

## Medical Policy Manual **Approved Revision: Do Not Implement until 6/30/21**

### Noninvasive Techniques for Evaluation and Monitoring of Chronic Liver Diseases

#### DESCRIPTION

Noninvasive techniques to diagnose and monitor liver fibrosis are being investigated as alternatives to liver biopsy in individuals with chronic liver disease. Options for noninvasive monitoring include multianalyte serum assays with algorithmic analysis and specialized radiologic methods including magnetic resonance elastography, transient elastography, acoustic radiation for impulse imaging and real-time transient elastography.

Multianalyte assays with algorithmic analyses are proposed as an alternative to simple serum tests (e.g., ALT, AST, platelet count and prothrombin index). They use a combination of serum biochemical markers of liver function and age, sex, height and weight. The algorithmic analysis provides a score that purportedly correlates with the degree of liver damage in individuals with a variety of liver diseases. These lab tests include, but are not limited to:

- **HCV FibroSURE®** (FibroTest™ in Europe) - 6 biomarkers (a2-macroglobulin, haptoglobin, bilirubin,  $\gamma$ -glutamyl transpeptidase (GGT), ALT, and apolipoprotein A1) yielding a prognostic algorithm scores for fibrosis and necroinflammatory activity
- **ASH FibroSURE®** - 10 biomarkers (a2-macroglobulin, haptoglobin, apolipoprotein A1, bilirubin, GGT, ALT, AST, total cholesterol, triglycerides, and fasting glucose) yielding a prognostic algorithm score for fibrosis, steatosis, and alcoholic steatohepatitis
- **NASH FibroSURE®** - 10 biomarkers (a2-macroglobulin, haptoglobin, apolipoprotein A1, bilirubin, GGT, ALT, AST, total cholesterol, triglycerides, and fasting glucose) yielding a prognostic algorithm score for fibrosis, steatosis, and nonalcoholic steatohepatitis
- **FibroSpect II™** - 3 biomarkers (hyaluronic acid, TIMP-1, and a2-macroglobulin) that directly measure fibrogenesis of the liver with algorithmic analysis

Noninvasive imaging is proposed as an alternative to liver biopsy to diagnose and evaluate the degree of fibrosis by mapping the elastic properties of soft tissue. Imaging techniques currently being investigated include:

- **Transient Elastography** (FibroScan®) - This technique transmits an elastic shear wave that propagates within the liver. The speed of the shear wave (the harder the tissue, the faster the shear propagates) is measured and quantified to determine the stage of fibrosis.
- **Acoustic radiation force impulses (ARFI)** (e.g., Acuson S2000™) - permits evaluation of liver stiffness in a smaller region.
- **Real-time tissue elastography** (e.g., HI VISION Preirus™) ultrasound able to display real-time elastography images.
- **Magnetic resonance elastography**- Combines MRI imaging with sound waves to create a visual map (elastogram) showing the stiffness of body tissues.

**Note: This policy does not address standard imaging with ultrasound or MRI.**

#### POLICY

- Transient elastography imaging (i.e., FibroScan®) when used to evaluate and/or monitor individuals with chronic liver disease is considered **medically necessary**.
- Magnetic resonance elastography is considered **medically necessary** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**



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- Transient elastography imaging (i.e., FibroScan®) when used to evaluate and/or monitor individuals with focal liver disease is considered **investigational**.
- All other noninvasive imaging that maps the elastic properties of soft tissue to evaluate and/or monitor individuals with chronic liver disease are considered **investigational**. These technologies include, but are not limited to, the following:
  - Acoustic radiation force impulse imaging (e.g., Acuson S2000™)
  - Real-time tissue elastography (e.g., HI VISION Preirus™)
- Multianalyte assays with algorithmic analyses (e.g., FibroSURE™) for the evaluation and/or monitoring of individuals with chronic liver disease are considered **investigational**.

