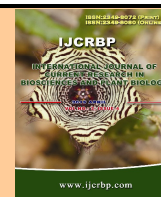




# International Journal of Current Research in Biosciences and Plant Biology

ISSN: 2349-8080 Volume 2 Number 4 (April-2015) pp. 112-116

[www.ijcrbp.com](http://www.ijcrbp.com)



## Review Article

### Diagnostic Techniques for the Determination of Hepatocellular Carcinoma - A Review

C. Venkatasalam<sup>1</sup> and A. Nagappan<sup>2\*</sup>

<sup>1</sup>Department of Electronics and Instrumentation Engineering, V.M.K.V. Engineering College, Salem-636 308, Tamil Nadu, India

<sup>2</sup>Department of Electronics and Communication Engineering, V.M.K.V. Engineering College, Salem-636 308, Tamil Nadu, India

\*Corresponding author.

Abstract	Keywords
<p>Hepatocellular carcinoma (HCC) is the most common form of liver cancer in adults. It begins in the hepatocytes-the main type of liver cell. About 3 out of 4 cancers that start in the liver are belonging to this type. HCC can have different growth patterns: some start as a single tumor that grows larger; only late in the disease does it spread to other parts of the liver; others seem to start in many spots throughout the liver, not as a single tumor. This is most often seen in people with ongoing liver damage (cirrhosis) and is the most common pattern noticed in India. Doctors can figure out the subtypes of hepatocellular cancer by looking at the cancer under a microscope. Most of these subtypes do not affect treatment or the patient's outlook. But one rare type, called fibrolamellar, has a much better outlook (prognosis) than other forms of liver cancer. The early detection of HCC is being obtained from the computed tomography (CT) and MRI scans. The various imaging techniques are also used to detect HCC. However, recent studies are much concerned with the early detection of HCC with more accuracy. The present study critically reviews the techniques which are helpful in enhancing the contrast and find the tumor in the early stage.</p>	<p>Cancer detection Hepatocellular carcinoma Imaging techniques Tumour Wavelets</p>

## Introduction

Hepatocellular carcinoma (HCC) is one of the major malignancies worldwide with the highest occurrence in Asia and sub-Saharan Africa (Bruix, 1997). The incidence of has increased all-inclusive and is now the 5<sup>th</sup> most common cancer representing approximately 5% of all cancer types in the world. More than

5,00,000 new cases are diagnosed every year and it is the third cause of cancer-related death and the first cause of death in patients with cirrhosis (Cho et al., 2010). Cirrhosis is the efficient and the most common recognized risk factor for HCC, particularly cirrhosis related to hepatitis C virus (HCV) and hepatitis B virus

(HBV) infections. (Lee et al., 1988; Chen, 2002; Bruix, 2005). In addition, HBV acquired in the perinatal period and early childhood is associated with increased risk of HCC even in the absence of cirrhosis. There are two components to the staging of HCC (1) Intrahepatic staging and (2) Extrahepatic staging. Intrahepatic staging requires delineation of the number and size of lesions and whether vascular invasion is or is not present. Optimally, lesion is present, staging technology would permit the distinction between *de novo* lesions and intrahepatic metastases. The distribution of these risk factors among patients with hepatocellular carcinoma is highly variable, depending on geographic region and race or ethnic group (El-Serag et al., 2007).

Most of these risk factors lead to the formation and progression of cirrhosis, which is present in 80 to 90% of patients with hepatocellular carcinoma. The 5-year cumulative risk for the development of hepatocellular carcinoma in patients with cirrhosis ranges between 5% and 30%, depending on the cause (with the highest risk among those infected with HCV), region or ethnic group (17% in the United States and 30% in Japan), and stage of cirrhosis (with the highest risk among patients with decompensated disease) (Fattovich et al., 2004). Worldwide, chronic HBV infection accounts for approximately 50% of all cases of hepatocellular carcinoma and almost all babyhood cases. In prevalent areas in Asia and Africa and India where HBV infection is transmitted from mother to infant, up to 90% of infected personnel have a chronic track, with common integration of HBV into host DNA. Although HBV can cause hepatocellular carcinoma in the absence of cirrhosis, the majority (70-80%) of patients with HBV-related hepatocellular carcinoma have cirrhosis.

