Correlation of Three-Dimensional Gradient Echo Dynamic MR Imaging with CT During Hepatic Arteriography in Patients with Hypervascular Hepatocellular Carcinomas: Preliminary Clinical Experience

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The purpose of this study is to elucidate the usefulness of dynamic MR study of the whole liver using 3DFISP with double dose gadolinium (Gd) enhancement in detecting enhancing lesions in 20 patients. Twenty patients with hepatocellular carcinoma (HCC) underwent 3DFISP dynamic study with double dose Gd. The demonstration of enhancing hypervascular lesions regardless of etiology was evaluated on a segment-by-segment basis with receiver operating characteristic (ROC) analysis, using findings on CT during hepatic arteriography as a gold standard. Diagnostic accuracy of 3DFISP in the detection of HCC was also evaluated. As to the demonstration of enhancing lesions, the Az value of the ROC curve was 88%. The detection rate of HCC with 3DFISP was 98%. 57% of enhancing pseudolesions were not detected on 3DFISP. We concluded that Dynamic MR study of the whole liver using 3DFISP with double dose Gd enhancement is a useful method to demonstrate hypervascular HCC. J. Magn. Reson. Imaging 2001;13:258–262. © 2001 Wiley-Liss, Inc.

Index terms: magnetic resonance; contrast enhancement; liver neoplasm; three-dimensional image; dynamic study

THE VALUE OF DYNAMIC MAGNETIC RESONANCE (MR) imaging has been reported for the diagnosis of liver tumors, particularly hepatocellular carcinomas (HCC) (1–9). Stress has been imposed on the importance of detecting early enhancement of the tumors which would represent their hypervascularity as observed on angiography (7–9). Previously, we have shown in phantom that three-dimensional (3D) fast-gradient echo sequence (fast imaging with steady precession (FISP), Siemens, Erlangen, Germany) is superior to two-dimensional (2D) fast low-angle shot sequence (FLASH) as a dynamic study pulse sequence when used with double dose Gd administration, because of its excellent signal-to-noise and contrast-enhancement ratios in addition to the inherently high spatial resolution (10). Our data also suggest that 3DFISP might be particularly useful in detecting and demonstrating hypervascular liver tumors (10).

In this report, we present our preliminary clinical data of 3DFISP in 20 patients with proven HCC, one of the most common hypervascular liver tumors. We first evaluated the performance of 3DFISP in demonstrating hypervascular lesions regardless of etiology, using the CT during hepatic arteriography (CTHA) as a gold standard, which is now considered the most accurate method to evaluate hepatic arterial vascularity (11,12). We also evaluated the diagnostic accuracy of 3DFISP in detecting HCC.

MATERIALS AND METHODS

Patient Population

Between January 1998 and August 1998, there were 38 consecutive patients with chronic liver damage who had double-dose Gd-enhanced 3DFISP dynamic MR liver imaging, and 20 of them underwent CT during hepatic arteriography (CTHA) and CT during arterial portography (CTAP) for possible transcatheter treatment of HCC. These 20 patients, all of whom had clinically and histologically proven viral hepatitis (N = 8) or cirrhosis (N = 12), form the study population in this evaluation in order to test the ability of 3DFISP to detect hypervascular lesions. There were 13 men and 7
women between 52 and 71 years (mean 62) of age. Body weights ranged from 43–67kg, with a mean of 52. The Gd contrast used was dimeglumine gadopentetate (Magnevist, Nihon Schering, Osaka, Japan). Because the maximum dose of Gd covered by public insurance in Japan is 20mL, 20mL of Gd was used even when the doubled dose was calculated to be > 20mL, which was the case in three patients. Thus, 17 patients received double dose (0.2mmol/kg) Gd, and three had 20mL (> 0.1mmol/kg, < 0.2mmol/kg) Gd; the average dose actually used for the patient population was 1.9 times the conventional (0.1mmol/kg) dose.

