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Dynamic enhancement of upper abdominal organs in normal volunteers with MRI and effects of contrast dose reduction

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Abstract

Background: To quantify enhancement parameters of the upper abdominal organs over time during magnetic resonance (MR) examinations and to evaluate the effect of a dose reduction of contrast medium on these parameters.

Methods: Ten volunteers underwent two separate dynamic enhanced MR examinations with 0.1 and 0.075 mmol/kg of contrast medium, respectively. Breath-hold gradient-echo T1-weighted images were acquired every second for 118 s followed by delayed images. The percentages of enhancement, the time to maximum enhancement, and the area under the time-versus-enhancement curve were calculated for each organ.

Results: The mean times to maximum percentage of enhancement were less than 25 s for the pancreas, kidneys, and spleen and 50 s for the liver. The mean values of maximum percentage of enhancement for the standard/reduced doses were 72%/62% (pancreas), 165%/155% (kidneys), 114%/87% (spleen), and 67%/53% (liver). This difference was significant when liver enhancement was considered ($p = 0.02$). In addition, when the areas under the time-versus-enhancement curves were compared, the difference between the standard dose and reduced dose was significant for all organs tested ($p < 0.05$).

Conclusions: Dynamic scanning of the upper abdomen should start early after contrast injection. Injection parameters should be standardized to capture arterial and venous enhancements in liver examinations. A 25% dose reduction did not significantly affect peak enhancement (except for the liver) but did significantly reduce overall enhancement.

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Key words: Magnetic resonance (MR)—Contrast enhancement—Contrast media—Experimental studies—Gadolinium.

Numerous studies have shown that intravenous administration of contrast material during magnetic resonance (MR) examinations improve detection and characterization of parenchymal lesions [1–4]. Gadolinium chelates are widely used in clinical practice at the dose of 0.1 mmol/kg body weight. However, the rate of injection and the time delay between injection and scanning have not been standardized because little is known about enhancement parameters during MR examinations.

The pharmacokinetics, biodistribution, and clinical indications of gadolinium chelates during MR examinations are similar to those of iodinated contrast agents used in computed tomography (CT) [5]. It has been shown in CT that differences in contrast enhancement between normal parenchyma and a lesion improve lesion conspicuity. Furthermore, rapid scanning at the time of peak enhancement during spiral CT optimizes enhancement parameters for a given dose of contrast medium, and some invesitgators have suggested the use of decreased doses of contrast material when using spiral CT [6]. Similarly, nonspecific contrast agents have been used with MR imaging to increase the lesion-to-tissue signal intensity ratio and to enhance lesion conspicuity. Because of the relatively long acquisition time, little emphasis has been given to the parameters of contrast injection. However, due to the recent advent of fast imaging sequences, an organ can now be scanned several times in a short period of time and several phases of parenchymal enhancement can be captured. The objectives of the present study were (a) to quantify enhancement parameters of the

liver, spleen, pancreas, and kidneys over time during MR examinations by using a standardized protocol of injection and controlled MR sequences that provides serial data over several minutes after contrast injection and (b) to evaluate the effect of a reduction of the dose of contrast medium on these enhancement parameters.

Materials and methods

Patients

Between October 1995 and February 1996, 10 healthy male volunteers each underwent two contrast-enhanced abdominal MR examinations, with a mean time interval of 67 days (range = 6–111 days) between each examination. The age range was 30–45 years, and the weight range was 63–92 kg (average = 73.8 kg). The volunteers were screened for general contraindications to MR imaging and for risk factors to contrast medium injection and were fully informed of the risks of the study. The protocol was approved by the Research Ethics Committee of our institution, and a written consent form was obtained from each volunteer.

Imaging technique

MR examinations were performed with a commercially available 1.5-T system (Signa 5.3; GE Medical Systems, Milwaukee, WI) with use of a phased-array torso multicoil. The same scanning parameters were used for each examination of every volunteer. Prior to scanning, a 10-mL syringe filled with mineral oil was placed on the right flank of each volunteer at the level of the upper abdomen to be used later as a standard of reference. All acquisitions were performed in the axial plane. Fat-suppressed T1-weighted spin-echo (SE) images (repetition time/echo time = 400/10 ms) covering the entire pancreas were initially obtained with a field of view of 40 cm, a 256 × 192 matrix, two signals acquired, 5-mm-thick sections, and 2-mm intersection gaps. Respiratory compensation and superior and inferior presaturation pulses were used. Images were acquired during shallow breathing by the patients.

