Magnetic Resonance Imaging 61 (2019) 116–123

Contents lists available at ScienceDirect

Magnetic Resonance Imaging

journal homepage: www.elsevier.com/locate/mri

Original contribution

Gadoxetate acid disodium-enhanced MRI: Multiple arterial phases using differential sub-sampling with cartesian ordering (DISCO) may achieve more optimal late arterial phases than the single arterial phase imaging

Yi Wei[a,1], Liping Deng[a,1], Yuan Yuan[a], Zixing Huang[a], Xiaopeng He[a], Xiaocheng Wei[b], Hancheng Yang[b], Bin Song[a,*]

[a] Department of Radiology, West China Hospital, Sichuan University, 610041 Chengdu, China
[b] GE Healthcare China, Beijing, China

ARTICLE INFO

Keywords:
Liver
Hepatocellular carcinoma
Magnetic resonance imaging
Contrast agents

ABSTRACT

Background: To prospectively determine whether the use of a multiple arterial phase imaging (DISCO) improve the capturing rate of late arterial phase with less motion artifact than single arterial phase obtained with gadoxetate acid disodium.

Materials and methods: From 06/2017 to 10/2018, prospectively acquired data of 132 patients who underwent either single ($n = 67$) or multiple arterial phase ($n = 65$) gadoxetate acid-enhanced MR imaging were analyzed. Two readers independently assessed arterial phase timing and the degree of motion artifact using a five-point scale. The *kappa* test was used to determine the agreement between the two readers, χ^2 or *fisher* exact test were used for the categorical variables and *Student t*-test or *Mann-Whitney U* test were used for the comparison of the motion artifacts.

Results: Good to perfect inter-observer agreement was obtained for the arterial phase timing and degree of motion artifact (all *kappa* value > 0.70). Optimal timing of arterial phase was observed in 95.4% (62/65) of multiple arterial phase compared with 73.1% (49/67) of single arterial phase ($\chi^2 = 12.209$, $p < 0.001$). Motion artifact score of the late arterial phase images measured using single arterial phase acquisition (3.22 ± 0.68) was significantly higher than the multiple arterial phase (2.42 ± 0.74) group ($t = 5.921$, $p < 0.001$). For the multiple arterial phase comparison, motion artifact score of the 2nd, 3rd and 4th phases were also significant reduced compared with 1st, 5th and 6th phases (all $p < 0.05$).

Conclusion: The use of multiple arterial phase acquisition with gadoxetate acid disodium can improve the capturing rate of well-timed late arterial phase with less motion artifact.

1. Introduction

Gadoxetate acid disodium is a widely used hepatobiliary specific contrast agents which can offer the hepatobiliary phase (HBP) in addition to the early dynamic phases obtained with other conventional extracellular gadolinium-based contrast media (GBCM), thus, enables more accurate detection, characterization of focal liver lesions [1–4]. However, accumulative evidences have shown that gadoxetate acid disodium yielded poorer arterial phase images compared with other conventional GBCM due to the high frequency happening of the transient severe motion that caused the severe motion artifacts [5–7]. Several strategies have been used to reduce the severe motion artifacts, including low injection rate, contrast dilution, shorten the scanning time and modified breath-holding method [8–12]. Of all these strategies, the data acquisition method was mainly based on the single arterial phase acquisition and once the transient severe motion occurs, the image quality cannot be guaranteed.

Differential sub-sampling with cartesian ordering (DISCO) is a high spatial-temporal resolution dynamic contrast-enhanced magnetic resonance (MR) technique that combines multiple features: a dual echo spoiled gradient echo (SPGR) acquisition for DIXON water-fat separation, a pseudo-random variable density *k-space* segmentation, parallel imaging and a view sharing reconstruction [13,14]. It offers the advantage of high imaging speed as the central *k-space* region were fully

* Corresponding author at: No. 37, GUOXUE Alley, Chengdu 610041, China.
E-mail address: songlab_radiology@163.com (B. Song).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.mri.2019.05.033
Received 10 February 2019; Received in revised form 16 May 2019; Accepted 21 May 2019

sampled every time while the outer regions were sub-sampled with a pseudo-random scheme [13]. Compared with the T1-weighted three-dimensional (3D) SPGR referred as LAVA-Flex sequence which was often used for single arterial phase acquisition, DISCO can achieve multiple arterial phase acquisitions in a single breath-hold period without sacrificing spatial resolution. Thus, with DISCO acquisition, it is high likely that at least one motion-free arterial phase image can be guaranteed. Furthermore, DISCO may also have the potential to increase the chance of capturing rate of the late arterial phase image as which is critical for the diagnosis of hepatocellular carcinoma (HCC) and other hypervascular metastasis [14]. To our knowledge, few studies have investigated the clinical benefit of multiple arterial phase images with DISCO in comparison with single arterial phase images in terms of the capturing rate of well-timed late arterial phase and reduce the motion artifact with gadoxetate acid-enhanced MR to date.

The purpose of this study was to prospectively determine the usefulness of multiple arterial phase imaging using DISCO can provide arterial phase images with less motion artifact and improve the capturing rate of well-timed late arterial phase in comparison to single arterial phase with gadoxetate acid-enhanced MR imaging.

2. Materials and methods

2.1. Participants

This study was approved by the institutional review board, and written informed consent was obtained from all patients. Between June 2017 and October 2018, a total of 175 patients who were suspected of having malignant focal hepatic lesions identified with ultrasonography or computed tomography (CT) underwent with preoperative gadoxetate acid-enhanced MR examination. A simple randomization was conducted before the MR examination according to random number table and all the patients were randomization divided into two groups. Including subcohort A patients underwent with multiple arterial phase imaging using DISCO, and subcohort B patients underwent single arterial phase imaging using LAVA sequence. Among these patients, 43 patients were excluded because of the exclusion criteria (Fig. 1): (*a*) patients underwent hepatectomy with preoperative transarterial chemoembolization ($n = 12$) or radiofrequency ablation ($n = 7$), (*b*) hepatic lesions were pathologically diagnosed as benign lesions ($n = 9$), intrahepatic cholangiocarcinoma ($n = 6$), (*c*) multiple HCCs ($n = 6$) and small HCC lesions in diameter < 1 cm ($n = 3$).

