The purpose of this study is to evaluate the plain and multiphasic dynamic Gd-enhanced MR imaging features of hepatic focal nodular hyperplasia (FNH) with breath-hold MR sequences.

Retrospectively, sixteen lesions of FNH in fifteen patients (ten male and five female) were reviewed. Among the sixteen lesions, three were proved by surgery, four by percutaneous biopsy, and the other nine by clinical follow-up. Patient’s age ranged from 21 to 62 years old (mean 33.1). MR examinations were performed with a 1.5-T superconducting whole body imager and phased-array body coil. All patients in pre-contrast scan were imaged with breath-hold T1-weighted fast low angle shot (FLASH), T2-weighted half-Fourier acquisition single-shot turbo-spin echo (HASTE) and T2-weighted fast spine echo (FSE) sequences. Multiphasic dynamic gadolinium (Gd)-enhanced MR images were obtained at 30 seconds, 70 seconds 3 minutes, 6 minutes and 10 minutes following a bolus of intravenous injection of 0.1 mmole/kg Gd-DTPA with fat-saturation breath-hold T1-weighted FLASH sequence.

FNH could be detected on T1-weighted FLASH images as hypointense lesions (n = 10, 63%) and T2-weighted FSE or HASTE images as hyperintense lesions (n = 11, 69%). Gd-enhanced dynamic MR imaging demonstrated homogeneous and complete enhancement (except central scar if present) on arterial-phase imaging (n = 16, 100%). Portal-venous-phase and delayed-phase imaging showed isointense (n = 8, 50%) or slightly hyperintense (n = 8, 50%). Central scar could be identified in twelve lesions and showed to be hypointense on T1-weighted (n = 9, 75%) and hyperintense on T2-weighted images (n = 9, 75%). In dynamic study, central scar demonstrated to be hypointense (n = 12, 100%) in arterial-phase images. Delayed enhancement of central scar could be depicted in portal-venous-phase images (n = 2, 17%) or a series of delayed scans: 3 minutes (n = 4, 33%), 6 minutes (n = 3, 25%), and 10 minutes (n = 3, 25%). Size of the central scar in seven lesions was smaller than 5 mm (58%), four was 5mm to 1cm (33%), and one was 2 cm in diameter (8%). Only one particular lesion demonstrated capsule formation.

Breath-holding plain and dynamic multiphasic MR imaging have been used broadly in the diagnosis of FNH. In the present study, both arterial- and delayed-phase images with Gd-enhanced T1-weighted sequences were thought to be superior to plain images in lesion detection. We also demonstrated that delayed scan longer than 6 minutes is essential to depict the tiny central scar. Typical MR imaging features of FNH included homogeneous solid mass with iso- or slightly hypointense on T1-weighted, iso- or slightly hyperintense on T2-weighted images as compared to surrounding normal liver parenchyma. Central scar presented as markedly hypointense on T1-weighted and iso- or hyperintense on T2-weighted images as compared to tumor. Dynamic study of main tumor demonstrated strong enhancement during arterial-phase imaging but central scar depicted strong enhancement during delayed-phase imaging.

Key words: Focal nodular hyperplasia, liver; multiphasic dynamic MRI

Focal nodular hyperplasia (FNH) is a benign tumor-like hepatic lesion with uncertain etiology.
Some researchers suggested that FNH represents a hyperplastic response of the liver parenchyma to a pre-existing vascular malformation [1].

MR imaging features of FNH had been reported in the previous literatures [2-13]. However, the results of published data are diverse, which may be caused by low magnetic field MR machine [2-5], conventional MR pulse sequence and body coil [6], different MR contrast agent [7, 8, 9] or lack of standard protocol for dynamic contrast-enhanced study [10, 11, 12, 13].

The aim of our retrospective study is to evaluate nonenhanced and dynamic Gd-enhanced MR imaging features of FNH with high magnetic field MR imager, phased-array body coil, and breath-hold pulse sequences. Tumor and central scar detectability in the individual MR sequences were assessed. Dynamic imaging acquisition in delayed phase plus ultra-delayed phase for central scar detection was focused and discussed.

