I.2

Principles of Contrast Medium Delivery and Scan Timing in MDCT

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Introduction

The advent of multidetector-row computed tomography (MDCT) technology has brought substantial advantages over single-detector-row CT (SDCT) in terms of image quality and clinical practice. The dramatically improved spatial and temporal resolution achievable on MDCT permits previously highly technically demanding clinical applications such as CT angiography and cardiac CT to be practiced routinely.

Another major advantage of MDCT over SDCT is that contrast medium can be used more efficiently and flexibly. However, in order to fully appreciate the benefits of MDCT, certain technical challenges involving scan timing and optimization of contrast enhancement need to be overcome. This chapter aims to review the numerous factors associated with contrast medium delivery and scan timing. Moreover, modifications to protocol design that are necessary for optimized contrast enhancement in MDCT are discussed, along with clinical considerations for CT angiography (CTA) and hepatic imaging.

Scan Timing and Factors Affecting Contrast Medium Delivery

The principal factors affecting contrast medium enhancement in CT imaging can be grouped into three broad categories: the patient, the injection of contrast medium, and the CT scan. Whereas factors associated with the former two categories determine the contrast enhancement process itself (independently of the CT scan), factors associated with the latter category (i.e., image acquisition parameters) play a critical role in permitting optimal visualization of the resulting contrast enhancement at specific time points. Whereas patient and injection factors involved in contrast enhancement are highly interrelated, some factors more closely affect the magnitude of contrast enhancement while others more closely affect the timing of contrast enhancement.

Patient Factors

The principal patient-related factors that influence contrast enhancement are body weight and cardiac output (cardiovascular circulation time). Other factors that can be considered of less significance include height, gender, age, venous access, renal function, and various pathological conditions.

Body Weight

The most important patient-related factor affecting the magnitude of vascular and parenchymal contrast enhancement is body weight [1–4]. Since large patients have larger blood volumes than small patients, contrast medium administered into the blood compartment of a large patient is diluted more than that administered to a small patient. The result is a reduced magnitude of contrast enhancement. Patient weight and the magnitude of enhancement are inversely related in a nearly one-to-one linear fashion. For a given administered dose of contrast medium, the magnitude of contrast enhancement is reduced proportionally to patient weight (Fig. 1). However, whereas the magnitude of contrast enhancement is strongly affected by patient weight, the timing of enhancement is largely unaffected by this parameter due to the concomitant proportional increase in both blood volume and cardiac output [3, 5, 6]. The result is a largely unaltered contrast medium circulation time that is independent of patient weight.

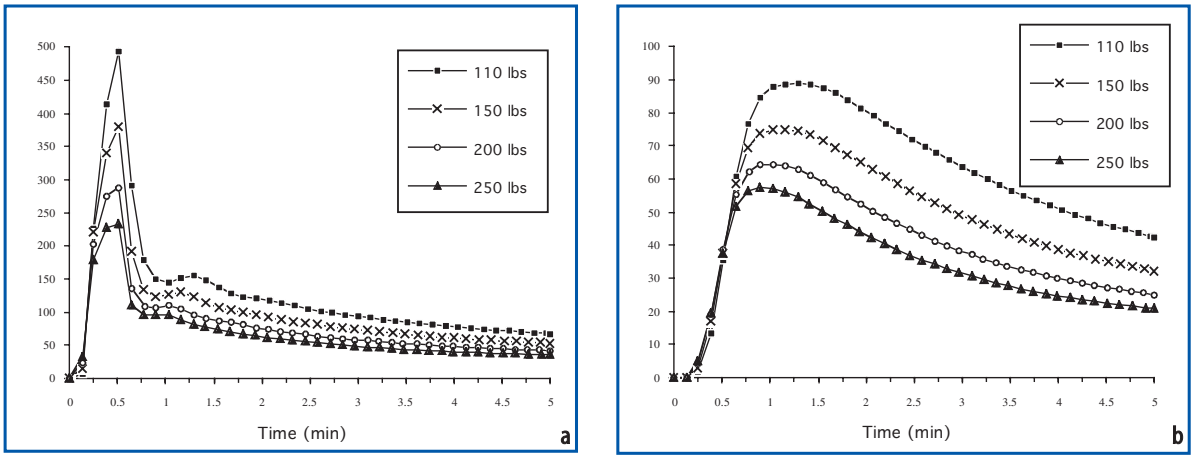

Fig. 1a, b. Simulated contrast enhancement curves with four different body weights. Simulated enhancement curves of the **a** aorta and **b** liver based on a hypothetical adult male with a fixed height (5'8" or 173 cm) and varying body weight (110, 160, 200, and 260 lbs, or 49.8, 72.5, 90.7, and 117.9 kg), subjected to injection of 125 ml of contrast medium at 5 ml/s (14). The magnitude of contrast enhancement is inversely proportional to body weight. (Reprinted from [53])

