World Journal of Clinical Sciences
ISSN: 2960-0286
DOI: 10.61784/wjcsv2n233

AN IN-DEPTH STUDY OF THE DIAGNOSTIC UTILITY OF MAGNETIC RESONANCE DIFFUSION-WEIGHTED IMAGING IN THE IDENTIFICATION OF EARLY-STAGE LIVER CANCER

Cecilia Thung
Department of Pathology, Icahn School of Medicine at Mount Sinai, New York, NY, 10029, USA.

Abstract: Liver cancer is one of the common malignant tumors in my country. Timely diagnosis and treatment of small liver cancer are crucial to improving patient prognosis and survival rate. In recent years, with the rapid development of MRI diffusion-weighted imaging (DWI) technology, it has been widely used in the diagnosis and treatment of abdominal diseases. Currently, the detection rate and diagnosis rate of MRI for small liver cancer are better than those of CT and ultrasound. The combined application of DWI sequence is of great significance for the diagnosis of small liver cancer. This article reviews the application value of DWI imaging technology in the clinical diagnosis of small liver cancer.
Keywords: Small liver cancer; Magnetic resonance imaging; Diffusion weighted imaging; Apparent diffusion coefficient

1 BASIC PRINCIPLES OF DWI

The incidence rate of hepatitis B is high in my country, and liver cancer related to it is one of the common malignant tumors in my country, with a fatality rate second only to lung cancer and gastric cancer. Early detection, diagnosis and treatment of small hepatocellular carcinoma (SHCC) have an important impact on improving patient prognosis and prolonging survival rate. Therefore, early detection and diagnosis of SHCC are of extremely important clinical significance. SHCC refers to liver cancer in which the maximum diameter of a single nodule of primary hepatocellular carcinoma is ≤3 cm or the sum of the maximum diameters of multiple nodules is ≤3 cm. SHCC lacks specific clinical manifestations in the early stage, with no or only mild liver function abnormalities, and tumor markers may also be negative. Therefore, its early diagnosis mainly relies on imaging examinations such as ultrasound, CT, or MRI. For liver cancer >3 cm, ultrasound, CT and conventional MRI are easy to observe, and the detection and diagnosis rates are high. However, due to the small size of SHCC and the atypical blood supply of some lesions, ultrasound and CT may be easily misdiagnosed or missed. The main reason is that ultrasound and traditional CT have poor soft tissue resolution, while MRI has high soft tissue resolution. In particular, dynamically enhanced MRI has obvious advantages in evaluating hemodynamics and detecting small liver cancers, and has been widely used in clinical practice. It is generally believed that MRI is better than traditional CT and ultrasound in detecting and diagnosing small liver cancers. DWI is currently the only non-invasive imaging method that can detect the microscopic movement of water molecules in living biological tissues. It was first used in the diagnosis of neurological lesions. In recent years, with the development and progress of MRI hardware and software technology, it has been more and more widely used in the body. DWI has high potential in the detection and diagnosis of liver cancer, and many reports have achieved good research results. The application of DWI imaging technology in the clinical diagnosis of small liver cancer is reviewed below.

DWI uses a special magnetic resonance imaging sequence to detect the diffusion movement of water molecules in human tissues. It is a functional examination method that images the movement characteristics of molecules. It can provide detection of the speed of the diffusion movement of water molecules in diseased tissues and reflect the disease. It is currently the only imaging method that can measure the diffusion movement of water molecules in vivo.

The factors that affect the DWI signal mainly include diffusion sensitivity coefficient (b value), diffusion coefficient (D), T2 transmission effect and anisotropy. The higher the b value, the more sensitive it is to diffusion motion, but the signal-to-noise ratio of the image will be lower; when the b value is lower, the signal-to-noise ratio is higher, but it is not sensitive to the detection of diffusion motion of water molecules, and the signal is susceptible to other motion images. , such as tissue blood perfusion, etc. The calculation formula of D value is bD=-lnS/S0, b is the diffusion sensitivity coefficient, S is the image signal intensity using diffusion-sensitive gradient field, and S0 is the image signal intensity without diffusion-sensitive gradient field. However, in the human body, DWI is not only affected by the diffusion of water molecules, but also affected by other factors such as respiration, exercise, perfusion, etc. Therefore, ADC is commonly used to represent the diffusion of living tissues. The ADC value calculation formula is: ADC=[ln(S1/S2)]/(b2 -b1), where S1 and S2 are the DWI signal strengths corresponding to the b1 and b2 values respectively. The T2 transmission effect means that when the T2WI signal of the examined tissue is high, part of the T2 image contrast can remain on DWI, causing the lesion to appear as high signal. T2 transmission effects can cause false positives of limited diffusion of lesions within the image. The diffusion anisotropy of water molecules means that the diffusion speed and direction of water molecules in different tissues in the human body are not exactly the same. For example, in the white matter fibers of the brain, it is easier for water molecules to diffuse in the direction parallel to the nerve fibers than in the vertical direction. To a certain extent can affect the DWI signal.

