if patient has NAFLD
- If FibroScan > 8.4, then calculate FAST score and if ≥ 0.35 order MRE
- Consider liver biopsy if MRE consistent with advanced fibrosis or cirrhosis depending on etiology

Algorithm on our website:

<https://anthc.org/wp-content/uploads/2021/01/Care-NAFLD-2021.pdf>

CONCLUSIONS

- All patients with chronic elevated liver enzymes should be evaluated for liver fibrosis
- Start with free markers and if low can re-evaluate again for fibrosis in 3-5 years
- FibroScan or equivalent elastography/SWE can eliminate many persons with intermediate APRI/FIB-4 results who have low fibrosis scores
- It's important to continue search for level of fibrosis, if present, to identify those with advanced fibrosis or cirrhosis who need regular surveillance for HCC

POST-DIDACTIC QUESTION

Choose the best answer...

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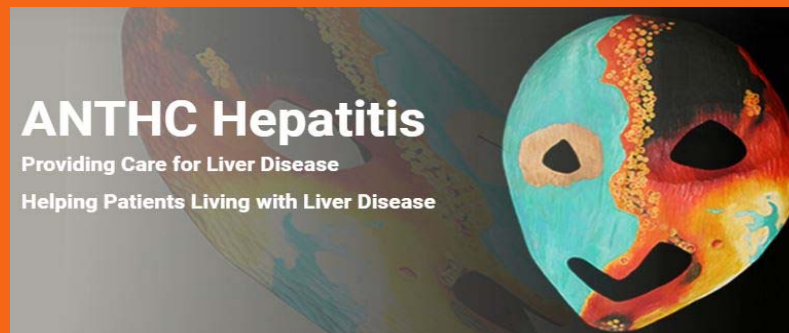
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LIVER DISEASE ECHO SCHEDULE AT A GLANCE

- April 15 Noninvasive Markers for Liver Fibrosis – Brian McMahon, MD
- May 21 Management of Ascites – Youssef Barbour, MD
- June 17 Motivational Interviewing – Lucia Neander, PhD
- July 15 Nutrition for the Liver – Anne Fleetwood, MS, RDN, CDCES
- August 19 Drug Induced Liver Injury – Brittney Keener, MPH, BCPS

ADDITIONAL LEARNING OPPORTUNITIES

- AK ID ECHO: HCV, HIV, PrEP, STIs
 - The 2nd Tuesday of every month from 12:00-1:00PM Alaska Standard Time
 - 1CE/CME offered per session
 - anthc.org/project-echo/hcv-hiv-prep-stis-echo
- LiverConnect Webinar Program
 - Second Tuesday of every month 8:00-9:00AM Alaska Standard Time
 - Full Hour didactic topics on Liver Disease and related topics 1CE/CME offered
 - anthc.org/what-we-do/clinical-and-research-services/hep/liverconnect/



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Thank you



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