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Contrast-enhanced magnetic resonance pancreatography with gadoteridol by heavily T2-weighted three-dimensional fluid-attenuated inversion recovery: preliminary results in healthy subjects

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ABSTRACT

The purpose of this study was to investigate the feasibility of contrast-enhanced magnetic resonance (MR) pancreatography with intravenously administered gadolinium-based contrast material (GBCM) in healthy subjects. Eight healthy male subjects (age: 29–53 years old, median: 37 years old) were enrolled. Contrast-enhanced MR pancreatography was scanned with heavily T2-weighted three-dimensional fluid-attenuated inversion recovery (hT2W-3D-FLAIR) before and after intravenous GBCM administration. Two radiologists evaluated the images, referring to three-dimensional MR pancreatography by consensus. Scanning was performed five times at 1.5-h intervals (at 0.5, 2, 3.5, 5, and 6.5 h) after GBCM administration. In all subjects, pre-contrast-enhanced hT2W-3D-FLAIR images demonstrated no visualization of the main pancreatic duct. After GBCM administration, the main pancreatic duct was visualized in all subjects at 0.5 h (n=4, 50%) and/or 2 h (n=7, 88%). The mean signal intensity of the main pancreatic duct was 3.17 ± 0.78 at pre-contrast enhancement, 7.96 ± 4.60 at 0.5 h, and 8.08 ± 4.64 at 2 h. The signal intensity ratio of the main pancreatic duct against the pancreatic parenchyma was statistically higher ($P < 0.01$) at the 0.5-h and 2-h scans than that of pre-contrast-enhanced scan. Intravenously administered GBCM seeped into the pancreatic duct in sufficient concentration to alter the appearance of the main pancreatic duct by hT2W-3D-FLAIR in healthy subjects.

Key Words: pancreas, pancreatography, magnetic resonance imaging, contrast material

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INTRODUCTION

Visualization of the pancreatic duct by secreted contrast material may be valuable for assessing pancreatic disease and pancreatic exocrine function. As for the biliary system, excretory cholangiography (e.g., scintigraphy of the biliary system, magnetic resonance (MR) cholangiography using gadoxetic acid (Gd-EOB-DTPA), drip infusion cholangiography with computed tomography, and so on) has been clinically useful for assessing biliary disease.¹⁻³⁾ However, there is no specific

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contrast material that is secreted into the pancreatic duct for pancreatography.

Gadolinium-based contrast material (GBCM) has been reported to slightly seep into cerebrospinal fluid in the subarachnoid space several hours after intravenous administration.⁴⁻⁷⁾ Though T1-weighted imaging does not allow visualization of these fluid contrast enhancements, heavily T2-weighted three-dimensional fluid-attenuated inversion recovery (hT2W-3D-FLAIR) imaging can allow visualization of even faint enhancement with low-concentration GBCM.⁸⁻¹⁰⁾ We hypothesized that low-concentration GBCM may also seep into the pancreatic secretions after intravenous administration, and that hT2W-3D-FLAIR imaging could allow visualization of the contrast enhancement of the main pancreatic duct.

The purpose of this preliminary study was to assess the feasibility of visualizing the contrast enhancement of the main pancreatic duct after intravenous administration of gadolinium-based contrast material (GBCM) by using 3-Tesla MR hT2W-3D-FLAIR.

MATERIALS AND METHODS

Our institutional review board approved this study of healthy subjects and written informed consent was obtained from all participants. Eight healthy male subjects (age: 29–53 years old, median: 37 years old) volunteered for this study. The subjects were required to fast for at least 3 hours before MR examination, and fasting continued during the examination. Only water intake was allowed.