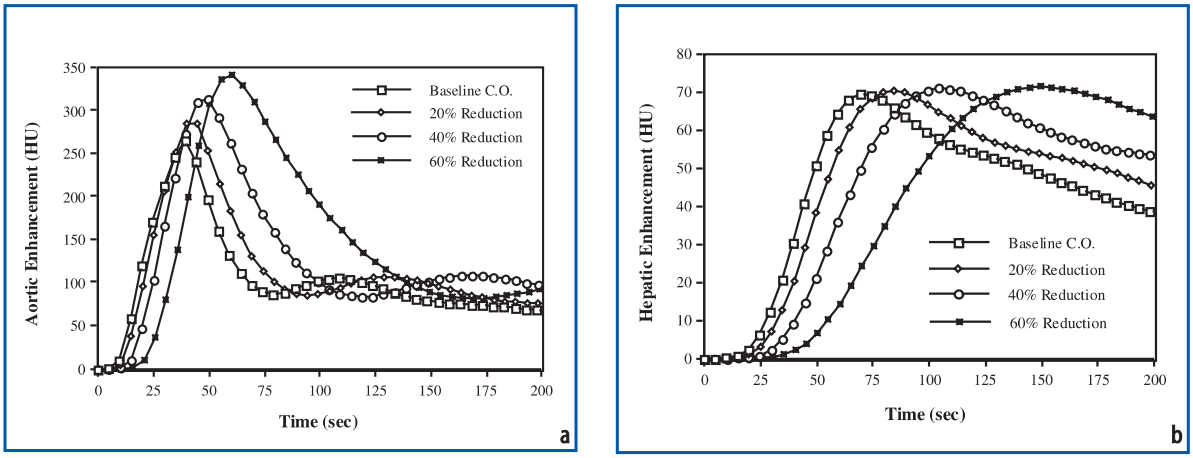

Fig. 2a, b. Simulated contrast enhancement curves at baseline and reduced cardiac outputs. Simulated enhancement curves of the **a** aorta and **b** liver based on a hypothetical adult male with a fixed height (5'8", or 173 cm) and body weight (150 lbs, or 68 kg), subjected to injection of 120 ml of contrast agent at 4 ml/s. A set of aortic and hepatic contrast enhancement curves was generated by reducing the baseline cardiac output, i.e., 6,500 ml/min, by 20%, 40%, and 60%. (Reprinted from [53])

Practical Tips

1. To maintain a constant degree of contrast enhancement in larger patients, one should consider increasing the overall iodine dose by increasing contrast medium volume and/or concentration. Increasing injection rate also increases the magnitude of vascular contrast enhancement (and hepatic enhancement in limited circumstances).
2. The timing of enhancement is largely unaffected by patient weight.

Cardiac Output

The most important patient-related factor affecting the timing of contrast enhancement is cardiac output (or cardiovascular circulation time) [7]. As cardiac output is reduced, the circulation of contrast medium slows, resulting in delayed contrast bolus arrival and delayed peak arterial and parenchymal enhancement (Fig. 2). The time delay between injection of the contrast medium bolus and the arrival of peak enhancement in the aorta and liver is highly correlated with, and linearly proportional to, cardiac output. Thus, in patients with reduced cardiac output, once the contrast bolus arrives in the central blood compartment, it is cleared more slowly, resulting in a higher, prolonged enhancement.

A consequence of the slower contrast bolus clearance in patients with reduced cardiac output is an increased magnitude of peak aortic and parenchymal enhancement. The rate of increase, however, is different in the aorta and liver. Whereas the magnitude of peak aortic enhancement increases substantially in patients with reduced cardiac output, the magnitude of peak hepatic enhancement increases only slightly.

