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The role of apparent diffusion coefficient values in characterization of solid focal liver lesions: a prospective and comparative clinical study

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We evaluated and compared the diagnostic accuracy (DA) of apparent diffusion coefficient (ADC) values with that of lesion-to-liver ADC ratios in the characterization of solid focal liver lesions (FLLs). This prospective study was approved by the Institutional Human Ethics Board, after waiving written informed consent. Diffusion-weighted imaging and other routine magnetic resonance imaging were performed on 142 consecutive patients with suspected liver disease. The mean ADC values and lesion-to-liver ADC ratios were compared between benign and malignant solid FLLs. Receiver operating characteristic analysis was performed. The study participants included 46 patients (28 men, 18 women; mean age, 52.5 years) with 57 solid FLLs (32 malignant and 25 benign FLLs). The mean ADC values and ADC ratios of benign solid FLLs were significantly higher than those of malignant lesions (P<0.01). The difference between the area under the receiver operating characteristic curve of the ADC values (0.699) and ADC ratios (0.752) was not significant. Our study suggests that the DA of the ADC ratio is not significantly higher than that of ADC in characterizing solid FLLs.

magnetic resonance, diffusion-weighted imaging, lesion characterization, liver, sensitivity, specificity

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INTRODUCTION

Accurate detection and characterization of solid focal liver lesions (FLLs) is important in clinical work, especially for patients with malignant FLLs, such as hepatocellular carcinoma (HCC) and metastases (Yau et al., 2014; Zhang et al., 2016; Yu et al., 2013). Cysts and hemangiomas can be easily characterized on the basis of their marked and homogeneous high signal intensity on T2-weighted images (T2WI). However, solid FLLs, including both malignant and benign lesions, are sometimes difficult to differentiate without using other conventional magnetic resonance imaging (MRI) sequences, because of their similar or slightly higher signal intensity relative to liver parenchyma on T2WI. With the advances in MRI technology, diffusion-weighted imaging (DWI) has been reported to be useful for the detection and characterization of FLLs (Kwon et al., 2015; Namimoto et al., 2015; Bouchaibi et al., 2015). DWI involves sensitive assessment of the diffusion properties of water molecules in the body, based on the quantitative measurement of the apparent diffusion coefficient (ADC) values, without using contrast agents. Several studies have reported that benign FLLs generally have higher ADC values compared with malignant FLLs (Parsai et al., 2015; Battal et al., 2011; Cieszanowski et al., 2012). How-

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ever, the practical application of a single ADC value threshold for accurate characterization of FLLs is not highly reliable, because of the variable degree of overlap in ADC values between benign and malignant FLLs (Parikh et al., 2008; Sandrasegaran et al., 2009). One reported study even found that ADC values did not allow differentiation of malignant from benign solid lesions (Parsai et al., 2015). In these studies, different *b* values, the acquisition techniques, and pulse triggering may have led to ADC value variability and overlapping for malignant and benign FLLs.

To reduce variability, the possibility of normalizing the ADC value using a reference organ such as spleen that remains relatively constant has been considered. Several studies have occasionally used lesion-to-liver ADC ratios in attempt to differentiate benign from malignant liver lesions (Sun et al., 2005; Sutherland et al., 2014; Agnello et al., 2012; Koc and Erbay, 2014). A recent article by Sutherland et al. evaluated the ADC ratio in the characterization of solid FLLs (Sutherland et al., 2014). They found that the lesion-to-normal liver ADC ratio could not reliably differentiate solid benign lesions from solid malignant lesions. However, the Koc and Erbay study found that the use of the lesion-to-normal parenchyma ADC ratio is more accurate than that of the lesion ADC alone in the differentiation of benign and malignant abdominal lesions (Koc and Erbay, 2014). These results were conflicting and, to our knowledge, no study has investigated and compared the diagnostic accuracy (DA) of ADC values and ADC ratios in the characterization of solid FLLs, in both non-cirrhotic and cirrhotic liver backgrounds.

The purpose of this study was to prospectively evaluate and compare the DA of ADC values and ADC ratios in benign and malignant solid FLLs.

RESULTS

Patients

The study population included 46 patients (28 men and 18 women; mean age 52.5 years, range 25−77 years) (Table 1). Fifty-seven solid FLLs (32 malignant and 25 benign) were included in this study. The 32 malignant lesions consisted of 22 HCCs, seven metastases, two cholangiocarcinomas (CCCs), and one hemangioendothelioma. Histopathological diagnoses were obtained for 12 HCCs, one metastatic lesion, two CCCs, and one hemangioendothelioma. The 25 benign lesions consisted of eight focal nodular hyperplasias (FNHs), eight solitary necrotic nodules (SNNs), four inflammatory pseudotumors (IPTs), two hepatic pseudolipomas, one angiomyolipoma, one hepatocellular adenoma (HCA), and one ectopic adrenal adenoma. Among the benign FLLs, two FNHs, one HCA, one ectopic adrenal adenoma, two inflammatory lesions, and one hepatic pseudolipoma were diagnosed pathologically. The diagnoses of the remaining FLLs were made clinically, according to the standard of reference.

