

Diagnostic accuracy of 3D breath-hold MR cholangiography using compressed sensing acceleration in visualizing non-dilated biliary system in living donor liver transplantation donors

Abstract

Background: Visualizing non-dilated biliary system is important for preoperative mapping of living donor liver transplantation (LDLT) donors.

Purpose: To evaluate diagnostic accuracy of three-dimensional (3D) magnetic resonance cholangiography (MRC) within a breath-hold (BH) using compressed sensing (CS) acceleration in visualizing non-dilated biliary system in LDLT donors.

Material and Methods: For this prospective study, 43 donors who underwent LDLT were enrolled. Preoperative MRC sequence included BH CS-MRC (17-second BH) and conventional respiratory-triggered (RT) MRC. Two radiologists evaluated biliary configurations of the hepatic hilum, left lobe, and cystic duct. Diagnostic accuracy was assessed using intraoperative cholangiography and surgical records as a reference standard. The association between severity of artifact in RT MRC and better accuracy of BH CS-MRC in visualizing hilar biliary configuration was also evaluated.

Results: Diagnostic accuracy of BH CS-MRC was not significantly different from that of RT MRC for biliary configurations of the hepatic hilum (69.8% vs. 76.7%, $P = 0.579$; and 72.1% vs. 74.4%, $P > 0.999$), left lobe (48.8% vs. 60.5%, $P = 0.332$; and 48.8% vs. 67.4%, $P = 0.080$) and cystic duct (90.7% vs. 93.0%, $P > 0.999$; and 95.3% vs. 95.3%, $P > 0.999$), though it showed a slight tendency to be lower. Severe artifacts seen in RT MRC were significantly associated with better accuracy of BH CS-MRC (both $P < 0.001$).

Conclusions: BH CS-MRC can be seen as complementary to RT MRC in visualizing non-dilated biliary anatomy in LDLT donors and be useful especially for subjects whose RT MRC images show severe artifacts.

Keywords

3D MR cholangiography; Compressed sensing; Breath-hold; SPACE.

Introduction

Three-dimensional (3D) magnetic resonance cholangiography (MRC) is a well-established noninvasive imaging modality for anatomical and morphological evaluation of biliary system (1). One of the important roles of 3D MRC is preoperative mapping of biliary anatomy for surgical procedures such as hepatic resection and transplantation (2). It is beneficial especially for living donor liver transplantation (LDLT), because invasive procedures like drip infusion cholangiography computed tomography or direct cholangiography should be avoided as far as possible in healthy living donors (3–6).

Currently, 3D MRC examinations are based on heavily T2-weighted fast spin-echo sequence using respiratory-triggering (7). Sampling perfection with application-optimized contrast using different flip angle evolutions (SPACE) is a fast spin-echo sequence that has shown to be useful for respiratory-triggered (RT) 3D MRC at 3T (8). However, RT sequences require prolonged scan times. Moreover, in subjects with irregular respiratory rhythms, RT may fail to trigger correctly and may result in deteriorated images with motion artifacts.

Compressed sensing (CS) is an emerging technique of image reconstruction from randomly undersampled data and has been applied to accelerate magnetic resonance imaging (MRI) for recent years (9–11). Using CS technique, some recent studies demonstrated that 3D MRC could be performed within a breath-hold (BH) (12–17). Although these studies showed that 3D MRC using CS provided good image quality compared with conventional RT 3D MRC, no studies have focused on diagnostic accuracy in visualizing non-dilated biliary system, which is important for preoperative mapping of healthy living donors (3–6). These previous studies are also limited by lack of a reference standard.

The purpose of our study is to compare diagnostic accuracy of BH CS-MRC for the depiction of non-dilated hilar biliary anatomy for preoperative assessment and delicate biliary ducts in left and cystic ducts in LDLT donors with conventional RT MRC using direct cholangiography and surgical records as a reference standard.

Material and Methods

Study population

This prospective single-center study was approved by the institutional review board at our institution (R0742). We enrolled consecutive potential donors for LDLT who underwent preoperative MRC between September 2016 and January 2018. Inclusion criteria were age 18 years and older and no contraindications to MRI. All study participants provided written informed consent. We identified 57 potential candidates, of whom 14 were excluded for the following criteria: (a) had not accomplished the MRC study protocol ($n = 0$); and (b) had not undergone LDLT and intraoperative cholangiography (IOC) ($n = 14$). A total of 43 participants were included in this study.