MRI technique

All MR imaging was performed on a 3-Tesla scanner (Skyra; Siemens, Erlangen, Germany) using a 32-channel array body coil. All subjects underwent heavily T2-weighted three-dimensional turbo spin echo (hT2W-3D-TSE) for usual MR pancreatography, and hT2W-3D-FLAIR for contrast-enhanced MR pancreatography. Both methods of pancreatography were scanned in the same oblique axial projection, and both images were obtained before and after a single dose of intravenous GBCM administration (gadoteridol, 0.2 mL/kg). Scanning was performed five times at 1.5-h intervals (at 0.5, 2, 3.5, 5, and 6.5 h) after GBCM administration. Parameters for usual MR pancreatography and hT2W-3D-FLAIR employed identical field of view (FOV), matrix size, and slice thickness to facilitate comparison.

Detailed scan parameters of usual MR pancreatography were: variable flip angle 3D turbo spin-echo technique (SPACE: sampling perfection with application-optimized contrasts by using different flip angle evolutions); repetition time (TR), 4900 ms; echo time (TE), 555 ms; frequency-selective fat-suppression pre-pulse; initial 180° refocusing flip angle rapidly decreased to 120° constant flip angle for the refocusing echo train; echo train length, 226; matrix size, 346 × 512; 12 oblique axial slices of 4-mm slice thickness; FOV, 253 × 300 mm; generalized autocalibrating partially parallel acquisition (GRAPPA) parallel imaging technique; acceleration factor of 3; number of excitations (NEX), 1.4; breath-hold acquisition time, 16 s.

Detailed scan parameter of contrast enhanced MR pancreatography were: SPACE sequence; TR, 4900 ms; TE, 555 ms; inversion time, 1700 ms; frequency-selective fat-suppression pre-pulse; initial 180° refocusing flip angle rapidly decreased to 120° constant flip angle for the refocusing echo train; echo train length, 226; matrix size, 346 × 512; 12 oblique axial slices of 4-mm slice thickness; FOV, 253 × 300 mm; GRAPPA parallel imaging technique with acceleration factor of 3; NEX, 1.4; breath-hold acquisition time, 16 s. On the basis of our preliminary experience before this study, an inversion time of 1700 ms was determined to nullify the main pancreatic duct signal.

Data analysis

The visualization of the main pancreatic duct on pre- and post-contrast-enhanced hT2W-3D-FLAIR images were evaluated by two radiologists (4 and 18 years of experience in the interpretation of abdominal MR imaging) by consensus. Usual MR pancreatography was used for anatomical reference in evaluating hT2W-3D-FLAIR images. The visual evaluation of the main pancreatic duct was graded as visible or not visible at the 3 pancreatic segments (pancreatic head, body, and tail).

The signal intensities of the main pancreatic duct and the pancreatic parenchyma of hT2W-3D-FLAIR images were measured by drawing circular regions of interest (ROIs). An ROI of 1-mm diameter for the main pancreatic duct and an ROI of 3-mm diameter for the pancreatic parenchyma were set on each pancreatic segment. If the main pancreatic duct was visible on hT2W-3D-FLAIR images, an ROI for the main pancreatic duct was set on hT2W-3D-FLAIR images directly. If the main pancreatic duct was not visible on hT2W-3D-FLAIR images, an ROI was copied from the image of the main pancreatic duct on usual MR pancreatography during the same session and was pasted onto the same position on the hT2W-3D-FLAIR images.

Then, the signal intensity ratio (SIR) of the main pancreatic duct to the pancreatic parenchyma was calculated as the relative value in each session. SIR was defined as the signal of the main pancreatic duct divided by the signal of the pancreatic parenchyma.

Statistical analysis

The average SIRs of the pre- and post-contrast-enhanced images were compared using the Mann-Whitney U test. We used SPSS 22 software (SPSS Inc., Chicago, IL) for statistical analyses and adopted 5% as the significance level for statistical testing. Mean data are expressed as means \pm standard deviations with their range.