Table 1 Clinical demographics of 46 patients (57 solid focal liver lesions)

Age range (mean age)	25−77 years (52.5 years)
Sex (Men/Women)	28/18
Location of the lesions	28 right lobes/18 left lobes
Benign (n=25)	eight FNHs four IPTs eight SNNs two hepatic pseudolipomas one angiomyolipoma one hepatocellular adenoma one ectopic adrenal adenoma
Malignant (n=32)	22 HCCs seven metastases two CCCs one hemangioendothelioma
Background liver	nine chronic hepatitis 13 liver cirrhosis seven steatosis 17 normal liver
Primary site of malignancy Patients (n=2)	one rectal-colon one pancreas

Quantitative evaluation

The results of the quantitative analysis are shown in Table 2. The mean ADC value was (1.59±0.47)×10^{-3} mm^2 s^{-1} for benign solid FLLs and (1.29±0.21)×10^{-3} mm^2 s^{-1} for malignant FLLs. ADC values for benign FLLs were significantly greater than malignant lesions (P<0.01) (Figure 1A). The calculated area under the receiver operating characteristic (ROC) curve (AUC) for diagnosing a malignant FLL was 0.699 (95% confidence interval, 0.563−0.813), with a sensitivity of 96.9%, a specificity of 52.0%, a positive predictive value (PPV) of 72.1%, and a negative predictive value (NPV) of 92.9%, using a cut-off ADC value of 1.60×10^{-3} mm^2 s^{-1}.

With the use of the ADC cut-off value, 12 false positive diagnoses of malignant FLLs (one ectopic adrenal adenoma, one angiomyolipoma, two FNHs, one HCA, two IPTs, three SNNs, and two pseudolipomas) and three false negative cases (one CCC, one hemangioendothelioma, and one metastasis) were noted. In general, the quantitative analysis of the ADC value yielded 15 misidentified FLLs, and the DA was 73.7% (42/57).

The calculated mean ADC ratio was 1.17±0.39 for benign solid FLLs and 0.95±0.22 for malignant FLLs. ADC ratios for malignant FLLs were significantly lower than benign lesions (P<0.01) (Figure 1B). In the ROC analysis, the AUC for the ADC ratio was 0.752 (95% confidence interval, 0.620−0.857). Using a cut-off value of 0.993, the ADC ratio had a sensitivity of 81.3%, a specificity of 76.0%, a PPV of 81.2%, and a NPV of 76.0%.

The use of the ADC ratio cut-off values resulted in six false positive diagnoses of malignant FLLs (one FNH, one ectopic

Table 2 Mean ADC values and ADC ratios of benign and malignant solid FLLs[a)]

Lesion type (number)	Mean ADC value ($\times10^{-3}$ mm^2 s^{-1})*	Mean ADC ratio
Benign lesions (n=25)	1.59±0.47	1.17±0.39
FNHs (n=8)	1.85±0.46	1.35±0.46
IPTs (n=4)	1.60±0.61	1.35±0.44
SNNs (n=8)	1.59±0.26	1.05±0.25
Hepatic pseudolipomas (n=2)	1.24 (1.10, 1.37)	0.94 (0.84, 1.04)
Angiomyolipoma (n=1)	1.42	1.13
Hepatocellular adenoma (n=1)	1.28	1.00
Ectopic adrenal adenoma (n=1)	0.7	0.72
Malignant lesions (n=32)	1.29±0.21	0.95±0.22
HCCs (n=22)	1.22±0.18	0.89±0.11
Metastases (n=7)	1.38±0.17	1.01±0.31
CCCs (n=2)	1.52 (1.63, 1.42)	1.30 (1.61, 0.99)
Hemangioendothelioma (n=1)	1.74	1.19

a) *, Data expressed as mean±SD. Numbers in parentheses are ranges.