**MATERIAL AND METHODS**

From 1994 to 2002, sixteen lesions of FNH in fifteen patients who had received MRI study at our hospital were analyzed. Only one patient had two lesions. The lesions were proved by surgery in three, percutaneous needle biopsy in four, and clinical follow-up in nine. Our criteria for clinical follow-up include typical ultrasound, CT, scintigraphy or MR imaging features for FNH, stationary lesion size and number on the follow-up sonography, and silent symptoms for at least one year [14]. There were ten

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**Figure 1.** A 49-year-old woman with FNH. **a.** Nonenhanced T1-weighted image showed the slightly hypointense lesion in the right lobe of the liver (arrows). Central scar was markedly hypointense (arrowhead). **b.** Corresponding HASTE T2-weighted image showed a slightly hyperintense tumor in contrast to surrounding liver (arrows) but central scar was hyperintense (arrowhead). **c.** Arterial phase presented strong lesion enhancement with the central scar being hypointense. **d.** 10-minute delayed-scan depicted contrast media uptake of the central scar.
male and five female with age ranging from 21 to 62 years (mean age: 33.1). Eleven patients were younger than 40 years old, three between 40 and 50, and one patient was older than 60.

In all patients, MR imaging was performed with a 1.5-Tesla superconducting magnet MR imager (Magnetum Vision Plus; Siemens, Erlangen, Germany) and phased-array body coil. All patients underwent imaging in the transaxial plane (6-mm slice thickness, 1.5-mm intersection gap). The entire liver was covered in the dynamic study during a single breath hold.

Examination parameters were as follows: T1-weighted gradient recalled echo (GRE) sequence with the FLASH technique (repetition time = 110-170 ms, echo time = 4.1 ms, flip angle = 80, acquisition time = 20 s, matrix = 128 x 256), T2-weighted FSE sequence (repetition time = 3600-4500 ms, echo time = 138 ms) and T2-weighted HASTE sequence (echo time = 90 ms, flip angle for refocusing pulse = 150, acquisition time = 20 seconds for 20 slices, matrix = 128 x 256).

Dynamic study was performed with fat-saturation T1-weighted GRE sequences following intravenous bolus injection of 0.1 mmol Gd-DTPA per kilogram of body weight. Images were obtained at 30 seconds for arterial phase, 70 seconds for portal venous phase, and 3, 6 & 10 minutes for delayed phase. Two radiologists reviewed the hard copy images with the knowledge for the diagnosis of FNH. The following MR features were recorded: size and location of the lesion, signal intensity of the lesion relative to that of normal liver parenchyma on T1-weighted image, T2-weighted image, & T1-weighted fat-suppressed dynamic study, homogeneity of the lesion signal intensity, presence of

Figure 2. A 24-year-old male with FNH presented as an isointense mass (arrows) on nonenhanced T1-weighted a. and T2-weighted b. images. Central scar (arrowhead) showed hypointensity on T1-weighted and hyperintensity on T2-weighted images. c. Arterial phase presented strong enhancement but central scar appeared hypointense. d. 6-minute delayed-scan depicted contrast media uptake of the central scar (arrowhead).
capsule or central scar, size of central scar, and the signal intensity change of the central scar in plain and dynamic study relative to tumor. Images were then compared with each other and final decisions were made by consensus.

RESULTS

Sixteen FNH lesions were found in fifteen patients and only one patient had two lesions. Mean diameter was 5.1 cm, ranging from 2 to 16 cm. Seven lesions (43%) were smaller than 3.5 cm and six lesions (38%) were larger than 5 cm in diameter. Fourteen patients presented with single lesion (94%) but one patient had double lesions. Seven lesions located in the right lobe (44%), eight in the left lobe (50%) and one in the caudate lobe (6%). Using Couinaud’s classification for specific anatomical localization, 6% in segment 1 (n = 1), 19% in segment 2 or 3 (n = 3), 31% in the segment 4 (n = 5), 25% in segment 5 or 6 (n = 4), and 18% in segment 7 or 8 (n = 3) were identified.

