Use of Two-dimensional Multiple-slice Magnetic Resonance Hydrography for Diagnosis of Hepatic Hemangiomas and Cysts

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Background/Purpose: Although hepatic hemangiomas and cysts display very high signal intensities on conventional T2 images, their appearances are quite distinct using magnetic resonance hydrography (MRH). We examined the feasibility of using MRH in distinguishing hepatic cysts from hemangiomas.

Methods: We recruited 97 patients with hepatic hemangiomas and 65 with hepatic cysts. All patients underwent magnetic resonance imaging (including two-dimensional multiple slice MRH, TR/TE: 8000/800) and the results were reviewed independently by two radiologists. The signal intensities of the lesions were measured. For each lesion, the variation in signal to noise ratio between MRH and the fat-saturated T2-weighted images was calculated, and the results were validated using a receiver operating characteristic curve.

Results: There was a significant difference between the signal to noise ratio of hepatic hemangiomas and cysts using MRH (p < 0.001). This difference could be identified by visual inspection. The receiver operating characteristic curve revealed that the ideal cut-off value for the signal intensity reduction ratio between hepatic cysts and hemangiomas was −0.1. Using this ratio, the derived sensitivity was 95.4%, specificity 99.0%, and accuracy 99.7%.

Conclusion: Hepatic hemangiomas and cysts have significantly different signal intensities on non-contrast two-dimensional multiple-slice MRH. This approach uses a non-invasive, reliable, and accurate imaging technique to differentiate the two diagnoses.

Key Words: contrast medium, hepatic cyst, hepatic hemangioma, magnetic resonance hydrography

Magnetic resonance hydrography (MRH) is the imaging of static and slow-flowing fluid using an magnetic resonance imaging (MRI) device.1,2 MRH has made possible various valuable clinical investigations in abdominal and pelvic regions, namely MR cholangiopancreatography,3 MR urography, and MRH of the fetus.4 Although hepatic cysts and hemangiomas display very high signal intensities (SIs) on conventional T2 images, their appearances are quite
distinct using MRH. Specifically, hepatic cysts have very high SI on heavily weighted T2 MRH, and hepatic hemangiomas display only a marginally higher intensity. Previous studies have suggested that for a 1.5T MRI device, the relaxation time of hemangiomas is 140–178 milliseconds, whereas that of hepatic cysts is 341–517 milliseconds.\(^5,6\) The use of true fast imaging with steady-state precision and half-Fourier acquisition single-shot turbo spin echo (HASTE) to depict liver tumors, including hemangiomas, has been reported.\(^7\) However, hepatic cysts and hemangiomas are still usually confirmed by contrast-enhanced MR studies. Recently, the hazards of using gadolinium-based MR contrast agent have been highlighted.\(^8\) According to a previous study, the incidence of nephrogenic systemic fibrosis was 0.7% with high-dose gadolinium-based contrast medium, which increased to 0.4% in chronic renal disease.\(^9\) Ideally, both of these benign conditions should be diagnosed without the use of an MR contrast agent.

The use of two-dimensional (2D) multiplanar MRH for the differentiation of hepatic cysts from hemangiomas has not yet been completely documented. Therefore, the purpose of this study was to investigate the feasibility of MRH as a non-contrast alternative that supplements routine MR pulse sequences to increase the diagnostic accuracy for these two common hepatic lesions.

### Patients and Methods

The study had the approval of the institutional review boards of our hospital. Informed consent for participation in the study was obtained from all patients prior to MR examination.