2.2. MR imaging

MR imaging was carried out by using a 3.0 T MR system (Discovery MR 750w, GE Healthcare, Milwaukee, USA). A sixteen-channel phased-array torsor coil (GE Medical System) was used for all examinations. In our study, DISCO divided the k-space data into 3 regions: 1 center region and 2 outer regions. The center regions are acquired every other acquisition while the outer groups are acquired less frequently and were shared with the nearest center regions for the final image reconstruction. For the subcohort A patients, multiple arterial phase images were acquired in an 18 s long breath hold with a 20 s delay after the injection of gadoxetate acid disodium (Primovist, Bayer Pharma AG, Berlin, Germany) with the injection rate of 1 ml/s. These data were reconstructed into sixth sequential phases with a temporal resolution of 3 s. Since the center *k-space* region were sampled every time and outer region were subsampled, the center *k-space* region images were reconstructed at 20 s, 23 s, 26 s, 29 s, 32 s, and 35 s (Fig. 2). For the subcohort B patients, the single arterial phase images were acquired in a 17 s long breath hold with a 20 s delay after the contrast injection. The mean delay time for portal venous phase, delayed phase and HBP were 60 s, 180 s and 20 min (Fig. 3), respectively. The routine liver MR sequence consisted of breath hold (BH) 2D T1 dual echo, respiratory triggered fat suppression T2-weighted imaging and diffusion weighted imaging (DWI) ($b = 0$, 200, 800, 1000) were also included. The detailed parameters of the DISCO, LAVA-Flex and routine liver MR sequence were listed in Table 1.

2.3. Imaging analysis

All the MR images were reviewed in our institutional picture archiving and communication system (Syngo-Imaging, version VB36A; Siemens Medical Solutions). Two independent radiologists reviewed the MR images. To avoid the measurement bias, arterial phase images of the two subcohorts was presented randomly and independently in a blinded manner. Each arterial phase images were reviewed for the timing of arterial phase and respiratory motion artifacts. The scoring system [15,16] for the timing phase was as follows: 1 = no contrast agents in the hepatic artery; 2 = early arterial phase (only contrast agents in the hepatic artery, but no enhancement in the portal vein and liver parenchyma); 3 = well-timed late arterial phase (hepatic artery and mild portal vein enhancement, without strong parenchymal enhancement or hepatic vein enhancement); 4 = portal venous phase (strong liver parenchymal and hepatic vein enhancement) (Fig. 4). When the two radiologists did not agree with the arterial phase timing, the consensus was reached by discussion. Motion artifacts was evaluated by using a 5-point scoring system that have been used in previously published articles [16,17] and demonstrated high interrater repeatability and the scoring system was:1 = no motion artifact; 2 = minimal artifact but have no effect on diagnostic quality; 3 = moderate motion artifact but not severe effect on diagnostic quality; 4 = severe motion artifact but the images were still interpretable; 5 = extensive artifact and the MR images were uninterpretable. Furthermore, typical truncation artifact presented as the ring artifact around the liver margin is not considered as the motion artifact. The motion artifact score was reached consensus by the two radiologists of each arterial phase images, and the optimal timing of arterial phase acquired with DISCO was used in comparison with the single arterial phase images. Furthermore, if there were more than one arterial phase with the same timing adequacy, the less motion score phase was selected for comparison.

2.4. Statistical analysis

Categorical variables are reported as the number of cases and percentages. *Kappa* test was firstly used to determine the agreement between the two independent radiologists in each item. A *kappa* value of 0 indicates no agreement, *kappa* values of 0.01–0.20 represent slight agreement, 0.21–0.40 fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 good agreement, 0.81–0.99 almost perfect agreement, and 1 perfect agreement. χ^2 or *fisher* exact test were used for the categorical variables. Continuous variables were firstly checked for normality by using *Kolmogorov-Smirnov* test, and *Student t*-test or *Mann-Whitney U* test were used for the comparison of the motion artifacts between the single arterial phase and the multiple arterial phase. *Kruskal-Wallis* test was used to compare the difference of motion artifact score with DISCO and LAVA-Flex imaging, and for the further multiple comparisons of arterial phases, the α' was corrected by using *Bonferroni* correction to reduce type I error. The α' is corrected according to the formula $\alpha' = \alpha \times m$ (numbers of comparion). A p value < 0.05 was considered to indicate a statistical significance. All statistical analyses were performed by using a statistical software package (SPSS 23.0 (SPSS Inc., Chicago, IL, USA)).

3. Results

3.1. Clinicopathologic characteristics

The final population included for analysis consisted of 132 patients (mean age, 51.66 ± 11.98 years; range, 24–75 years), including 90 men (51.63 ± 11.42 years; range, 33–75 years) and 42 women