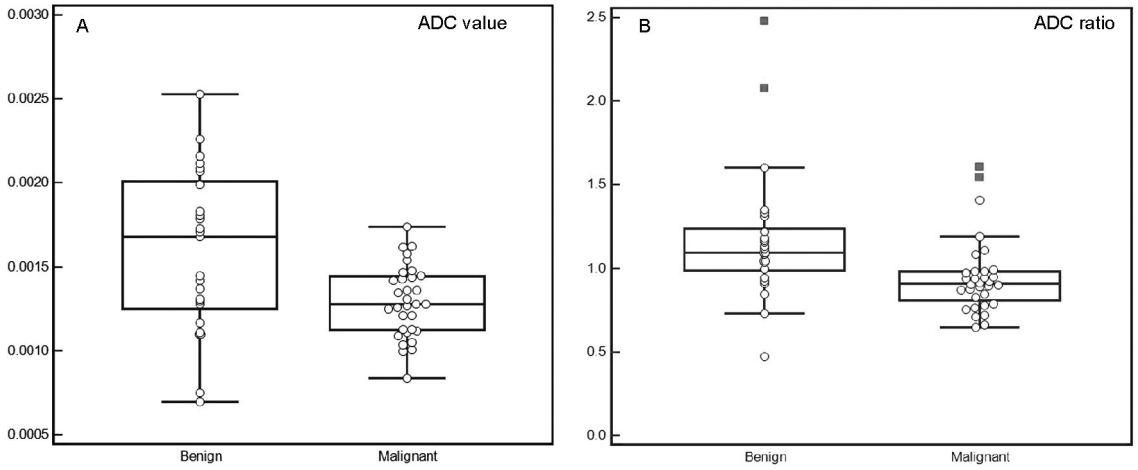

Figure 1 Box-and-whisker plot of ADC value (A) and ADC ratio (B) of benign and malignant solid FLLs. Horizontal line in the middle of each box, median ADC value; horizontal line at top and bottom of each box, 75th and 25th percentiles of values, respectively; whiskers, range of values; ■, outlier.

adrenal adenoma, one IPT, two SNNs, and one pseudolipoma) (Figure 2) and seven false negative cases (two HCCs, two CCCs, two metastases, and one hemangioendothelioma) (Figure 3). Hence, 13 FLLs were misidentified using ADC ratio quantification, and the DA was 77.2% (44/57).

The mean ADC value of the liver was (1.41±0.40)$\times10^{-3}$ mm^2 s^{-1} for the benign group, and (1.39±0.20)$\times10^{-3}$ mm^2 s^{-1} for the malignant group. The difference in the ADC value of the liver between benign and malignant groups was not significant. The difference in the AUC for the ADC value and ADC ratio was also not significant (Z=0.861, P=0.389) (Figure 4).

DISCUSSION

Our study showed that, although ADC values for benign FLLs were significantly greater than malignant lesions (P<0.01), the practical application of a single ADC value threshold for characterizing solid FLLs was not highly reliable. Several studies have reported different ADC cut-offs (1.4×10^{-3}–1.6×10^{-3} mm^2 s^{-1}), with variable sensitivity of 74% to 100% and variable specificity of 77% to 100%, for diagnosing malignant lesions (Taouli and Koh, 2010; Bharwani and Koh, 2013; Taouli et al., 2003; Bruegel et al., 2008). In our study, using a cut-off of 1.60×10^{-3} mm^2 s^{-1}, the ADC value showed reasonably good sensitivity (96.87%) and NPV (92.9%), but a relatively low specificity (52.0%) and DA (73.7%).

We found that the limited benefit of the ADC in FLL characterization was attributed to high overlap in the values of the lesions. In our study, high ADC values were observed in some of the malignant FLLs, including one CCC, one hemangioendothelioma, and one metastasis. In addition, low ADC

