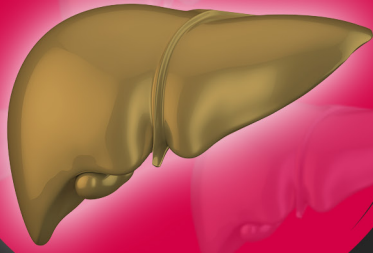


AFP-L3 & DCP



HCC Surveillance Algorithm

UCSD routine surveillance algorithm

A regular surveillance program for patients at risk for development of Hepatocellular Carcinoma (HCC) is recommended by clinical practice guidelines worldwide [1-6]. The following surveillance algorithm is currently in place at the University of California San Diego (UCSD) [Figure]. Dr. Yuko Kono, an Associate Clinical Professor at the UCSD Health System, performs regular surveillance on her patients at risk for HCC development. Serum biomarkers lectin-reactive alpha-fetoprotein (AFP-L3), alpha-fetoprotein (AFP) and des-gamma-carboxy prothrombin (DCP) are performed routinely in combination with ultrasound at a frequency of every 6 months. If ultrasound is negative, but one or more of the HCC biomarkers are positive, the patients are escalated to enhanced imaging for further evaluation.

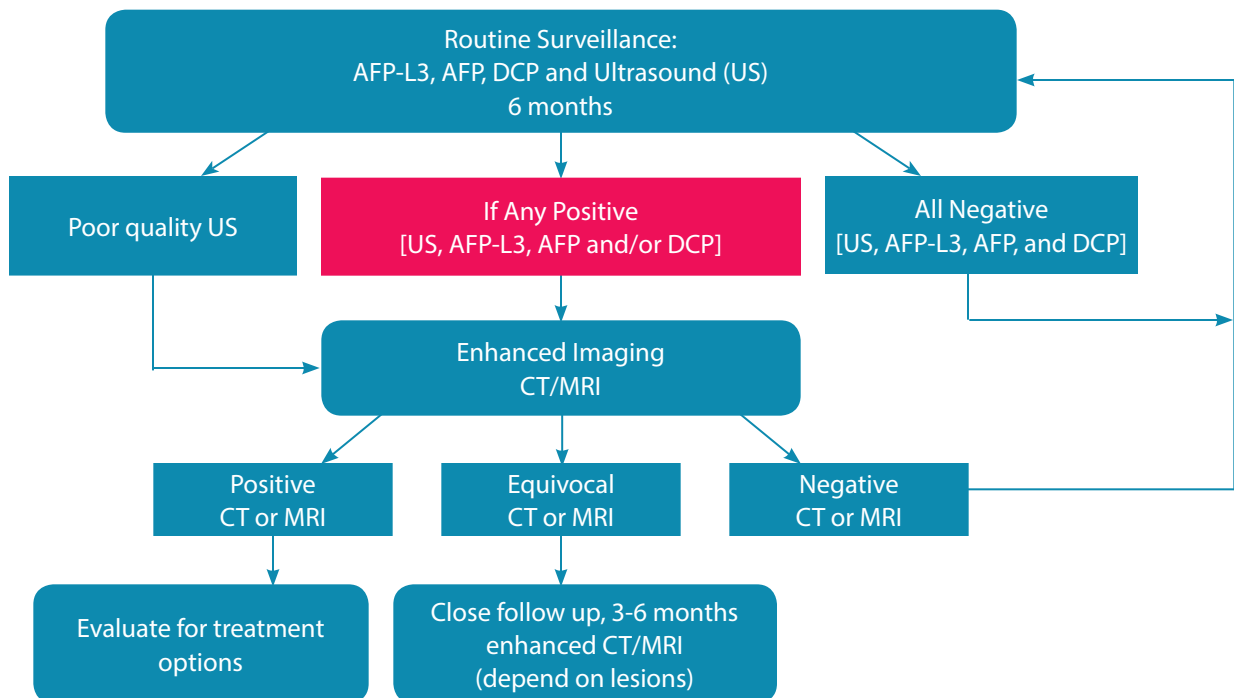


Figure: UCSD routine surveillance algorithm.
Cutoff points for positive results: AFP-L3 \geq 10%; DCP \geq 7.5 ng/mL; AFP \geq 20 to 200 ng/mL (depending on clinical scenario)

Studies have shown that although each biomarker can be clinically useful on its own for risk assessment of HCC, due to the heterogeneity of HCC tumors, using the biomarkers in combination can yield better clinical performance [7-9]. As such, the HCC biomarkers in combination (AFP-L3, AFP and DCP) are increasingly becoming part of surveillance protocols in U.S. clinics [10].

Table: Practice guidelines for HCC surveillance

Organizations	Surveillance Recommendation
AASLD American Association for the Study of Liver Diseases [1]	Ultrasound every 6 months
EASL European Association for the Study of the Liver [2]	Ultrasound every 6 months (AFP denoted as risk marker)
APASL Asian-Pacific Association for the Study of the Liver [3]	AFP + ultrasound every 6 months (AFP-L3/DCP noted as options based on medical circumstance)
NCCN National Comprehensive Cancer Network [4]	AFP + ultrasound every 6-12 months
VA United States Department of Veterans Affairs [5]	AFP + ultrasound every 6-12 months
JSH Japan Society of Hepatology [6]	AFP/AFP-L3/DCP + ultrasound every 3-6 months

ACKNOWLEDGEMENT

We want to thank Dr. Yuko Kono for sharing the University of California San Diego (UCSD) Health System surveillance algorithm. Dr. Yuko Kono is a practicing Hepatologist with expertise in contrast enhanced ultrasound imaging and has a special interest in HCC Surveillance.

REFERENCES

- 1 Bruix J, Sherman, M. AASLD Practice Guideline. Management of hepatocellular carcinoma, An Update. *Hepatology* 2011;53(3): 1020-1022.
- 2 European Association for the Study of the Liver; European Organisation for Research and Treatment of Cancer. EASL-EORTC clinical practice guidelines: management of hepatocellular carcinoma. *J Hepatol.* 2012;56(4):908–943.
- 3 Omata M. et. al. Asian Pacific Association for the Study of the Liver consensus recommendations on hepatocellular carcinoma. *Hepatol Int.* 2010;4(2):439–474.
- 4 National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology, hepatobiliary cancers. https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf. Version 1, 2017 [March 1, 2017]. Accessed March 17, 2017
- 5 United States Department of Veterans Affairs. Management of hepatocellular carcinoma. <http://www.hepatitis.va.gov/pdf/2009HCC-guidelines.pdf>. Published September 2009. Accessed March 17, 2017.
- 6 Makuuchi M, et al. Development of evidence-based clinical guidelines for the diagnosis and treatment of hepatocellular carcinoma in Japan. *Hepatol Res.* 2008;38:37-51.
- 7 Ertle JM, et al. A Combination of α -Fetoprotein and Des- γ -Carboxy Prothrombin Is Superior in Detection of Hepatocellular Carcinoma. *Digestion.* 2013;87:121-31.
- 8 Choi JY, et al. Diagnostic value of AFP-L3 and PIVKA-II in hepatocellular carcinoma according to total-AFP. *World J Gastroenterol.* 2013;19:339-46.
- 9 Hann HW, et al. Usefulness of highly sensitive AFP-L3 and DCP in surveillance for hepatocellular carcinoma in patients with a normal alpha-fetoprotein. *J Med Microb Diagn.* 2014;3:130.
- 10 Gish R. Early Detection of Hepatocellular Carcinoma through surveillance using biomarkers, *Gastroenterology and Hepatology.* 2014;10:121-3.