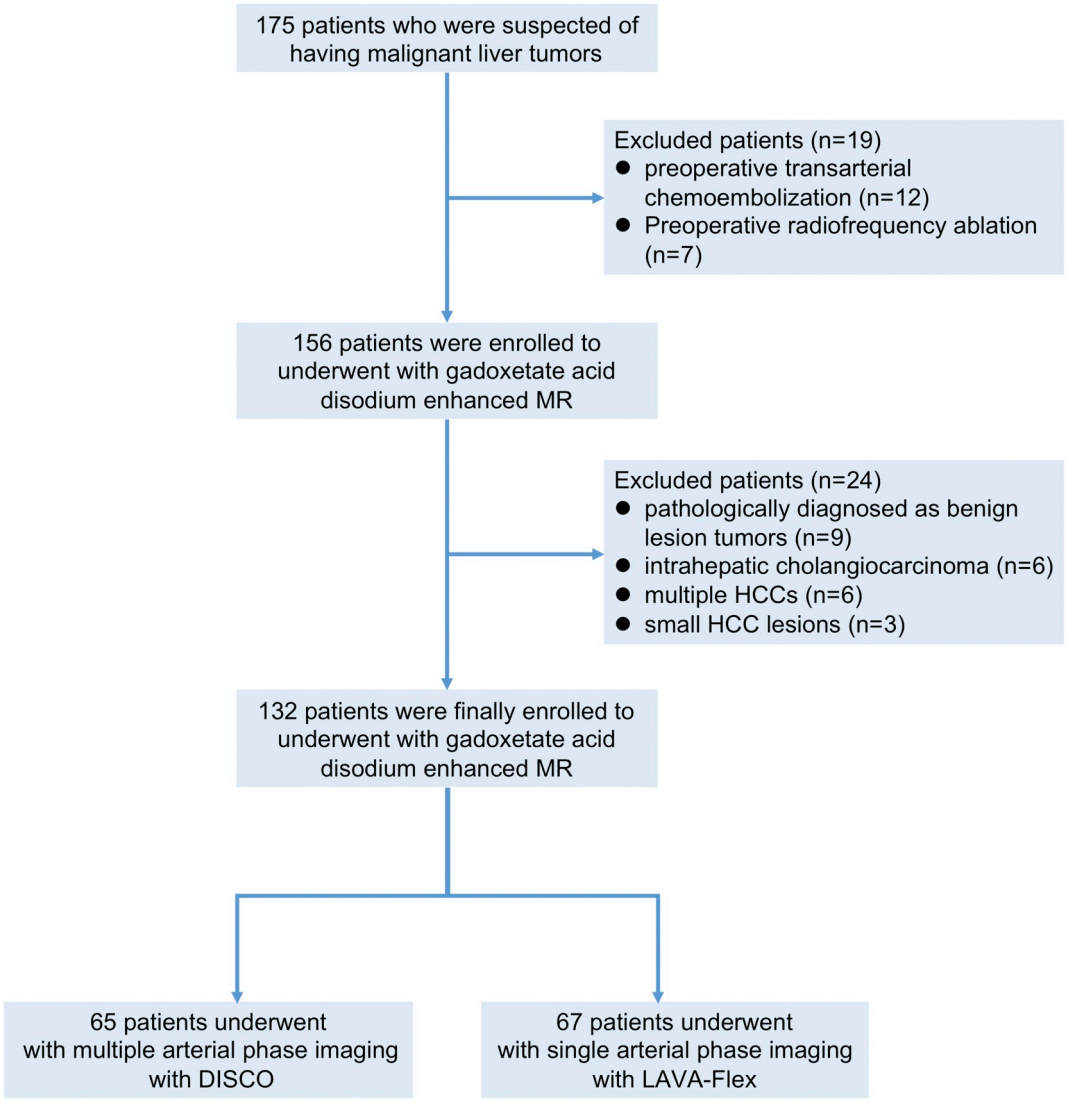

Fig. 1. Flowchart of the inclusion and exclusion criteria. Patients underwent with gadoxetate acid disodium enhanced MR were randomized divided into two groups with multiple arterial phase imaging with DISCO or single arterial phase imaging with LAVA-Flex.

(51.71 ± 13.28 years; range, 25–69 years). Of these, 65 patients (51.52 ± 11.94 years) including 67 tumors (6.46 ± 3.98 cm) underwent with the multiple arterial phase imaging with DISCO acquisition and 67 patients (51.79 ± 12.13 years) including 72 tumors (6.72 ± 3.72 cm) underwent with the single arterial phase imaging with LAVA-Flex. Histologically, there were 24 HCCs with Edmondson-Steiner (E-S) grade 1, 63 HCCs with E–S grade 2, 33 HCCs with E–S grade 3 and 19 HCCs with E–S grade 4. In addition, there were 87 tumors without microvascular invasion, and 52 tumors with microvascular invasion. No significant differences of the baseline characteristics were obtained between the patients with multiple arterial phase imaging and single arterial phase imaging groups (all $p < 0.05$), and baseline characteristics of all patients were summarized in Table 2.

3.2. Inter-observer repeatability

The inter-observer agreement of the artifact score were almost perfect agreement for 2nd (*kappa*:0.874; 95% Confidence interval [CI]:0.785–0.962), 3rd (*kappa*: 0.862; 95% CI:0.762–0.962) and 4th (*kappa*: 0.854; 95% CI:0.752–0.957) phase; and good agreement was obtained for 1st (*kappa*: 0.752; 95% CI:0.597–0.907), 5th (*kappa*: 0.772; 95% CI:0.636–0.909) and 6th (*kappa*: 0.709; 95% CI:0.564–0.855) phase. Reader agreement for the timing of arterial phase, almost perfect agreement was obtained for 1st (*kappa*: 0.824; 95% CI:0.699–0.948), 5th phase (*kappa*: 0.898; 95% CI:0.781–1.000) and 6th phase (*kappa*: 0.954; 95% CI:0.864–1.000); and good agreement was obtained for 2nd (*kappa*: 0.707; 95% CI:0.545–0.868), 3rd (*kappa*: 0.797; 95% CI:0.648–0.946) and 4th (*kappa*: 0.777; 95% CI:0.650–0.903) phase. For the single arterial phase imaging with LAVA-Flex, good agreement was obtained for the artifact score (*kappa*: 0.798; 95% CI:0.675–0.922) and timing of arterial phase (*kappa*: 0.760; 95% CI:0.603–0.918).

3.3. Timing phase capturing and motion artifact comparison

In patients with DISCO acquisition, the late arterial phase was achieved in 95.4% (62/65) of the patients and missed in 4.6% (3/65) of patients in whom only the portal venous phase was obtained. For the 1st, 2nd, 3rd, 4th, 5th and 6th phase, the late arterial phase was obtained in 9.2% (6/65), 30.8% (20/65), 76.9% (50/65), 49.2% (32/65), 21.5% (14/65) and 10.8% (7/65) respectively (Fig. 5). Furthermore, with DISCO acquisition, the phase 3 demonstrated the highest capturing rate of well-timed late arterial phase and was also significantly higher than phase 4 (76.9% [50/65] *vs* 49.2% [32/65]; $\chi^2 = 10.054$, $p = 0.002$). In patients with single arterial phase acquisition, the late