Contrast-enhanced imaging was performed with a fast spoiled gradient-recalled echo sequence using a single section plane with multiple acquisitions at the same slice position. Imaging parameters were selected to provide T1-weighted image contrast and a short imaging time: repetition time/echo time = 11.6/4.2 ms, flip angle of 30°, 256 × 128 matrix, one signal acquired, 7-mm-thick sections, and no incrementation.

One hundred fifty images were acquired at the same level over 118 s, which resulted in one image acquired approximately every 0.8 s. Images were acquired during a single breath-hold after hyperventilation of pure oxygen. The ability of the volunteers to hold their breath during 120 s after ventilation in an oxygen atmosphere was tested prior to the study. Breath-hold was initiated at the end of a normal expiration. Scanning was initiated 12 s (range = 8–14 s) after the start of contrast medium injection so that the initial images were unenhanced. At the end of the 118-s acquisition, a short sequence including five images was performed every 30 s until 5 min after injection (mean = 292 s) by using the same parameters. A postcontrast T1-weighted SE sequence was performed 471 s (range = 420–579 s) after contrast medium injection. This delay was similar for each of the paired examinations for the same volunteer, with a mean variation of 26 s in the delay between the paired examinations. Imaging parameters of pre- and postcontrast T1-weighted SE sequences were identical.

Injection parameters

A few minutes before the dynamic acquisition, 20 mg of Buscopan (Boehringer-Ingelheim Canada Ltd., Burlington, ON, Canada) were injected intravenously to diminish bowel peristalsis and motion artifacts. All volunteers received 0.1 mmol/kg and 0.075 mmol/kg of gadopentetate dimeglumine (Gd-DTPA; Magnevist, Berlex Laboratories, Wayne, NJ) during the first and second MR examinations, respectively. Potential changes in the weight of the volunteers between the first and second examinations were not taken into consideration. The contrast material was administered as a rapid bolus (3 cc/s) by means of hand injection through five pieces of extension tubing of 30 inches each, connected to a 20-gauge intravenous catheter placed in a right antecubital vein. The use of the extension tubing made it possible to keep the volunteers in the imager during the injection. The time delay between the start of injection and scanning was 12 s (range = 8–14 s). Immediately after the contrast material was injected, the extension tubing and intravenous catheter were flushed with 21 mL of sterile normal saline at the same rate (21 cc in 7 s = 3 cc/s). Because no power injector was commercially available for MR examinations at the time of the study, all contrast injections were performed by the same operator. Prior to the study, more than 200 simulated injections were performed by this operator, until a rate of injection of 3 mL/s could be obtained consistently. All timing parameters related to contrast injection and triggering of acquisitions were monitored and recorded manually by three people using two stopwatches.

Data analysis

Signal intensity (SI) measurements of the pancreatic, hepatic, splenic. and renal parenchyma were obtained by means of an operator-defined region of interest (ROI) on the SE and gradient-echo sequences. The ROIs were placed over the tail of the pancreas, the posterior aspect of the right lobe of the liver, the mid-portion of the spleen, and the posterior aspect of the left renal cortex. Effort was made to maintain the ROIs at the same location for the successive measurements over time. The mean ROI sizes were 247 mm^2, 321 mm^2, 633 mm^2, and 115 mm^2 for the tail of the pancreas, spleen, liver, and kidneys, respectively. Pancreatic enhancement could be measured only in nine volunteers and splenic enhancement in eight because in two cases the organ was not included in the imaged volume and one volunteer had had a splenectomy.

Because single section techniques do not acquire data in a steady state, there may be variation of signal from slice to slice. However, the signal intensity was measured only after a pseudosteady state had been obtained in the following fashion: for each examination, the signal intensities of each of the organs studied was measured (a) every second between 12 and 45 s after contrast injection, (b) every 5 s between 45 and 80 s, (c) every 20 s between 80 and 120 s, and (d) every 30 s between 120 and 300 s. The actual time of each image section was calculated by adding the time delay between contrast medium injection and image acquisition recorded by the stopwatches to the image time indicated on the MR scanner. Because the acquisition time of each image was not 1 s but 0.8 s, the image acquired closest to the time unit was selected for measurement. All measurements were made by the same observer who was blinded to the volume of contrast medium injected. The effect of contrast medium on the signal intensity of the different abdominal organs studied was calculated as follows [7]:

$$\%E = [(SI_{tissue}/SI_{ref})\mathbf{post} - \mathbf{(SI}_{tissue}/SI_{ref})pre]/[(SI_{tissue}/SI_{ref\ stand})pre]$$

where %E is the percentage of enhancement, (SI_{tissue}/SI_{ref})pre is the ratio between the signal intensity of the organ and that of the standard tissue on the precontrast images, and (SI_{tissue}/SI_{ref})post is the ratio between the signal intensity of the organ and that of the standard tissue on the postcontrast images at a given time.

