

HelioLiver Dx Provides a Molecular Lead-Time Advantage for Earlier HCC Risk Stratification

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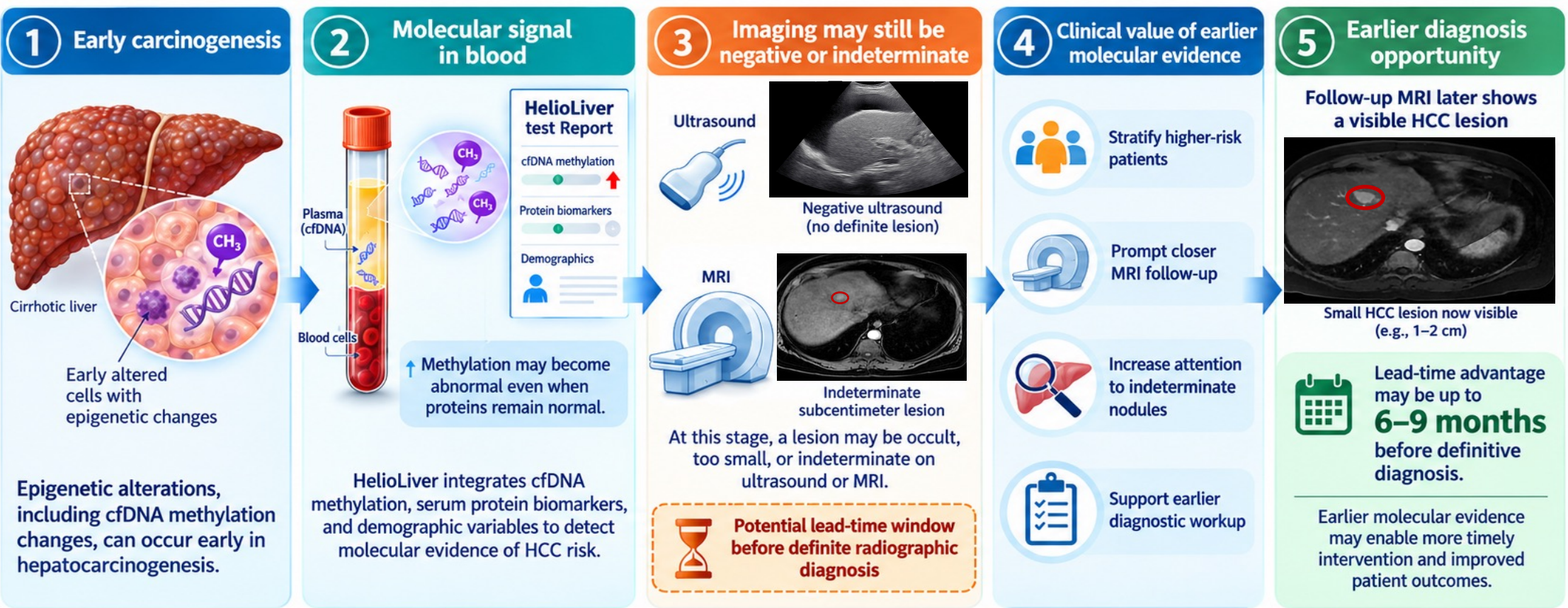
OVERVIEW

Early HCC can remain radiographically occult or indeterminate even on multiphasic MRI. Because cfDNA methylation changes can arise early in hepatocarcinogenesis, HelioLiver Dx may detect tumor-associated molecular signals before a lesion is definitively visible on imaging, providing a potential lead-time advantage of up to 6–9 months in these real-world cases and enabling closer surveillance and earlier diagnostic evaluation.

INTRODUCTION

Multiphasic magnetic resonance imaging (MRI) is a principal modality for the noninvasive diagnosis of hepatocellular carcinoma (HCC), yet very small or early-stage tumors may remain radiographically occult or fail to meet definitive imaging criteria¹. This creates a diagnostic window during which tumor biology may already be present despite negative or indeterminate imaging. Epigenetic dysregulation is an early event in hepatocarcinogenesis, and tumor-associated cell-free DNA (cfDNA) methylation changes may therefore become detectable in blood before a lesion can be visualized or definitively classified by imaging². HelioLiver™ Dx is a multi-analyte blood test for early HCC detection that integrates cfDNA methylation with serum protein biomarkers and demographic variables. In the prospective CLIMB study, HelioLiver demonstrated greater sensitivity than ultrasound, with a particularly notable advantage in small and T1 tumors³. Earlier molecular evidence of HCC may help identify patients who warrant closer imaging surveillance, shorter-interval follow-up, or additional diagnostic evaluation, potentially reducing delays until radiographic confirmation while disease remains within a stage amenable to potentially curative therapy. This analysis presents patient-level evidence illustrating the potential of HelioLiver to detect tumor-associated molecular signals before HCC becomes radiographically visible or classifiable.