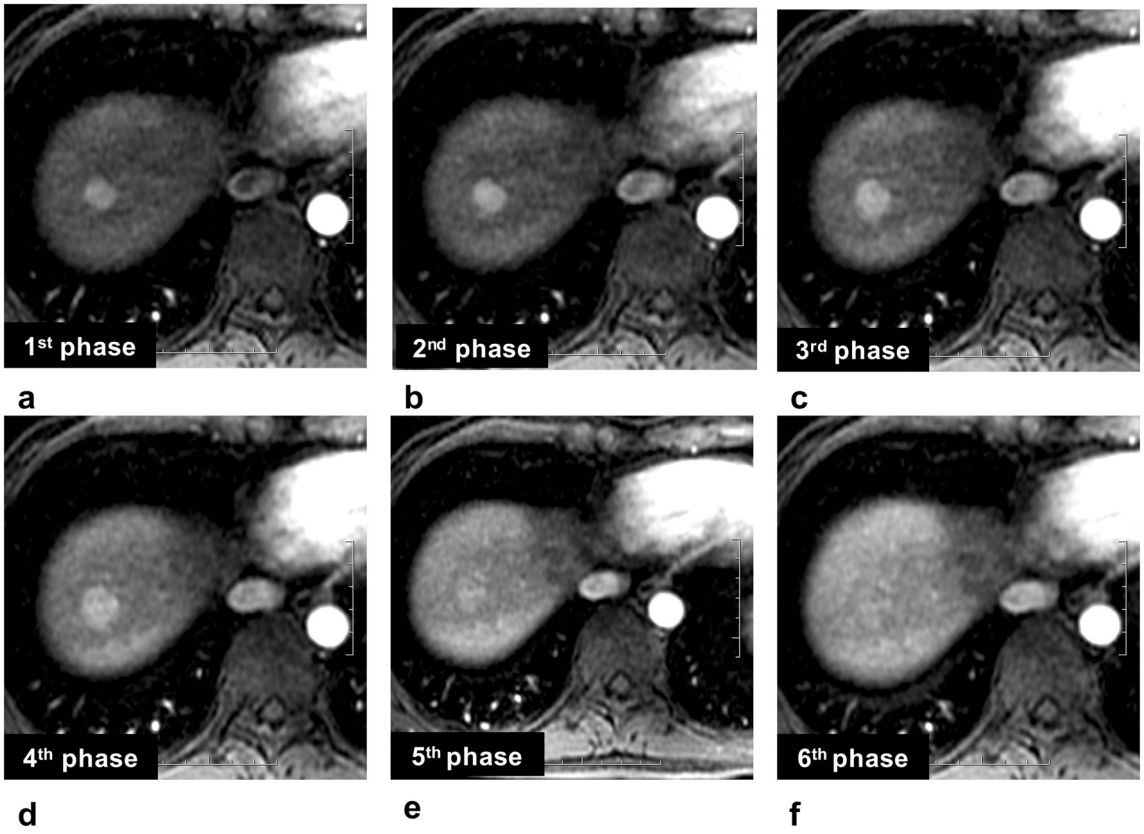

Fig. 2. A 53-year-old man with hepatocellular carcinoma underwent gadoxetic acid disodium-enhanced liver MR images. The 1st to 6th multiple arterial phase (a–f) images of gadoxetate acid disodium acquired at 20 s, 23 s, 26 s, 29 s, 32 s and 35 s, respectively. Note no to minimal motion artifact was found from 1st to 6th phase, and the tumor showed typically enhancement pattern of "wash-in" from 1st to 4th phase (a–d), and typically enhancement pattern of "wash-out" from 5th to 6th phase (e–f).

arterial phase was observed in 73.1% (49/67) of the patients, however, 17.9% (12/67) of patients were presented with early arterial phase, 9.0% (6/67) of patients were presented with portal venous phase. In short, the chance of well-timed late arterial phase capturing rate using multiple arterial phase imaging with DISCO acquisition was significant higher than the single arterial phase imaging with LAVA-Flex acquisition (95.4% [62/65] *vs* 73.1% [49/67]; $\chi^2 = 12.209$, $p < 0.001$); but no significant difference was found between phase 3 and LAVA-Flex (76.9% [50/65] *vs* 75.4% [49/67]; $\chi^2 = 0.253$, $p = 0.615$).

Late arterial phase images showed severe motion artifact (motion artifact score ≥ 4) was obtained in 6.5% (4/62) of the patients using DISCO compared to 36.7% (18/49) of the patients using LAVA-Flex ($\chi^2 = 15.794$, $p < 0.001$), and late arterial phase images showed no to minimal artifact (motion artifact score ≤ 2) was obtained in 56.5% (35/62) of the patients using DISCO compared to 14.3% (7/49) of the patients using LAVA-Flex ($\chi^2 = 20.689$, $p < 0.001$). The motion artifact score of the late arterial phase images measured using LAVA-Flex (3.22 ± 0.68) group was significantly higher than the DISCO (2.42 ± 0.74) group ($t = 5.921$, $p < 0.001$). For the patients with DISCO acquisition, in detail, the severe motion artifact was happened in 12.3% (8/65), 9.2% (6/65) and 10.8% (7/65) of the patients with the 2nd, 3rd and 4th phases and were significant lower than the 1st phase with the incidence rate of 27.7% (18/65) [1st *vs* 2nd: $\chi^2 = 4.808$, $p = 0.028$; 1st *vs* 3rd: $\chi^2 = 7.358$, $p = 0.007$; 1st *vs* 4th: $\chi^2 = 5.992$, $p = 0.014$], but no significant differences were found between each two comparisons of 2nd, 3rd and 4th phases (all $p > 0.05$). For the multiple comparisons of motion artifact obtained with DISCO and LAVA-Flex, statistical significance was obtained between these different phases ($\chi^2 = 115.50$, $p < 0.001$). The motion artifact score of the 2nd (2.66 ± 0.76), 3rd (2.34 ± 0.78) and 4th (2.71 ± 0.72) phases were also significant reduced compared with 1st (3.29 ± 0.70), 5th (3.28 ± 0.57), 6th (3.58 ± 0.75) phases and LAVA-Flex (3.24 ± 0.70) (all $p < 0.05$), and no statistical significance was also found between 2nd and 3rd ($p = 0.471$), 3rd and 4th ($p = 0.172$) phases (Table 3-4, Fig. 6).

4. Discussion

The results of this study demonstrated that the use of multiple arterial phase acquisition with DISCO captured well-timed hepatic late arterial phase images more frequently than single arterial phase imaging with LAVA-Flex. Furthermore, less motion artifacts were also observed of the late arterial phase images using multiple arterial phase imaging compared with the single arterial phase imaging. Thus, multiple hepatic arterial phase acquisition may result in more optimal late arterial phase and provide high image quality with less motion artifacts.

There have been several studies comparing the capturing rate of well-timed late arterial phase using multiple arterial phase acquisition and conventional single arterial phase acquisition [16–21]. Park et al. [18] found that the optimal timing of hepatic arterial phase was observed in 98.5% (66/67) of multiple arterial phase acquisitions and 89.6% (60/67) of single arterial phase acquisitions ($p = 0.015$). Yoon et al. [19] showed that late arterial phase was captured at least once in 96.4% (159/165) of the multiple arterial phase group and in 84.2% (494/587) of the single arterial phase group ($p < 0.001$). Another study conducted by Gruber et al. [21] also found that the late arterial phase was captured in 84.4% (76/90) of the multiple arterial phase using CAIPIRINHA-Dixon-TWIST-VIBE compared with 56.7% (51/90) of the single arterial phase using VIBE ($p < 0.001$). Our results showed that the late arterial phase capturing rate at multiple arterial phase was