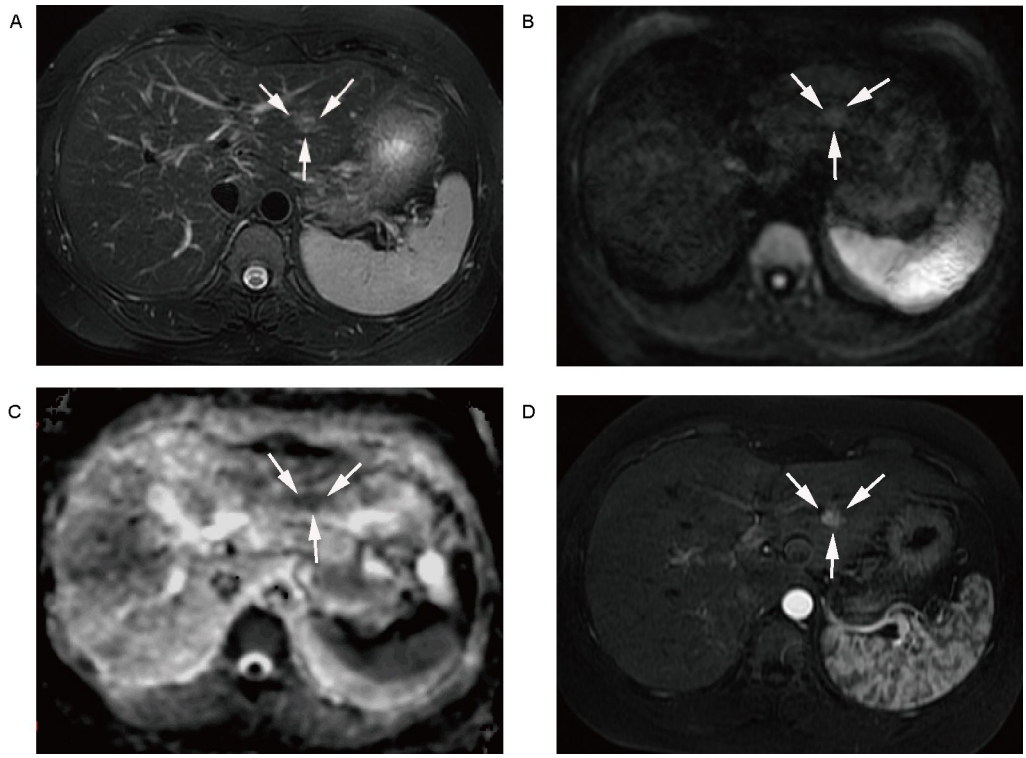

Figure 2 Transverse magnetic resonance imaging of focal nodular hyperplasia in a 43-year-old woman. A, Fat-suppressed T2-weighted fast spin-echo image shows a slightly hyper-intense lesion in the liver with a central scar. B, Diffusion-weighted imaging shows a hypo-intense lesion in the liver. C, Apparent diffusion coefficient map shows a hypo-intense lesion in the liver. D, Contrast-enhanced T1-weighted image in arterial phase demonstrates strong enhancement of the lesion.

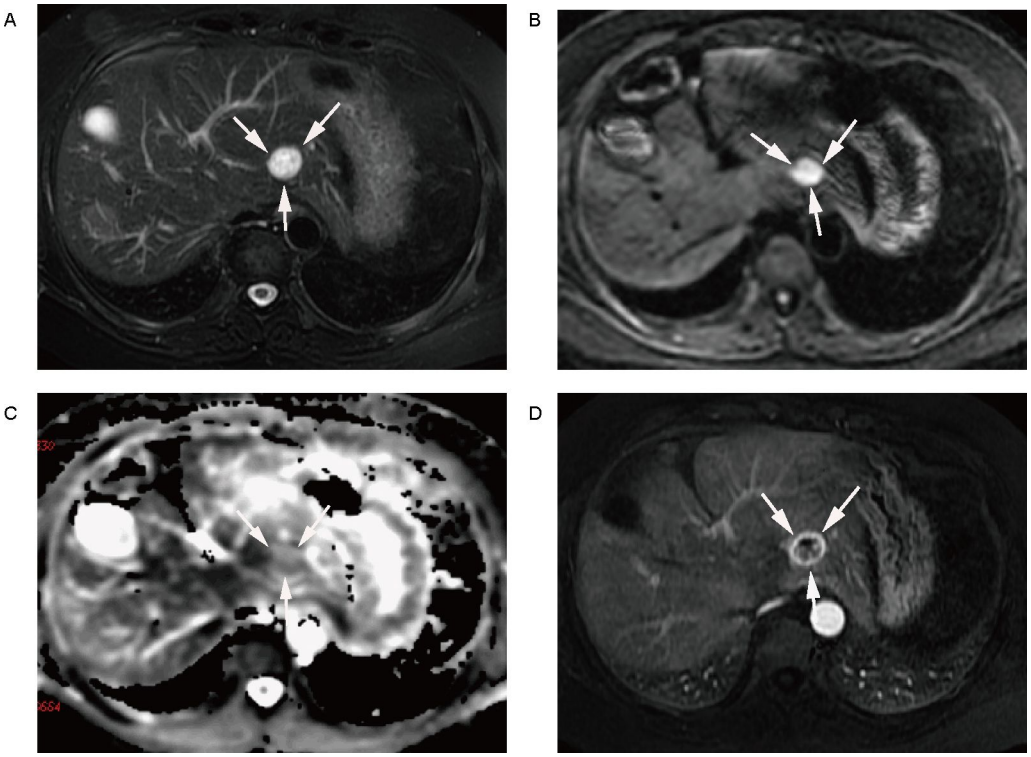

Figure 3 Transverse magnetic resonance imaging of a hemangioendothelioma in a 49-year-old woman. A, Fat-suppressed T2-weighted fast spin-echo image shows a hyper-intense lesion in the liver. B, Diffusion-weighted imaging shows a strongly hyper-intense lesion in the liver. C, Apparent diffusion coefficient map shows a slightly hyper-intense lesion in the liver. D, Contrast-enhanced T1-weighted image in arterial phase demonstrates a strong, irregular, and ring-like enhancement of lesion.

