

## The Hercules study: A prospective real-world evaluation of screening whole-body MRI (sWB-MRI) for multi-cancer detection and general preventive healthcare.

Yosef Chodakiewitz, Jeffrey Michael Venstrom, Daniel J. Durand, Sean London, Ty Vachon, Vikash Modi, Jason Itri, Amar Patel, Pratik Shingru, Sam Hashemi, Perry Kaneriyia; Prenuvo, Vancouver, BC, Canada; Prenuvo, Redwood City, CA; Hercules Research Center, Watertown, MA

**Background:** Cancer remains a leading cause of mortality, with major gaps in early detection contributing to later-stage diagnoses and poorer outcomes. While single cancer screening methods are effective for specific populations, they leave most cancers undiagnosed such that only 14% of cancers are detected through screening. Multi-cancer detection technologies, such as screening whole-body MRI (sWB-MRI), address this gap by enabling simultaneous systemic cancer risk stratification. Advances in sWB-MRI protocols, including whole-body diffusion-weighted imaging, improve tumor detection without the use of ionizing radiation or contrast agents. This positions sWB-MRI as a non-invasive, radiation-free tool for preventive care suitable for longitudinal monitoring. The need for prospective studies using standardized image acquisition and reporting frameworks, larger cohorts, and long-term follow-up data motivated this study. **Methods:** The Hercules Project is a prospective real-world data study evaluating the predictive accuracy and utility of sWB-MRI for detecting cancer and other clinically significant diagnoses (CSD). Radiological scoring frameworks used include: ONCO-RADS: A validated 5-point scale stratifying cancer risk, from no oncological relevance (ONCO-1) to highly suspicious (ONCO-5). CSD Framework: A novel 5-point scale categorizing pathologies (not limited to cancer) from no clinical relevance (CSD-1) to findings requiring expedited follow-up (CSD-5). Radiologists assign ONCO-RADS and CSD scores during scan interpretation, applied to structured reports by body region and organ system. These frameworks support sensitivity, specificity, PPV and NPV analyses by type of diagnosis. Follow-up at 12–18 months compares findings with diagnostic confirmation and clinical outcomes, enabling analysis of diagnostic pathways and long-term patient impact. Participants are enrolled via one of two arms: Pragmatic: Self-funded participants paying participation-fees reflecting typical U.S. out-of-pocket costs for sWB-MRI. Health Equity: Subsidized access (10–50% of cohort) reduces financial barriers for underserved populations, with sliding-scale subsidies (50–100%) based on socioeconomic factors. Endpoints: Primary endpoints include diagnostic accuracy (sensitivity, specificity, ROC AUC, PPV, NPV), time-to-diagnosis, stage at detection, healthcare utilization (e.g. TCOC), and cost-effectiveness (e.g., QALY). Exploratory endpoints assess the impact of socioeconomic and biological factors on disparities, and the utility of sWB-MRI enabled multi-dimensional diagnostics structured by ONCO-RADS and CSD frameworks. Trial Info: The study is active at a research-dedicated MRI center in Boston, with IRB approval for multi-center expansion to 20 locations. Clinical trial information: NCT06212479. Research Sponsor: None.