The estimated risk of hepatocellular carcinoma is 15 to 20 times as high among persons infected with HCV as it is among those who are not infected, with most of the excess risk limited to those with advanced hepatic fibrosis or cirrhosis (Donato et al., 2002). There are ten Markers of HCV infections are found in 80 to 90% of patients with hepatocellular carcinoma in Japan, 44 to 66% in Italy, and 30 to 50% in the United States. It has been projected that cases of HCV-related hepatocellular carcinoma will continue to increase in the United States over the next two to three decades. Risk factors for hepatocellular carcinoma among

persons infected with HCV include an older age at the time of infection, male sex, co infection with the human immunodeficiency virus or HBV.

### **Assessment tools and techniques for detecting HCC**

HCC screening is suggested for high-risk patients. In a randomized prescribed trial of nearly 19,000 Hepato bacculo virus infected patients in China, it was revealed that HCC observation with testing of serum -fetoprotein (AFP) and performance of abdominal ultrasound (US) at repeated 6-month intervals improves continued existence. Even though observance to surveillance was comparatively low (less than 60%), a 37% reduction in HCC-related mortality was reported. A similar, randomized clinical trial study in China, on the other hand, reported that surveillance for HCC is not beneficial in the absence of curative therapies after the cancer was diagnosed (Zhang et al., 2004).

In addition, several nonrandomized trials, as well as observational studies, have observed the survival advantage in those identified with small and early tumors (Chen et al., 2003). Noninvasive diagnosis of HCC is best limited to patients with cirrhosis and to patients with a focal hepatic mass of 2 cm. In contrast, the suggested diagnostic approach for tumors 2 cm or tumors that do not meet above criteria is such that, when nodules within 1–2 cm on screening of a cirrhotic liver are typical of HCC (hypervascular with washout) on 2 imaging modalities, the lesion should be treated as HCC. In an atypical lesion where the vascular summary is not steady between the techniques, a biopsy of the lesion should be considered. Another criterion is smaller nodules that are 1 cm, and should be followed with ultra sound at 3 to 6 months interval. If, over a period of 2 years, growth has not been observed, a return to routine surveillance at 6-month intervals is suggested (Zhang et al., 1999).

### **Ultra Sound Scan for HCC screening**

Liver ultra sound scan is the most widely used tools for HCC surveillance. Based on the estimated HCC doubling time, the recommended surveillance interval is 6 months, although a one year period may be uniformly effective. The performance of ultra sound scan depends on the experience of the examiner, the

technology used, the body habitus, the presence of cirrhosis, and the size of the tumor. The current studies normally point out 60% sensitivity, and 90% specificity. The sensitivity of ultra sound to detect tumor nodules in cirrhotic livers is particularly low (Waki et al., 2010). Once a screening test is abnormal or there is a clinical suspicion that a patient may have HCC, imaging is very important for the diagnosis and staging of this tumor. The most reliable diagnostic tests are triple-phase helical computed tomography (CT) and triple-phase dynamic contrast enhanced magnetic resonance imaging (MRI) (Wong et al., 2000).

### **Use of Computed Tomography (CT) and Magnetic Resonance Imaging (MRI)**

The technical efficiency of ablation is commonly assessed by findings on contrast-enhanced CT or MRI. A tumor cell should be considered to have been successfully ablated when there were no longer any improved regions within the entire tumor regions during the arterial phase and at least a 0.5 cm margin of apparently normal hepatic tissue surrounding the tumor during the portal phase (Ni et al., 2005; Mori et al., 2009). Hepatocellular carcinoma is the liver cancer and the majority of primary liver cancers are not suitable for curative resection at the time of diagnosis. The major Difficulties of surgical resection may be related to size, site, and number of tumors, vascular and extrahepatic involvement as well as liver function of the patient (Cho et al., 2010; Rust and Gores, 2001; Lee et al., 2008).

