# MODERN RADIOLOGICAL DIAGNOSIS OF HEPATOCELLULAR CARCINOMA

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## ABSTRACT

**Hepatocellular carcinoma is the most common primary tumour of the liver. It is characterized by a quick evolution and poor prognosis. The hepatocellular carcinoma is found out in patients with chronic liver diseases, mostly with chronic hepatitis B and C, where the risk is by 100 times higher than in the patients with cirrhosis of other etiology. The treatment is operative. Chemotherapy and radiotherapy don't exert any significant effect. The hepatocellular carcinoma is diagnosed by imaging examination methods. This review shows the opportunities of different contemporary methods for diagnosis of the hepatocellular carcinoma, its staging and subsequent treatment.**

**Key words:** *hepatocellular carcinoma, imaging method, ultrasound, computer tomography, magnetic resonance imaging, intraoperative ultrasound*

Final diagnosis in oncology is pathomorphological. However, the detection of hepatocellular carcinoma (HCC) is based on imaging methods and it is always a problem for the physicians. In the past, scintigraphy was the basic method for HC diagnosis. This does not represent a diagnostic method of choice anymore.

Usually, ultrasound examination (US) is the first and cheapest imaging instrumental method used in patients suspicious of presence of focal lesions of the liver. The main limitations of this method are the dependency on US specialist's experience and the equipment used, the difficulty in diffuse liver disease and the low specificity (25). The percutaneous US can't be used as the only method of diagnosis of HCC, however, it is suitable for screening (24). The sensitivity and specificity of US regarding the focal hepatic lesions increase with the introduction of the contrast-enhanced US (CEUS) and the method gets comparable to the contrast-enhanced computer tomography (CT) and magnetic resonance imaging (MRI) (27). This places CEUS in the diagnostic algorithm for distinguishing the malignant from the benign lesions before the puncture techniques (21).

In the end of the 70's, fine needle biopsy (FNB) under US control was introduced in the clinical practice to differentiate the focal lesions in liver parenchyma. FNB is not recommended for most cases because it is connected with poor survival rates after hepatic resection (22).

Spiral CT with contrast enhancement is the fundamental examination for initial staging and observation of HCC (8). This is extremely important for the malignant lesions in hepatic cirrhosis. Nowadays CT with arterioportography and CT arteriography are the most sensitive methods for detection of malignant hepatic lesions (10). However, they are invasive and expensive and lead to highly frequent falsely positive results.

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MRI is the basic method of additional imaging evaluation of the liver (29). In view of its high cost, MRI examination is performed when either the attending physician decides that it is necessary, or the patient is allergic to iodine.

Founding whatever lesion depends on its size and 'the difference in the contrast' between the lesion and the surrounding hepatic parenchyma (8). For that reason, contrast materials are obligatorily used providing greater difference ('contrast') between the intact and pathological tissue. HCC radiological characteristic consists in the arterial vascularity and venous wash off (14). This means that during the examination (CT, MRI or CEUS), the tumour has a brighter signal then the liver in the arterial phase, and in the venous or late phase of the examination the lesion is less contrasted then the surrounding hepatic parenchyma (23).

Positron-emission tomography (PET) is a very precise method in determining the presence or absence of hepatic metastases. However, its role in HCC is limited because its diagnostic sensitivity is 50-60% only (28).

The invasive methods of examination enhance the diagnostic opportunities. The image of the left lobe of the liver with a high resolution can be obtained with endoscopic US and FNB can be performed under its control (1). Laparoscopy and laparoscopic US are other invasive methods to diagnose and determine the optimal strategy of treatment of HCC (13).

Ultimately, the choice of imaging modality to detect, evaluate and follow-up the tumours of the liver must be based not only on the patient and its clinical conditions, but also on the experience in the imaging modalities within each medical institution.

Although there are many imaging methods, based on the preferences and experience of the institutions, CT is the most common imaging method of graphic examination of the liver in the diagnostics of patients with suspicious HCC (5).