The tube of mineral oil placed on either the flank or the abdominal fat of the volunterr was used as a standard for comparison. The mean maximum percentage of enhancement and the mean time to maximum percentage of enhancement (time to peak) were calculated for each organ studied and for each of the doses of contrast medium used. In addition, the mean values of percentages of enhancement were plotted against time. The area under the time-versus-percentage of enhancement curve was calculated for each organ and for each of the doses of contrast medium used for the intervals 12–30 s, 12–45 s, 12–60 s, and 12–120 s. The effect of the dose of contrast medium on delayed enhancement was calculated by comparing the enhancement values obtained on the postcontrast SE T1-weighted sequences. The effect of dose reduction was tested for significance at a level of $p < 0.5$ with the Wilcoxon sign-rank test. The confidence interval at 95% was obtained for every value.

Results

The MR examinations were well tolerated by all volunteers. One volunteer, however, developed an unexplained redness on the back during the test, which disappeared rapidly. No volunteer had difficulty holding their breath during the 2-min duration of the gradient-echo sequence. The mean values of maximum percentages of enhancement with the standard/reduced dose and for the pancreas, liver, kidneys, and spleen were 72.03%/61.56% (pancreas), 66.59%/52.80% (liver), 164.57%/154.63% (kidneys), and 114.39%/86.64% (spleen) (Table 1). Although the injection of a reduced dose resulted in a lower percentage of enhancement with all organs studied, the difference only reached statistical significance for liver enhancement ($p = 0.02$). The mean values of time-to-peak enhancement were 20 s, 23.44 s, and 23.63 s for the kidney, pancreas, and spleen, respectively, and 50 s for the liver with the 0.1-mmol/kg dose (Table 2). Interestingly, reducing the dose to 0.075 mmol/kg resulted in shortening the time to peak uniformly, although the difference was not significant except for renal enhancement ($p = 0.04$; Table 2).

Parenchymal enhancement dropped rapidly after reaching its maximum; 20 s after peak enhancement was reached, pancreatic, splenic, renal, and hepatic enhancement had dropped by 23%, 23%, 38%, and 9%, respectively (Figs. 1–4). Twenty seconds later, enhancement had dropped by 31%, 32%, 29%, and 14%, respectively. The area under the time-versus-enhancement curve that lay between 12 and 30 s decreased significantly when the reduced dose of contrast material was used and when pancreatic, renal, and splenic enhancement were considered ($p = 0.0017$, $p = 0.0020$, $p = 0.0078$, respectively; Table 3). For liver enhancement, the difference reached statistical significance only when the segment of the curve lying between 12 and 120 s was considered. Although a reduced dose of contrast medium resulted in a decreased percentage of enhancement measured on the postcontrast SE T1-weighted images, the differences observed did not reach statistical significance (Table 4).

Table 1. Mean (range) percentage of enhancement by dose and by organ

Dynamic sequences	0.1 mmol/kg	0.075 mmol/kg	*p**
Pancreas, 95% CI	72.03 (60–83)	61.56 (47–76)	0.16
Liver, 95% CI	66.59 (54–78)	52.80 (44–61)	0.02
Kidneys, 95% CI	164.57 (153–176)	154.63 (102–185)	0.25
Spleen, 95% CI	114.39 (87–141)	86.64 (59–114)	0.10

* Wilcoxon test

Table 2. Mean (range) time to peak (seconds) by dose and by organ

Dynamic sequences	0.1 mmol/kg	0.075 mmol/kg	*p**
Pancreas 95% CI	23.44 (17–29)	17.78 (14–21)	0.09
Liver 95% CI	50 (34–66)	38.10 (31–44)	0.16
	64.8 (29–100)	38.10 (31–44)	0.12
Kidneys 95% CI	20.00 (18–22)	17.00 (14–19)	0.04
Spleen 95% CI	23.63 (17–30)	24.25 (13–36)	0.74

* Wilcoxon test

Discussion

The use of gradient-echo sequences for imaging of abdominal organs allows examination during suspended respiration. Moreover, repeated acquisitions at short time intervals after the administration of the paramagnetic contrast agent Gd-DTPA enables the study of organ perfusion. Proper timing of the contrast material administration relative to the data acquisition is critical with the rapid acquisition technique. If imaging is improperly timed, data may be acquired prior to or after maximal peak enhancement, which results in an examination with suboptimal contrast.