**Patients**

This study was conducted over 11 months. Patients who were found to have focal hepatic tumors by sonography and for whom further assessment was indicated, were referred for MRI. A total of 109 patients were found to have lesions that had a “light-bulb” appearance on T2-weighted imaging. The light-bulb appearance was defined as very high, internal homogeneous SI (similar to the signal of the thecal sac) and well-defined margins on T2-weighted imaging (T2WI).\(^10\) The appearance of all the lesions was confirmed by the on-site radiologist (R.C. Chen, C.S. Li, W.T. Chen or J.M. Li). An additional MRH sequence was performed on the above patients. Focal lesions > 1.0 cm were included to avoid the partial volume effect. For patients with multiple lesions, only the largest three from each patient were included. The results revealed 99 patients with 97 hepatic hemangiomas and 65 hepatic cysts. The diagnosis of hepatic cyst relied on its characteristic MR findings, which included a low T1 and a very high T2 SI without enhancement in a contrast-enhanced series. Hemangioma was confirmed by its distinctive MR characteristics, which was a very high T2 SI, enhanced in a peripherally nodular or rapidly homogeneous pattern during the early arterial phase, followed by fill-in or persistent homogeneity during the late and delayed phases.\(^11,12\)

The diameter of the hemangiomas ranged from 1.0 cm to 4.6 cm (mean: 1.9 ± 1.1 cm) and the diameter of the cysts varied from 1.0 cm to 6.5 cm (mean: 2.2 ± 1.5 cm). After their MR examinations, all patients were followed up by sonography for a minimum of 6 months (range: 6–18 months). The largest diameters of the lesions were recorded for comparison.

**Imaging**

Sonographic examinations were performed with a Logiq 700 sonography unit (GE Medical Systems, Milwaukee, WI, USA) using a 3.5–4.0 MHz probe. MR images were acquired using a 1.5T MR scanner (Philips Gyroscan ACS-NT, Eindhoven, the Netherlands) and a phased-array body coil. Dual T1-weighted images (TR/TE: 210/2.3 and 4.6; slice thickness, 8 mm; gap, 0.8 mm; matrix, 256 × 204; axial) were performed within one breath hold. Turbo spin-echo (TSE) T2-weighted images (TR/TE: 1800–2500/100; TSE factor, 23; NSA, 4; slice thickness, 8 mm; gap, 0.8 mm;
matrix, 256 × 154; axial), with and without fat saturation, and coronal T2-weighted images were obtained with respiratory triggering.

The MRH was an axial 2D single shot, with multi-slice sequences and fat saturation, which was acquired within one breath hold (TR/TE, 8000/800; TSE factor, 128; 12 slices; slice thickness, 8 mm; gap, 0.8 mm, matrix, 256 × 204; NSA, 2). The total acquisition time was only 16 seconds and all patients were examined using the same technique. The total thickness of tissue scanned for each 2D MRH session was typically 10 cm. Using the above parameters, the entire liver could be scanned within two breath holds.

Dynamic MR images were obtained by applying a T1-weighted fast field echo sequence (175–210/1.3–2.1; flip angle, 80°; NSA, 1; slice thickness, 8 mm; gap, 0.8 mm; matrix, 256 × 154) before intravenous contrast administration and at 18–20 seconds (early arterial-dominant phase), 50–55 seconds (portal venous phase), and 5 minutes (5-minute delayed phase) after the manual intravenous administration of gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany; 0.1 mmol/kg body weight). Other delayed phase axial images and coronal images were acquired about 10 minutes after intravenous contrast agent administration (10-minute delayed phase). These pulse sequences were all obtained using single acquisitions during one breath hold.

**Image analysis**

The task of image analysis was subdivided between three separate radiologists who were blinded to the lesion type. One measured the mean value of SI of the lesions of the fat-saturated T2WI and MRH. This was performed on a picture archiving and communication system (PACS; Centricity Radiology RA600 v6.1 Diagnostic; GE Medical Systems) with a high-resolution monitor using an operator-defined region of interest that was defined as an ovoid area 5–10 mm in diameter. The standard deviation (SD) of background noise was measured in a background area anterior to the lesion without phase-shift artifacts. The signal to noise ratio (SNR = SI/SD_{background}) of the lesions in the two series were calculated.