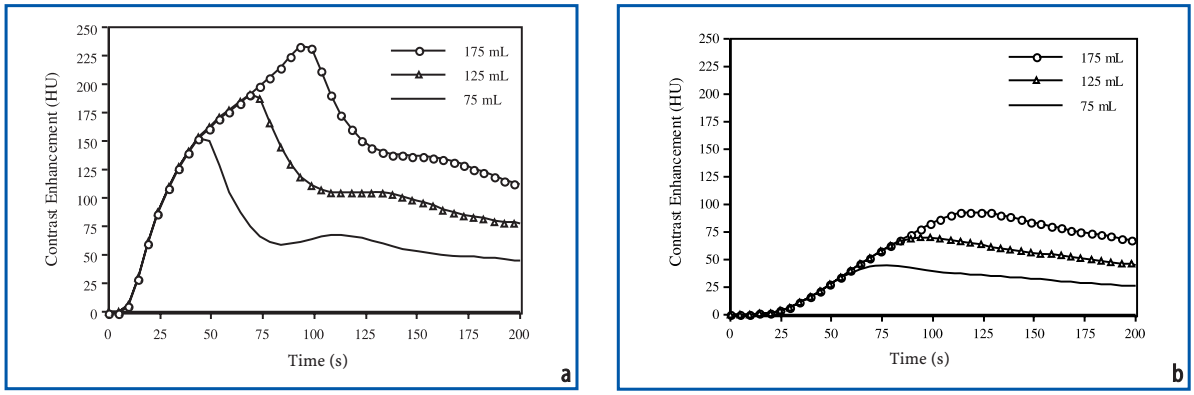

Fig. 3a, b. Simulated contrast enhancement curves with three different contrast medium volumes. Simulated enhancement curves of the **a** aorta and **b** liver based on a hypothetical adult male with a fixed height (5'8", or 173 cm) and body weight (150 lbs, or 68 kg), subjected to injection of 75, 125, and 175 ml of contrast medium at 2 ml/s. Time-to-peak and magnitude of enhancement peak increases with contrast medium volume. (Reprinted from [53])

Practical Tips

1. When scan timing is critical, it is important to individualize the scan delay to account for variations in cardiac output among patients. Scan delay can be individualized by using a test bolus or a bolus tracking technique.

Contrast Injection Factors

Key factors related to the injection of contrast medium include injection duration, injection rate, contrast medium volume (injection duration × rate), concentration, and use of a saline flush.

Injection Duration

Injection duration, which is determined by the volume of contrast medium and the rate at which it is administered (injection duration = contrast volume ÷ injection rate), critically affects both magnitude and timing of contrast enhancement [8–13]. Increased injection duration at a fixed rate of injection leads to greater deposition of iodine mass. This results in increased magnitude of vascular and parenchymal enhancement, which is proportional to injection duration (Fig. 3).

The appropriate injection duration is determined by scanning conditions and the clinical objectives of the examination. Injection duration should be prolonged for a long CT scan to maintain good enhancement throughout image acquisition. An injection duration that is too short leads to insufficient contrast enhancement. On the other hand, too long an injection duration results in a waste of contrast medium and the generation of undesirable tissue and venous contrast enhancement. Pertinent clinical factors to be considered in determining injection duration include body size, the vessel or organ of interest, and the desired level of enhancement [14].

A sufficiently long injection is particularly crucial in portal-venous phase imaging of the liver because the principal determinant of hepatic enhancement is total iodine dose administered [9–11, 13, 15–21]. Thus, for a fixed injection rate, the injection duration for a large patient should be longer than that for a small patient. On the other hand, for a fixed injection duration and contrast medium concentration, the injection rate should be adjusted according to the patient's body size to deliver the appropriate amount of iodine mass. In this case, larger patients require faster injections.

The duration of contrast medium injection is the most important technical factor that affects scan timing. In patients with normal cardiac output, peak arterial contrast enhancement is achieved shortly after termination of a contrast medium injection [20]. As the volume of contrast medium increases, so too does the time required to reach the peak of arterial or parenchymal contrast enhancement (Fig. 3). Conversely, a shorter time-to-peak enhancement is noted for a fixed volume of contrast medium injected at a faster injection rate (Fig. 4).