Under CT fluoroscopy using either CT arteriography or iodized oil injection, the target and puncture hepatic malignancies using a percutaneous ethanol injection needle. Real-time CT fluoroscopy is application for needle puncture and monitors the size of malignancies. guide the needle puncture and to monitor ethanol injection in small hepatic malignancies (Ding et al., 2001). The alternative method is Ultrasound scan images. The specific procedure directed procedures are necessary but limited for tumors located under the diaphragm. However, saline solution introduction into the pleural cavity can break up the lung and liver on B-mode in ultra sound scan, to be precise, artificial pleural effusion acts as an acoustic window. The literature finds that on the probability and safety of RFA with artificially induced pleural effusion for HCC

located in the right subphrenic region (Takayasu et al., 1999; Minami et al., 2004). Conversely, contrast enhanced harmonic ultra sound scan imaging is capable to estimate small hypervascular HCCs even when B-mode ultra sound scan cannot sufficiently characterize the tumors (Wang et al., 2007; Minami et al., 2007; Quiaia et al., 2004).

Significant advances have been made in the capability to analyze HCC. These advances relate to the acknowledgment that patients with cirrhosis are at high risk for this disease, resulting in the accomplishment of screening strategies. Cross-sectional imaging modalities are including CT and MRI scan images, consent imaging during the arterial phase of contrast administration. The contrast is vital role in the imaging of tumor especially HCC. The lesions are surrounded with tumor are higher vascular micro tumors are identified by means of contrast tumors frequently are identified by means of contrast enhancement during MRI and CT. In a cirrhotic liver, the mass lesion of tumor is more than 2cm is opted for detecting in CT and MRI without increasing contrast, Diagnosis of a small HCC nodule  $\geq 2$  cm in diameter is still demanding and requires advances in imaging modalities and/or cytological approaches (Byrnes et al., 2007). For determination of lesion of HCC below 2cm is required for treating the liver chirrrosis is must for the detecting and treatment.

The accurate diagnosis of HCC lesions 2 cm in diameter can be made non-invasively, based on radiographic criteria in patients with cirrhosis. The ability to diagnose these tumors non-invasively is based on the high occurrence of HCC in patients with cirrhosis, the neovascularity of HCC, and the possibility of finding to equate neovascularity with contrast enhancement on rapid-sequence cross-sectional imaging studies are most effective in the finding of HCC. Consensus diagnostic tools have been developed and extensively accepted. The important provisions for establishing a radiologic diagnosis of HCC include the presence of a focal lesion 2 cm in diameter, recognized by using 2 imaging modalities and showing arterial hyper vascularization in at least 1 of the imaging modalities. Contrast enriched CT, MRI and angiography are used most commonly to identify these features in clinical performance (Sangiovanni et al., 2004).

CT and MRI are significant assessment for the detection and characterization of liver tumors (Bolondi et al., 2001). The CT and MRI images were retrospectively analyzed by two radiologists who have 10 and 15 years of experience in diagnosing abdominal diseases. Neither radiologist was conscious of the patients' clinicopathological data. Reviews were achieved in cooperation and by agreement. The presence of liver cirrhosis, tumor size, the enhancement pattern on dynamic contrast scanning, the presence of pseudo capsule, tumor rupture, portal vein thrombus, and lymph node metastasis were recorded. A distinctive HCC improvement pattern was defined as early enhancement at HAP and rapid contrast medium washout at PVP or EP with hypo-attenuation/intense signal or iso-attenuation intense signal (Sherman et al., 1999).