Two radiologists independently reviewed all MR images in two steps without prior knowledge of diagnosis. The images were pre-set to the optimal window level and center, and sent to the PACS by the technologists. The non-contrast images including MRH were given to the radiologists for review, and they were asked to record the SI of the lesions on T2-weighted fat-saturated images and MRH based on the pre-set images. They were not allowed to change the window level and centers. The SI of the lesions was graded as isointense, intermediate hyperintense, or very hyperintense as compared to the SI of the liver parenchyma. Next, they were asked to compare the SIs in the three series and record the changes between the MRH and other pulse sequences, and then to make a diagnosis by visual inspection. If the SI of the lesion by MRH was comparable with or higher than that by fat-saturated T2WI, it was labeled a hepatic cyst. If the reverse occurred and the MRH SI of the lesion was lower than that of the fat-saturated T2WI, the lesion was regarded as a hemangioma. The signal for hemangioma was low, but all the lesions were still visible by MRH. To establish the reference standard, the radiologists reviewed all sonographic and MR images (including the dynamic MR images with contrast enhancement) as well as the follow-up sonography and/or MR images, to reach a consensus. The established diagnosis was recorded separately from the preliminary diagnoses based on visual inspection.

**Statistical analysis**

For statistical analysis of the SNR of the lesions in the different MR series, we used the Student t test. A p value < 0.05 was considered to be statistically significant. The signal variation ratio of the SNRs of the lesions between MRH and T2WI with fat saturation defined by the formula

$$\text{SNR}_{\text{MRH}} - \text{SNR}_{\text{T2 fat sat}} / \text{SNR}_{\text{T2 fat sat}}.$$ 

The resultant variation derived from this formula was evaluated and validated by a ROC curve from which an ideal cut-off value was obtained. Thus, lesions with SI variation that fell beneath the
cut-off value were diagnosed as hemangiomas, and those with SI variation above the cut-off value were considered to be hepatic cysts. The sensitivity and specificity of this method were also obtained from the ROC curve. In addition, the sensitivity and specificity of the visual assessment by two radiologists were calculated and the inter-observer variation was analyzed by the \( \kappa \) test.

**Results**

All diagnoses of hepatic hemangiomas and cysts were confirmed by contrast-enhanced MRI. All of the cysts were hypointense by T1-weighted imaging, hyperintense by T2WI, and did not enhance throughout the study. All of the hemangiomas were hypointense by T1-weighted imaging, hyperintense by T2WI, and demonstrated one of two types of enhancement. One type of enhancement was rapid, homogeneous, and persisted into the delayed phase. The other was progressive centripetal enhancement that also persisted into the delayed phase. There was no disagreement between the two radiologists over the final diagnoses of the hemangiomas and cysts.

For the preliminary diagnosis based on their visual assessment of SI variations, the first radiologist successfully diagnosed 96 out of 97 hepatic hemangiomas and 63 out of 65 hepatic cysts. The sensitivity was 98.97%, the specificity was 96.92%, and the accuracy was 98.15%. The second radiologist was able to make the correct diagnoses in all the 97 hemangiomas and 64 of the 65 cysts with a sensitivity of 100%, specificity of 99.46%, and accuracy of 99.38%. The inter-observer agreement was excellent (\( \kappa = 0.948 \)). There were four disagreements in which three of the lesions were cysts and one of the lesions was hemangioma. The mean size of these four lesions was relatively small at 1.1 cm (range: 1.0–1.3 cm).

We also attempted to quantify the SI variation that distinguished the two lesions. For hemangiomas, the mean SNR was 80.80 ± 38.45 on the fat-saturated T2-weighted images and 17.09 ± 8.79 on the MRH images (Figure 1). For cysts, the SNR was 98.74 ± 44.07 on the fat-saturated T2-weighted images and 215.03 ± 107.11 on the MRH images (Figure 2). Using the Student \( t \) test, the difference in SNR variation between the hemangiomas and cysts was consistent and statistically significant (\( p < 0.001 \)). Based on this analysis, MRH was clearly a superior approach to conventional MR when discriminating these two lesions.