MRC protocol

All examinations were conducted in the supine position using a 3T MR scanner (MAGNETOM Skyra, Siemens Healthcare, Erlangen, Germany), with a combination of 18-channel body-matrix coil and 32-channel spine-matrix coil. In all participants, two 3D MRCs were applied using a SPACE sequence: BH CS-MRC sequence and conventional RT MRC sequence (Table 1).

CS-MRC is a work-in-progress prototype based on the SPACE sequence using a variable-density Poisson-disk random undersampling pattern of the two phase-encoding dimensions with CS reconstruction (18). The acquisition time of BH CS-MRC is 17sec with a k-space sampling rate of 3.7%, which is corresponding to 27-fold acceleration. We performed CS reconstruction using an L1 norm-based regularization term (19), with a built-in reconstruction system (Siemens Healthcare). The CS specific reconstruction parameters, the regularization parameter and the number of iterations, were set to 0.002 and 40 for each reconstruction. The reconstruction time for each subject was approximately 10 min.

Other image sequences, axial and coronal 2D multi-slice half-Fourier acquisition single shot turbo spin echo (HASTE) and 2D thick-slab rapid acquisition with relaxation enhancement (RARE) MRC in the coronal and two coronal-oblique planes, were also obtained in all subjects; however, these images were not used to evaluate diagnostic

performance.

IOC

IOC was performed in all subjects by surgeons before lobe resection. After cholecystectomy, the cystic duct remnant was cannulated and iopamidol (Iopamiron, Bayer, Osaka, Japan) was hand injected to visualize biliary system. Anteroposterior views of IOC were obtained in all subjects.

Image analyses

BH CS-MRC and RT MRC images were randomly ordered and assessed by two independent board-certified abdominal radiologists (H.N. [reader 1] and S.K. [reader 2], with 7 and 8 years of experience, respectively). The readers knew that the images had been acquired preoperatively for LDLT donors, but were blinded to any other information, including IOCs and surgical records. The coronal source images and the coronal maximum intensity projection (MIP) reconstructions were used for evaluation. To minimize any learning bias, we scheduled a 4-week interval between the first and second interpretation sessions.

1. Diagnostic performance for visualizing biliary anatomy

We assessed diagnostic accuracy of MRC for the depiction of biliary anatomy of the hepatic hilum (3–6). For this analysis, reader 1 and reader 2 evaluated the confluence patterns of the right anterior hepatic duct (RAHD), right posterior hepatic duct (RPHD) and left hepatic duct (LHD). All anatomical variants, including accessory or aberrant ducts into common bile duct (CBD), right hepatic duct (RHD) or LHD, were recorded (20,21).

In addition, we assessed diagnostic accuracy of MRC for the depiction of biliary configuration of the left lobe (confluence patterns of bile ducts from segment II, III, and IV – B2, B3 and B4, respectively) and the insertion site of the cystic duct. Though biliary anatomy of the left lobe and cystic duct is not necessarily required for preoperative mapping in LDLT, we used them in order to evaluate diagnostic performance of MRC in visualizing delicate

ducts.

The reference standards of biliary configurations of the hepatic hilum, left lobe, and cystic duct were defined in advance by consensus of two other board-certified abdominal radiologists (A.O. and S.A., with 9 and 15 years of experience, respectively) by referencing IOCs and surgical records. They also referred preoperative MRC images to verify the reference standards.

2. Qualitative analysis for artifact

Reader 1 and reader 2 also evaluated the severity of motion or blurring artifact in BH CS-MRC and RT MRC for each subject using the following three-point scale: 1, no to mild artifacts with no impact on diagnostic assessment; 2, moderate artifacts with slight impact on diagnostic assessment; 3, severe artifacts with considerable impact on diagnostic assessment. If the two readers disagreed, a third radiologist (A.O. with 9 years of experience) arbitrated the results.