Practical Tips

1. The use of a higher contrast medium concentration or a faster injection rate facilitates faster delivery of the total iodine load, allowing use of a shorter injection to achieve the desired degree of contrast enhancement.
2. A rapid contrast delivery rate and short injection duration are desirable for arterial enhancement with MDCT but are much less important for parenchymal or venous enhancement.
3. A short injection duration (i.e., low volume and/or high injection rate) results in earlier

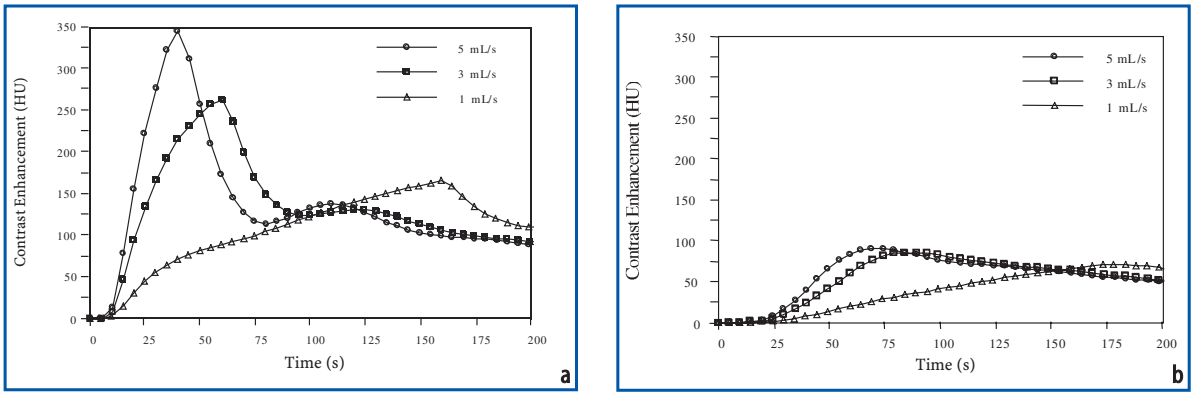

Fig. 4a, b. Simulated contrast enhancement curves with three different contrast medium injection rates. Simulated enhancement curves of the **a** aorta and **b** liver based on a hypothetical adult male with a fixed height (5'8", or 173 cm) and body weight (150 lbs, or 68 kg) subjected to 150 ml of contrast medium injected at 1, 3, and 5 ml/s. The curves show that for a fixed volume of contrast medium, as the rate of injection increases, the magnitude of contrast enhancement increases and the duration of high-magnitude contrast enhancement decreases. (Reprinted with permission from Bae KT (2005) Technical aspects of contrast delivery in advanced CT. Applied Radiology 32 [Suppl]: 12-19)

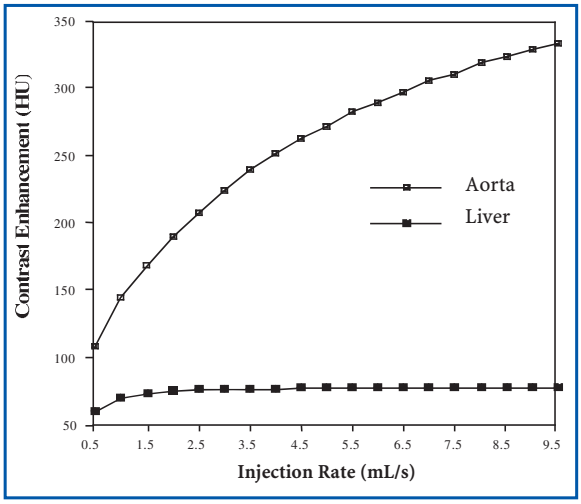

Fig. 5. Effect of contrast medium injection rate on the magnitude of peak contrast enhancement. Simulation of peak aortic and hepatic contrast enhancement at different injection rates based on a hypothetical adult male with a fixed height (5'8", or 173 cm) and body weight (150 lbs, or 68 kg) subjected to injection of 120 ml of contrast medium. (Reprinted with permission from Bae KT, Heiken JP, Brink JA (1998) Aortic and hepatic peak enhancement at CT: effect of contrast medium injection rate-pharmacokinetic analysis and experimental porcine model. Radiology 206:455-464)

peak arterial and parenchymal enhancement and requires a short scan delay. A long injection duration (i.e., high volume and/or low injection rate) results in later peak enhancement, and thus a longer scan delay is preferable.

Injection Rate

Both rate of delivery and total delivered mass of iodine are increased when the injection rate is increased at a fixed duration of injection. The magnitude of peak vascular and parenchymal enhancement increases with a wider temporal window of desired contrast enhancement. On the other hand, when the injection rate is increased at a fixed volume of contrast medium, the peaks of enhancement increase in magnitude and occur earlier and the duration of high-magnitude enhancement decreases (Fig. 4). However, for a given increase in injection rate, the rate of increase in the magnitude of aortic contrast enhancement is substantially greater than that of the liver (Fig. 5) [22–24].

