

HelioLiver Dx as a Molecular Adjunct for Resolving Indeterminate Liver MRI Imaging and Access Limitations: A Four-Case Real-World Series

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OVERVIEW

Indeterminate liver findings can delay definitive HCC diagnosis and treatment, particularly when repeat CT or MRI is inconclusive, inaccessible, or contraindicated. HelioLiver may provide complementary molecular evidence to help reduce diagnostic uncertainty and support more informed surveillance and management decisions.

INTRODUCTION

Indeterminate liver observations represent an important diagnostic gap in patients with cirrhosis who are at risk for hepatocellular carcinoma (HCC). Liver Imaging Reporting and Data System category 3 (LR-3) observations carry an intermediate probability of malignancy, with an estimated 38% ultimately representing HCC¹. Current guidance recommends repeat CT or MRI within 3–6 months². However, cross-sectional imaging may remain inconclusive, be delayed, or be contraindicated. Such delays may be clinically meaningful, as the pooled HCC tumor-volume doubling time is approximately 4.6 months, and about 35% of tumors demonstrate rapid growth with doubling times under 3 months³. Prolonged diagnostic uncertainty may therefore allow disease progression and reduce opportunities for curative treatment. HelioLiver™ Dx is a multi-analyte blood-based test integrating cell-free DNA methylation, serum protein biomarkers, and demographic variables. It may provide complementary molecular evidence when imaging is equivocal or when access to multiphasic CT or MRI is limited. This analysis presents patient-level, real-world evidence evaluating the clinical utility of HelioLiver in scenarios involving indeterminate liver MRI findings or barriers to definitive cross-sectional imaging.

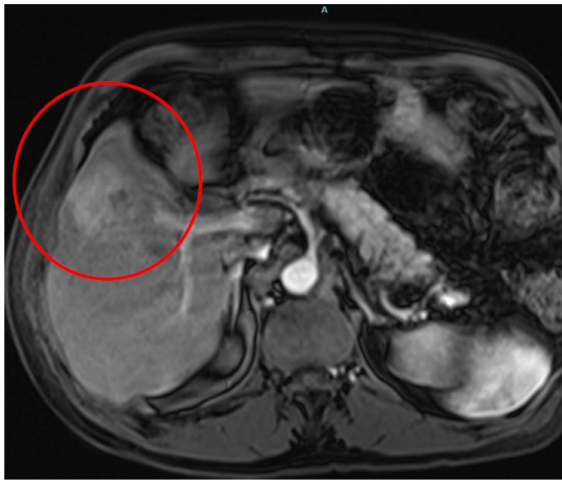
METHODS

We present a real-world case series of 4 patients with cirrhosis and either unresolved imaging findings or limited access to MRI. Clinical characteristics, imaging, AFP, HelioLiver results, follow-up, and the impact of testing on clinical management were evaluated.

RESULTS

Case #1

63-year-old male with hepatitis B-related cirrhosis, asymptomatic and referred for evaluation of a newly detected liver lesion. MRI demonstrated a 3.5 cm segment 5/8 mass with arterial enhancement and central delayed enhancement, but no washout, classified as LI-RADS 3 (LR-3).



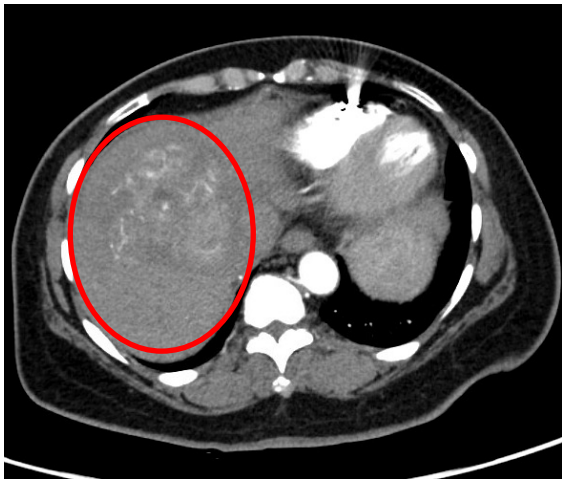
HelioLiver Result: Abnormal/Positive

Test	Value
AFP	12.7 ng/mL (ref range 0.3 – 12.1 ng/mL)
AFP-L3%	18.1 % (ref range <10 %)
DCP	Normal (ref range < 7.7 ng/mL)
Methylation score	0.86 (ref range < 0.57)

- The abnormal HelioLiver result prompted biopsy of the liver mass, which confirmed moderately differentiated HCC.
- Without a positive HelioLiver result, biopsy may have been delayed, and management would likely have involved serial imaging every 3 months, allowing further tumor growth in the interim.
- The patient subsequently underwent successful Y-90 radioembolization and is now awaiting liver transplant.

Case #2

62-year-old female with MASH cirrhosis, MELD 15, and severe congestive heart failure (EF 20–30%), precluding liver transplantation. An AICD prevented MRI evaluation, and she was on lifelong Plavix. CT demonstrated a large 8 cm arterially enhancing hepatic mass with equivocal washout; AFP was normal.