Statistical analysis

Diagnostic accuracy of BH CS-MRC and RT MRC was compared using exact McNemar test. The artifact scores were also compared using exact Wilcoxon signed-rank test. Regarding diagnosis accuracy for biliary configurations of hepatic hilum, the subjects were divided into two groups as “BH CS-MRC > RT MRC” and “BH CS-MRC $\leq$ RT MRC” according to the comparison of the result (accurate or inaccurate) of the two sequences: (1) BH CS-MRC > RT MRC, those in whom BH CS-MRC was accurate while RT MRC was inaccurate; and (2) BH CS-MRC $\leq$ RT MRC, those in whom BH CS-MRC was inaccurate while RT MRC was accurate or both sequences were accurate or inaccurate. To assess the association between the severity of artifact in RT MRC (score 3 or 1–2) and these two groups (BH CS-MRC > RT MRC or BH CS-MRC $\leq$ RT MRC), Fisher’s exact test was used. We also calculated estimated diagnostic accuracy assuming that accurate diagnosis by either BH CS-MRC or RT MRC can be regarded as accurate.

Interobserver agreement in diagnostic accuracy was evaluated using not only the

kappa coefficient but also the percent agreement because the kappa coefficient can be misleadingly low in situations where data show uneven distribution (22). The following kappa values were used to interpret agreement strength: 0–0.20 indicated slight agreement, 0.21–0.40 indicated fair agreement, 0.41–0.60 indicated moderate agreement, 0.61–0.80 indicated substantial agreement, and 0.81 and above indicated almost perfect agreement (23).

Statistical analyses were performed using R version 3.4.0 (R Foundation for Statistical Computing, Vienna, Austria) with the `exactRankTests`, `exact2x2` and `irr` package. All tests were two sided with a significance level of $P = 0.05$.

Results

A total of 43 participants (18 men and 25 women) were enrolled in this study. The median age was 37 years (interquartile range, 29.5–51.5 years; range, 21–64 years).

The acquisition time for BH CS-MRC was 17 sec for each subject. This was about 12–49 times shorter than the time required for RT MRC (median, 506 sec; range, 201–835 sec).

Anatomical variants of biliary configurations of the hepatic hilum included (24): (a) RPHD joining RHD in 30 patients (69.8%), (b) trifurcation in 2 patients (4.7%), (c) RPHD joining LHD in 4 patients (9.3%), (d) RPHD joining CBD in 1 patients (2.3%), and (e) other variations including the accessory duct joining CBD, RHD or LHD in 6 patients (14.0%). Anatomical biliary variants in the left lobe included: (a) common trunk of B2 and B3 joining B4 in 31 patients (72.1%), and (b) B2 joining common trunk of B3 and B4 in 12 patients (27.9%). Variants of the insertion site of the cystic duct included: (a) CBD in 42 patients (97.7%), and (b) other site in 1 patient (2.3%).

Diagnostic accuracy of BH CS-MRC and RH MRC for biliary configurations of the hepatic hilum, left lobe, and cystic duct were presented in Table 2. The difference was not statistically significant for both readers, although diagnostic accuracy of BH CS-MRC had a slight tendency to be lower than that of RT MRC (Table 2, Fig 1, Fig 2). The artifact score was not significantly different between BH CS-MRC and RH MRC ($P > 0.999$; both median

score 1). The number of subjects whose images showed the artifact score 3 was four (9.3%) for BH CS-MRC, and five (11.6%) for RT MRC. Regarding diagnostic accuracy for hilar biliary anatomy, the artifact score 3 in RT MRC was significantly associated with the group BH CS-MRC > RT MRC for both readers (Table 3, Fig. 2). All five RT MRC images with artifact score 3 were non-diagnostic for biliary configurations of the hepatic hilum. Assuming that accurate diagnosis by either BH CS-MRC or RT MRC can be regarded as accurate, diagnostic accuracy for hilar biliary anatomy of RT MRC and BH CS-MRC would be improved from 76.7% to 88.4% (reader 1) and from 74.4% to 83.7% (reader 2) in comparison with that of RT MRC.

Interobserver agreement (the kappa coefficient and percent agreement) for diagnostic accuracy was as follows, respectively. (1) BH CS-MRC: hepatic hilum, $\kappa = 0.61$, 83.7%; left lobe, $\kappa = 0.63$, 81.4%; and cystic duct, $\kappa = 0.29$, 90.7%. (2) RT MRC: hepatic hilum, $\kappa = 0.56$, 83.7%; left lobe, $\kappa = 0.45$, 74.4%; and cystic duct, $\kappa = 0.79$, 97.7%.