2 THE SIGNIFICANCE OF DWI SIGNAL INTENSITY IN THE QUALITATIVE DIAGNOSIS OF SHCC AND THE DIAGNOSIS OF TUMOR DIFFERENTIATION

DWI is sensitive to changes in the tissue microenvironment and can objectively reflect the diffusion of water molecules within the lesion through the signal intensity and apparent diffusion coefficient ADC value in DWI. HCC tumor cells are dense and the diffusion activity of water molecules is limited. They usually show high or slightly high signal on DWI and low signal on ADC diagram. DWI has high sensitivity for diffusion-limited lesions, and can clearly display small lesions that cannot be displayed by conventional MRI. Research by Yang Bei et al. shows that when the b value is 400 s/mm2, the sensitivity of DWI in diagnosing small liver cancer is 88.4%, which is higher than the 75.4% of conventional MRI [1]. Yue Zheng et al. conducted a meta-analysis on the DWI diagnostic results of 359 patients and 444 lesions, and concluded that the DWI summary sensitivity was 91% and the summary specificity was 91% [2]. Xu Anbo et al[3] and Liu Yan[4] compared the detection rates of SHCC by DWI and enhanced MRI respectively. The detection rates of DWI were 81.55% and 80.74% respectively, and the detection rates of enhanced MRI were 84.52% and 85.93 respectively. %, the two groups of studies concluded that there was no significant difference in the detection of SHCC between DWI and contrast-enhanced MRI alone, but the detection rate of the combined use of DWI and contrast-enhanced MRI was due to the two alone.

The naked eye evaluation of DWI signal intensity is easily affected by adjacent tissues and lacks accuracy and objectivity. Therefore, some scholars analyze the signal intensity value (SI) of the lesion and the signal intensity ratio (RCR) of the lesion and normal liver tissue. Some scholars pointed out that the higher the tumor grade, the greater the SI value of the lesion. Research by He Jiawei [5] and others has shown that the SI value of moderately differentiated HCC lesions is smaller and can be distinguished from the SI values of highly and poorly differentiated HCC, while there is no significant difference in SI value between well-differentiated and poorly differentiated lesions; RCR is a tumor The higher the grade, the greater the RCR value. The RCR values of high, moderate and poorly differentiated SHCC were (1.37±0.13), (1.57±0.13) and (1.71±0.10) respectively, and the difference in RCR values between each group was statistically significant. Moigne FL et al. [6] also showed that RCR has a higher reference value than SI value in identifying SHCC with different degrees of differentiation.

The formation of liver cancer in cirrhotic liver is a gradual process, which gradually develops from regenerative nodules to dysplastic nodules (DN). Hepatocellular carcinoma foci appear in DN and eventually develop into SHCC. Liver cirrhosis DN is recognized as a precancerous lesion of hepatocellular carcinoma, and the identification of DN and SHCC has important guiding value for clinical treatment. Zhang Shaoping [7] applied multi-b-value DWI for differential diagnosis of DN and SHCC and found that the best display of DN and SHCC was when the b-value = 600 s/mm2; and as the b-value increased, DN/liver parenchyma The signal intensity ratio of SHCC gradually decreased slightly, while the signal intensity ratio of SHCC and normal liver tissue gradually increased.

3 ADC VALUE FOR QUALITATIVE DIAGNOSIS OF SHCC AND DIAGNOSIS OF TUMOR DIFFERENTIATION DEGREE

DWI can quantitatively analyze the degree of water molecule diffusion in the lesion through the ADC value, and then identify SHCC and other intrahepatic lesions. Some studies believe that the ADC value is liver cyst > hepatic hemangioma > benign liver tumor > HCC and liver metastases. The research results of Ding Fang et al. showed that the ADC value of SHCC was significantly different from that of normal liver, cirrhotic nodules and hepatic hemangioma, while there was no significant difference between the ADC value of SHCC and metastases [8]. The application of DWI and ADC values is also valuable in distinguishing SHCC from other benign tumor lesions of the liver, but there are certain differences in the selection of b values and ADC values. Xie Pingkun et al. [9] studied that when the b value is 800 s/mm2 and the ADC critical value is ≤1.21×10-3 s/mm2, the sensitivity and specificity of distinguishing benign and malignant lesions reach 82.35% and 93.24% respectively. Chen Yuehua et al. [10] studied that when the b value is 600 s/mm2 and the ADC critical value is 1.51× 10-3 s/mm2, the diagnostic sensitivity reaches 100%, but the specificity is only 50%. Based on the results of many studies, the b value has a high signal-to-noise ratio and accuracy when it is 400~900 s/mm2; there is no unified standard for selecting ADC, and benign and malignant lesions still overlap.