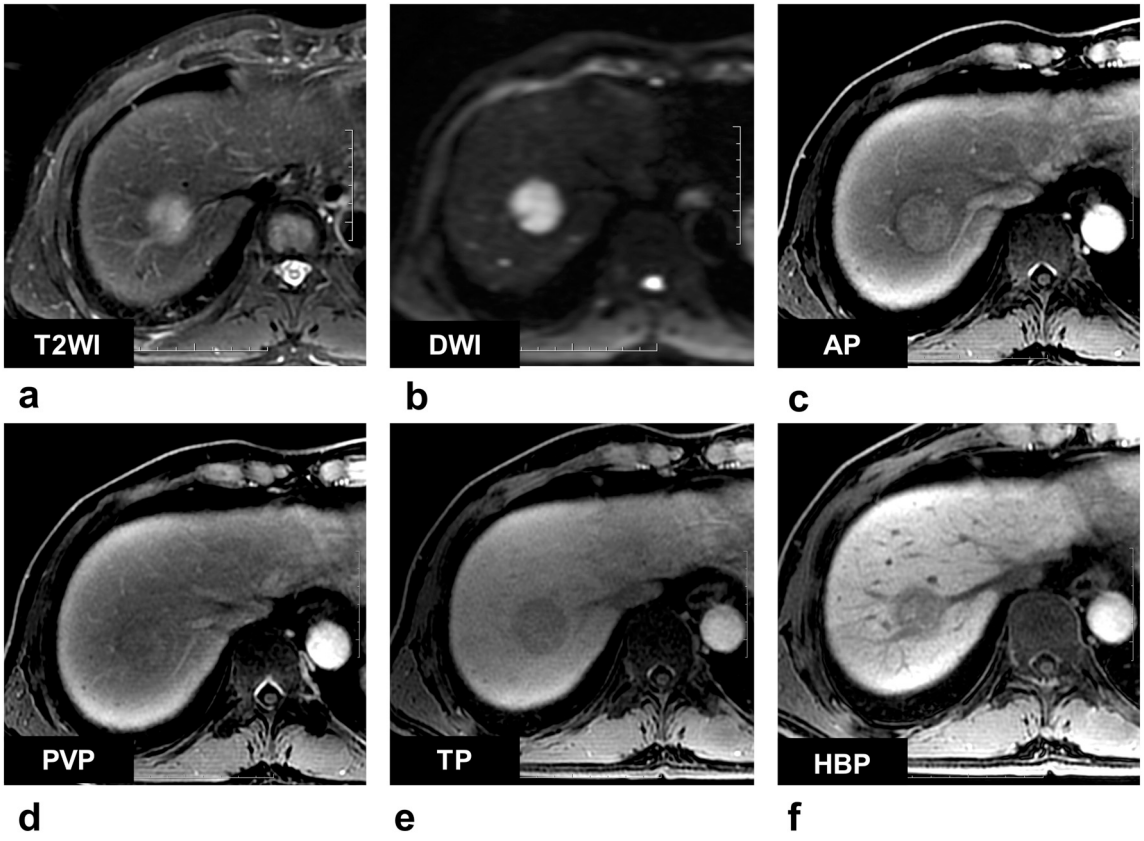

Fig. 3. A 56-year-old man with hepatocellular carcinoma underwent gadoxetic acid disodium-enhanced liver MR images. The T2WI (a) showed a slightly hyperintensity tumor on the right liver lobe, the DWI (b) showed markedly diffusion restriction. The single arterial phase (c) image showed typical enhancement pattern of "wash-in" and the portal venous showed "wash-out" (d), the equilibrium phase (e) and hepatobiliary phase showed hypointensity. Arterial phase (AP), diffusion weighted imaging (DWI), equilibrium phase (EP), hepatobiliary phase (HBP).

Table 1
Parameters of DISCO, LAVA, T1-weighted imaging, T2-weighted imaging and LAVA sequence.

Parameter	DISCO	LAVA-Flex	In/out of phase T1-weighted imaging	T2-weighted imaging	DWI
Repetition time (msec)	4.9	4.5	150	6500–7200	7500
Echo time (msec)	1.1	1.8	2.4/5.8	83.0	77
Field of view (cm^2)	40 × 32	40 × 32	42 × 42	40 × 40	40 × 30
Scan matrix	320 × 192	320 × 192	288 × 192	320 × 320	80 × 128
Slice thickness (mm)	3	4	6	6	6
Slice gap (mm)	…	…	2	2	2
Motion compensation	Breath hold	Breath hold	Breath hold	Respiratory trigger	Respiratory trigger
Flip angle	15	12	75	90	90
Number of slices	54	54	24	24	24
Number of excitation	1	1	1	2	1/4/4
Fat saturation	Dixon	Dixon	None	Fat saturation	Fat saturation
Pixel size (mm)	1.25 × 2.08	1.25 × 2.08	1.46 × 2.19	1.25 × 1.25	5.0 × 3.13

higher compared with that at single arterial phase ($\chi^2 = 12.209$, $p < 0.001$) acquisition.

Compared with the previous studies [18,19], the current study showed comparable well-timed late arterial phase capturing rate of multiple arterial phase acquisition, but a little lower late arterial phase capturing rate of single arterial phase acquisition. This might be explained by that the single arterial phase acquisition was obtained with a fixed delay time in this study, however, the bolus tracking method was used in other studies as which could greatly reduce the impact of individual variations such as body weight index, heart rate and circulation time [22] and thus to achieve a great chance to grasp late arterial phase. Furthermore, previous studies [18–20] often adopted 2 or 3 arterial phases as the multiple arterial phase acquisition to obtain well-timed late arterial phase. In our study, 6 arterial phases were obtained with a high temporal resolution of 3 s in each phase, therefore, there would be more chance to observe the dynamic enhancement pattern of the tumor not only focused on the late arterial phase but emphasized on the enhancement pattern of the whole arterial phase process. Our results found that the highest rate of late arterial phase was appeared in the 3rd phase and more early arterial phase was appeared in the 1st or 2nd phase, early portal venous phase or portal venous phase appeared in the 5th or 6th phase, thus, with the 6 phases multiple arterial phase acquisition, the tumor enhancement pattern from early arterial phase to portal venous phase can be covered and which is of pivotal importance for the diagnosis for the hypervascular liver tumors. In addition, from imaging technique point of view, most published studies [16,18,19,21] utilize time-resolved angiography with stochastic trajectories (TWIST) in their multiple arterial phases dynamic imaging. In the TWIST