cfDNA methylation abnormalities may emerge before small HCC lesions are clearly visible on imaging



 **HelioLiver** may complement imaging by revealing early molecular evidence of HCC before lesions are clearly visible, helping to enable earlier risk stratification, closer follow-up, and more timely diagnostic workup.

METHODS

We reviewed 2 real-world cases of patients with cirrhosis. Clinical characteristics, imaging, AFP, HelioLiver Dx results,, and longitudinal follow-up were collected to assess the impact of testing on clinical management and diagnostic evaluation.

RESULTS

Case #1

Patient Overview: 77-year-old man with well-compensated cirrhosis secondary to MASH



Treatment and Management

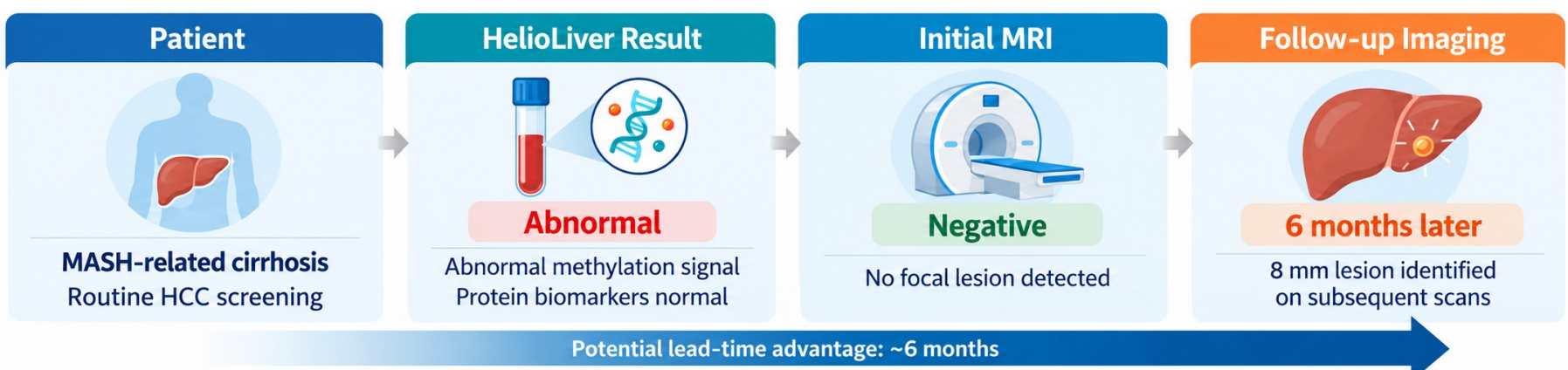
- The patient received five rounds of SBRT and was referred for liver-transplant evaluation.

Key Takeaway

- HelioLiver detected a molecular signal of HCC approximately six months before the tumor became visible on imaging, enabling closer surveillance and timely clinical intervention.

Case #2

Patient Overview: Patient with MASH-related cirrhosis



Treatment and Management

- The patient will undergo close imaging surveillance with repeat MRI every 3 months.

Key Takeaway

- The initial MRI failed to detect the early-stage tumor, likely due to its small size and atypical vascular pattern
- HelioLiver identified biological signals before the tumor became radiographically visible

CONCLUSIONS

- HelioLiver Dx may detect HCC before lesions become radiographically visible or definitively classifiable, providing a potential lead-time advantage in some patients.
- Tumor-associated cfDNA methylation signals may emerge before structural abnormalities are detectable on MRI, suggesting that some apparent HelioLiver “false positives” may instead reflect occult disease not yet visible on imaging.
- Because an occult lesion generally cannot be treated until it is localized and diagnostically confirmed, the immediate value of an abnormal HelioLiver Dx result may be to better risk-stratify patients and identify those who warrant intensified surveillance or shorter imaging intervals.
- Earlier escalation of surveillance may allow HCC to be identified while tumors remain small, and patients are still eligible for potentially curative treatment.
- Systematic real-world evidence collection is ongoing to further define clinical trajectories in which cfDNA methylation signals precede MRI confirmation.

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