The method we used to measure enhancement in the present study aimed at controlling as many variables as possible. The long period of breath-hold allowed us to record multiple data points during the dynamic phase of enhancement. This ensured capture of peak enhancement and provided data during different phases of enhancement until late into the equilibrium phase. Our sequence parameters were chosen to ensure sequential acquisition, where all the lines in *k* space are completed for each image before the next image is acquired. With the sequence parameters chosen, one image was acquired in approximately 0.8 s, which allowed us to acquire all dynamic images during a single sequential acquisition, at the same location, and with strictly controlled parameters. These same parameters were applied during the second examination for each volunteer. The flip angle of 30° used in the spoiled gradient-echo sequence was a compromise between T1 contrast and the need to maintain enough of a signal intensity. In clinical practice, however, we favor the use of a fast multiplanar spoiled gradient-recalled imaging technique with interleaved acquisition [7, 8].

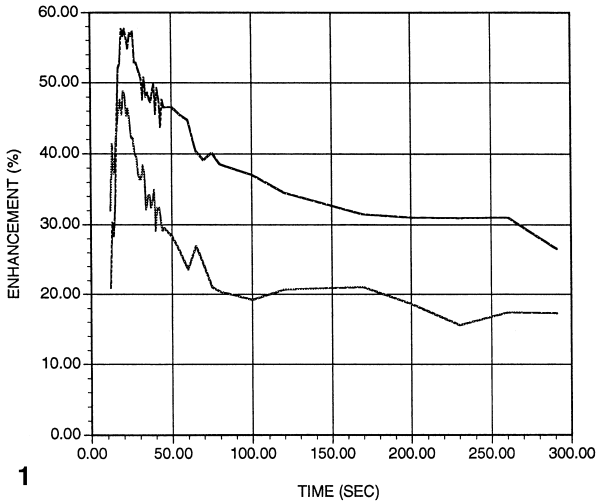

Fig. 1. Pancreas enhancement. (—) Dose: 0.1 mmol/kg; (---) dose: 0.075 mmol/kg.

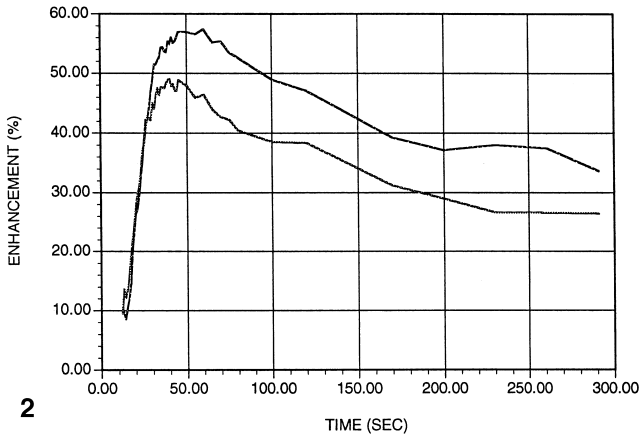

Fig. 2. Liver enhancement. (—) Dose: 0.1 mmol/kg; (---) dose: 0.075 mmol/kg.

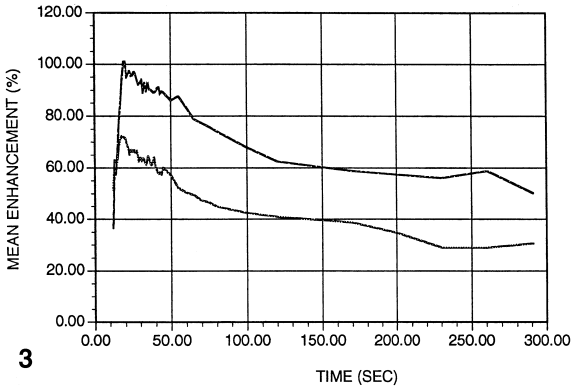

Fig. 3. Spleen enhancement. (—) Dose: 0.1 mmol/kg; (---) dose: 0.075 mmol/kg.