ADC can indirectly reflect the differences in the microstructure of liver tissue through changes in the diffusion speed and range of water molecules in the tissue, thereby providing a diagnostic basis for the identification and quantification of DN and SHCC lesions. Research results by Chen Yuehua et al. show that when the b value is 600 s/mm2, the ADC value of cirrhotic nodules is (1.50 ±0.34) × 10 -3 s/mm2, and the ADC value of SHCC lesions is (1.26 ± 0.18) × 10 -3 s/ mm2, the ADC value is significantly different [10]. The research results of Ding Fang et al. [11] showed that when the b value was 800 s/mm2, the ADC value of the liver cirrhosis nodule group (1.65±0.29) × 10-3 s/mm2 was significantly higher than the ADC value of the SHCC group (1.24±0.27)×10-3 s/mm2. Hu Weizhuo et al. [12] found that when the b value was 700 s/mm2, the ADC values of the liver cirrhosis regenerative nodule group and the HCC group were (1.86±0.10)×10-3 s/mm2 and (1.31±0.24)×10- 3 s/mm2, a significant difference.

The lower the degree of differentiation of HCC, the denser the tumor cells, which in turn leads to a reduction in the intracellular and extracellular spaces and a more obvious restriction of the diffusion of water molecules within the tumor. He Jiawei et al.'s study found that ADC value can effectively distinguish the degree of tissue differentiation of SHCC. When ADC value = 1.39×10-3 s/mm2, the sensitivity and specificity of distinguishing well-differentiated HCC from moderately-poorly differentiated HCC reached 85% and 85% respectively. 93.7%[5]. Hu Weizhuo et al. [12] also found that the ADC values of HCC with various degrees of differentiation are different. The ADC values of highly, moderately and poorly differentiated HCC are (1.65±0.22)×10-3 s/mm2 and (1.28±0.14) respectively. ×10-3 s/mm2 and (1.15±0.16) ×10-3 s/mm2, but the difference in ADC values of moderately and poorly differentiated HCC is only 0.13×10-3 s/mm2, which has no practical clinical significance. However, the results obtained by some scholars believe that there is no statistical difference in ADC values between high, medium and poorly differentiated SHCC.

4 APPLICATION OF INTRA-VOXEL INCOHERENT MOTION IMAGING IN SHCC DIAGNOSIS

In recent years, DWI's new technology intravoxel incoherent motion imaging (IVIM) has been widely researched and applied in multiple systems. A large number of studies have confirmed that in addition to reflecting the diffusion of water molecules in the tissue, the ADC value is also affected by the microcirculation perfusion in the tissue. Therefore, it cannot accurately and objectively show the diffusion movement of water molecules in the tissue and lacks stability. IVIM is to obtain quantified pure diffusion coefficient D values and microcirculatory perfusion-related diffusion coefficient D* values through the bi-exponential model by applying multi-b-value diffusion-weighted imaging. The D value reflects the pure diffusion rate of extravascular water molecules within the lesion, which is relatively slow; the D* value reflects the pseudo-diffusion of intravascular water molecules, which flows faster, and this perfusion effect will affect the ADC of intrahepatic lesions. value. The perfusion-related volume fraction F represents the proportion of microcirculatory perfusion diffusion in the total diffusion effect. IVIM can obtain more essential D value, D* value and F value, which is helpful for the qualitative diagnosis and tumor grading of SHCC. Ying Mingliang et al. [13] found that D value is better than traditional ADC value in the qualitative diagnosis of liver malignant lesions, with sensitivity and specificity reaching 92.3% and 95.45%, and accuracy and AUC reaching 95.83% and 0.945 respectively. . Woo S et al.'s study concluded that the higher the pathological grade of HCC, the lower the D value and ADC value of the lesion, and the sensitivity of D value in the differential diagnosis of high and low grade HCC is higher than the traditional ADC value [14]. Granata V et al. concluded that ADC value has better performance in distinguishing high-grade and low-grade HCC [15], which is contrary to Woo S's conclusion. There may be differences in results due to differences in sample number, inspection parameters, etc.

