



## CASCADE 2027 NON-CONFIDENTIAL SUMMARY »

# Early Biopsy-Free Liver Cancer Diagnosis on Existing Ultrasound Scanners

## Overview

On contrast-enhanced ultrasound (CEUS), a low-cost, radiation-free liver exam, about 7 in 10 lesions labeled “probably cancer” turn out to be cancer, yet the scan alone can’t confirm them. Patients are left with repeat imaging or a needle biopsy, and timing matters: five-year survival is 37% when liver cancer is found while still localized, versus 3% once it has spread. UW researchers have developed a simple add-on to the standard CEUS exam. In preclinical studies, a brief ultrasound pulse, applied while the usual FDA-approved microbubble contrast agent circulates, temporarily stops blood flow inside tumors while normal liver tissue stays perfused, so a follow-up contrast scan shows any tumor as a dark void.

- **A clearer answer without a biopsy:** The test aims to resolve suspicious lesions at the scan itself, reducing reliance on needle biopsy, which in liver cancer carries about a 2.7% risk of spreading tumor cells along the needle path.
- **Runs on equipment hospitals already own:** It is delivered as a programmed pulse sequence on clinical ultrasound scanners, using contrast agents already approved for patient use; a small stand-alone pulse device is an alternative embodiment.
- **Beyond the liver:** The approach may extend to other solid tumors reachable by ultrasound, including deadly cancers such as kidney, prostate, pancreatic, and ovarian cancer, for which no proven routine screening test exists today.

## Description

This is a diagnostic imaging method for oncology, initially aimed at patients whose liver lesions are being evaluated for hepatocellular carcinoma (HCC), the most common primary liver cancer. It builds on a phenomenon the Averkiou lab calls transient tumor perfusion loss (TTPL): tumor blood vessels are small, immature, and poorly formed, so they respond to the mechanical forces of oscillating microbubbles by briefly shutting down, while normal vessels do not. The workflow has three steps: inject a standard ultrasound contrast agent, deliver a short ultrasound pulse to the organ of interest, then re-inject contrast and run a standard CEUS scan, in which tumors appear as contrast-free voids. Rather than relying only on how a lesion looks, the test measures how it responds to a controlled challenge, giving clinicians an additional, independent signal.

- **Key differentiator:** Because the response appears specific to tumor vessels, the pulse can in principle be applied across a whole organ without knowing in advance where a lesion is, and the result is read in the same exam on the same scanner.

### COMOTION REFERENCE »

BDP 9290

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- **Proof of concept:** In published mouse studies of liver cancer, the team induced tumor-selective loss of blood flow using a modified commercial clinical scanner and clinically approved microbubbles, without significant tissue damage at moderate settings. Blood flow largely recovered within about 15 minutes at moderate settings, while the highest settings caused some tissue injury.
- **Development status:** Work to date was carried out in a therapeutic (drug-delivery) context, and the diagnostic use, including how well the test separates cancers from benign lesions, has not yet been tested. The previous work was done on two mouse tumor models, one subcutaneous nude athymic mice and one orthotopic genetically engineered pten-null mouse model. Planned next steps are optimizing the pulse on a standard abdominal ultrasound probe in an orthotopic liver-cancer mouse model, followed by an initial feasibility study in patients with malignant and benign liver lesions.

## Technology Readiness Level (TRL)

**TRL 3 —Experiments and analysis demonstrate critical functions and/or proof of concept.** The core effect, a tumor-selective and reversible loss of blood flow visible on CEUS, has been demonstrated in multiple mouse models of liver cancer using a modified clinical ultrasound scanner and clinically approved contrast agents. A diagnostic prototype, manufacturing, and validation in patients have not yet been completed.

## Value Proposition

- **Earlier diagnosis:** Aims to flag cancers that current CEUS scoring leaves indeterminate, so patients can be treated while curative options remain.
- **Fits the existing exam:** Adds a brief step to a standard CEUS exam, using the same FDA-approved contrast agents and ultrasound settings that are slightly modified but still within FDA diagnostic limits.
- **Runs on existing scanners:** Delivered as a programmed pulse sequence on clinical ultrasound equipment, with no new imaging system to buy; alternatively, the pulse could ship as a small stand-alone device as a distributable product.
- **Lower cost and broader access:** Ultrasound is cheaper, portable, and radiation-free compared with CT and MRI, which could bring better liver cancer detection to community and rural settings and, potentially, to handheld devices.
- **Fewer biopsies and inconclusive follow-ups:** A clearer answer at the ultrasound exam could spare patients needle biopsies and ambiguous CT or MRI scans.

## Intellectual Property Position

Patent application pending.

## Market Opportunity

- **Customers and users:** Hospital radiology departments and imaging centers that evaluate liver lesions are the primary customers, with radiologists and sonographers as users. Ultrasound scanner manufacturers are natural licensing and distribution partners.

- **Market drivers:** HCC accounts for an estimated 750,000 new diagnoses per year worldwide, and incidence is rising with chronic liver disease from viral hepatitis, alcohol, and metabolic (fatty liver) disease. Fewer than about 30% of patients are diagnosed early enough for curative treatment.
- **Unmet need:** On CEUS, the standard “definite cancer” category (LI-RADS LR-5) catches only about 70% of liver cancers, while about 70% of “probable” (LR-4) and 40% of “intermediate” (LR-3) lesions prove to be cancer. Those patients wait through repeat imaging or undergo biopsy before treatment can start. Similar unmet needs exist in detecting other cancers.
- **Competitive landscape:** The method complements rather than replaces contrast CT, MRI, and existing CEUS criteria by adding an independent signal for indeterminate lesions, though with strong results it could replace some of those exams. Its commercial value will depend on showing that benign lesions do not respond the same way.
- **Expansion opportunities:** Clearer tumor margins could also support treatment planning by revealing small satellite lesions that drive recurrence. Other solid tumors are a larger prize: pancreatic cancer has no recommended screening test for average-risk adults (five-year survival 13% overall, 44% when localized), and screening for ovarian cancer, including with transvaginal ultrasound, has not been shown to reduce deaths (five-year survival 92% when localized, 32% once spread).

## References

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