RESULTS

In all subjects, pre-contrast-enhanced hT2W-3D-FLAIR images demonstrated no visualization of the main pancreatic duct (Fig. 1). After GBCM administration, the main pancreatic duct was detectable in at least one segment of the pancreas in 4 of 8 subjects (50%) at 0.5 h, 7 subjects (88%) at 2 h, 2 subjects (25%) at 3.5 h, 2 subjects (25%) at 5 h, and 1 subject (13%) at 6.5 h (Fig. 2). The main pancreatic duct was visualized in all subjects at 0.5 h and/or 2 h. Visualization of the main pancreatic duct was most frequently observed at the pancreatic body.

The mean signal intensity of the main pancreatic duct was 3.17 ± 0.78 at pre-contrast enhancement, 7.96 ± 4.60 at 0.5 h, 8.08 ± 4.64 at 2 h, 4.66 ± 1.86 at 3.5 h, 4.18 ± 1.58 at 5 h, and 3.84 ± 0.73 at 6.5 h. That of the pancreatic parenchyma was 2.83 ± 0.72 at pre-contrast enhancement, 3.85 ± 1.23 at 0.5 h, 3.13 ± 0.98 at 2 h, 3.31 ± 0.82 at 3.5 h, 3.05 ± 0.71 at 5 h, and 3.31 ± 0.93 at 6.5 h. The SIR of the pancreatic duct against the pancreatic parenchyma on the same scan is shown in Table 1. The SIR of the first scan and the second scan against that of the pre-contrast-enhanced scan shows a statistically significant difference ($P < 0.01$).

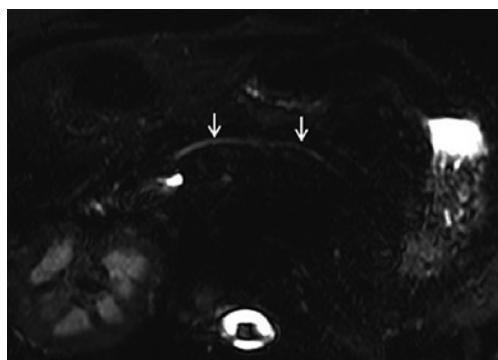


Fig. 1a

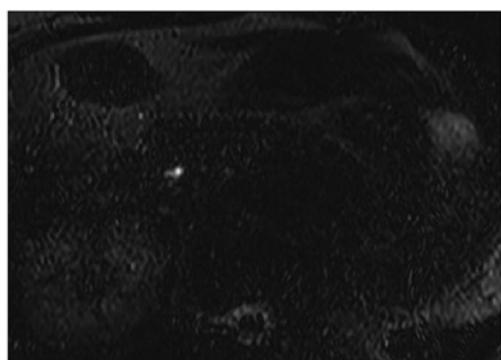


Fig. 1b

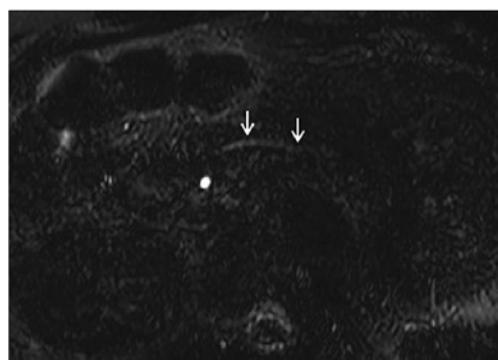


Fig. 1c

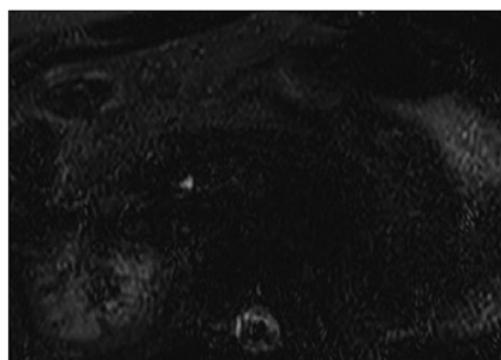


Fig. 1d

Fig. 1 A 53-year-old subject. (A) Usual MR pancreatography using hT2W-3D-TSE shows normal pancreatic duct at the pancreatic body and tail (arrow). (B) hT2W-3D-FLAIR image of pre-contrast material administration shows no visualization of the main pancreatic duct. (C) hT2W-3D-FLAIR image after 0.5 h shows the main pancreatic duct at the pancreatic body. (D) hT2W-3D-FLAIR image after 6.5 h shows no visualization of the main pancreatic duct.