The finding of HCC has diverse over time as size limit has progressively decreased; Patients with single tumors  $\leq 2$  cm each are usually included. On the other hand, pathological and clinical data shows that some of these tumors are not early at all, while some are very early HCC or carcinoma *in situ* (CIS). CIS is a small, very well discriminate HCC with a nonspecific nodular appearance with no invasion of malignant cell structure. Cancer invasion and spread (microvascular invasion and satellites) may have effect even in tumors  $< 1$  cm but others are CIS (Willatt et al., 2008). Both entities may be detected by US, but CIS may be identified if there is no arterial provide as it is a minute, non-arterial enhanced nodule. The ordinary history of untreated early HCC is not known since these patients are regularly treated with medicine. The literature shows 65% three year survival in patients with single tumors (McGahan et al., 2001).

## Conclusion

The imaging features and determination of HCC in the various CT and MRI have infrequently been reported in the early literature (Trevisani et al., 2001). The purpose of this update is to describe the scanning images with high contrast for finding of tumor cells below 2 cm in the scale. The medical image qualities depends on different features with contrast characteristics indicate that the choice of wavelet transform is playing an important role in detecting and comparing them to determine the HCC cells in early stage.

## References

- Bolondi, L., Sofia, S., Siringo S., 2001.. Surveillance programme of cirrhotic patients for early diagnosis and treatment of hepatocellular carcinoma: a cost effectiveness analysis. *Gut*, 48, 251–259.
- Bruix, J., Sherman, M., 2005. Management of hepatocellular carcinoma. *Hepatology*, 42, 1208–1236.
- Bruix, J., 1997. Treatment of hepatocellular carcinoma. *Hepatology*, 25, 259-262.
- Byrnes, V., Shi, H., Kiryu, S., 2007. The clinical outcome of small (20 mm) arterially enhancing nodules on MRI in the cirrhotic liver. *Am. J. Gastroenterol.* 102, 1654–1659.
- Chen, J.G., Parkin, D.M., Chen, Q.G., 2003. Screening for liver cancer: results of a randomised controlled trial in Qidong, China. *J. Med. Screen.* 10, 204–209.
- Chen, T.H., Chen, C.J., Yen, M.F., 2002. Ultrasound screening and risk factors for death from hepatocellular carcinoma in a high-risk group in Taiwan. *Int. J. Cancer* 98, 257–261.
- Cho, Y. K., Kim, J.K., Kim, W.T., Chung, J.W., 2010. Hepatic resection versus adiofrequency ablation for very early stage hepatocellular carcinoma: a Markov model analysis. *Hepatology*. 51(4), 1284–1290.
- Ding, H., Kudo, M., Onda, H., 2001. Evaluation of post-treatment response of hepatocellular carcinoma with contrast enhanced coded phase-inversion harmonic US: comparison with dynamic CT. *Radiol.* 221, 721–730.
- Donato, F., Tagger, A., Gelatti, U., 2002. Alcohol and hepatocellular carcinoma: the effect of lifetime intake and hepatitis virus infections in men and women. *Am. J. Epidemiol.* 155, 323-331.
- El-Serag, H.B., Rudolph, K.L., 2007. Hepatocellular carcinoma: epidemiology and molecular carcinogenesis. *Gastroenterol.* 132, 2557-2576.
- Fattovich, G., Stroffolini, T., Zagni, I., Donato, F., 2004. Hepatocellular carcinoma in cirrhosis: incidence and risk factors. *Gastroenterol.* 127, Suppl. 1, S35-S50.
- Lee, S.W., Tsou, A.P., Chan, H., Thomas, J., Petrie, K., Eugui, E.M., Allison, A.C., 1988. Glucocorticoids selectively inhibit the transcription of the interleukin 1 beta gene and decrease the stability of interleukin 1 beta mRNA. *Proc. Natl. Acad. Sci. USA* 85, 1204-1208.
- Lee, W. S., Yun, S.H., Chun, H. K., 2008. Clinical outcomes of hepatic resection and radiofrequency