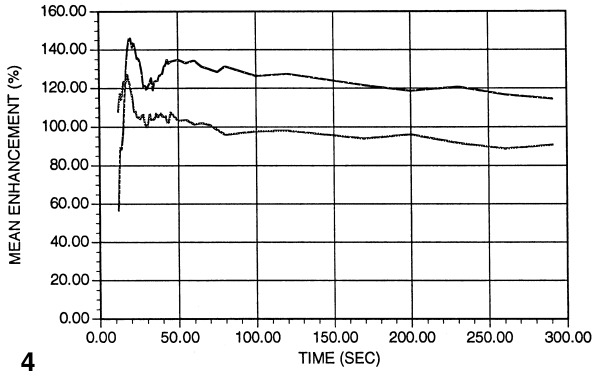

Fig. 4. Kidney enhancement. (—) Dose: 0.1 mmol/kg; (---) dose: 0.075 mmol/kg.

Our results show that maximum enhancement for the organs with a predominantly arterial supply such as the pancreas, spleen, and kidneys occurred very rapidly ($<$25 s), with a rapid decrease thereafter. These numbers differ from those reported by Hammed et al. [9], but in their protocol, scanning was repeated only every 30 s during the first 2 min and then every 60 s for up to 10 min. In the present study, peak liver enhancement occurred approximately 50 s after injection, and this was comparable to the results reported by Shmiedl et al. [10]. In fact, liver enhancement is mainly dependent on portal vascularization. However, it has now been established both with CT and MR imaging that scanning during the arterial phase and not during the peak enhancement phase increases detection of hypervascular tumors such as hypervascular metastases, hepatocellular carcinomas, focal nodular hyperplasia, and liver cell adenomas.

The rate of injection, the time delay between injection and scanning, and the time of each postcontrast acquisition are important factors to consider when planning a dynamic gadolinium-enhanced sequence. Although the volume of contrast material injected is much less with MR than with CT, a slow injection over 15–20 s, which corresponds to a rate of less than 1 mL/s, is inappropriate for dynamic scanning. Because of its high viscosity, it is difficult to hand-inject gadolinium at a rate superior to 3 mL/s. However, with minimal practice, one investigator was able to consistently achieve a rate of injection of 3 mL/s both in vitro and during the 20 MR examinations. The first report using an MR-compatible power injector has been published [11] and has demonstrated its superiority over hand injection in reproducing consistent injection rates. However, such an injector was not available at our institution at the time of the study.

Because the scan is initiated rapidly after injection of contrast material, the patient needs to be kept in the imager during the contrast injection. Therefore, long extension tubes filled with normal saline are used. However,

Table 3. Areas under curve (% enhancement × seconds) by organ and by dose

Dynamic sequences	0.1 mmol/kg	0.075 mmol/kg	*p**
Pancreas			
12–30 s	998	946	0.0017
12–45 s	1689	1645	0.0032
Liver			
12–30 s	475	537	0.76
12–45 s	1249	1210	0.92
12–60 s	1988	1949	0.55
12–120 s	4406	4289	0.0001
Kidneys			
12–30 s	2382	2301	0.0020
12–45 s	4287	4193	0.0020
Spleen			
12–30 s	1601	1469	0.0078
12–45 s	3043	2950	0.79

* Wilcoxon test

a 120-inch extension tube, as used in the present study, made of five tubes of 30 inches each, has a capacity of 19 mL, which represents a dead space during contrast injection and impedes the accurate timing of injection. Also, sometimes only a portion of the bolus of contrast penetrates the patient's veins when the extension tubing is flushed with normal saline, which fractions the bolus and results in an additional delay of 5–10 s. One way to achieve reproducible injection rates and delays is to use a extension tube long enough so that its capacity equals or exceeds the volume of contrast to be injected (Table 5). Immediately prior to injection, the contrast agent can slowly fill the tube extension, but the actual bolus injection only starts when the extension tube is flushed with 20 mL of normal saline. Using in vitro experimentation, however, we demonstrated that there was mixing of normal saline with contrast medium at the junction during this maneuver. In addition, the use of extension tubes of different lengths may theoretically result in different degrees of resistance, thereby limiting the ability of using a consistent rate of injection. This limitation should not exist if a power injector is used.

In our study, peak enhancement of the pancreas, spleen, and kidney and arterial hepatic enhancement occurred 20–25 s after the start of contrast injection and decreased by almost 25% during the 20 s following peak enhancement. Because the acquisition time of a fast spoiled gradient-recalled sequence covering the entire pancreas or liver changes between 20 and 25 s and because the time interval between two sequence acquisitions is approximately 10 s, one should trigger the first acquisition 10 s after the entry of the bolus into the patient's venous system. Because some individual variables cannot be controlled, a bolus tracking software that would trigger the acquisition when a predetermined contrast enhancement is achieved could be valuable to further optimize dynamic gadolinium-enhanced MR scanning.