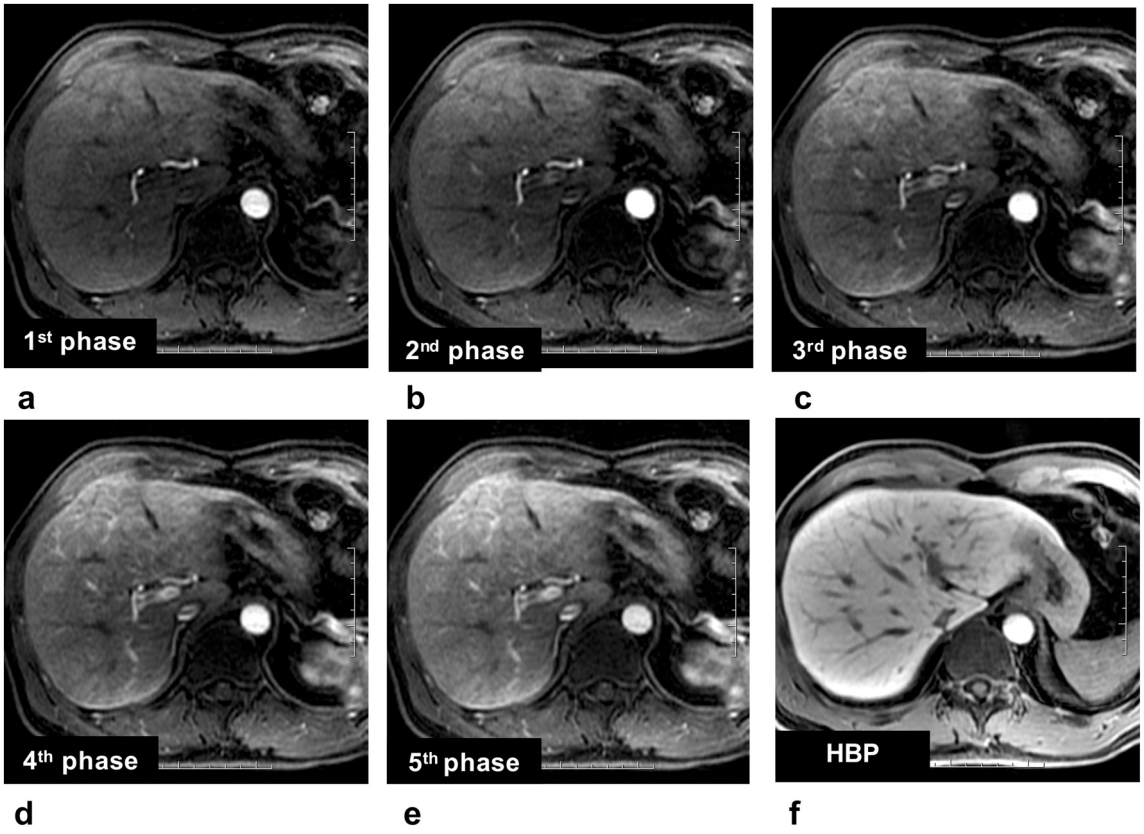

Fig. 4. A 63-year old man with hepatocellular carcinoma underwent gadoxetic acid disodium-enhanced liver MR images. The 1st to 5th multiple arterial phase (a–e) images of gadoxetate acid disodium acquired at 20 s, 23 s, 26 s, 29 s and 32 s, respectively. The 1st and 2nd phase showed early arterial phase with contrast agents only appeared in the hepatic artery (a, b); 3rd and 4th showed well-timed late arterial phase with mild portal vein enhancement (c, d); 5th (e) showed early portal venous phase with liver parenchymal enhancement and the hepatobiliary phase showed strong liver parenchymal enhancement (f).

Table 2
Baseline characteristics of the study population.

Variables	Multiple AP (n = 65)	Single AP (n = 67)	p value
Age, mean (SD), y	51.52 ± 11.94	51.79 ± 12.13	0.898
Sex	…	…	0.622
Male	43	47	…
Female	22	20	…
Hepatitis B virus	42	45	0.757
BMI	23.36 ± 1.18	23.22 ± 1.28	0.495
Liver cirrhosis	42	46	0.622
Ascites	8	11	0.501
COPD[a]	3	5	0.718
Pleurary effusion	2	3	NA
Asthma	0	0	NA
Congestive heart failure	1	2	NA

Note: Data are means ± standard deviation. COPD: chronic obstructive pulmonary diseases.
[a] Data are examined with *fisher* exact test.

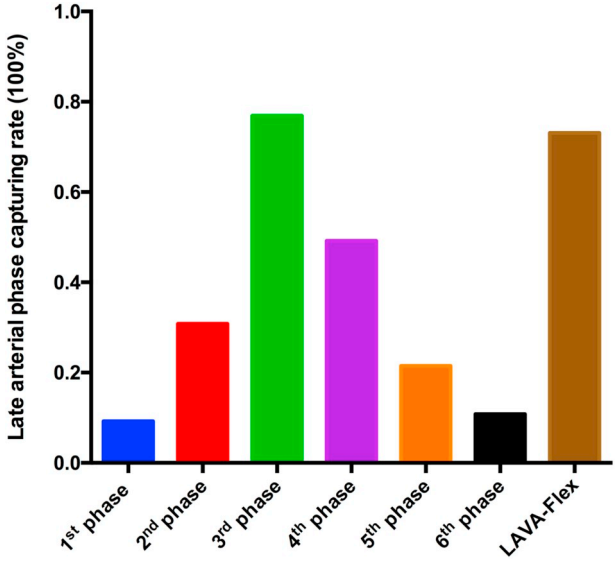

Fig. 5. Well-timed late arterial phase capturing rate of each subphase using multiple arterial phase acquisition and single arterial phase acquisition. The 3rd phase of multiple arterial phase acquisition demonstrated the highest late arterial phase capturing rate of 76.9% (50/65) and was slightly higher than the single arterial phase acquisition of 75.4% (49/67).

sequence, all K-space points are sorted according to their radial distance in K-space; K-space is divided into A (center region) and B (outer region) [23]. While region A is completely sampled, region B is undersampled by a factor of n. The k-space trajectory within the region B follows a spiral pattern in the ky-kz plain with every trajectory in B being slightly different. The less frequently acquired B region were then shared among more frequently acquired A regions to form high temporal images [24]. DISCO, which is used in our study, is quite similar compared to TWIST, except the outer region in DISCO is acquired in a pseudo-random pattern. This difference between aforementioned two techniques may have impact on the final image quality, because pseudo-random acquisition is believed to have better dispersal of artifacts induced by under-sampling of outer K-space. The less structured, more noise-like artifact may be beneficial for small size lesion detection.

Table 3
Captured arterial phase, motion artifact in multiple arterial phase and conventional single arterial phase acquisition.