DISCUSSION

The results of this study show that GBCM remains in the main pancreatic duct after intravenous administration, and hT2W-3D-FLAIR images allow visualization of the contrast enhancement in the pancreatic duct.

The concept that intravenously administered GBCM might seep into the pancreatic secretions is novel. After review of the literature, to the best of our knowledge, this has not been reported. The exact mechanism of how GBCM seeps into the pancreatic secretions is unknown. Intravenously administered GBCM is distributed into the blood and the extracellular space and is renally excreted. GBCM is not distributed into the intracellular compartment.¹¹⁾ Thus, it is presumed that GBCM is not excreted from the pancreatic acinar cells with the pancreatic secretions, and that GBCM slowly diffuses into the pancreatic duct from the pancreatic parenchyma.

In this study, we used hT2W-3D-FLAIR to detect contrast enhancement in the main pancreatic duct. The method to detect low concentrations of GBCM using 3D-FLAIR has been reported,⁴⁻⁷⁾ and further sensitivity to low concentrations has been reported using hT2W-3D-FLAIR.^{8, 9)} The T2 value of fluid with a low concentration of GBCM is long enough to be detected with a heavily

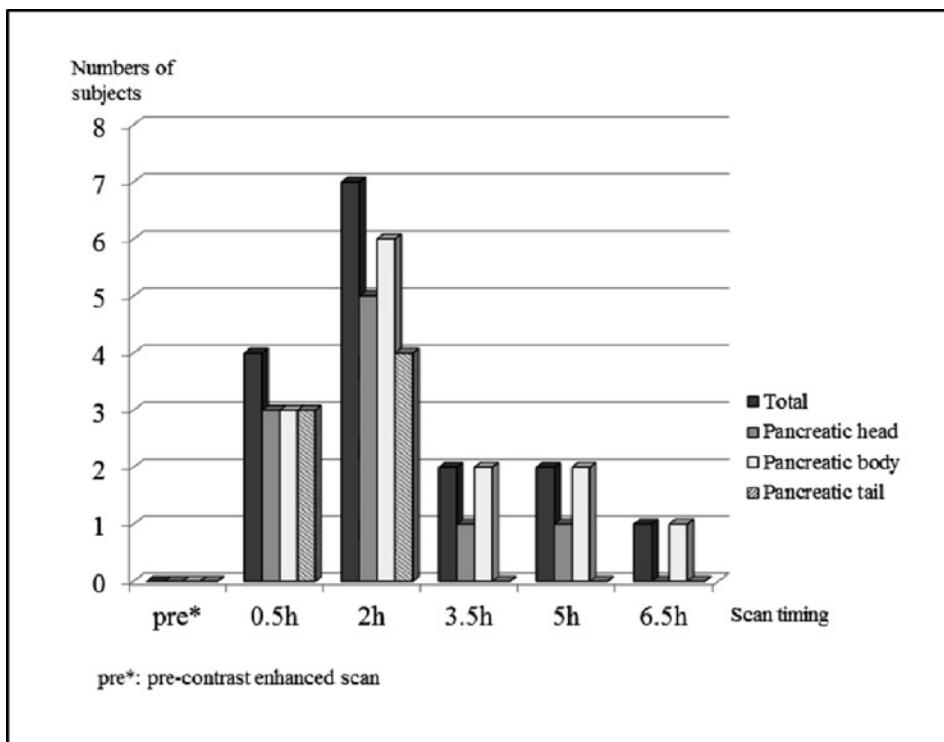


Fig. 2 Visualization of the main pancreatic duct on hT2W-3D-FLAIR images and time course. The main pancreatic duct was not detectable in all subjects on the pre-contrast-enhanced scan. The main pancreatic duct was detectable in 4 subjects at 0.5 h and in 7 subjects at 2 h. At 6.5 h, the main pancreatic duct was detectable in only 1 subject.

