Differentiation of hypointensity nodules on gadoxetic acid-enhanced hepatobiliary phase MRI using non-balanced spin-echo SSFP (T2FFE)

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TARGET AUDIENCE: Researchers and clinicians interested in body/liver imaging and disease.

PURPOSE: Gadoxetic acid has excellent utility in liver MR imaging for diagnosing hepatocellular carcinoma (HCC), distinguishing hypervascular pseudolesions from small HCCs, and facilitating the discrimination between focal nodular hyperplasia and hepatic adenoma [1,2]. Furthermore, gadoxetic acid-enhanced hepatobiliary (HB) phase images significantly improve the detection of hepatic metastases compared with pre-contrast and dynamic MRI [1-5]. Although HB phase hypointensity is seen in malignancy [6], it is not specific, because many benign tumors such as cysts and hemangiomas also have low signal intensity on HB phase images. In particular, hemangiomas may often pose a serious problem because differentiation from metastases can be challenging due to a similar appearance on unenhanced and contrast-enhanced imaging [1,2,7,8]. In this study, we attempted to use a non-balanced spin-echo SSFP (T2FFE) sequence in the HB phase to differentiate malignant from benign (particularly cysts and hemangiomas) lesions. The purpose of this study was optimize sequence parameters and then to perform an initial evaluation in patients with focal hepatic lesions.

METHODS: A total of 38 patients were examined with a 1.5-Tesla whole-body clinical system (Achieva, Philips Healthcare). The study was approved by the local institutional review board, and written informed consent was obtained from all subjects.

1) Flip angle optimization of T2FFE for gadoxetic acid-enhanced MRI: A total of 10 patients without focal hepatic lesions were examined. T2FFE is a type of SSFP technique, allowing for the acquisition of whole-liver 3D black-blood images in a breath-holding scan [9]. T2FFE typically provides T2-weighted contrast because it actually generates the spin echo despite the variant of a gradient echo sequence [10]. Interestingly, however, T2FFE theoretically has high sensitivity to T1 shortening effects due to gadoxetic acid. It was thought that the degree of this sensitivity depends on the flip angle. Therefore, we compared flip angles for maximizing the sensitivity to T1 shortening on gadoxetic acid-enhanced MRI of the liver. First, to investigate the gadolinium sensitivity of T2FFE, we measured the signal-to-noise ratio (SNR) of stepwise-diluted gadoxetic acid solution for each flip angle, and we compared the SNR with conventional T2 weighted turbo spin-echo (T2W TSE) and T1 weighted turbo field-echo (T1W T1TFE). Subsequently, to optimize the flip angle in the HB phase, we calculated and compared the enhanced liver-to-muscle contrast ratio ($CR_{Liver\text{-}Muscle}$) at three flip angles of 20°, 50° and 80°. The $CR_{Liver\text{-}Muscle}$ of the different flip angles were compared by using one-way repeated measures analysis of variance (ANOVA) and the post-hoc Tukey test. Finally, to further optimize the flip angle, image quality of three flip angles was visually evaluated by two board-certified radiologists in a random and blinded manner. Quality of contrast, degree of artifacts, and contamination by small vessels were assessed using a three-point grading scale. Visual grades were compared among three flip angles using the Kruskal–Wallis test and the post-hoc Steel–Dwass test.

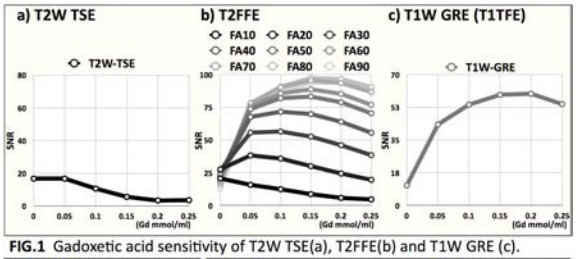

FIG.1 Gadoxetic acid sensitivity of T2W TSE(a), T2FFE(b) and T1W GRE (c).

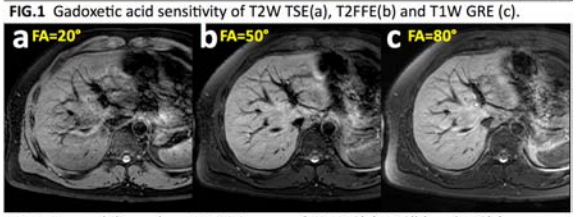

FIG.2 Hepatobiliary phase T2FFE images of FA=20°(a), 50°(b) and 80°(c).

2) Feasibility evaluation: A total of 28 patients with 34 lesions (including 8 cysts, 7 hemangiomas, 11 HCCs, and 8 metastases) were examined. First, to demonstrate the actual sensitivity to T1 shortening owing to gadoxetic acid in the optimized T2FFE sequence, $CR_{Liver\text{-}Muscle}$ was compared with conventional 3D T1W T1TFE. Spearman's correlation coefficient in $CR_{Liver\text{-}Muscle}$ between T1TFE and T2FFE sequence was calculated. Subsequently, to demonstrate the differences of image contrast between T2FFE and conventional T1W images, lesion-to-enhanced liver contrast ($CR_{Lesion\text{-}Liver}$) was compared with T1TFE in all lesions. The $CR_{Lesion\text{-}Liver}$ of the different lesions was assessed by using one-way repeated measures ANOVA and the post-hoc Tukey-Kramer test.