The variation ratio calculated by the equation \( \frac{\text{SNR}_{(\text{MRH})} - \text{SNR}_{(\text{T2 fat sat})}}{\text{SNR}_{(\text{T2 fat sat})}} \) was different for the hemangiomas and cysts. A ratio of \(-0.1\) was a good cut-off value for discriminating hemangiomas and cysts, and this allowed only a few exceptions (Figure 3). This meant that lesions with SI reduction ratio \(< -0.1\) should have been considered to be hemangiomas, whereas lesions for which the ratio was \( > -0.1\) should have been diagnosed as cysts. The area under the ROC curve was 0.997. Quantitative analysis of the MRH results with respect to differentiation of hemangioma from cysts revealed a sensitivity of 95.4%, a specificity of 99.0%, and an accuracy of 99.7%.

There were five exceptions using \(-0.1\) as the cut off value: three cysts and two hemangiomas. For four lesions, this might have been caused by the relatively high standard deviation of the background noise (three cysts with high SD by MRH and one hemangioma with high SD by fat-saturated T2WI). One hemangioma (SI reduction ratio = \(-0.1\)) fell in the borderline area of the cut off value.

**Discussion**

Hepatic hemangiomas and cysts are very common benign hepatic lesions, most of which can be diagnosed by sonography. However, difficulties can arise with some obese patients. These are usually diagnosed by contrast-enhanced MRI. Some atypical hemangiomas can show marked delay in enhancement, and in these cases 10-minute delayed scans are needed, thus prolonging the MR study. For some small hemangiomas, their T2-weighted SIs are bright, yet they can be difficult to identify in the T1-weighted images before and after contrast enhancement due to their size.
For these atypical or small hemangiomas, MRH, which is quick and easy to perform in nearly all MR machines and does not require additional contrast medium, might be a helpful method for their characterization.

MRH is able to highlight static or very slow-flowing fluid by applying a heavily T2-weighted pulse sequence. In Fenlon’s study, extreme T2WI with a TE of 125 milliseconds was useful for distinguishing benign and malignant hepatic lesions. Other investigators have also used heavily T2-weighted MRI and true fast imaging with steady-state precision sequences to differentiate hepatic cysts and hemangiomas from other solid tumors. Jafari et al have measured the T1 and T2 SIs of liver, spleen and hemangioma using a rapid acquisition relaxation enhanced sequence with a 0.5T MR device, setting the TE at 500 milliseconds. They noted that even with the TE set at 500 milliseconds, the SI of the hemangioma remained high. In view of this phenomenon, we increased the TE to 800 milliseconds for our 2D multiple slice MRH, and a significant drop in the signal intensity of the hemangiomas could be noticed compared to that with the cysts; this phenomenon can be confidently recognized by visual inspection.

Hepatic lesions with a light-bulb appearance by T2WI were the lesions of interest in our study. All lesions with a light-bulb appearance were either cysts or hemangiomas. Traditionally, to diagnose these during an MR scan involves the use of a contrast agent, which has recently been found to be associated with nephrogenic systemic fibrosis in patients with renal insufficiency. On the other hand, contrast agent is seldom used in routine health examinations, to avoid any possible reaction. Both lesions are benign; therefore, the use of

Figure 1. Magnetic resonance imaging in a 37-year-old woman showed hepatic hemangioma. (A) Axial T2-weighted and (B) axial T2-weighted with fat saturation MR images showed a very high-signal hepatic hemangioma (arrow). (C) Magnetic resonance hydrography (8000/800) showed a significant signal drop (arrow) compared with (A) and (B). (D) The post-contrast delayed-phase T1-weighted image showed homogeneous enhancement of the lesion (arrow).
a potentially hazardous agent in their diagnosis is not appropriate. Nevertheless, despite the fact that both diagnoses are benign, patients often prefer to have a definite diagnosis. MRH offers a fast (16 seconds) and reliable method for the differentiation of cysts from hemangiomas, without the use of an MR contrast agent.