Parameter	Multiple arterial phase						Single arterial phase
	1st phase	2nd phase	3rd phase	4th phase	5th phase	6th phase	
Timing of arterial phase							
Early arterial phase (%)	75.38% (49/65)	69.23% (45/65)	18.46% (12/65)	12.31% (8/65)	4.62% (3/65)	3.08% (2/65)	17.91% (12/67)
Late arterial phase (%)	9.23% (6/65)	30.77% (20/65)	76.92% (50/65)	49.23% (32/65)	21.54% (14/65)	10.77% (7/65)	73.13% (49/67)
Portal venous phase (%)	0% (0/65)	0% (0/65)	4.62% (3/65)	38.46% (25/65)	73.85% (48/65)	86.15% (56/65)	8.96% (6/67)
Mean artifact score	3.29 ± 0.70	2.66 ± 0.76	2.34 ± 0.78	2.71 ± 0.72	3.28 ± 0.57	3.58 ± 0.75	3.24 ± 0.70

Multiple arterial phase acquisitions may have some disadvantages as a tradeoff exists between the high temporal resolution and spatial resolution [17,25]. However, with DISCO acquisition, the disadvantage may be overcome because of the specific *k-space* sampling strategy as an elliptically ordered central k-space region every time, and sub-samples the outer regions with pseudo-random segmentation [13,14]. Our results found that the late arterial phase showed severe motion artifacts (motion artifact score ≥ 4) using DISCO was less than the single arterial phase using LAVA-Flex ($\chi^2 = 15.794$, $p < 0.001$), and late arterial phase showed no to minimal artifact (motion artifact score ≤ 2) was higher using DISCO than that using LAVA-Flex ($\chi^2 = 20.689$, $p < 0.001$). The mean motion artifact score of the late arterial phase using LAVA-Flex was also higher than the DISCO acquisition, thus, using of a multiple arterial phase provided at least one well-timed and respiratory motion artifact compromised late arterial phase images. In addition, previous study [18,19] showed that respiratory motion artifact in multiple arterial phase acquisition were significant higher than single arterial phase acquisition, our studies found that the motion artifact score of the 2nd, 3rd and 4th phase was significant lower than the single arterial phase (all $p < 0.001$), but comparable respiratory motion artifact was found between the 1st, 5th, 6th and single arterial phase. The higher motion artifact score of the previous study may be explained by the less arterial phases settings (usually dual or triple arterial phases), as with view-sharing technique, when the 1st phase was affected by the motion artifacts caused by the stimulation of contrast agents, the other phases would also share peripheral *k-space* data and the motion artifact areas may be also shared [20,26]. However, with 6 arterial phases settings, the effect of view-sharing technique of peripheral *k-spaces* data would be effectively mitigated.

It is noteworthy that the mean motion artifact score of the 6 multiple arterial phases were significantly higher in the 1st phase than 2nd and 3rd phase. Our study results were consistent with the previous study conducted by Park [18] and Yoon [19] who also reported that the worst motion artifact occurred in the first subphase when conducted with the dual or triple arterial phases. Furthermore, it's also found that nearly half of the transient severe motion artifacts were observed in the early phase of multiple arterial phase acquisition. Thus, this may be used to explain why the first subphase of multiple arterial phase showed more severe motion artifact. In addition, our study found that the motion artifacts slightly increased from 4th to 6th phases, therefore, we carefully infer that the slightly increased motion artifacts may be because of the challenge to sustain a well breath-hold after nearly 10 s breath-hold time.

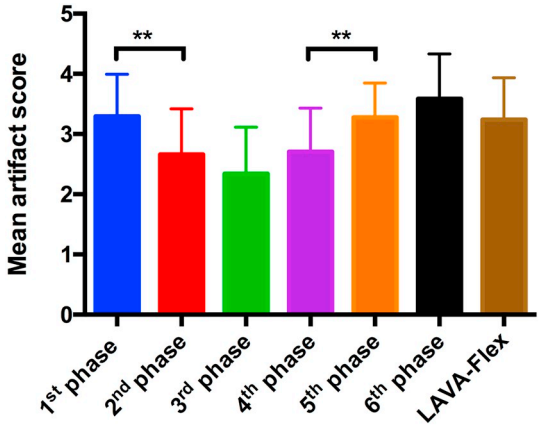

Fig. 6. Mean motion artifact scores between multiple arterial phase and single arterial phase acquisition. Note a tendency toward decreased mean artifact score from 2nd to 3rd phase, and subsequently increased from 4th to 6th phase. The lowest artifact score was observed in 3rd phase (2.34 ± 0.78) and was significantly lower than the single arterial phase (3.24 ± 0.70) acquisition ($t = 7.011$, $p < 0.001$). "*" significant difference ($p < 0.05$), "**" significant difference ($p < 0.01$).

Our study had several limitations. First, the protocol parameters of the single arterial phase were not totally matched with the multiple arterial phase as which could affect the image quality such as the spatial resolution and signal-to-noise ratio. However, previous study has directly compared the overall image quality and fat suppression between DISCO and LAVA-Flex [13], thus, we did not analyze image quality parameters other than motion artifact. Second, transient dyspnea occurring before arterial phase acquisition may lead to the underestimation of incidence of transient motion and related motion artifact, however, a same time was fixed before starting the arterial phase acquisition, so the incidence of the transient motion before starting the acquisition between the two groups can be neglected. Furthermore, our

Table 4
Multiple comparisons of motion artifact of the multiple arterial phases using DISCO and single arterial phase using LAVA-Flex.

Parameters	1st phase	2nd phase	3rd phase	4th phase	5th phase	6th phase
2nd phase	< 0.001	…	…	…	…	…
3rd phase	< 0.001	0.471	…	…	…	…
4th phase	0.002	1.000	0.172	…	…	…
5th phase	1.000	< 0.001	< 0.001	0.001	…	…
6th phase	1.000	< 0.001	< 0.001	< 0.001	1.000	…
LAVA-Flex	1.000	0.001	< 0.001	0.003	1.000	0.715

Note: the α' was corrected by using *Bonferroni* correction according to the formula $\alpha' = \alpha \times m$ (numbers of comparion). A p value < 0.05 was considered to indicate a statistical significance.

primary goal of this study was not to investigate the incidence of transient motion. Third, several studies have already investigated the usefulness of multiple arterial phase imaging in the capturing of late arterial phase. Nevertheless, the previous studies were mainly retrospective design with a limited study population and the researches were conducted by using TWIST-VIBE sequence. In this study, a large number of patients have been included with a prospective study design nature, and the DISCO sequence has been applied. Finally, we did not evaluate the diagnostic performance of the various arterial phase acquisitions in lesion detection and conspicuity, but an improved capturing rate of optimal late arterial phase was achieved in our study, as which is of great clinical importance to make an accurate diagnosis.

In conclusion, the use of multiple arterial phase acquisition with gadoxetate acid disodium can improve the capturing rate of well-timed late arterial phase with less motion artifact.

References

[1] Duncan JK, Ma N, Vreugdenburg TD, Cameron AL, Maddern G. Gadoxetic acid-enhanced MRI for the characterization of hepatocellular carcinoma: a systematic review and meta-analysis. J Magn Reson Imaging 2017;45:281–90.