IVIM does not require the use of contrast agents. The D value can quantitatively display the degree of water molecule diffusion and microcirculatory blood perfusion in normal tissues and tumor tissues, providing clinicians with a more accurate and objective basis for diagnosis. Choi IY et al. [16] found that when b=0,900 s/mm2, compared with traditional ADC values, D value and F value can better distinguish HCC and intrahepatic cholangiocarcinoma, and D value can distinguish liver malignancy. The viable tissue area, necrosis area and fibrosis of the tumor are significantly correlated with the degree of tumor necrosis. Studies such as Zhou Yue [17] have shown that in the diagnosis of SHCC, D value has the highest performance in distinguishing tumor boundaries from normal liver tissue, which is better than ADC value, D* value and F value. IVIM can differentially diagnose liver cirrhosis nodules and SHCC. Huang Mengna [18] found that the ADC value, D value and D* value of the liver cirrhosis nodule group were significantly higher than those of the SHCC group, and the diagnostic performance of the D value was different from that of traditional ADC. The values are similar, and both are significantly higher than the D* value, while the average F value between the cirrhosis nodule group and the SHCC group has no significant difference. Even if the tumor size of moderately and poorly differentiated liver cancer is small, most of them have invaded microvessels, and their malignancy should be taken into consideration when selecting treatment options. Li Hongxiang et al. [19] used IVIM to compare the negative group and the positive group for microvascular invasion and found that the ADC value and D value of the negative group were higher than those of the positive group, and the D value had the best diagnostic performance, with the D value threshold being 1.02×10-3 s/mm2, the sensitivity reaches 94.4%, which can predict the microvascular invasion of liver cancer before surgery.

5 APPLICATION OF DWI IN PROGNOSTIC ASSESSMENT OF LIVER CANCER AND DIAGNOSIS OF POSTOPERATIVE RECURRENCE

The prognosis of HCC is related to various factors such as tumor size, degree of differentiation, occurrence of intrahepatic metastasis, and vascular invasion. DWI can play a significant role in the evaluation of the above factors and thus the prognosis of this lesion. As discussed above, IVIM can distinguish tumor boundaries from normal liver tissue, and can distinguish tumor tissue, necrosis, and fibrosis. RCR, ADC and D value play a guiding role in identifying the degree of differentiation of liver cancer. The D value has good diagnostic performance for microvascular invasion of liver cancer. Patients with liver cancer are often accompanied by tumor thrombus formation in the portal vein. DWI shows high signal like tumor thrombus and tumor tissue, and can be distinguished from low signal thrombus. Intrahepatic metastases of liver cancer are highly malignant, and DWI also has high value for small metastases. Wang Jirong [20] found that DWI has a higher detection rate for micro-hepatocellular carcinoma than dynamic contrast-enhanced MRI.

DWI also has a role in residual and recurrence of liver cancer after surgery. Gao Huiqing [21] et al. conducted a comparative study on preoperative and postoperative TACE for liver cancer and found that the ADC value of liver cancer lesions after surgery was higher than that before surgery, and the ADC value of the postoperative effective group was greater than that of the ineffective group. Yin Tingting et al. [22] used DWI combined with dynamic contrast-enhanced MRI to judge intrahepatic recurrence of micro-hepatocellular carcinoma after liver cancer resection. The sensitivity and specificity reached 89.5% and 97.1% respectively.

In summary, DWI is of great value in the diagnosis and differential diagnosis of SHCC. It can distinguish liver cirrhosis nodules from SHCC, provide a certain basis for the grading of SHCC tumors, and can evaluate the prognosis and recurrence of liver cancer. It has important clinical guiding value. However, due to its low signal-to-noise ratio and low resolution, it still needs to be combined with conventional MRI, dynamic enhanced MRI and other inspection methods to diagnose lesions.

COMPETING INTERESTS

The authors have no relevant financial or non-financial interests to disclose.