To obtain a fast arterial CT scan (e.g., for MDCT angiography applications), an increased injection rate resulting in a shortened but elevated magnitude of arterial enhancement is beneficial. On the other hand, a longer injection duration resulting in more prolonged vascular enhancement is preferable for slower CT scans. Faster injection rate and shorter injection duration result in a longer interval between peak arterial enhancement and hepatic parenchymal equilibrium enhancement. Thus, a faster injection results not only in a higher magnitude of arterial enhancement but also in a greater temporal separation between the arterial and venous phases of hepatic enhancement (Fig. 6).

Practical Tips

1. The magnitude of peak aortic enhancement increases almost linearly with increases of injection rate (up to 8–10 ml/s) while peak hepatic enhancement increases much more gradually and is apparent only at relatively low injection rates (<3 ml/s).
2. A fast injection improves the separation of contrast-enhancement phases and thus is beneficial for multiphase examinations of the liver, pancreas, and kidneys, as optimized enhancement during each contrast enhancement phase may improve lesion detection and characterization.

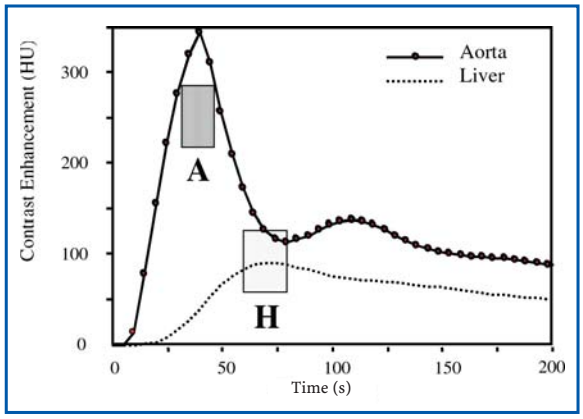

Fig. 6. Simulated aortic and hepatic contrast enhancement curves with a high contrast injection rate. Aortic (*solid line*) and hepatic (*dashed line*) contrast enhancement curves are simulated using a physiologically based compartment model (body weight 150 lbs, or 68 kg, and height 5'8", or 173 cm) subjected to a high injection rate protocol (150 ml of contrast medium injected at 5 ml/s) (14). A high injection rate not only increases the magnitude of arterial enhancement, but it also provides greater temporal separation between the arterial (*A*) and venous (*H*) phases of enhancement. This distinct phase separation is beneficial for multiphase scanning of the liver, pancreas, and kidneys. (Reprinted from [94])

Concentration

The availability of contrast media with high iodine concentrations (350 mgI/ml and above) has attracted a great deal of interest recently for MDCT applications [21, 25–39]. For injections of fixed duration, rate, and volume, a contrast medium with a high iodine concentration will deliver a larger total iodine load more rapidly. The resulting magnitude of peak contrast enhancement is increased, and the temporal window at a given level of enhancement is wider. Conversely, time-to-peak enhancement is unaffected because duration and rate of injection remain constant.

On the other hand, when the need is to maintain a constant total iodine mass and injection rate, injection volume and duration vary with contrast medium concentration. Under these conditions, the injected volume of a contrast medium with high iodine concentration is smaller than that of a contrast medium with low iodine concentration. The duration of enhancement is shorter with the higher concentration agent because of reduced contrast medium volume. Nevertheless, contrast medium with a higher iodine concentration delivers more iodine mass per unit time and thus results in earlier and greater peak aortic enhancement (Fig. 7). The effect is the same as that seen with the use of a high injection rate.

Practical Tips

1. For a fast MDCT scan, a high iodine delivery rate is desirable to maximize arterial enhancement for CTA and to depict hypervascular tumors.
2. Use of a contrast medium with high iodine concentration is an alternative approach to using an increased injection rate to increase iodine delivery rate.

Saline Flush

A saline flush "pushes" the tail of the injected contrast medium bolus into the central blood volume and thus makes use of contrast medium that would otherwise remain unused in the injection