Discussion

We demonstrated that diagnostic accuracy of BH CS-MRC in visualizing non-dilated biliary anatomy of the hepatic hilum, left lobe, and cystic duct was not significantly different from that of RT MRC. However, diagnostic accuracy of BH CS-MRC showed a slight tendency to be lower than that of RT MRC. BH CS-MRC might be less accurate at visualizing delicate bile ducts. This tendency was in accordance with previous studies which reported that BH CS-MRC was less accurate at visualizing the delicate bile or pancreatic ducts (16,17). Our study subjects were healthy living donors whose bile ducts were likely to be thinner than older subjects with biliary or pancreatic disease in other studies (25). Depiction of delicate ductal structures of younger subjects seems to be a challenge for BH CS-MRC. In addition, severe motion or blurring artifacts with compromise in diagnostic assessment can not be completely eliminated in BH CS-MRC, even though 17-second BH acquisition is achieved. These artifacts may be caused by failure to hold the breath or other motion during BH (26).

Our results suggest that BH CS-MRC can be seen as complementary rather than alternative to RT MRC for preoperative mapping of hilar biliary anatomy in LDLT in clinical practice. BH CS-MRC has some strong advantages. In this study, four or five subjects showed better accuracy of BH CS-MRC in visualizing hilar biliary anatomy. We demonstrated that severe motion or blurring artifacts seen in RT MRC were significantly associated with better accuracy of BH CS-MRC. Another advantage is the total scan time, which was about 12–49 times shorter for BH CS-MRC. Considering these advantages, BH CS-MRC can be a complementary technique. Severe artifacts on RT MRC are not extremely rare as shown in this and a previous study (25). Repeat RT MRC for such situation requires a longer scan time and is not acceptable in clinical routine. For preoperative mapping in LDLT, additional acquisition of BH CS-MRC is expected to improve diagnostic accuracy, especially for subjects whose RT MRC images show severe artifacts. The 17-second BH will not be a heavy burden for most subjects.

Regarding diagnostic accuracy of RT MRC for the biliary configurations of the hepatic hilum, our result (74.4–76.7%) was lower than previously reported (84.6–92.5%) (3–6). There are two possible reasons for this result: (a) we evaluated all anatomical variants including accessory or aberrant ducts, which were not described or included in other studies; and (b) we did not exclude RT MRC images with severe artifacts causing problems for diagnostic assessment unlike other studies.

There is room for improvement in BH CS-MRC technique. The reconstruction time of CS-MRCP was almost 10 min in this study. Shorter reconstruction time must be better for the clinical implementation, and recent upgrading of our reconstruction system enables 6 min. Therefore, it is expected that improvement of the reconstruction system will achieve realistic reconstruction time in the clinical situation. Moreover, the fully optimized acquisition and reconstruction parameters for BH CS-MRC are still in development (17). The rapid development of CS and other undersampled MR techniques may also improve the accuracy of BH MRC (9,27).

We did not perform conventional quantitative analyses such as signal-to-noise ratio and contrast-to-noise ratio since they may not be valid when applied to CS, which inherently

reduces noise-like artifacts by its nonlinear image reconstruction (12).

Our study has several limitations. First, a relatively small number of subjects may limit the statistical power. Further study is needed to clarify the possible superiority of diagnostic accuracy of RT MRC. However, regardless of whether the superiority of RT MRC was statistically significant or not, additional BH CS-MRC for preoperative mapping can be recommended since RT acquisitions fail sometimes. Second, we did not perform subgroup analysis based on anatomical biliary variants due to the relatively small number of subjects. Third, the readers were not totally blinded to the MR sequence, because image characteristics of BH CS-MRC and RT MRC are different enough to distinguish between them. Fourth, kappa values for the diagnostic accuracy tend to be lower. However, this could be attributed to a high proportion of accurate diagnosis since percent agreements were high. Fifth, we compared diagnostic accuracy of 3D BH CS-MRC only with 3D RT MRC which is a standard procedure for preoperative mapping of biliary anatomy in LDLT donors (3–6), but not with 2D MRC.

In conclusion, diagnostic accuracy of BH CS-MRC in visualizing non-dilated biliary anatomy of the hepatic hilum, left lobe, and cystic duct of LDLT donors was not significantly different from that of RT MRC, though it showed a tendency to be lower. BH CS-MRC can be seen as complementary rather than alternative to RT MRC for preoperative biliary mapping in LDLT and be useful especially for subjects whose RT MRC images show severe artifacts.