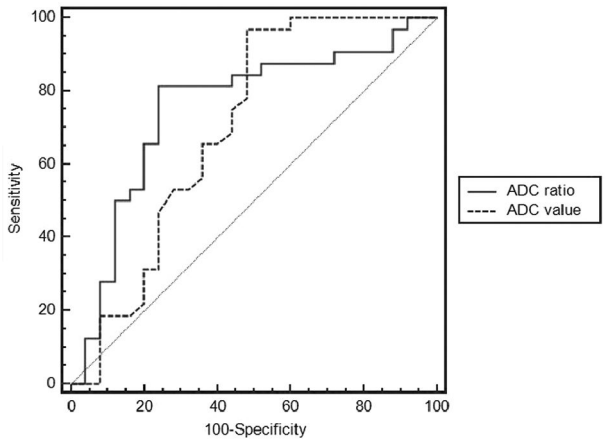

Figure 4 ROC curves show that the area under the ROC curve for ADC ratio (0.752) was not significantly larger than that of ADC value (0.699).

values were found in a few benign lesions including FNHs (n=2), IPTs (n=2), SNNs (n=3), and a HCA (n=1). Agnello et al. reported that benign hepatocellular lesions, such as FNH and HCA, often demonstrate restricted diffusion, with hyper-intense signals at high b values DWI compared with the liver, making these benign lesions indistinguishable from malignant lesions (Agnello et al., 2012). Parikh et al. found no significant differences between the ADC values of benign hepatocellular lesions (five HCAs and four FNHs) and those of metastases and HCCs (Parikh et al., 2008). Sandrasegaran et al. also confirmed that DWI had minimal additional value over standard MRI for characterizing solid liver lesions, because of the high overlap in ADC values (Sandrasegaran et al., 2009).

In order to eliminate the effect of inherent ADC variability, we used the ADC value of surrounding normal liver parenchyma as an internal control, and calculated the ADC ratios of lesion-to-liver. Our study showed that ADC ratios of benign solid FLLs were significantly higher than malignant lesions (P<0.01). Despite the larger AUC for the ADC ratios compared with those of the ADC values, the ADC ratio did not significantly improve the DA for solid FLLs.

The ADC ratio was influenced by both the ADC value of the FLL and the liver. The ADC value of the background hepatic parenchyma varied according to its histopathological condition. The Sandrasegaran et al. study found that ADC values in cirrhotic livers were significantly lower than those in normal livers, with a moderate correlation between the ADC value and the degree of liver fibrosis (Sandrasegaran et al., 2009). Since most of the malignant FLLs occurred in cirrhotic or hepatitis backgrounds, our study also found that the mean ADC value of the surrounding liver in the malignant group was lower than in the benign group. However, the difference did not reach significance. Conversely, malignant FLLs, such as CCCs and the hemangioendothelioma, showed relatively higher ADC values compared with HCCs in our study. Bruegel et al. found that the mean ADC value of hemangioendothelioma (1.86×10^{-3} mm^2 s^{-1}) was higher than those of other hepatic malignancies (Bruegel et al., 2011). Kaya and Koc reported that the highest ADC values in malignant lesions were observed in cases of cholangiocarcinomas (Kaya and Koc, 2014). In general, lesion-to-liver ADC ratios are not reliable for differentiating benign and malignant liver lesions, in the presence of a mixture of cirrhotic and normal liver parenchyma and in malignant lesions with relatively high ADC values.

There were several limitations of our study. First, not all FLLs were confirmed pathologically. However, clinical diagnosis was firmly established on the basis of the consensus of experienced abdominal radiologists and follow-up data. Most benign FLLs were contraindicated for surgical resection. Second, only two b values (0 and 600 s mm^{-2}) were used for the ADC calculations. Using a higher number of b values may lead to more accurate ADC values, yet would require a longer acquisition time and potentially cause more motion artifacts. Third, the number of benign solid FLLs was relatively small. However, our results are valid because the study cohort was a series of consecutive patients and covered topics of common disease.