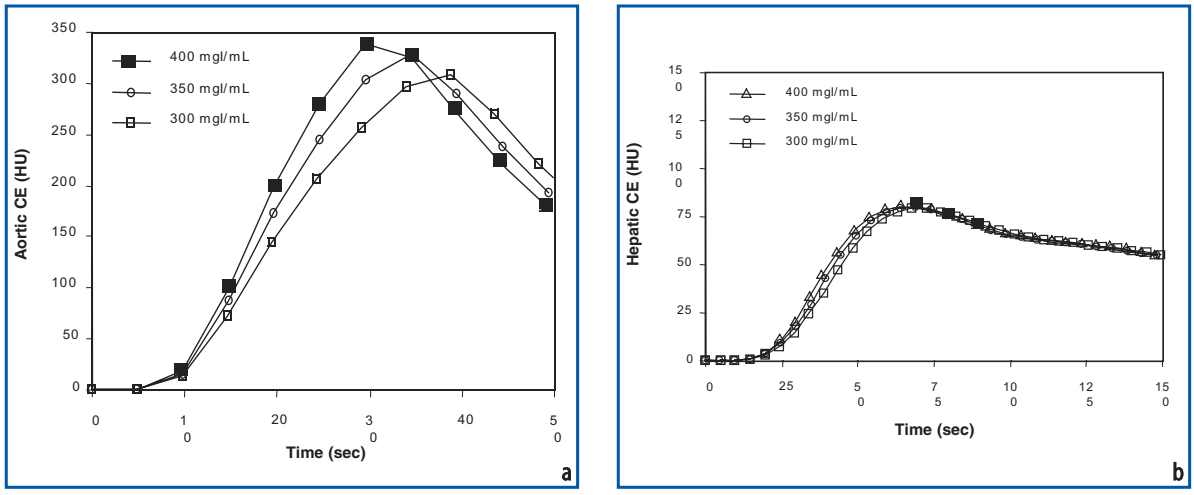

Fig. 7a, b. Simulated contrast enhancement curves with a fixed amount of iodine mass but three different contrast medium concentrations injected at a constant rate. Simulated enhancement curves of the **a** aorta and **b** liver based on a hypothetical adult male with a fixed height (5,8", or 173 cm) and body weight (150 lbs, or 68 kg) subjected to 5 ml/s injection of the same amount of iodine mass but at three different concentrations and volumes: 300 mgI/ml, 140 ml; 350 mgI/ml, 120 ml; and 400 mgI/ml, 105 ml. The aortic time-enhancement curves demonstrate that the use of high-concentration contrast material is associated with earlier and greater peak aortic enhancement. The effect of high iodine concentration contrast material on liver enhancement is minimal if iodine mass is unchanged. (Reprinted with permission from Bae KT (2003) Technical aspects of contrast delivery in advanced CT. Applied Radiology 32 [Suppl]:12-19)

tubing and peripheral veins. A saline flush therefore increases both the level of contrast enhancement and the efficiency of contrast medium utilization [40–47]. Additional advantages of a saline flush include improved bolus geometry due to reduced intravascular contrast medium dispersion and, on thoracic CT studies, reduced streak artifact from dense contrast material in the brachiocephalic vein and superior vena cava. A saline flush is particularly beneficial when a small volume of contrast medium is used. For this reason, a saline flush is commonly used for gadolinium-enhanced magnetic resonance imaging (MRI) but has not been widely used in CT, in part because a double-barrel CT contrast injector has not been commercially available until recently. With the increasing use of MDCT and the increasing clinical application of CTA, use of a saline flush is rapidly becoming accepted in clinical practice to compensate for the use of smaller contrast medium volumes.

The volume of contrast medium that can be substituted by saline flush without affecting the degree of contrast enhancement depends on the "dead space" volume of the injection tubing and the peripheral venous blood volume between the brachial vein and the superior vena cava. The peripheral venous blood volume is in turn related to patient size or weight. In a typical clinical setting, the amount of contrast medium saving may be anything between 12 ml and 20 ml.

Practical Tips

1. A saline flush improves contrast enhancement, the efficiency of contrast medium use and reduces artifacts; this is particularly beneficial when a small total amount of contrast medium is used.
2. Twenty to thirty milliliters of saline flush may be sufficient, and injection of a larger quantity might not further improve contrast enhancement.

Arterial CT Angiography

MDCT readily permits acquisition of images with high spatial and temporal resolution. The benefits of MDCT angiography are such that most conventional catheter-based diagnostic angiography examinations have been replaced by this technique.

For example, pulmonary CTA is now the most commonly practiced CTA application in the routine clinical setting. Improved spatial resolution on MDCT permits excellent delineation of peripheral pulmonary arteries and detection of small emboli. Improved temporal resolution deriving from increased scan speeds on the more recent 16- and 64-slice MDCT scanners permits a pulmonary CTA examination to be performed within a few seconds. Moreover, better temporal resolution results in reduced motion artifacts, with improved contrast enhancement and image quality. Advances in MDCT and electrocardiogram (ECG)-gating technology enable acquisition of high-resolution, motion-free images of the heart and coronary CTA within a single short breath hold. Aortic CTA and peripheral run-off CTA are additional routine applications with MDCT.