### MEDICAL APPROPRIATENESS

- Magnetic resonance elastography is considered **medically appropriate** if **ALL** of the following are met:
  - Chronic liver disease, as indicated by **ANY ONE** of the following:
    - Nonalcoholic fatty liver disease, and hepatic fibrosis or cirrhosis is known or suspected
    - Chronic liver disease excluding nonalcoholic fatty liver disease (e.g., chronic hepatitis C virus infection, chronic hepatitis B virus infection) and need to assess for advanced fibrosis or cirrhosis with **ANY ONE** of the following:
      - BMI of 30 or greater
      - Vibration-controlled transient elastography is unavailable, contraindicated, or results are indeterminate
  - No moderate or severe hepatic iron overload documented (e.g., hemochromatosis, hemosiderosis)

### IMPORTANT REMINDERS

- Any specific products referenced in this policy are just examples and are intended for illustrative purposes only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available. These examples are contained in the parenthetical e.g. statement.
- We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits, or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

### ADDITIONAL INFORMATION

The evidence to support the use of noninvasive radiologic methods other than transient and magnetic resonance elastography for liver fibrosis measurement is limited. The evidence is insufficient to determine the effects of the technology on health outcomes.

### SOURCES

American Association for the Study of Liver Disease / Infectious Disease Society of America. (2019, November). *Recommendations for testing, managing, and treating hepatitis C*. Retrieved June 1, 2020 from <http://www.hcvguidelines.org>.

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American Association for the Study of Liver Disease. (2018). *The diagnosis and management of nonalcoholic fatty liver disease: practice guideline from the American Association for the Study of Liver Disease*. Retrieved March 17, 2021 from <https://www.aasld.org/publications/practice-guidelines>.

American College of Radiology. (2019). *ACR appropriateness criteria, Chronic liver disease*. Retrieved March 9, 2021 from <https://www.acr.org/Clinical-Resources/ACR-Appropriateness-Criteria>.

American Gastroenterological Association. (2017). *American Gastroenterological Association Institute guideline on the role of elastography in the evaluation of liver fibrosis*. Retrieved March 9, 2021 from <https://gastro.org/guidelines/liver-diseases/>.

BlueCross BlueShield Association. Evidence Positioning System. (12:2020) *Noninvasive techniques for the evaluation and monitoring of patients with chronic liver disease*. (2.04.41). Retrieved March 9, 2021 from <https://www.evidencepositioningsystem.com/>. (87 articles and/or guidelines reviewed)

Harris, R., Harman, D., Card, T., Aithal, G., & Guha, I. (2017). Prevalence of clinically significant liver disease within the general population, as defined by non-invasive markers of liver fibrosis: a systematic review. *The Lancet: Gastroenterology & Hepatology*, 2 (4), 288-297. Abstract retrieved July 18, 2017 from PubMed database

Hashemi, S., Alavian, S., Gholami-Fesharaki, M. (2016). Assessment of transient elastography (FibroScan) for diagnosis of fibrosis in non-alcoholic fatty liver disease: a systematic review and meta-analysis. *Caspian Journal of Internal Medicine*, 7 (4), 242-252. Abstract retrieved July 18, 2017 from PubMed database.

Houot, M., Ngo, Y., Munteanu, M., Marque, S., & Polynard, T. (2016). Systematic review with meta-analysis: direct comparisons of biomarkers for the diagnosis of fibrosis in chronic hepatitis C and B. *Alimentary Pharmacology and Therapeutics*, 43 (1), 16-29. Abstract retrieved July 18, 2017 from PubMed database.

Lam, S., Nettel-Aguirre, A., Van Biervliet, S., Roeb, E., Sadler, M., Friedrich-Rust, M., et al. (2019). Transient elastography in the evaluation of cystic fibrosis-associated liver disease: systematic review and meta-analysis. *Journal of the Canadian Association of Gastroenterology*, 2 (2), 71-80. (Level 2 evidence)

Li, Y., Huang, Y., Wang, Z., Yang, Z, Sun, F., Zhan, S. (2016). Systematic review with meta-analysis: the diagnostic accuracy of transient elastography for the staging of liver fibrosis in patients with chronic hepatitis B. *Alimentary Pharmacology and Therapeutics*, 43 (4), 458-469. Abstract retrieved July 18, 2017 from PubMed database.