[2] McInnes MD, Hibbert RM, Inacio JR, Schieda N. Focal nodular hyperplasia and hepatocellular adenoma: accuracy of gadoxetic acid-enhanced MR imaging-a systematic review. Radiology 2015;277:927.

[3] Jiang HY, Chen J, Xia CC, Cao LK, Duan T, Song B. Noninvasive imaging of hepatocellular carcinoma: from diagnosis to prognosis. World J Gastroenterol 2018;24:2348–62.

[4] Joo I, Lee JM, Lee DH, Jeon JH, Han JK, Choi BI. Noninvasive diagnosis of hepatocellular carcinoma on gadoxetic acid-enhanced MRI: can hypointensity on the hepatobiliary phase be used as an alternative to washout? Eur Radiol 2015;25:2859–68.

[5] Motosugi U, Bannas P, Bookwalter CA, Sano K, Reeder SB. An investigation of transient severe motion related to Gadoxetic acid-enhanced MR imaging. Radiology 2016;279:93–102.

[6] Yoon JH, Lee JM, Yu MH, et al. Evaluation of transient motion during Gadoxetic acid-enhanced multiphasic liver magnetic resonance imaging using free-breathing Golden-angle radial sparse parallel magnetic resonance imaging. Invest Radiol 2018;53:52–61.

[7] Bashir MR, Castelli P, Davenport MS, et al. Respiratory motion artifact affecting hepatic arterial phase MR imaging with gadoxetate disodium is more common in patients with a prior episode of arterial phase motion associated with gadoxetate disodium. Radiology 2015;274:141–8.

[8] Tamada T, Ito K, Yoshida K, et al. Comparison of three different injection methods for arterial phase of Gd-EOB-DTPA enhanced MR imaging of the liver. Eur J Radiol 2011;80:e284–8.

[9] Akai H, Yasaka K, Nojima M, et al. Gadoxetate disodium-induced tachypnoea and the effect of dilution method: a proof-of-concept study in mice. Eur Radiol 2018;28:692–7.

[10] Kim YK, Lin WC, Sung K. Reducing artifacts during arterial phase of gadoxetate disodium-enhanced MR imaging: dilution method versus reduced injection rate. 2017;283:429–37.

[11] Park YS, Lee CH, Kim IS, et al. Usefulness of controlled aliasing in parallel imaging results in higher acceleration in gadoxetic acid-enhanced liver magnetic resonance imaging to clarify the hepatic arterial phase. Invest Radiol 2014;49:183–8.

[12] Song JS, Choi EJ, Park EH, Lee JH. Comparison of transient severe motion in gadoxetate disodium and gadopentetate dimeglumine-enhanced MRI: effect of modified breath-holding method. Eur Radiol 2018;28:1132–9.

[13] Saranathan M, Rettmann DW, Hargreaves BA, Clarke SE, Vasanawala SS. DIfferential subsampling with Cartesian ordering (DISCO): a high spatio-temporal resolution Dixon imaging sequence for multiphasic contrast enhanced abdominal imaging. J Magn Reson Imaging 2012;35:1484–92.

[14] Clarke SE, Saranathan M, Rettmann DW, Hargreaves BA, Vasanawala SS. High resolution multi-arterial phase MRI improves lesion contrast in chronic liver disease. Clinical and investigative medicine. Medecine Clin. Exp. 2015;38:E90–9.

[15] Hope TA, Saranathan M, Petkovska I, Hargreaves BA, Herfkens RJ, Vasanawala SS. Improvement of gadoxetate arterial phase capture with a high spatio-temporal resolution multiphase three-dimensional SPGR-Dixon sequence. J. Magn. Reson. Imaging 2013;38:938–45.

[16] Pietryga JA, Burke LM, Marin D, Jaffe TA, Bashir MR. Respiratory motion artifact affecting hepatic arterial phase imaging with gadoxetate disodium: examination recovery with a multiple arterial phase acquisition. Radiology 2014;271:426–34.

[17] Davenport MS, Viglianti BL, Al-Hawary MM, et al. Comparison of acute transient dyspnea after intravenous administration of gadoxetate disodium and gadobenate dimeglumine: effect on arterial phase image quality. Radiology 2013;266:452–61.

[18] Park YS, Lee CH, Kim JW, Lee YS, Paek M, Kim KA. Application of high-speed T1 sequences for high-quality hepatic arterial phase magnetic resonance imaging: intraindividual comparison of single and multiple arterial phases. Invest Radiol 2017;52:605–11.

[19] Yoon JH, Lee JM, Yu MH, Kim EJ, Han JK. Triple arterial phase MR imaging with gadoxetic acid using a combination of contrast enhanced time robust angiography, keyhole, and viewsharing techniques and two-dimensional parallel imaging in comparison with conventional single arterial phase. Korean J Radiol 2016;17:522–32.

[20] Min JH, Kim YK. Artifacts during the arterial phase of gadoxetate disodium-enhanced MRI: multiple arterial phases using view-sharing from two different vendors versus single arterial phase imaging. Eur Radiol 2018;28:3335–46.

[21] Gruber L, Rainer V, Plaikner M, et al. CAIPIRINHA-Dixon-TWIST (CDT)-VIBE MR imaging of the liver at 3.0T with gadoxetate disodium: a solution for transient arterial-phase respiratory motion-related artifacts? Eur Radiol 2018;28:2013–21.

[22] Adibi A, Shahbazi A. Automatic bolus tracking versus fixed time-delay technique in biphasic multidetector computed tomography of the abdomen. Iran. J. Radiol. 2014;11:e4617.

[23] Lim RP, Shapiro M, Wang EY, et al. 3D time-resolved MR angiography (MRA) of the carotid arteries with time-resolved imaging with stochastic trajectories: comparison with 3D contrast-enhanced Bolus-Chase MRA and 3D time-of-flight MRA. Am J Neuroradiol 2008;29:1847–54.

[24] Vogt FM, Eggebrecht H, Laub G, et al. High spatial and temporalresolution MRA (TWIST) in acute aortic dissection. Proceed-ings of the 15th annual meeting of ISMRM, Berlin. 2007.

[25] Agrawal MD, Spincemaille P, Mennitt KW, et al. Improved hepatic arterial phase MRI with 3-second temporal resolution. J. Magn. Reson. Imaging 2013;37:1129–36.

[26] Goshima S, Noda Y, Kajita K, et al. Gadoxetic acid-enhanced high temporal-resolution hepatic arterial-phase imaging with view-sharing technique: impact on the LI-RADS category. Eur J Radiol 2017;94:167–73.