Regardless of the attainments of the technologies, the sensitivity of the preoperative imaging modalities remains 60-80% (20). The small lesions in the liver may be early HCC, regenerative and dysplastic nodules. The early lesions must be operated with a high probability of recovery (19). They are most difficult to diagnose. In contrast to the classic HCC, early HCC is hypovascular due to a reduced portal venous supply of the lesion as well as because the arterial vascularization is not completely developed. There is a radiological pathognomonic sign of HCC, i. e., arterial vascularity and venous wash out (23).

Tumour markers don't have any high sensitivity nd specificity as well as they present with less organ specificity for diagnosing primary tumours or metastatic disease of the liver. Hopes are high that genome and proteome tumour markers will gain ground as early markers of malignancy.

Alpha-fetoprotein is widely used in following-up the primary HC, especially in patients with cirrhosis (16). Other perspective markers are des-gamma-carboxy-prothrombine (DCP) and AFP-L3%, the agglutinin reactive fraction of AFP (7,17). The role of AFP markers is challenged in the era of the sensitive imaging modalities (9), moreover, it is not included in the guidelines of observation of primary liver carcinoma of the American Association of Studying the Hepatic Diseases (18). The sensitivity and specificity of the AFP assay at entry at the cut off level of 20 ng/dL are 41% and 82%, respectively, with a positive predictive value of 46% and negative predictive value of 85% (3). AFP values >400 ng/mL are indicative of HCC. Thirty-percent of the patients with HCC <2 cm present with normal AFP and levels 20-250 ng/dL are common in regenerative nodules or viral cirrhosis. AFP elevation with time is actually of diagnostic value for HCC (4).

Hepatic resection surgery is still the golden standard in the treatment of the primary liver tumours with results unattainable for the other therapeutic methods - a five-year survival rate over 50% for HCC (15). Local treatment is the alternative of the operative treatment consisting in the so-called percutaneous methods such as cryoablation, radiofrequent ablation, microwave ablation, laser ablation, injecting of ethanol which are recommended in small tumours sized at an average up to 5 cm, and better, in smaller ones - up to 3 cm when there are contraindications for operative treatment (2). The experience with chemotherapy for HCC is disappointing, too, because of the low response and high toxicity. Sorafenib, an oral multikinase with activity toward tumour cellular proliferation and



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angiogenesis, has a moderate effect in advanced primary HC without any significant toxicity (12).

During operation, the surgeons routinely examine the liver by inspection and palpation. So, small and deeply localized lesions can be easily missed. The solid and uneven surface of the liver makes detecting by palpation the small HCC nodules quite difficult (30). Many of these impalpable lesions provide greater chances for the patient (11).

This deficiency must be compensated and thus the intraoperative ultrasound (IOUS) has been introduced in the clinical practice. In a study performed in the Naval Hospital of Varna, Military Medical Academy of Sofia, in 12 operated HCC patients, 11 men and one woman at a mean age of 58 years, during the period from 2007 to 2011, IOUS establishes additional malignant lesions, not detected by US and CT, in four (33,33%) and five (41,67%) patients, respectively. This is due to detecting the small lesions (<20 mm), where IOUS finds out 12 small lesions of a total of 25 ones, while US and CT detect one lesion each. The additional information from IOUS led to change of the operative plan in four patients (33,33% of the cases) (26).

In conclusion, we should note that the precise preoperative imaging diagnostics with defining the number, size and form of HCC, its localization and the interrelation with the intra- and extra-hepatic structures such as vascular and biliary vessels and neighbouring organs is of crucial significance for the effective operative removal of any detectable hepatic tumours. Unfortunately, notwithstanding the technologic progress in imaging diagnostic methods, the abovementioned literature data unambiguously indicate that at this stage, the non-operative staging of the liver tumours is not precise enough for the planning of effective treatment yet.

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