On nonenhanced T1-weighted images, FNH appeared minimally hypointense to the surrounding normal liver parenchyma in ten lesions (63%), isointense in five lesions (31%), and slightly hyperintense in one lesion (6%). Nonenhanced T2-weighted images of FNH presented to be mildly hyperintense in eleven lesions (69%), and isointense in five lesions (31%).

When combined with T1-weighted and T2-weighted imaging features, five specific patterns could be identified as follows: (1) hypointense on T1-weighted and isointense on T2-weighted (n = 3), (2) hypointense on T1-weighted and hyperintense on T2-weighted (n = 7) (Fig. 1), (3) isointense on T1-

Figure 3. A 23-year-old male with FNH presented to be an isointense mass (arrows) on T1-weighted a. and hyperintense on T2-weighted b. images, but without central scar. c. Arterial-phase image showed strong enhancement but delayed-phase d. image altered to be slightly hyperintense as compared to surrounding liver.
weighted and isointense on T2-weighted \((n = 2)\) (Fig. 2), (4) isointense on T1-weighted and hyperintense on T2-weighted \((n = 3)\) (Fig. 3), (5) hyperintense on both T1-weighted and T2-weighted \((n = 1)\) (Fig. 4).

In dynamic studies during the arterial-phase imaging, sixteen lesions \((100\%)\) appeared markedly hyperintense compared to surrounding normal liver parenchyma but rapidly washed out to be mildly hyperintense \((n = 8, 50\%)\) or isointense \((n = 8, 50\%)\) during portal-venous-phase and delayed-phase images. Central scar could be detected in twelve lesions and they showed hypointense on T1-weighted images \((n = 9, 75\%)\) and hyperintense on T2-weighted images \((n = 9, 75\%)\). In dynamic study, all the central scars demonstrated to be hypointense \((n = 12, 100\%)\) in arterial-phase images. Delayed enhancement of central scars could be depicted in portal-venous-phase images \((n = 2, 17\%)\), or a series of delayed scans in 3 minutes \((n = 4, 33\%)\), 6 minutes \((n = 3, 25\%)\), and 10 minutes \((n = 3, 25\%)\). The diameter of central scars in seven lesions was smaller than 5 mm \((58\%)\), 5 mm to 8 mm in three \((25\%)\), 1 cm in one \((8\%)\), and 2 cm in one \((8\%)\).

The majority of the lesions did not have capsule formation but only one lesion \((6\%)\) was encapsulated with fibrous tissue, which was proved by pathology. Lesion contents in most patients were homogeneous \((n = 14, 88\%)\).

**DISCUSSION**

FNH is the second most common benign hepatic tumor following hemangioma, constituting about 8% of primary hepatic tumors in autopsy series \([14]\). It is usually asymptomatic and is often an incidental finding during physical check-up. It has no malignant potential. FNH primarily occurs among adult female \((85\%)\) around young and middle age \([15]\). Pathologically, it is characterized by nodules of hyperplastic hepatocytes that circle around a central scar \([1]\). The scar often structures in a stellate-like manner and consists of fibrous bands, hyperplastic vessels, and aberrant bile ducts embedded in a loose myxomatous stroma \([1]\).

Typical and atypical MR imaging features of FNH have been reported but most of the articles revealed diverse results and were difficult to compared with each other \([2-13]\), mainly because of using low magnetic field MR imager \([2-5]\), conventional non-breath-hold sequence and body coil \([6]\), different MR contrast agent \([7, 8, 9]\) or different dynamic imaging acquisition protocol \([10, 11, 12, 13]\).

We used high magnetic field MR imager \((1.5T)\) with phased-array body coil and breath-hold sequence for high-resolution MR images. Arterial phase imaging in dynamic study becomes possible while using breath-hold T1-weighted gradient recalled echo FLASH imaging, which is compatible with spiral CT and angiography. Therefore, radiologist could obtain higher quality and more convincible MR imaging data for the diagnosis of FNH.