Table 1 Mean signal intensity ratio (SIR) against the pancreatic parenchyma

	SIR
Pre-contrast-enhanced scan	1.15 ± 0.24
0.5-h scan	2.16 ± 1.24
2-h scan	2.81 ± 1.84
3.5-h scan	1.53 ± 0.83
5-h scan	1.46 ± 0.75
6.5-h scan	1.24 ± 0.38

*: $P < .01$

**: $P < .001$

T2-weighted sequence, and inversion pulse could nullify the signal of the main pancreatic duct on the pre-contrast-enhanced images. Thus, hT2-3D-FLAIR allowed visualization of contrast-enhanced MR pancreateography.

Regarding the scan timing, the 2-h scan demonstrated the pancreatic duct most frequently,

and the 0.5-h scan demonstrated the duct second-most frequently. The main pancreatic duct was visualized in all subjects at 0.5 h and/or 2 h, and the SIRs of the 0.5-h scan and the 2-h scan showed a statistically significant difference. Therefore, the optimal scan timing in this study was considered 2 h after intravenous GBCM administration. However, this preliminary study set the scan timing from 0.5 h to 6.5 h at 1.5-h intervals. Thus, the true peak of GBCM concentration in the main pancreatic duct may be between 0.5 h and 2 h, and the results of this study showed that the scans after 3.5 h were too late to allow visualization of the contrast-enhanced pancreatic duct sufficiently.

To assess pancreatic disease and/or pancreatic function using MRI, secretin-enhanced MR pancreatography has been performed.^{12, 13)} Secretin provides better detail of the pancreatic ductal anatomy, and recently, cine-dynamic MRCP with a spatially selective inversion-recovery pulse has also been reported to estimate pancreatic exocrine function and flow of pancreatic secretions noninvasively.^{14, 15)}

If the concentration of GBCM in the pancreatic duct is reflective of pancreatic function or pancreatic disease, this contrast-enhanced MR pancreatography may be useful as a new tool for evaluating the pancreas. However, it is unknown whether or not the seepage of GBCM into the pancreatic duct correlates with pancreatic function. This preliminary study was performed only in healthy subjects. These points should be clarified in further studies.

This study had some limitations. First, the pancreatic position in usual pancreatography and the hT2W-3D-FLAIR image may not have been exactly the same because both image acquisitions were performed with a breath-hold technique. Therefore, in cases where the main pancreatic duct was not visualized on hT2W-3D-FLAIR imaging, the ROI positions pasted from the usual pancreatography in the same session may have been out of alignment. Second, the signal intensities of the main pancreatic duct were weak and the SIRs were also relatively low. However, the influence of signal noise was not considered. Third, the evaluation of the visibility of the main pancreatic duct was subjective and was, either positively or negatively, based on the consensus of two radiologists, but inter-observer agreement was not assessed.

In conclusion, intravenously administered GBCM seeped into the pancreatic secretions in sufficient concentration to alter the appearance of the main pancreatic duct by hT2W-3D-FLAIR in healthy subjects. This contrast-enhanced MR pancreatography may be useful as a new tool for evaluating the pancreas.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

REFERENCES

- 1) Lambie H, Cook AM, Scarsbrook AF, Lodge JP, Robinson PJ, Chowdhury FU. Tc99m-hepatobiliary iminodiacetic acid (HIDA) scintigraphy in clinical practice. *Clin Radiol*, 2011; 66: 1094–1105.
- 2) Tschirch FT, Struwe A, Petrowsky H, Kakales I, Marincek B, Weishaupt D. Contrast-enhanced MR