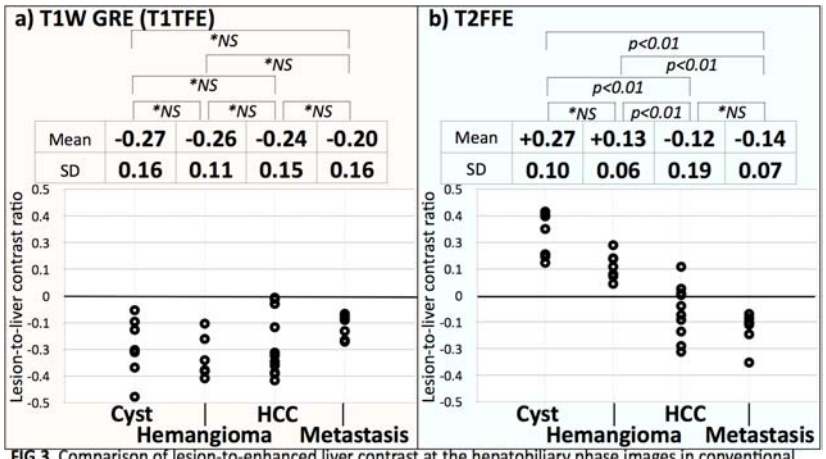

FIG.3 Comparison of lesion-to-enhanced liver contrast at the hepatobiliary phase images in conventional T1W GRE(a) and T2FFE(b).

RESULTS and DISCUSSION: 1) Gadoxetic acid sensitivity of T2FFE increased as flip angle increased (**FIG.1**). With flip angles of 50° or more, it became approximately constant. The $CR_{Liver\text{-}Muscle}$ for flip angles of 20°, 50° and 80° were 0.06±0.07, 0.41±0.08 and 0.50±0.10, respectively. Significant differences were observed in $CR_{Liver\text{-}Muscle}$ between flip angles of 20° and 50°, but were not observed between flip angles of 50° and 80° degrees. Representative images are shown in **FIG.2**. The visual grades of quality of contrast and degree of artifacts showed similar results between flip angles of 50° and 80°; there were no significant differences. On the other hand, the visual grades of contamination by small vessels were significantly better for a flip angle of 50° than 80°. Generally, large flip angles deteriorate black blood effect because they increase inflow effect (causing increase of blood signal). Thus, we employed an optimal flip angle of 50°.

2) The $CR_{Liver\text{-}Muscle}$ measured in T2FFE with flip angle of 50° correlated well with the one measured in conventional T1TFE (R=0.87, P<0.0001). The $CR_{Lesion\text{-}Liver}$ of T1TFE and T2FFE in all lesions are shown in **FIG.3**. In T1TFE, all types of lesions (both benign and malignant) showed negative contrast. On the other hand, in T2FFE, benign lesions showed positive contrast whereas malignant lesions showed negative contrast. This is because an increase of liver parenchyma signal due to gadoxetic acid unexpectedly became a reference point of signal level and therefore this sequence could clearly show the slight differences of T2 relaxation times or T1/T2 relaxation times ratio [11] in each lesion on the images. Representative images are shown in **FIG.4**. Although all metastases clearly showed negative contrast, HCCs showed positive contrast in some cases. Thus, in particular, T2FFE might be useful for discrimination of metastases and benign tumors (cysts and hemangiomas). However, in patients with cirrhosis, similar results may not be obtained because hepatocellular uptake of gadoxetic acid is reduced [12]. This issue should be noted as a drawback.

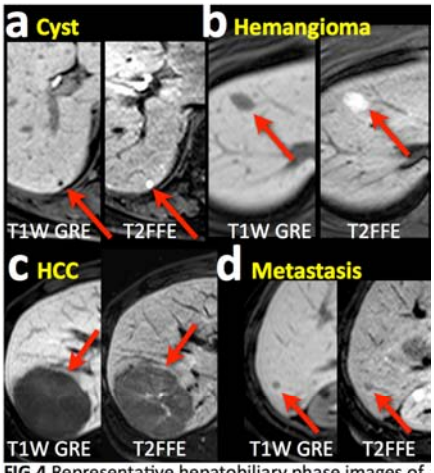

FIG.4 Representative hepatobiliary phase images of conventional T1W GRE and T2FFE in patients with cyst(a), hemangioma(b), HCC(c) and metastasis(d).

CONCLUSION: This study introduced a novel approach to differentiate hypointense nodules on HB phase images by use of T2FFE sequence. This approach might particularly be useful for distinguishing metastases and hemangiomas.

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