Plain MR images of FNH in the present study demonstrated iso- or slightly hypointense on T1-weighted and iso- or slightly hyperintense on T2-weighted images. The minimal change in signal intensity between FNH and normal liver parenchyma.
possibly reflects the components of this benign lesion, which primarily is composed of proliferation of normal hepatocytes and Kupffer cells but lacks normal hepatic architecture arrangement [1, 2].

HASTE sequence was used for T2-weighted images in most of the lesions in our study, which reflected to be equal or superior to FSE on lesion to liver contrast-noise ratio, motion artifact suppression, and image quality. [13, 16, 17].

In dynamic study, most lesions showed rapid and dramatic enhancement in arterial-phase images relative to the surrounding normal liver parenchyma. Early enhancement pattern reflects the hypervascular nature of the FNH and the main blood supply arising from the hepatic artery [18]. Some lesions also showed persistently mild hyperintensity relative to normal liver parenchyma on delayed phase, which might be due to the presence of hyper-functioning hepatocytes within lesions [6].

The central scar could be detected in 75% of our cases. Most of them showed hypointensity on T1-weighted and hyperintensity on T2-weighted images. The hyperintensity of the central scar on T2WI may be due to the presence of bile ducts and blood vessels, which radiate along the septa of the collagenous scar [1, 2]. Absence of central scar on plain and dynamic studies could be due to the small size or isointensity to the surrounding tumor.

Dynamic imaging protocol for liver tumor evaluation in breath-hold sequence of most recent reports covered arterial phase, portal venous phase, and delayed phase in 3 and 6 minute-scans [19, 20]. But the 10-minute post-contrast images allow the observation of delayed retention of contrast material within fibrous-tissue tumor (such as: cholangiocarcinoma, or colon cancer with liver metastasis), washout patterns in most of hepatocellular carcinoma, the presence or absence of centripetal enhancement in peripherally enhancing lesions, and central scar differentiation [12, 21]. During arterial-phase imaging in dynamic study, hypointense stellate-like central scar became more conspicuous than noneenhanced scans. Enhancing central scar could be detected on portal venous and delayed phase images on 3, 6, and 10 minutes follow-up scans, indicating that the sequential follow-up of dynamic images more than 6 minutes is necessary in order to pick up the central scar. This conclusion is compatible with one previous report in dynamic CT study [26] but another report showed difference in the percentage of scars that can be early-enhanced on arterial- and portal-venous-phase images (94.8% in their result [13] and 17% in ours). It is hard to explain this discrepancy and the possible etiology might be due to different population or tumor size or central scar size. Small (tumor size < 2 cm) FNH accounts for 13% in the present study (n = 2, 2/16 = 13%) and 28.6% in the previous report [14]. The size of central scar was not mentioned by previous report [13]. But in our study, small central scar (size < 8 mm) were demonstrated in 10 lesions (10/12, 83%), which also suggested that detailed and meticulous evaluation of this anatomical landmark was crucial for differential diagnosis.

Delayed enhancement of central scar in different time interval may be related to variable tissue density between vascular channels and traversing fibrous tissue [19]. Therefore, we postulated that differential delayed enhancement of central scar may be due to difference in vascular channel density comparing to surrounding fibrous tissue. However, no up-to-date pathological verification has been published.

FNH is usually not encapsulated. However, one particular lesion had a low signal rim on both T1-weighted and T2-weighted images. Pathologic evaluation proved it to be a well-defined capsule, which was very unusual but not obsolete and it had been reported in the literature [3]. The signal intensity of this case also demonstrated inhomogeneously high signal on T1-weighted and T2-weighted images and the etiology was proved to be steatosis under pathological examination, which has also been reported [3].

Other imaging modalities such as Tc-99m sulfur colloid liver-spleen scintigraphy, Color-Doppler ultrasound, and dynamic spiral CT scan, were reported to be helpful for the diagnosis of FNH. Eighty percent of FNH showed uptake in Tc-99m sulfur colloid liver scans but it was not a pathognomonic feature, which may be induced by other hepatocellular neoplasms, including hepatic adenoma and hepatocellular carcinoma [23]. Color Doppler ultrasound examination is another useful tool to evaluate the flow within the central scar but it cannot reveal dynamic changes without contrast agents [24, 25]. On the other hand, spiral CT offers similar dynamic changes as MRI but no T1-weighted and T2-weighted images could be served as a reference before contrast injection is provided. Higher sensitivity of the central scar detection may be related to better lesion to liver contrast-noise ratio of MR imaging as compared to CT [27].