In conclusion, the ADC ratio did not significantly improve the DA in characterizing solid FLLs, compared with the ADC value. Accurate and reliable characterization of solid FLLs should not be based on the ADC value or ADC ratio alone. The diagnosis must be made using a combination of DWI and other available sequences, such as dynamic contrast-enhanced MRI.

MATERIALS AND METHODS

Patients

This prospective study was approved by the Institutional Human Ethics Board, and the requirement of a written informed consent was waived. From June 2012 to December 2012, 142 consecutive patients underwent magnetic resonance imaging and DWI for the evaluation of suspected FLLs. The exclusion criteria were as follows: (i) regional therapy or systemic chemotherapy before MRI (n=8), (ii) lack of sufficient data for diagnosis (n=6), (iii) DWI with severe image distortion due to artifacts (n=3), (iv) no FLLs detected (n=37), and (v) solid FLLs with less than 10 mm maximum diameter (n=42).

MR imaging

A 1.5 T MRI whole-body scanner (Signa Twin-Speed HD, GE Healthcare, USA) with an eight-element phased array coil was used for signal reception. Gradient strength was 23/40 mT m^{-1}, and the gradient slew rate was 80/150 mT m^{-1} ms^{-1}. Diffusion-weighted images were obtained in the axial plane using a respiratory-triggered single-shot echo-planar imaging sequence with the following parameters: Repetition time/Echo time, 2–3 respiratory cycles/minimum ms; echo

train length, 128; bandwidth, 80–120 Hz/pixel; field of view (FOV), 320–380 mm; rectangle FOV, 90%–100%; matrix size, 128×128; number of signal averages, 4; section thickness/gap, 6/1.5 mm; parallel acceleration factor, 2; and acquisition time, 2–3 min. Tri-directional motion probing gradients with two *b* values (0 and 600 s mm^{-2}) were used in the acquisition of diffusion-weighted images, and fat-saturation pulses were used to prevent severe chemical shift artifacts.

Other MR sequences, including in- and opposed-phase spoiled gradient-recalled echo T1-weighted imaging, respiratory-triggered T2-weighted fast spin-echo imaging with fat-suppression, and contrast-enhanced fat-suppressed three-dimensional spoiled gradient recalled echo imaging were also performed.

Image analysis

ADC values for each lesion were measured by a single observer (J.Y.G., with five years of experience in abdominal imaging), who was blinded to the clinical history, imaging reports, and pathologic results. ADC maps were obtained on the MR console using post-processing software. ADC value measurements were performed by placing the regions of interest (ROIs) on ADC maps and carefully drawing manually to encompass the entire lesions, without necrotic cores if present. For lesions not easily identified on DWI, the locations were determined using T2-weighted and/or contrast-enhanced T1-weighted images. The ROIs in the surrounding normal liver parenchyma avoided intrahepatic vessels and motion artifacts. The average value of each ADC was obtained based on three measurements.

A lesion-to-liver ADC ratio was then calculated for each lesion as ADC_{Le}/ADC_{Li}, in which ADC_{Le} represented the ADC value of the lesion and ADC_{Li} was the ADC value of the surrounding liver parenchyma.

Reference standard

The standard of reference for FLL characterization was optimally established on the basis of histopathological findings. In the absence of histopathological data, clinical diagnoses were established using the combination of clinical history, typical MRI findings, and follow-up MRI after a minimum interval of six months. The clinical diagnoses of benign lesions, including FNH, IPTs, SNNs, and hepatic pseudolipomas, were made using validated criteria and by their stability at follow-up MRI after a minimum of six months (Ronot and Vilgrain, 2014; Zech et al., 2008; Park et al., 2014; Wang et al., 2012; Prasad et al., 2005). HCCs were diagnosed clinically based on the presence of cirrhosis, typical imaging findings (Krinsky et al., 2001; Silva et al., 2009), the American Association for the Study of Liver Disease criteria for HCC (Bruix et al., 2005), elevated levels of tumor markers (e.g., α-fetoprotein), and progressive enlargement at follow-up. Metastases were diagnosed on the basis of the presence of known primary malignancy, MR imaging findings (Danet et al., 2003; Hardie et al., 2010), and follow-up imaging results showing progression.

Statistical analysis

The Kolmogorov-Smirnov test was used to assess normal distribution. Data were expressed as the mean±SD. The ADC value and ADC ratio of the benign and malignant solid FLLs were compared using Mann-Whitney *U* tests. A ROC curve analysis was performed to determine the optimal cut-offs for the ADC value and ADC ratio, in order to provide the best discrimination in terms of maximum sensitivity and specificity. The sensitivity, specificity, PPV, NPV, and DA were calculated. The DA of the ADC value or ADC ratio was determined by calculating the AUC. Comparisons between the differences in AUC values of quantitative parameters (ADC value versus ADC ratio) were made. The statistical analysis was performed using statistical package MedCalc software (MedCalc, Mariakerke, Belgium, version 13.1.2.0), and $P<0.05$ was accepted as statistically significant.