**Imaging Protocol**

All MR images were obtained with a 1.5T unit (Magnetom Vision, Siemens, Erlangen, Germany) using a four-element phased array coil and FOV of 24–33cm on the axial plane during patients’ breath-holding. T2-weighted images were obtained either with turbo-spin-echo sequence (TR/eff.TE = 2900–3000/120msec; echo train, 29; matrix, 138 × 256; slice thickness/interstice gap = 6/1.5mm; one excitation), half-Fourier rapid acquisition with relaxation enhancement (TR/eff.TE = ∞/87msec; echo train = 128; matrix size = 240 × 256; slice thickness/interstice gap = 5/0mm; one excitation), or both. T1-weighted images were obtained utilizing a FLASH sequence (TR/TE = 100/5msec; flip angle = 70°; matrix size = 112 × 256; slice thickness/interstice gap = 6/1.5mm; one excitation), with and without frequency selective fat saturation technique. Double-dose Gd-enhanced 3DFISP imaging (TR/TE = 5/2msec; flip angle = 25°, matrix 144 × 256; slab thickness = 13–15cm; partition = 24; one excitation, as determined in our phantom study (10)) was then performed before and at intervals of 30 sec, 60 sec, 90 sec, and 360 sec after commencement of the intravenous Gd injection in the upper extremities. Gd contrast medium was injected manually at an approximate rate of 2mL/sec. Subsequently, T1-weighted FLASH images were again obtained.

CTHA and CTAP were performed using a Toshiba X Vigor unit at the time of conventional angiography within a week of the MR examination in all 20 patients. All CTAP were obtained with a helical technique with a 1:1 pitch, 5mm collimation, 5mm reconstruction, 120kV, 150–200mA, and 25-sec delay following contrast injection (Iopamiron 150, 150mgI/ml) through a number 5 French catheter placed in the superior mesenteric artery via a femoral approach at a rate of 2.5mL/sec for a total volume of 100mL. A Liple vasodilator (Yoshitomi Pharmaceutical, Osaka, Japan) was injected through the catheter just before contrast injection for better portal opacification. All CTHA studies were performed with a helical technique using the same parameters as CTAP. Contrast was injected through a number 5 French catheter placed at the proper hepatic artery, or the right or left hepatic arteries separately via a contralateral or ipsilateral femoral approach as for CT arterial portography, at a rate of 1–3mL/sec with a 5-sec delay.

**Image Interpretation and Data Analysis**

CTHA of the 20 patients were evaluated by consensus by two radiologists (HA and KS) for the presence of enhancing lesions on a segment-by-segment basis, and this was used as the gold standard. CTAP were referenced at the time of interpretation. The nomenclature to describe hepatic segments was based on Couinaud’s system (13). There were a total of 140 segments available for evaluation. When enhancement of the suspected lesion was equivocal on CTHA, diminished portal perfusion at the corresponding site on CTAP was considered to support the presence of an enhancing lesion. Two other radiologists (KY and MJ), who were unaware of the results of CTHA, separately evaluated the 30-sec 3DFISP images of the same patient group on a segment-by-segment basis, and the presence of enhancing lesions, regardless of etiology, was evaluated. Thirty-sec films were selected for evaluation because they were considered to represent arterial or arterial-dominant phase (1.4,7). The level of confidence was recorded for each segment using a 5-point scale; a rating of 1 indicated definitely absent; 2, possibly absent; 3, indeterminate; 4, possibly positive; 5, definitely positive. A binomial receiver operating characteristic (ROC) curve was fitted to each reader’s confidence rating by using a maximum likelihood estimation (14,15). The area under the curve (Az value) was evaluated for the diagnostic accuracy of the two readers. The difference between ROC curves of the two readers was tested by the CORROC algorithm (14,15). The presence of hypovascular lesions, such as cysts or early HCC, was disregarded for the purpose of this study. Agreement between the two readers was evaluated by kappa statistics. Kappa values greater than zero were considered to indicate positive agreement; values up to 0.4, positive but poor agreement; values of 0.4–0.75, good agreement; and values greater than 0.75, excellent agreement. 3DFISP films were reviewed again by the same two readers by consensus, and disagreements were then resolved. Sensitivity and specificity were calculated for ratings of 4 or greater as positive. The etiology of the enhancing lesions was also determined and recorded by consensus at this time, referring to other MR images. HCC were diagnosed when T1- and T2-weighted images demonstrated abnormal signal intensity, and late-phase 3DFISP images showed low signal intensity as compared to the surrounding liver tissue at the site corresponding to the enhancing lesion seen on 30 sec 3DFISP images (3,4,7). Pseudolesions were diagnosed when there was no abnormal signal on T1- and T2-weighted images, and also on late phase 3DFISP images at the site of enhancing lesions, which were typically wedge-shaped and located at the periphery of the liver. When small nodular enhancements were seen apart from the surface of the liver with no signal change on T1- and T2-weighted images and late-phase 3DFISP images, these were considered small HCC. Hemangioma was diagnosed when characteristic very high signal intensity on T2-weighted images and prolonged enhancement on the late phase 3DFISP images were seen (16).
Confirmation of the Etiology of the Lesions