REFERENCES

[1] Yang Bei, Wang Xiang, Jin Chaolin. Application of MRI diffusion-weighted imaging in the early diagnosis of liver cancer with diameter < 2 cm in patients with cirrhosis. Liver, 2015, 20(3): 183-185.
[2] Yue Zheng, Jiang Yi, Wang Yanwei. Meta-analysis of the diagnostic value of DWI for small liver cancer in the context of liver cirrhosis. Chinese Journal of CT and MRI, 2017, 15(5): 81-84.
[3]Xu Anbo, Ding Chaopeng, Meng Fanjie. Analysis of the application of dynamic enhanced magnetic resonance and DWI in the diagnosis of liver nodular lesions and small liver cancer. Journal of Medical Imaging, 2017, 27(5):954-957.
[4] Liu Yan. Discussion on the value of multi-b value DWI combined with MRI dynamic enhanced scanning in the diagnosis of hepatocellular carcinoma. Chinese Modern Doctor, 2018, 56(24): 119-122,169.
[5] He Jiawei, Xu Zhifeng, Hou Shinan. The value of quantitative analysis of MR diffusion-weighted imaging in predicting the differentiation degree of small liver cancer. Journal of Clinical Radiology, 2017, 36(10): 1452-1455.
[6]Moigne FL, Boussel L, Haquin A. Grading of small hepatocellular carcinomas (≤2 cm): correlation between histology, T2 and diffusion weighted imaging. Br J Radiol, 2014 (87): 20130763.
[7] Zhang Shaoping, Guo Bingbing, Ma Hailong. The value of multi-b value DWI combined with DCE-MRI in the differential diagnosis of cirrhotic dysplasia nodules and small liver cancer. Chinese and Foreign Medicine, 2018, 37(33): 1-6.
[8] Ding Fang, Gu Hongmei. Research on the application of magnetic resonance diffusion-weighted imaging in small liver nodule lesions. Journal of Nantong University (Medical Edition), 2016, 36(3): 193-196.
[9] Xie Pingkun, Zou Yu, Li Tiefeng. The application value of diffusion-weighted imaging and ADC value in the differential diagnosis of suspected small liver cancer. Journal of Clinical Radiology, 2014, 33(10): 1524-1528.
[10] Chen Yuehua, Lu Jian, Miao Xiaofen. The value of diffusion-weighted imaging and its apparent diffusion coefficient in the diagnosis of small liver cancer. Jiangsu Medicine, 2016, 42(1):94-96.
[11] Ding Fang, Gu Hongmei, Ge Yongqian. The differential diagnostic value of magnetic resonance DWI and R2* imaging for small liver cancer and sclerotic nodules. Journal of Clinical Radiology, 2018, 37(11): 1844-1847.
[12] Hu Weizhuo, Liu Zhonghu, Qin Hongjuan. Preliminary clinical study on MRI of primary liver cancer with different degrees of differentiation. Progress in Modern Biomedicine, 2017, 17(26): 5074- 5078.
[13] Ying Mingliang, Shu Jin'er, Pan Jiangfeng. The value of single and double exponential model diffusion weighted imaging in the differential diagnosis of benign and malignant liver hypervascular lesions. Chinese Journal of Clinical Medical Imaging, 2017, 28(1): 3943.
[14]Woo S,Lee JM,Yoon JH. Intravoxel incoherent motion diffusion -weighted MR imaging of hepatocellular carcinoma: correlation with enhancement degree and histologic grade. Radiology, 2014, 270(3):758-767.
[15]Granata V, Fusco R, Catalano O. Intravoxel incoherent motion (IVIM) in diffusion-weighted imaging (DWI) for Hepatocellular carcinoma: correlation with histologic grade. Onco-target, 2016, 7(48):79357-79364.
[16]Choi IY,Lee SS,Sung YS. Intravoxel incoherent motion diffusion -weighted imaging for characterizing focal hepatic lesions: correlation with lesion enhancement .J Magn Reson Imaging, 2017, 45(6):1589-1598.
[17] Zhou Yue, Gao Jianbo, Qu Jinrong. Diagnostic value of diffusion-weighted imaging single-exponential model and double-exponential model for VX2 small liver cancer in rabbits. World Chinese Journal of Digestion, 2015(36):5760-5767.
[18] Huang Mengna. Evaluation of the diagnostic value of different diffusion models of magnetic resonance for small liver cancer and cirrhosis nodules. Zhengzhou University, 2018.
[19] Li Hongxiang, Xu Yikai, Zhang Jing. The value of voxel-incoherent motion DWI in predicting microvascular invasion of liver cancer. Journal of Clinical Radiology, 2018, 37(9): 1475-1479.
[20] Wang Jirong. The value of 1.5T magnetic resonance enhanced scanning combined with diffusion-weighted imaging in the diagnosis of micro-hepatocellular carcinoma. Qinghai Medical Journal, 2017, 47(7): 80-82.
[21] Gao Huiqing, Yu Yixing, Hu Chunhong. Application of diffusion-weighted imaging combined with general magnetic resonance imaging in the evaluation of efficacy after TACE for liver cancer. Journal of Interventional Radiology, 2016, 25(9): 774-778.
[22] Yin Tingting, Gu Hong, Yang Runiu. Analysis of the value of MRI combined with DWI and DCE scanning sequences in detecting intrahepatic recurrence of small cancer foci after liver cancer resection. Journal of Practical Hepatology, 2017, 20(5): 625-626.