National Institute for Health and Care Excellence. (2017). *Hepatitis B (chronic): diagnosis and management*. Retrieved August 6, 2018 from [www.nice.uk/guidance](http://www.nice.uk/guidance).

Roulot, D., Roudot-Thoraval, F., NKontchou, G., Kouacou, N., Costes, J., Elourimi, G., et al. (2017). Concomitant screening for liver fibrosis and steatosis in French type 2 diabetic patients using Fibrosan. *Liver International*, 37 (12), 1897-1906. Abstract retrieved July 18, 2017 from PubMed database.

Shen, Y., Wu, S.D., Wu, L., Wang, S.Q., Chen, Y., Liu, L.L., et al. (2019). The prognostic role of liver stiffness in patients with chronic liver disease: a systematic review and dose-response meta-analysis. *Hepatology International*, 13 (5), 560-572. Abstract retrieved July 19, 2019 from PubMed database.

Singh, S., Venkatesh, S.K., Wang, Z., Miller, F.H., Motosugi, U., Low, R.N., et al. (2015). Diagnostic performance of magnetic resonance elastography in staging liver fibrosis: a systematic review and meta-analysis of individual participant data. *Clinical Gastroenterology and Hepatology*, 13 (3), 440-451.e6. (Level 2 evidence)

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U.S. Food and Drug Administration. (2013, April). Center for Devices and Radiological Health. 510(k) *Premarket Notification Database*. K123806 (FibroScan®). Retrieved July 18, 2017 from <https://www.accessdata.fda.gov>.

Winifred S. Hayes, Inc. Medical Technology Directory. (2020, July). *Ultrasound transient elastography for detecting hepatic fibrosis in patients with hepatitis C*. Retrieved March 9, 2021 from [www.Hayesinc.com/subscribers](http://www.Hayesinc.com/subscribers). (80 articles and/or guidelines reviewed)

Winifred S. Hayes, Inc. Health Technical Assessment. (2019, April; last update search August 2020). *Acoustic radiation force impulse (ARFI) elastography for detecting hepatic fibrosis In patients with hepatitis C*. Retrieved March 9, 2021 from [www.Hayesinc.com/subscribers](http://www.Hayesinc.com/subscribers). (84 articles and/or guidelines reviewed)

Winifred S. Hayes, Inc. Health Technology Assessment. (2016, January; last update search June 2020). *Magnetic resonance elastography for detecting and staging liver fibrosis*. Retrieved July 18, 2019 from [www.Hayesinc.com/subscribers](http://www.Hayesinc.com/subscribers). (55 articles and/or guidelines reviewed)

Winifred S. Hayes, Inc. Health Technology Assessment. (2020, April). *Magnetic resonance elastography for prognosis of liver disease progression*. Retrieved March 9, 2021 from [www.Hayesinc.com/subscribers](http://www.Hayesinc.com/subscribers). (58 articles and/or guidelines reviewed)

Xiao, H., Shi, M., Xie, Y., & Chi, X. (2017). Comparison of diagnostic accuracy of magnetic resonance elastography and Fibroscan for detecting liver fibrosis in chronic hepatitis B patients: A systematic review and meta-analysis. *PLoS ONE*, 12 (11), e0186660. Abstract retrieved March 9, 2021 from PubMed database.

Xu, X., Kong, H., Song, R., Zhai, Y., Wu, X., Ai, W., et al. (2013). The effectiveness of noninvasive biomarkers to predict hepatitis B-related significant fibrosis and cirrhosis: A systematic review and meta-analysis of diagnostic test accuracy. *PLOS One*. 9 (6), e100182. (Level 2 evidence)

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