- ablation in patients with solitary colorectal liver metastasis. *J. Clin. Gastroenterol.* 42(8), 945–949.
- McGahan, J. P., Dodd III, G. D., 2001. Radiofrequency ablation of the liver: current status. *Am. J. Roentgenol.* 176, 3–16.
- Minami, Y., Kudo, M., Chung, H., 2007. Contrast harmonic sonography-guided radiofrequency ablation therapy versus Bmode sonography in hepatocellular carcinoma: prospective randomized controlled trial. *Am. J. Roentgenol.* 188, 489–494.
- Minami, Y., Kudo, M., Kawasaki, T., Chung, H., Ogawa, C., Shiozak, H., 2004. Percutaneous radiofrequency ablation guided by contrast-enhanced harmonic sonography with artificial pleural effusion for hepatocellular carcinoma in the hepatic dome. *Am. J. Roentgenol.* 182, 1224–1226.
- Mori, K., Fukuda, K., Asaoka, H., 2009. Radiofrequency ablation of the liver: determination of ablative margin at MR imaging with impaired clearance of ferucarbotran-feasibility study. *Radiol.* 251, 557–565.
- Ni, Y., Chen, F., Mulier, S., 2006. Magnetic resonance imaging after radiofrequency ablation in a rodent model of liver tumor: tissue characterization using a novel necrosis-avid contrastagent. *Eur. Radiol.* 16, 1031–1040.
- Quaia, E., Calliada, F., Bertolotto, M., 2004. Characterization of focal liver lesions with contrast-specific US modes and a sulfur hexafluoride-filled microbubble contrast agent: diagnostic performance and confidence. *Radiol.* 232, 420–430.
- Rust, C., Gores, G.J., 2001. Locoregional management of hepatocellular carcinoma: Surgical and ablation therapies. *Clin. Liver Dis.* 5, 161–173.
- Sangiovanni, A., Del Ninno, E., Fasani, P., De Fazio, C., Ronchi, G., Romeo, R., Morabito, A., de Franchis, R., Colombo, M., 2004. Increased survival of cirrhotic patients with a hepatocellular carcinoma detected during surveillance. *Gastroenterol.* 126, 1005-1014.
- Sherman, M., Peltekian, K.M., Lee, C., 1999. Screening for hepatocellular carcinoma in chronic carriers of hepatitis B virus: incidence and prevalence of hepatocellular carcinoma in a North American urban population. *Hepatology.* 22, 432–438.
- Takayasu, K., Muramatsu, Y., Asai, S., Muramatsu, Y., Kobayashi, T., 1999. CT fluoroscopy-assisted needle puncture and ethanol injection for hepatocellular carcinoma: a preliminary study. *Am. J. Roentgenol.* 173, 1219–1224.
- Trevisani, F., D’Intino, P.E., Morselli-Labate, A.M., 2001. Serum fetoprotein for diagnosis of hepatocellular carcinoma in patients with chronic liver disease: influence of HBs Ag and anti-HCV status. *J. Hepatology.* 34, 570–575.
- Waki, H. K., Aikata, Y. Katamura, 2010. Percutaneous radiofrequency ablation as first-line treatment for small hepatocellular carcinoma: results and prognostic factors on long-term followup. *J. Gastroenterol. Hepatology.* 25, 597–604.
- Wang, Z., Tang, T., An, L., 2007. Contrast-enhanced ultrasonography for assessment of tumor vascularity in hepatocellular carcinoma. *J. Ultrasound Med.* 26, 757–762.
- Willatt, J.M., Hussain, H.K., Adusumilli, S., Marrero, J.A., 2008. MR Imaging of hepatocellular carcinoma in the cirrhotic liver: challenges and controversies. *Radiol.* 247, 311-330.
- Wong, L.L., Limm, W.M., Severino, R., 2000. Improved survival with screening for hepatocellular carcinoma. *Liver Transpl.* 6, 320–325.
- Zhang, B., Yang, B., 1999. Combined  $\alpha$ -fetoprotein testing and ultrasonography as a screening test for primary liver cancer. *J. Med. Screen.* 6, 108–110.
- Zhang, B.H., Yang, B.H., Tang, Z.Y., 2004. Randomized controlled trial of screening for hepatocellular carcinoma. *J. Cancer Res. Clin. Oncol.* 130, 417–422.