The etiology of enhancing lesions was confirmed as follows: in 118 segments in 17 patients, surgical resection was performed, and pathologic and intraoperative findings were correlated; when no pathology was detected in the resected specimen or by intraoperative ultrasonography, CTHA or 3DFISP findings were considered to be pseudolesions, including arterioportal shunts and non-portal splanchic venous supply such as cholecystic or aberrant right gastric venous drainage (17,18). In the remaining 22 segments in 3 patients, percutaneous biopsy was performed without surgery, and histologic evidence of HCC was obtained for at least one of the lesions. Iodized-oil injection emulsified with a chemotherapeutic agent (19) was performed in these three patients. When follow-up CT obtained 2 weeks after the therapy demonstrated dense accumulation of iodized oil in lesions other than the biopsy-proven one, they were considered to be HCC. Hemangiomas were confirmed when characteristic pooling of contrast was identified on the angiography (20). Enhancing lesions without iodized oil accumulation were all considered pseudolesions.

RESULTS

In all of the 20 patients, the entire liver was imaged with the imaging slab of 3DFISP. In 19 of 20 patients, good arterial or arterial dominant-phase images were obtained when strong aortic and hepatic arterial enhancement and minimal or slight enhancement of the intra-hepatic portal venous branches without opacification of hepatic venous branches were defined as findings of arterial dominant phase. In one patient a 30 sec image was considered an arterio-portal phase rather than a true arterial phase, demonstrating strong enhancement of both hepatic arterial and intrahepatic portal venous branches without opacification of hepatic venous branches.

Detection of Enhancing Lesions

There were 75 hepatic segments with 78 enhancing lesions observed on hepatic CTA. The Az values of the two readers who evaluated 3DFISP images were 0.89 and 0.87 (Fig. 1). There was no statistically significant inter-observer difference (P = .90). The kappa value between these two readers was 0.68, which suggests good agreement. The sensitivity and specificity of detecting enhancing lesions were 87% and 97%, respectively, when the findings on CTHA were regarded as the gold standard.

Detection of HCC

There were 56 enhancing HCCs, 1 hemangioma and 21 pseudolesions. HCC measured 3mm to 5cm in diameter, with a mean of 2.6cm. All enhancing HCCs but one, which was a histologically proven 3-mm intrahepatic metastasis, were correctly identified on 3DFISP, with a 98% detection rate of enhancing HCC (Fig. 2). Of the 21 pseudolesions seen on CTHA, 9 (43%) were not detected on 3DFISP, all of which were small arterioportal shunts measuring less than 5mm in their largest dimension and located in the periphery of the liver (Fig. 3). Three (14%) were interpreted as small HCC, all of which were small round-shaped arterioportal shunts located in the central portion of the liver. One hemangioma was correctly diagnosed. Thus, the etiology of the lesions was correctly diagnosed in 65 (96%) of 68 enhancing lesions depicted on 3DFISP.