To remove the confounding factor of indigenous SI differences in different lesions, the difference between SIs of the lesions using MRH and fat-saturated T2WI was expressed as a ratio. It was mentioned that the ideal cut-off value was $-0.1$ according to the ROC curve and the dot diagram. This gave MRH a sensitivity of 95.4%, a specificity of 99.0%, and an accuracy of 99.7%. This ideal cut off value will vary depending on the MR facility and the parameters used. However, qualitative assessment by radiologists using the naked eye gave comparable results. Therefore, we suggest that MRH is an excellent tool for differentiating hepatic hemangiomas from cysts and that qualitative assessment should suffice in day-to-day practice.

Figure 2. A 56-year-old woman with multiple hepatic cysts. (A) Axial T2-weighted and (B) axial T2-weighted with fat saturation magnetic resonance images showed multiple hepatic cysts. (C) MR hydrography (8000/800) showed a persistent high T2 signal for all the cysts. (D) The post-contrast late-phase T1-weighted magnetic resonance image showed negative enhancement in these lesions.

Figure 3. The signal intensity variation ratio of the magnetic resonance hydrography and T2 fat-saturated images was calculated using $\frac{SI_{(MRH)} - SI_{(T2 \ fat \ sat)}}{SI_{(T2 \ fat \ sat)}}$. The ideal cut-off value was found to be $-0.1$. Almost all hemangiomas were $<-0.1$, whereas almost all cysts were $>-0.1$. SI = signal intensity; MRH = magnetic resonance hydrography.
One study has explored the feasibility of differentiating hepatic cysts from hemangiomas using multi-section fluid-attenuated inversion recovery (FLAIR)-HASTE. In that study, only 85% of the cysts could be null effectively by FLAIR-HASTE. In our study, the accuracy of MRH was 98.15–99.7%. Therefore, we suggest that MRH seems to be a more reliable technique when differentiating these two lesions.

In our current day-to-day practice, delayed-phase post-contrast MRI sequences are still occasionally required for confirmation of hepatic cysts or hemangiomas and the exclusion of other lesions. This typically adds 5–10 minutes to the study duration. In comparison, MRH does not require contrast enhancement, takes only 16 seconds for 12 images, and can be done as an add-on as soon as the prior MR sequences reveal suspicious hepatic lesions. Most importantly, it is both sensitive and specific, with or without ROI measurement.

One of the limitations of the present study was that all the hemangiomas and cysts were typical cases. Jang et al have reported several atypical hemangiomas that could not be differentiated from malignant tumors by computed tomography, conventional MR, and sonography. It would be interesting to investigate the MR hydrographic appearance of such sclerosed or hemorrhagic hemangiomas. Future investigation in this area would be helpful. However, the present study still provided a rapid MR sequence that helped with the diagnosis of cysts and hemangiomas without the use of contrast medium. Another limitation was that pathological examination was not available. This was a study of hepatic benign lesions such as cysts and hemangiomas. All of them showed characteristic MR appearances and no interval changes during the 6–18 months follow-up studies. This is a shortcoming in most comparative studies.

There were inter-observer discrepancies in the preliminary diagnosis of four lesions; all of which were relatively small. This discrepancy might have been due to the relatively thick 2D slices (8 mm) and the resultant partial volume artifacts. This can be easily mitigated by employing a three-dimensional method that is able to achieve a much thinner slice thickness, although at the expense of a longer examination time of 4–8 minutes. However, the accuracy of the present study was high. Thus a time-consuming three-dimensional method might not be necessary given such a satisfactory result.

In conclusion, hepatic lesions with a light-bulb appearance in T2WI are almost always cysts or hemangiomas. These two types of lesions, even if they are small in size (the smallest was 1.0 cm), can be reliably differentiated by 2D multiple-slice MRH. This is a fast and reliable technique and does not require the administration of potentially hazardous gadolinium chelates. Hemangiomas demonstrate a noticeable signal drop during MRH, whereas cysts retain a light-bulb appearance. The sequence is useful for the patients who cannot use gadolinium chelate contrast agents and for those who receive MR health examinations.

References