Contrast Enhancement Magnitude

As discussed above, the magnitude of arterial contrast enhancement for CTA depends on a number of patient-related and injection-related factors, including body weight and cardiac output, contrast medium volume and concentration, injection rate, type of contrast medium, and saline flush. The magnitude of arterial enhancement increases in direct proportion to the rate of iodine delivery, which is dependent on injection rate and contrast medium concentration (Figs. 4 and 7). In addition, when contrast medium is injected at a constant rate, enhancement increases continuously over time, with increasing injection duration due to the cumulative effects of new incoming contrast medium and recirculated contrast medium. Without recirculation, contrast enhancement reaches a steady-state plateau. The use of a contrast medium with a higher iodine concentration results in a greater magnitude of aortic contrast enhancement, even if the total iodine dose and injection rate are unchanged. This is due to the increased rate of iodine delivery into the vascular system.

The amount of contrast medium required for CTA is determined by the desired level of enhancement, vessels of interest, and scan duration. Although the magnitude of hepatic enhancement needed to detect focal lesions has been investigated extensively, to date, only a few studies have addressed the minimum degree of enhancement needed for CTA. Becker et al. [26] considered an attenuation of 250–300 HU to be optimal for coronary CTA since this attenuation permitted adequate differentiation of low-density coronary artery atherosclerotic lesions (which typically have a density of approximately 40 HU), intermediate fibrous plaques (approximately 90 HU), and calcified plaques (>350 HU) without obscuring coronary calcifications. However, when imaging is performed to identify significant stenoses, visualization of the lumen is more important, and higher vascular attenuation (>300 HU) may improve visualization of small coronary vessels [39]. In our opinion, for most CTA applications, contrast enhancement of 250–300 HU (i.e., attenuation of

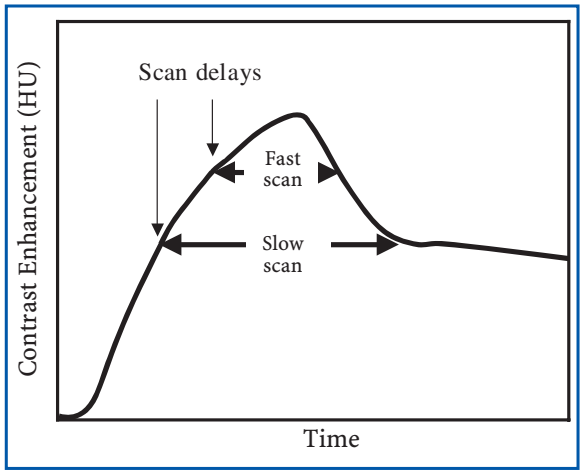

Fig. 8. Simulated aortic contrast enhancement curve with two different scan delays designated for the fast and the slow scans. For given duration of contrast enhancement or injection, the shorter the scan duration, the longer the additional delay needed to ensure that imaging takes place during the peak of aortic enhancement

300–350 HU) is adequate for the diagnosis of a wide range of vascular pathology.

In a coronary CTA study performed on a 4-row MDCT scanner, Becker et al. [26] reported that 40 g iodine (gI) (equivalent to 114 ml of a 350 mgI/ml concentration) injected at a flow rate of 1 gI/s (equivalent to 3.3 ml/s of a 350 mgI/ml concentration) resulted in an attenuation of 250–300 HU although no information was given about patient weight. In a similar but more elaborate comparative coronary CTA study with 16-row MDCT, Cademartiri et al. [39] reported that 42–49 gI at an injection rate of 1.2–1.4 gI/s generated a mean coronary artery attenuation of 273–333 HU (average patient weight 72–74 kg). In our experience, with a 64-row MDCT scanner, a volume of approximately 1.2 ml/kg of 350 mgI/ml contrast medium injected at a rate of 4 ml/s (i.e., 0.4 gI/kg of contrast medium injected at 1.4 gI/s) yields a contrast enhancement of approximately 250 HU in the pulmonary artery. Based on these observations, we thus estimate that diagnostically adequate coronary artery enhancement may be obtained for a 70-kg patient with (1) 45 gI injected at 1.2 gI/s (e.g., 128 ml of 350 mgI/ml concentration @ 3.3 ml/s) over 40 s for 4-row MDCT, (2) 42 gI injected at 1.4 gI/s (e.g., 120 ml of 350 mgI/ml concentration @ 4 ml/s) over 30 s for 16-row MDCT, and (3) 35 gI injected at 1.4 gI/s (e.g., 100 ml of 350 mgI/ml concentration @ 4 ml/s) over 25 s for 64-row MDCT. With these contrast medium administration schemes, a mean coronary artery attenuation of 300–350 HU can be expected for a 70-kg patient. A saline flush may further reduce the contrast medium requirement by 15–25 ml as well as helping to reduce the level of artifact in the superior vena cava and right heart. In order to maintain an equivalent degree of contrast enhancement, larger patients require a larger iodine dose while smaller patients require a smaller iodine dose.