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Table 1. Scan parameters of sequences in MRC protocol

	BH CS-MRC	RT MRC
Dimension	3D	3D
Plane	Coronal	Coronal
TR (ms)	1700	1000
TE (ms)	501	504
Flip angle (°)	115	120
Field of view (mm)	350 × 350	340 × 340
Matrix size	384 × 384	384 × 384
Section thickness (mm)	1.14	1.14
Intersection gap (%)	0	0
Fat suppression	SPAIR	SPAIR
Parallel imaging	None	GRAPPA
Parallel imaging factor	None	3
Respiratory triggering	None	PACE
Acquisition time (sec)	17	506 (201 to 835)
Slice number	112	112

Data for acquisition time of RT MRC are median (range). SPAIR = spectral attenuated inversion recovery. GRAPPA = generalized autocalibrating partially parallel acquisitions. PACE = prospective acquisition correction.

Table 2. Diagnostic accuracy of BH CS-MRC and RT MRC for biliary anatomy

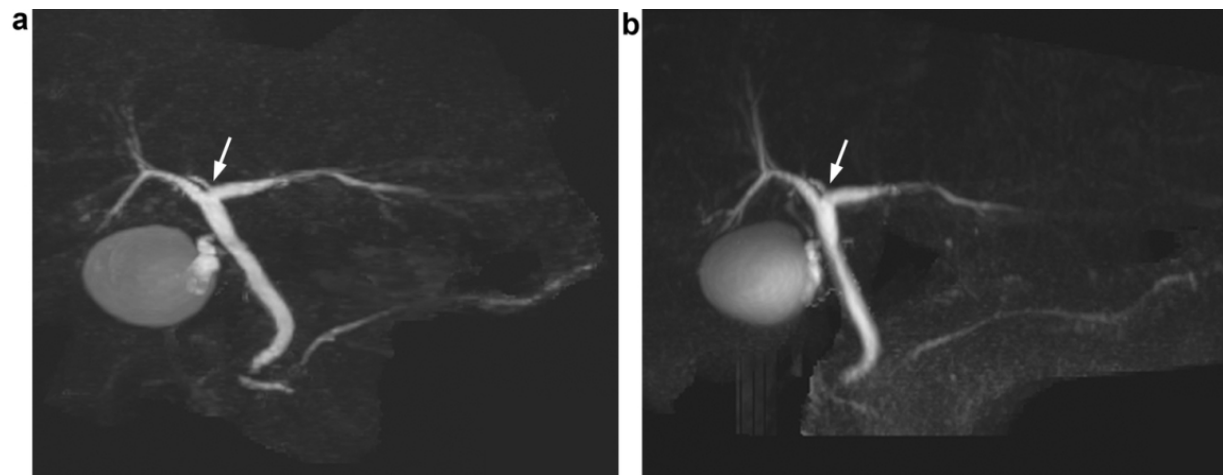
	BH CS-MRC	RT MRC	<i>P</i> value	Odds Ratio [95% CI]
Hepatic hilum				
Reader 1	69.8% (30/43)	76.7% (33/43)	0.581	0.63 [0.16–2.17]
Reader 2	72.1% (31/43)	74.4% (32/43)	> 0.999	0.80 [0.16–3.72]
Left lobe				
Reader 1	48.8% (21/43)	60.5% (26/43)	0.332	0.54 [0.17–1.61]
Reader 2	48.8% (21/43)	67.4% (29/43)	0.077	0.33 [0.08–1.10]
Cystic duct				
Reader 1	90.7% (39/43)	93.0% (40/43)	> 0.999	0.5 [0.008–9.60]
Reader 2	95.3% (41/43)	95.3% (41/43)	> 0.999	1.0 [0.07–13.80]

Data are % (n/N). CI = confidence interval.