- cholangiography with Gd-EOB-DTPA in patients with liver cirrhosis: visualization of the biliary ducts in comparison with patients with normal liver parenchyma. *Eur Radiol*, 2008; 18: 1577–1586.
- 3) Okada M, Fukada J, Toya K, Ito R, Ohashi T, Yorozu A. The value of drip infusion cholangiography using multidetector-row helical CT in patients with choledocholithiasis. *Eur Radiol*, 2005; 15: 2140–2145.
 - 4) Hirai T, Ando Y, Yamura M, Kitajima M, Hayashida Y, Korogi Y, et al. Transthyretin-related familial amyloid polyneuropathy: evaluation of CSF enhancement on serial T1-weighted and fluid-attenuated inversion recovery images following intravenous contrast administration. *AJNR Am J Neuroradiol*, 2005; 26: 2043–2048.
 - 5) Mamourian AC, Hoopes PJ, Lewis LD. Visualization of intravenously administered contrast material in the CSF on fluid-attenuated inversion-recovery MR images: an in vitro and animal-model investigation. *AJNR Am J Neuroradiol*, 2000; 21: 105–111.
 - 6) Bert RJ, Caruthers SD, Jara H, Krejza J, Melhem ER, Kolodny NH, et al. Demonstration of an anterior diffusional pathway for solutes in the normal human eye with high spatial resolution contrast-enhanced dynamic MR imaging. *Invest Ophthalmol Vis Sci*, 2006; 47: 5153–5162.
 - 7) Naganawa S, Komada T, Fukatsu H, Ishigaki T, Takizawa O. Observation of contrast enhancement in the cochlear fluid space of healthy subjects using a 3D-FLAIR sequence at 3 Tesla. *Eur Radiol*, 2006; 16: 733–737.
 - 8) Naganawa S, Kawai H, Sone M, Nakashima T. Increased sensitivity to low concentration gadolinium contrast by optimized heavily T2-weighted 3D-FLAIR to visualize endolymphatic space. *Magn Reson Med Sci*, 2010; 9: 73–80.
 - 9) Naganawa S, Yamazaki M, Kawai H, Sone M, Nakashima T. Contrast enhancement of the anterior eye segment and subarachnoid space: detection in the normal state by heavily T2-weighted 3D FLAIR. *Magn Reson Med Sci*, 2011; 10: 193–199.
 - 10) Naganawa S, Suzuki K, Yamazaki M, Sakurai Y. Serial scans in healthy volunteers following intravenous administration of gadoteridol: time course of contrast enhancement in various cranial fluid spaces. *Magn Reson Med Sci*, 2014; 13: 7–13.
 - 11) Aime S, Caravan P. Biodistribution of gadolinium-based contrast agents, including gadolinium deposition. *J Magn Reson Imaging*, 2009; 30: 1259–1267.
 - 12) Mensel B, Messner P, Mayerle J, Fluhr G, Völzke H, Lerch MM, et al. Secretin-stimulated MRCP in volunteers: assessment of safety, duct visualization, and pancreatic exocrine function. *AJR Am J Roentgenol*, 2014; 202: 102–108.
 - 13) Sanyal R, Stevens T, Novak E, Veniero JC. Secretin-enhanced MRCP: review of technique and application with proposal for quantification of exocrine function. *AJR Am J Roentgenol*, 2012; 198: 124–132.
 - 14) Torigoe T, Ito K, Yamamoto A, Kanki A, Yasokawa K, Tamada T, et al. Age-related change of the secretory flow of pancreatic juice in the main pancreatic duct: evaluation with cine-dynamic MRCP using spatially selective inversion recovery pulse. *AJR Am J Roentgenol*, 2014; 202: 1022–1026.
 - 15) Yasokawa K, Ito K, Tamada T, Yamamoto A, Hayashida M, Tanimoto D, et al. Noninvasive investigation of exocrine pancreatic function: Feasibility of cine dynamic MRCP with a spatially selective inversion-recovery pulse. *J Magn Reson Imaging*, 2015; 42: 1266–1271.