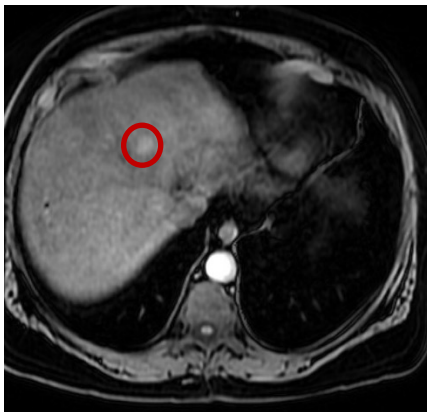
HelioLiver Result: Abnormal/Positive

Test	Value
AFP	3.5 ng/mL (ref range 0.3 – 12.1 ng/mL)
AFP-L3%	NC (ref range <10 %)
DCP	Normal (ref range < 7.7 ng/mL)
Methylation score	0.95 (ref range < 0.57)

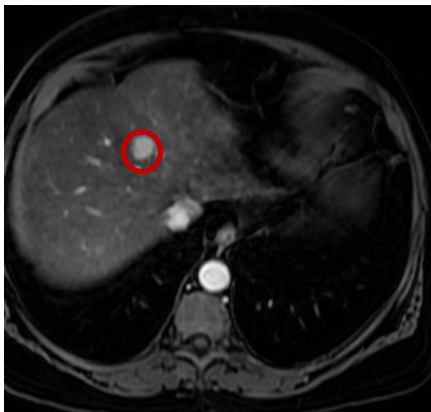
- The case demonstrates that a large infiltrative HCC can still present with a normal AFP.
- Given the clinical concern for HCC, an abnormal HelioLiver helped confirm the diagnosis of HCC and avoid the need for a high-risk biopsy (on lifelong Plavix).
- The patient proceeded with palliative Y90 radioembolization.

Case #3

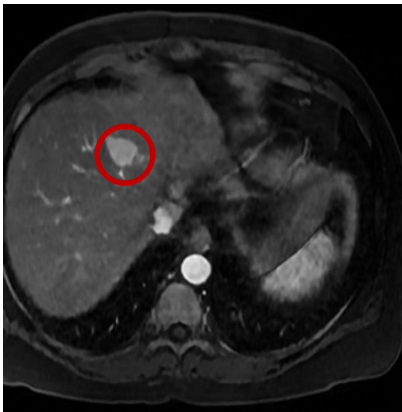
65-year-old female with hereditary hemochromatosis-related cirrhosis (MELD score 15). Routine HCC surveillance MRI identified a 1.4 cm in segment IV lesion with arterial enhancement without washout. The radiology interpretation favored a dysplastic nodule or benign nodule related to iron deposition.



8/2025 – 1.4 arterial enhancing lesion, no washout. Segment IVA. Read as dysplastic nodule. *Helio liver lab result below



12/2025 – 1.6 arterial enhancing lesion, no washout. Segment IVA. LR3



3/2026 – 2.0 cm arterial enhancing lesion, now with washout. Segment IVA. LR5.

HelioLiver Result: Abnormal/Positive

Test	Value
AFP	2.6 ng/mL (ref range 0.3 – 12.1 ng/mL)
AFP-L3%	19.8 (ref range <10 %)
DCP	0.4 (ref range < 7.7 ng/mL)
Methylation score	0.78 (ref range < 0.57)

- A positive HelioLiver result in August 2025 increased clinical suspicion that the initially favored benign/dysplastic nodule represented early HCC.
- The case illustrates the potential value of HelioLiver in prompting closer evaluation of indeterminate liver lesions.
- The lesion was closely monitored and has now reached 2 cm; the patient is planned for Y-90 radioembolization followed by liver transplant listing.

Case #4

34-year-old male, who presented with abdominal pain, CT found to have a 11.8 x 11.5 x 9.9 cm mass at the junction of right and left lobes. Described as a heterogeneous mass with microscopic fat, faint pseudocapsule with equivocal washout.



HelioLiver Result: Normal/Negative

Test	Value
AFP	1.8 ng/mL (ref range 0.3 – 12.1 ng/mL)
AFP-L3%	NC
DCP	0.7 ng/mL (ref range < 7.7 ng/mL)
Methylation score	0.37 (ref range < 0.57)

- Given the negative HelioLiver result, biopsy was pursued before considering a potentially complex surgical resection due to the lesion's location.
- Multiple core biopsies showed benign liver tissue with no malignant cells.
- Repeat imaging 6 months later showed no interval growth, further supporting a benign diagnosis.
- The negative HelioLiver result helped avoid a potentially high-risk major surgery for a benign liver mass.

CONCLUSIONS

- When MRI findings are inconclusive or MRI cannot be performed, HelioLiver helps resolve diagnostic uncertainty and supports more confident patient management.
- A positive result can prompt timely targeted imaging, biopsy, or closer follow-up, creating an opportunity for earlier HCC detection and treatment.
- A negative result can provide clinical reassurance, help avoid unnecessary procedures, and allow clinicians to focus surveillance resources on patients at higher risk.
- These cases demonstrate the potential clinical utility of HelioLiver Dx as an adjunct for diagnostic imaging in patients with indeterminate lesions or limited access to CT/MRI. Incorporating a blood-based molecular signal into diagnostic pathways may help resolve ambiguity, reduce delays, and support timely, risk-appropriate management before potentially curable HCC progresses. .

REFERENCES

- Lee S, et al. Percentages of hepatocellular carcinoma in LI-RADS categories with CT and MRI: A systematic review and meta-analysis. Radiology. 2023;307(1):e220646. doi:10.1148/radiol.220646
- Singal AG, et al. AASLD Practice Guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. Hepatology. 2023;78(6):1922-1965. doi:10.1097/HEP.0000000000000466.
- Nathani P, et al. Hepatocellular carcinoma tumour volume doubling time: A systematic review and meta-analysis. Gut. 2021;70(2):401-407. doi:10.1136/gutjnl-2020-321040.