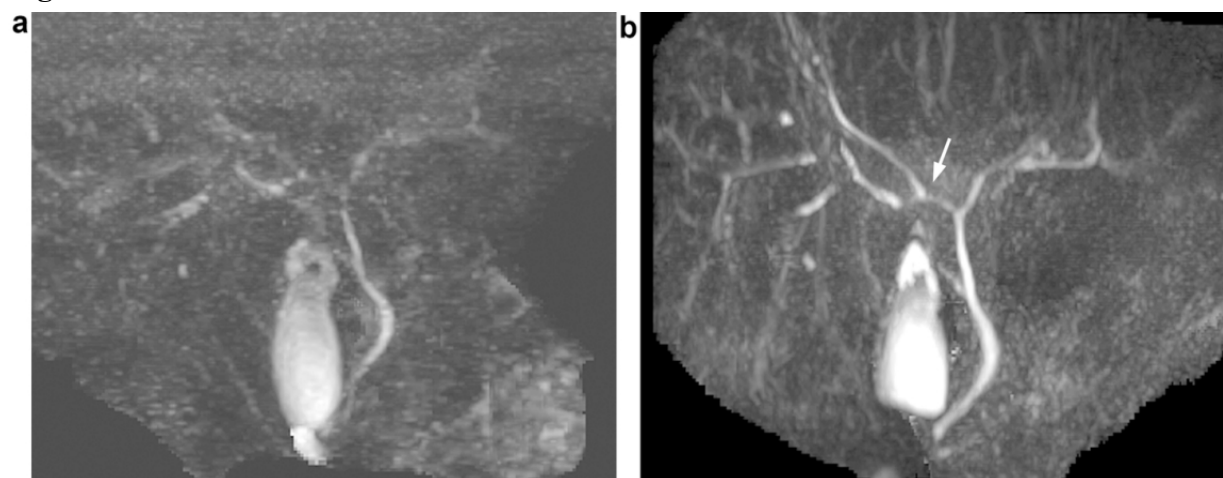
Table 3. Association between the severity of artifact in RT MRC and “BH CS-MRC > RT MRC” or “BH CS-MRC $\leq$ RT MRC” group in visualizing the biliary configuration of the hepatic hilum

	Artifact score 3 in RT MRC	Artifact score 1–2 in RT MRC	<i>P</i> value
Reader 1			
BH CS-MRC > RT MRC	4	1	< 0.001
BH CS-MRC ≤ RT MRC	1	37	
Reader 2			
BH CS-MRC > RT MRC	4	0	< 0.001
BH CS-MRC ≤ RT MRC	1	38	

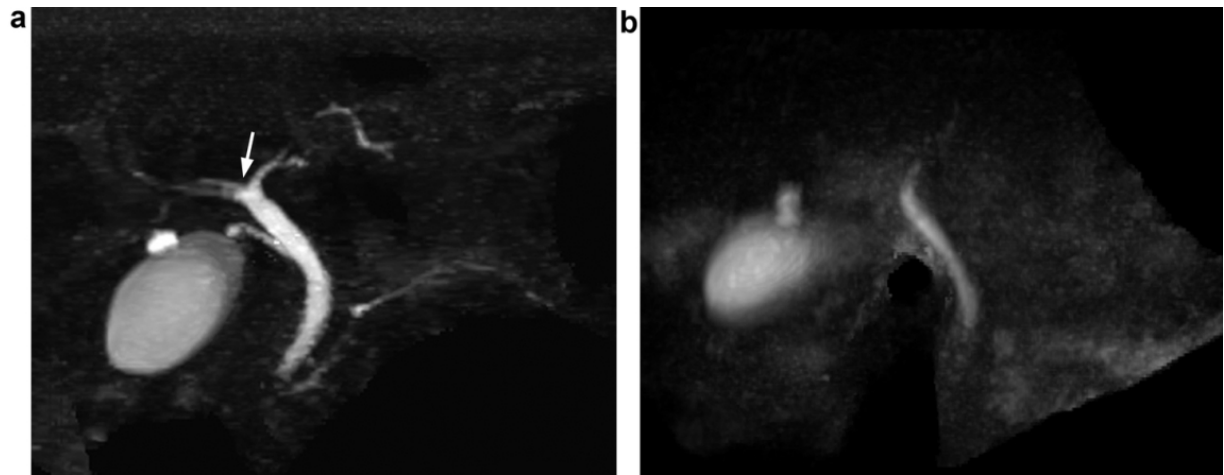
Figures

Figure 1

(a) BH CS-MRC MIP image and (b) RT MRC MIP image. The hilar biliary anatomy (RPHD joining LHD) was well depicted on both BH CS-MRC and RT MRC (arrows).

Figure 2

(a) BH CS-MRC MIP image and (b) RT MRC MIP image. The hilar biliary anatomy (RPHD joining RHD) was well depicted on RT MRC (arrow) while BH CS-MRC was considered non-diagnostic.

Figure 3

(a) BH CS-MRC MIP image and (b) RT MRC MIP image. The hilar biliary anatomy (trifurcation) was well depicted on BH CS-MRC while RT MRC was considered non-diagnostic because of severe motion artifacts (artifact score 3).