Table 4. Mean (range) percentage of enhancement by dose and by organ

T1W delayed sequences	0.1 mmol/kg	0.075 mmol/kg	*p**
Pancreas, 95% CI	30 (9–51)	17 (0–33)	0.37
Liver, 95% CI	40 (2–78)	31 (0–62)	0.92
Kidneys, 95% CI	138 (107–167)	103 (65–142)	0.06
Spleen, 95% CI	81 (29–131)	56 (25–86)	0.54

* Wilcoxon test

Table 5. Length of extension tubing as a function of patient's weight

Weight (kg)	Amount of Contrast (cc)	Length of catheter (inches)[a]
50	10	3 × 30 (11.5 cc)
55	11	3 × 30 (11.5 cc)
60	12	2 × 30 + 2 × 20 (13.8 cc)
65	13	3 × 30 + 2 ×t 20 (13.8 cc)
70	14	3 × 30 + 1 × 20 (14 cc)
75	15	4 × 30 (15.2 cc)
80	16	3 × 30 + 2 × 20 (17.5 cc)
85	17	4 × 30 + 1 × 20 (18 cc)
90	18	4 × 30 + 1 × 20 (18 cc)
95	19	5 × 30 (19 cc)
100	20	4 × 30 + 2 × 20 (20.5 cc)

20 inches tubing extension = 2.9 ml
30 inches tubing extension = 3.8 ml

Overall, a 25% reduction of the dose of contrast medium negatively affected all enhancement parameters; however, with the exception of the liver, the differences observed in maximum enhancement were not significant. The areas under the time-versus-enhancement curve were significantly decreased in the group of examinations performed with a lower dose of contrast medium. This was true, however, only when the segments of the time-versus-enhancement curve analyzed included the peak parenchymal enhancement of the organ considered.

Our study also demonstrates that conventional SE sequences performed after contrast injection do not capture peak enhancement of the abdominal organs and therefore should not be used unless information, such as slow filling or washout of a lesion, is needed on delayed enhancement. In fact, enhancement parameters were consistently higher during the early fast spoiled gradient-recalled acquisition obtained with the lower dose of contrast material than during the conventional SE sequence obtained with the higher dose. These findings may have practical implications depending on the clinical situation and must be analyzed further. Analysis of the time-versus-enhancement curve showed that differences in enhancement produced by the two different doses of contrast medium were constant until 5 min after injection (Figs. 1–4). Comparison of enhancement with the two doses during the time interval of 8–14 min (conventional

SE delayed sequences) was not statistically significant ($p > 0.05$).

In our study, the same rate of injection was maintained during all examinations, but the volume of contrast material changed. The time from injection to maximum enhancement was shorter with the lower dose (except for the spleen, $p = 0.74$), but this was not statistically significant except for the kidneys ($p = 0.04$). The results of previous studies performed with CT have shown that the time-to-peak liver enhancement depends mainly on the duration of injection and that shorter injection times result in shorter times to peak enhancement [12]. The same phenomenon was observed in the present study when the amount of contrast medium was reduced; however, the effect was not as great because the actual reduction in volume and injection time was minimal. For example, in a 70-kg volunteer, the contrast medium was reduced by 3.4 cc between the two examinations, resulting in a shortening of the injection of only 1.2 s.

One limitation of the present study is that all subjects were young and healthy and thus not representative of a usual patient population. However, because the subjects were compared with themselves, the between-subject variability factor was controlled when enhancement was compared with two different doses of contrast medium. Also, we only analyzed enhancement of normal parenchymal tissues, and our data cannot be directly extrapolated to lesion conspicuity produced by two different doses of contrast medium.

Conclusions

Dynamic imaging of the upper abdomen enables the capture of the maximum enhancement of abdominal organs. Peak pancreatic, renal, and splenic enhancement occur early during the arterial phase of enhancement; therefore, these organs should be scanned within 25 s of contrast injection. In the liver, peak enhancement only occurs later; however, multiple acquisitions may be useful for capturing the arterial and portal venous phases of enhancement. Delayed SE T1-weighted sequences are not acquired during the optimal enhancement window. A 25% reduction of the dose of contrast medium negatively affects overall parenchymal enhancement. However, the actual effect on lesion conspicuity needs to be studied.

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