DISCUSSION

The usefulness of demonstrating lesion enhancement on early phase CT or MR imaging has been stressed in the diagnosis of HCC because most HCC’s are hypervascular (7–9). Our previous phantom study suggested that 3DFISP has better signal profile to demonstrate lesion enhancement than 2DFLASH when used with double dose Gd (10). Although a full double-dose administration was not possible in three patients in the present study, usefulness of 3DFISP in demonstrating hypervascular lesions was suggested in our study, yielding relatively high diagnostic accuracy with an Az value of 0.88 and sensitivity and specificity of 87% and 97%, respectively, when CTHA findings were considered the gold standard. Most of the lesions which 3DFISP failed to detect were small arterioportal shunts located in the periphery of the liver. In one case, 3DFISP beautifully demonstrated tumor vascularity that was only faintly seen on CTHA (Fig. 2). CTHA is currently considered the most accurate method to detect arterial vascularity of hepatic lesions (16,17), but it is an invasive procedure requiring angiography. Dynamic MR imaging of the liver using 3DFISP with double-dose Gd enhancement may be a non-invasive alternative to CTHA for detecting hypervascular HCCs, particularly in patients for whom angiography is contraindicated. Further investigation using a larger series is needed to confirm this issue.

In the present study, 98% of the enhancing HCC’s were correctly detected with 3DFISP. The sensitivity of
detecting HCC using helical CT or dynamic MR study have been reported to be from 60% to 90% (7–9). Although our results cannot simply be compared to these previous data because of the difference in the study design and background, dynamic study of the liver with 3DFISP is a promising method to improve demonstration and analysis of HCC.

There are several limitations in this study. First, because we focused on the detection of enhancing lesions rather than characterization of lesions, we excluded non-enhancing lesions from the evaluation, including early HCC. Actually, there were five early HCC’s included in the surgical specimens in this study, which were all well differentiated and hypovascular on CTHA or 3DFISP (21). The value of 3DFISP in evaluating these hypovascular lesions should be further investigated. Second, proof of pathology was not obtained for all nodules detected on 3DFISP. Third, because we could not obtain whole liver specimens, some small lesions might not have been detected with any imaging technique. We therefore could not determine false-negative ratios in this study.

**Figure 2.** A 66-year-old man with proven HCC by histology. A: 30-sec 3DFISP image. An enhancing lesion of 1.5cm diameter (arrow) is evident. A small cyst (curved arrow) is seen. B: CT during hepatic arteriography. The area corresponding to the mass seen in A is only faintly enhanced (arrow) compared to the surrounding normal liver tissue. An insufficient injection rate may be the cause of faint enhancement in this particular case. A small cyst (curved arrow) is seen. C: CT during arterial portography. There is an area of portal perfusion defect (arrow) corresponding to the mass seen in A. A small cyst (curved arrow) is seen.

**Figure 3.** A 59-year-old man with proven HCC (not shown). A: 30-sec 3DFISP image. No definite enhancing lesion is seen in the left lobe. A small hemangioma (curved arrow) with arterioportal shunting is shown in the right lobe. B: CT during hepatic arteriography. Two small enhancing lesions (arrows) are noted in the left lobe of the liver. No definite lesions were detected at these sites on conventional CT, any sequence of MR, nor the intraoperative ultrasonography, and these lesions were considered pseudolesions (arterioportal shunts). A hemangioma is barely evident because the contrast medium was injected mainly into the left hepatic artery.
In conclusion, 3DFISP was shown to be a useful method to demonstrate hypervascular lesions in the liver, yielding 87% sensitivity and 97% specificity when CTHA findings were used as a gold standard. The detection rate of hypervascular HCC’s was 98%.

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