Compliance and ethics *The author(s) declare that they have no conflict of interest. We conformed to the Helsinki Declaration of 1975 (as revised in 2008) concerning Human and Animal Rights, and we followed our policy concerning Informed Consent as shown on Springer.com.*

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Agnello, F., Ronot, M., Valla, D.C., Sinkus, R., Van Beers, B.E., and Vilgrain, V. (2012). High-*b*-Value diffusion-weighted MR imaging of benign hepatocellular lesions: quantitative and qualitative analysis. Radiology 262, 511–519.

Battal, B., Kocaoglu, M., Akgun, V., Karademir, I., Deveci, S., Guvenc, I., and Bulakbasi, N. (2011). Diffusion-weighted imaging in the characterization of focal liver lesions: efficacy of visual assessment. J Comput Assist Tomogr 35, 326–331.

Bharwani, N., and Koh, D.M. (2013). Diffusion-weighted imaging of the liver: an update. Cancer Imaging 13, 171–185.

Bouchaibi, S.E., Coenegrachts, K., Bali, M.A., Absil, J., Metens, T., and Matos, C. (2015). Focal liver lesions detection: comparison of respiratory-triggering, triggering and tracking navigator and tracking-only navigator in diffusion-weighted imaging. Eur J Radiol 84, 1857–1865.

Bruegel, M., Holzapfel, K., Gaa, J., Woertler, K., Waldt, S., Kiefer, B., Stemmer, A., Ganter, C., and Rummeny, E.J. (2008). Characterization of focal liver lesions by ADC measurements using a respiratory triggered diffusion-weighted single-shot echo-planar MR imaging technique. Eur Radiol 18, 477–485.

Bruegel, M., Muenzel, D., Waldt, S., Specht, K., and Rummeny, E.J. (2011). Hepatic epithelioid hemangioendothelioma: findings at CT and MRI including preliminary observations at diffusion-weighted echo-planar imaging. Abdom Imaging 36, 415–424.

Bruix, J., Sherman, M., and Sherman, M. (2005). Management of hepatocellular carcinoma. Hepatology 42, 1208–1236.

Cieszanowski, A., Anysz-Grodzicka, A., Szeszkowski, W., Kaczynski, B., Maj, E., Gornicka, B., Grodzicki, M., Grudzinski, I.P., Stadnik, A., Krawczyk, M., and Rowinski, O. (2012). Characterization of focal liver