In conclusion, arterial-phase images for tumor detection and delayed-phase images for central scar detection are superior to noneenhanced images in the diagnosis of FNH. We had reviewed and compared the literatures and concluded that typical MR imaging features showed iso- or slight hypointensity on T1-
weighted image, and iso- or slight hyperintensity on T2-weighted images. Central scar in plain MRI showed low signal intensity on T1-weighted images and high signal intensity on T2-weighted images. The most common dynamic appearance of FNH demonstrated to be homogeneous (except the scar), strong enhancement during arterial-phase, and isointense or slightly hyperintense during portal-venous-phase and delayed-phase imaging. Most of the central scars disclosed enhancement on delayed scans.

Multiphasic dynamic MRI is a very useful imaging modality for the diagnosis of FNH, but atypical lesions need biopsy or surgery to rule out other hypervascular neoplasms, such as adenoma [28], hepatocellular carcinoma, or hypervascular metastasis [6].

REFERENCE

肝臟局部結節增生之多相動態磁振造影

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本研究之目的為評估肝臟局部結節增生於多相動態磁振造影上之表徵。我們回顧分析過去8年間3個經由手術，4個經由切片，以及9個經由臨床追蹤，而證實為肝臟局部結節增生之15位病患的16個病灶。其中10位病患為男性，5位為女性，年齡層分佈為21至62歲，平均年齡為33.1歲。我們使用1.5-Tesla磁振造影掃描儀及phased-array體表線圈。先取得T1-weighted FLASH和T2-weighted HASTE & FSE影像後，再經由靜脈注射每公斤體重0.1 mmole劑量的Gd-DTPA，以取得fat-suppressed T1-weighted FLASH動態影像。動脈相時間設定在第30秒，門靜脈相設定在第70秒，延遲影像則取第3分鐘，6分鐘及10分鐘。

大部分的病灶在T1-weighted FLASH影像上呈現出些微的低訊號（n = 10, 63%），而在T2-weighted HASTE & FSE影像上呈現出些微的高訊號（n = 11, 69%）；動態影像上呈現出均勻高血管性的動脈相（n = 16, 100%）；到了門靜脈相和延遲影像則呈現出等訊號（n = 8, 50%），或略高於肝臟實質之訊號（n = 8, 50%）。有12個病灶在影像上反應出中心疤痕組織；中心疤痕組織於T1-weighted FLASH影像上呈現出低訊號（n = 9, 75%），在T2-weighted HASTE & FSE影像上呈現高訊號（n = 9, 75%），而動態影像上於動脈相呈現出低訊號（n = 12, 100%），但每一病灶均會呈現延遲顯影之高訊號，分別在門靜脈相（n = 2, 17%），延遲3分鐘影像（n = 4, 33%），6分鐘影像（n = 3, 25%），及10分鐘影像（n = 3, 25%）。中心疤痕組織有7例小於5 mm，4例介於5 mm至1 cm，1例大於2 cm。僅有1例外包覆有一層纖維膜。

磁振造影已成為廣泛應用於診斷肝臟局部結節增生的良好工具，我們的研究中發現，使用顯影劑之多相動態磁振造影被認為優於未打顯影劑之影像，而6分鐘以上之延遲影像是顯示中心疤痕組織的必要條件。典型的肝臟局部結節增生影像的特徵是均勻的（通常為單一個）腫塊於T1-weighted影像上呈現出與肝臟實質相等或略低的訊號，而於T2-weighted影像上呈現相等或略高的訊號；而中心疤痕組織相對於腫瘤在T1-weighted影像上呈現更低的訊號，但T2-weighted影像上則呈現高訊號。腫瘤於多相動態影像之動脈像呈現出增強顯影，而中心疤痕組織則於延遲影像呈現出增強顯影。

關鍵詞：肝臟局部結節增生，多相動態磁振造影