SUPERIOR DIAGNOSTIC PERFORMANCE: THE GALAD SCORE

In a new approach, investigators led by Prof. Dr. P.J. Johnson from the UK established an algorithm, in which **G**ender, **A**ge, AFP-**L**3, **A**FP and **D**CP are calculated. This **GALAD** score can detect early stages of HCC at a sensitivity of at least 75% and a specificity of 89%[7].

Recently the GALAD model was validated in an international setting by analysing nearly 7000 datasets from the UK, Germany, Japan and Hong Kong. AUROC analysis in all cohorts showed better values for GALAD compared to individual or combined markers. The performance of the model didn't vary when comparing different aetiologies such as HBV, HCV and "others". Similarly, for small and early HCC the model gave AUC values of at least 0,85 and could successfully discriminate between HCC and other hepatobiliary cancers[8].

DETERMINATION OF AFP-L3 AND DCP

The tests can be ordered from the following laboratories:

Institution:	**University Hospital Essen**
Department:	Prof. Dr. med. Gerken Clinic of Gastroenterology and Hepatology
Contact to the lab:	**Dr. med. Wichert**
e-mail:	marc.wichert@uk-essen.de

Institution:	**Hannover Medical School (MHH)**
Department:	Prof. Dr. med. Manns Department of Gastroenterology, Hepatology and Endocrinology
Contact:	**Prof. Dr. med. Vogel**
e-mail:	vogel.arndt@mh-hannover.de
Contact to the lab:	**Prof. Dr. med. Wedemeyer**
e-mail:	wedemeyer.heiner@mh-hannover.de

Institution:	**Institute for Medical Diagnostics**
	Berlin-Potsdam MVZ GbR
Contact to the lab:	**Dr. med. Rasenack**
e-mail:	t.rasenack@imd-berlin.de

In other countries, the tests are available by:

Country:	**Romania**
Distributor:	Proton Impex 2000 S.R.L.
Contact person:	**Mr. Eugen Ioan**
e-mail:	eugen.ioan@proton.com.ro

LITERATURE

1 EASL-EORTC Clinical Practice Guidelines: Management of hepatocellular carcinoma. J Hepatol 2012 (56): 908-943
2 Kagebayashi C et al. Automated immunoassay system for AFP-L3% using on-chip electrokinetic reaction and separation by affinity electrophoresis. Anal Biochem 2009, 15;388 (2): 306-11
3 Ertle J et al. A combination of α-fetoprotein and des-γ-carboxy prothrombin is superior in detection of hepatocellular carcinoma. Digestion 2013;87(2):121-31
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5 Toyoda et al. Clinical utility of highly sensitive Lens culinaris agglutinin-reactive alpha-fetoprotein in hepatocellular carcinoma patients with alpha-fetoprotein <20 ng/mL. Cancer Sci. 2011;102(5):1025-31
6 Choi JY et al. Diagnostic value of AFP-L3 and PIVKA-II in hepatocellular carcinoma according to total-AFP. World J Gastroenterol 2013 Jan 21; 19(3):339-346
7 Johnson P et al. The detection of hepatocellular carcinoma using a prospectively developed and validated model based on serological biomarkers. Cancer Epidemiol Biomarkers Prev. 2014 Jan;23(1):144-53
8 Berhane S et al. Role of the GALAD and BALAD-2 Serologic Models in Diagnosis of Hepatocellular Carcinoma and Prediction of Survival in Patients. Clin Gastroenterol Hepatol. 2016 Jan 13; Epub ahead of print

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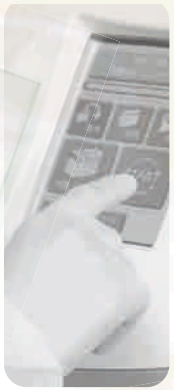
- HCC
- High Sensitivity
- Early Serological Recognition

DCP
AFP-L3

DETECTION OF HEPATOCELLULAR CARCINOMA

In Europe, about 70% of all Hepatocellular Carcinoma (HCC) cases are diagnosed at an advanced stage. Curative treatment options are only available for a minority of patients. Optimal surveillance of at risk patients for the early detection of HCC is of crucial importance.