lesions using quantitative techniques: comparison of apparent diffusion coefficient values and T2 relaxation times. Eur Radiol 22, 2514–2524.
Danet, I.M., Semelka, R.C., Leonardou, P., Braga, L., Vaidean, G., Woosley, J.T., and Kanematsu, M. (2003). Spectrum of MRI appearances of untreated metastases of the liver. Am J Roentgenol 181, 809–817.
Hardie, A.D., Naik, M., Hecht, E.M., Chandarana, H., Mannelli, L., Babb, J.S., and Taouli, B. (2010). Diagnosis of liver metastases: value of diffusion-weighted MRI compared with gadolinium-enhanced MRI. Eur Radiol 20, 1431–1441.
Kaya, B., and Koc, Z. (2014). Diffusion-weighted MRI and optimal *b*-value for characterization of liver lesions. Acta Radiol 55, 532–542.
Koc, Z., and Erbay, G. (2014). Optimal *b* value in diffusion-weighted imaging for differentiation of abdominal lesions. J Magn Reson Imaging 40, 559–566.
Krinsky, G.A., Lee, V.S., Theise, N.D., Weinreb, J.C., Rofsky, N.M., Diflo, T., and Teperman, L.W. (2001). Hepatocellular carcinoma and dysplastic nodules in patients with cirrhosis: prospective diagnosis with MR imaging and explantation correlation. Radiology 219, 445–454.
Kwon, G., Kim, K.A., Hwang, S.S., Park, S.Y., Kim, H.A., Choi, S.Y., and Kim, J.W. (2015). Efficiency of non-contrast-enhanced liver imaging sequences added to initial rectal MRI in rectal cancer patients. PLoS ONE 10, e0137320.
Namimoto, T., Nakagawa, M., Kizaki, Y., Itatani, R., Kidoh, M., Utsunomiya, D., Oda, S., and Yamashita, Y. (2015). Characterization of liver tumors by diffusion-weighted imaging. J Comput Assist Tomogr 39, 453–461.
Parikh, T., Drew, S.J., Lee, V.S., Wong, S., Hecht, E.M., Babb, J.S., and Taouli, B. (2008). Focal liver lesion detection and characterization with diffusion-weighted MR imaging: comparison with standard breath-hold T2-weighted imaging. Radiology 246, 812–822.
Park, J.Y., Choi, M.S., Lim, Y.S., Park, J.W., Kim, S.U., Min, Y.W., Gwak, G.Y., Paik, Y.H., Lee, J.H., Koh, K.C., Paik, S.W., and Yoo, B.C. (2014). Clinical features, image findings, and prognosis of inflammatory pseudotumor of the liver: a multicenter experience of 45 cases. Gut Liver 8, 58–63.
Parsai, A., Zerizer, I., Roche, O., Gkoutzios, P., and Miquel, M.E. (2015). Assessment of diffusion-weighted imaging for characterizing focal liver lesions. Clin Imaging 39, 278–284.
Prasad, S.R., Wang, H., Rosas, H., Menias, C.O., Narra, V.R., Middleton, W.D., and Heiken, J.P. (2005). Fat-containing lesions of the liver: radiologic-pathologic correlation. Radiographics 25, 321–331.
Ronot, M., and Vilgrain, V. (2014). Imaging of benign hepatocellular lesions: current concepts and recent updates. Clin Res Hepatol Gastroenterol 38, 681–688.
Sandrasegaran, K., Akisik, F.M., Lin, C., Tahir, B., Rajan, J., and Aisen, A.M. (2009). The value of diffusion-weighted imaging in characterizing focal liver masses. Acad Radiol 16, 1208–1214.
Sandrasegaran, K., Akisik, F.M., Lin, C., Tahir, B., Rajan, J., Saxena, R., and Aisen, A.M. (2009). Value of diffusion-weighted MRI for assessing liver fibrosis and cirrhosis. Am J Roentgenol 193, 1556–1560.
Silva, A.C., Evans, J.M., McCullough, A.E., Jatoi, M.A., Vargas, H.E., and Hara, A.K. (2009). MR imaging of hypervascular liver masses: a review of current techniques. Radiographics 29, 385–402.
Sun, X.J., Quan, X.Y., Huang, F.H., and Xu, Y.K. (2005). Quantitative evaluation of diffusion-weighted magnetic resonance imaging of focal hepatic lesions. World J Gastroenterol 11, 6535–6537.
Sutherland, T., Steele, E., van Tonder, F., and Yap, K. (2014). Solid focal liver lesion characterisation with apparent diffusion coefficient ratios. J Med Imaging Radiat Oncol 58, 32–37.
Taouli, B., and Koh, D.M. (2010). Diffusion-weighted MR imaging of the liver. Radiology 254, 47–66.
Taouli, B., Vilgrain, V., Dumont, E., Daire, J.L., Fan, B., and Menu, Y. (2003). Evaluation of liver diffusion isotropy and characterization of focal hepatic lesions with two single-shot echo-planar MR imaging sequences: prospective study in 66 patients. Radiology 226, 71–78.
Wang, L.X., Liu, K., Lin, G.W., and Zhai, R.Y. (2012). Solitary necrotic nodules of the liver: histology and diagnosis with CT and MRI. Hepat Mon 12, e6212.
Yau, T., Tang, V.Y.F., Yao, T.J., Fan, S.T., Lo, C.M., and Poon, R.T.P. (2014). Development of Hong Kong Liver Cancer staging system with treatment stratification for patients with hepatocellular carcinoma. Gastroenterology 146, 1691–1700.e3.
Yu, J.P., Ma, Q., Zhang, B., Ma, R.J., Xu, X.G., Li, M.S., Xu, W.W., and Li, M. (2013). Clinical application of specific antibody against glypican-3 for hepatocellular carcinoma diagnosis. Sci China Life Sci 56, 234–239.
Zech, C.J., Grazioli, L., Breuer, J., Reiser, M.F., and Schoenberg, S.O. (2008). Diagnostic performance and description of morphological features of focal nodular hyperplasia in Gd-EOB-DTPA-enhanced liver magnetic resonance imaging: results of a multicenter trial. Invest Radiol 43, 504–511.
Zhang, B., Dong, W., Luo, H., Zhu, X., Chen, L., Li, C., Zhu, P., Zhang, W., Xiang, S., Zhang, W., Huang, Z., and Chen, X.P. (2016). Surgical treatment of hepato-pancreato-biliary disease in China: the Tongji experience. Sci China Life Sci 59, 995–1005.