The current guideline from the European Association for the Study of the Liver (EASL) and the European Organization for Research and Treatment of Cancer (EORTC) recommends that at-risk patients be screened at 6 month intervals using abdominal ultrasound[1]. However, the detection of HCC in a cirrhotic or fatty liver by ultrasound can be challenging.

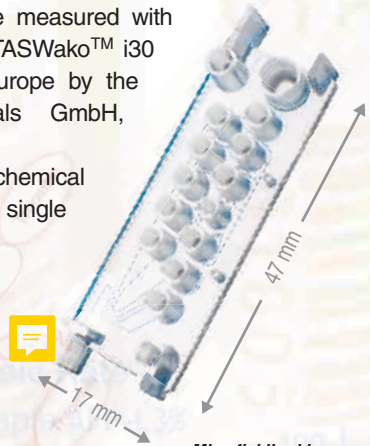
The biomarkers lectin-reactive alpha-fetoprotein (AFP-L3) and des-gamma-carboxy prothrombin (DCP) have been shown to be specific for the risk assessment of hepatocellular carcinoma (HCC). Their combined use aids in the clinical assessment for early detection. Adding AFP-L3 and DCP to HCC surveillance can increase the chances of detecting early HCC and therefore should be incorporated into regular surveillance practices. Both tests are now available in Europe as CE-marked *In Vitro* Diagnostics.

WHAT ARE AFP-L3 AND DCP?

AFP-L3 is an isoform of AFP with an additional fucose residue. This isoform interacts with the lectin *Lens culinaris* agglutinin (LCA). AFP-L3% is the ratio of AFP-L3 to total AFP as a percentage.

DCP (des-gamma-carboxy prothrombin) is an immature form of the coagulation protein, prothrombin. In normal liver, the prothrombin precursor undergoes post-translational vitamin K dependent carboxylation. In the case of HCC this reaction is impaired, resulting in secretion of non-carboxylated forms. DCP is also known as „Protein Induced by Vitamin K Absence or Antagonist II" (PIVKA-II).

AFP, AFP-L3 and DCP are measured with high sensitivity using the μTASWako™ i30 instrument distributed in Europe by the company Wako Chemicals GmbH, Neuss, Germany.
In this system, several biochemical analyses are carried out in a single microfluidic chip[2].

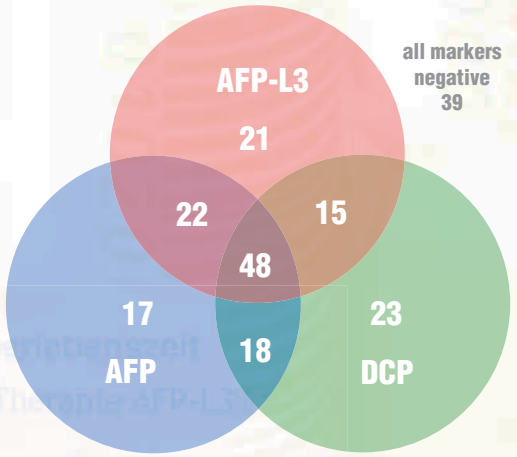


Microfluidic chip
original size

HOW TO USE AFP-L3 AND DCP?

Both, AFP-L3 and DCP, are intended for *in vitro* diagnostic use as an aid in the risk assessment for the development of HCC in conjunction with imaging studies, clinical assessment and other laboratory findings. Patients with elevated AFP-L3 values (≥10%) have been shown to have an increase in the risk of developing HCC within the next 21 months and should be more intensely evaluated for evidence of HCC according to existing HCC practice guidelines.

Several studies have shown that AFP-L3 and DCP are complementary markers. The combined use of these markers provides higher clinical sensitivity and is effective for the early detection of HCC[3/4].



Distribution of HCC patients with various patterns of positivity for the HCC biomarkers[4]

The determination of the markers enables the serum based detection of tumors in early stages even if the AFP shows negative results. In a broad investigation of 270 HCC patients, all of them with serum AFP less than 20 ng/ml, the use of the biomarkers in combination detected 49% of all patients with tumors ≤ 2cm[5]. All three markers AFP, AFP-L3 and DCP combined can detect HCC with a sensitivity of about 80% at a specificity of 90%[6].