For peripheral run-off CTA, the amount of contrast medium required for adequate enhancement of the abdominal aorta and peripheral arteries depends on patient weight and scan duration. For a patient with a body weight of 60–80 kg, an injection rate of 1.4 gI/s (4 ml/s of a 350 mgI/ml concentration) is probably sufficient. This is similar to the scheme for pulmonary and coronary CTA described above. The rate can be increased or decreased depending on the patient's body weight and the concentration of contrast medium used.

A common approach to selecting the injection duration for a CTA examination with a long scan time (>25 s) is to keep injection duration identical to scan duration. This approach, however, does not work with a short scan time (<15 s). If scan time and injection duration are equally short, then the result will be poor overall enhancement. Although enhancement can be improved by using a faster injection rate or a higher iodine concentration, there are clear practical restrictions on the extent to which these parameters can be increased to compensate for a short injection duration or low contrast volume.

Practical Tips

1. When contrast medium volume is reduced for CT angiography with MDCT, an increased injection rate and high contrast medium concentration can compensate for the somewhat decreased magnitude of aortic enhancement achieved with the smaller contrast medium volume.
2. One approach to estimating the injection duration for a short scan may be to add a constant factor to the scan duration. For a patient with body weight of 60–80 kg who receives contrast medium injected at 1.4 gI/s (e.g., 4 ml/s of 350 mgI/ml concentration), our proposed injection duration is "15 s + $^{1}/_{2}$ scan duration" with a saline flush or "20 s + $^{1}/_{2}$ scan duration" without a saline flush. The injection rate can be increased or decreased depending on body weight and the concentration of contrast medium used.

Scan Timing

Three factors should be considered for determination of scan delays for CTA or parenchymal imaging: (1) contrast medium injection duration, (2) contrast arrival time (*Tarr*), and (3) scan duration. In patients with normal cardiac output, peak arterial contrast enhancement is achieved shortly after termination of the contrast medium injection [20,

23]. Thus, in general, an injection of short duration (i.e., low volume and/or high injection rate) results in earlier peak arterial and parenchymal enhancement. In such cases, a short scan delay is required for CTA. On the other hand, an injection of long duration (i.e., high volume and/or low injection rate) results in later peak enhancement, and thus a longer scan delay is needed for CTA (Figs. 3 and 4).

In addition to injection duration, variation among patients in cardiac output (cardiovascular circulation time) should be taken into account when individualizing the scan delay for CTA studies. *Tarr* is related to the patient's cardiac output and can be measured using a test-bolus or bolus-tracking method. In our experience, the bolus-tracking method is a more efficient and practical approach although some radiologists prefer the test-bolus method because it provides an additional opportunity to "test" the integrity of the venous access prior to injecting the full bolus of contrast medium. With both techniques, a region of interest (ROI) is usually placed just proximal to the organ of interest, e.g., on the main pulmonary artery or right ventricle for pulmonary CTA or on the ascending aorta or left ventricle for coronary CTA.

Traditionally, for slow CTA studies (single-row and 4-detector-row scanners), the scan delay was chosen to equal a patient's *Tarr*. However, this approach does not provide precise scan timing when faster MDCT scanners and shorter injection durations are utilized. This is because *Tarr* merely represents time of contrast arrival rather than optimal scan delay. For fast (i.e., 16- and 64-row) MDCT scanners, an "additional or diagnostic delay" must be included to determine the appropriate scan delay [20, 28]. The significance of the additional delay for optimal enhancement has been demonstrated both empirically [48] and theoretically [49]. Determination of the appropriate additional delay, which is related to scan speed and injection duration, is critical for fast MDCT. The shorter the scan duration, the longer the additional delay needed to ensure that imaging takes place during the peak of aortic enhancement (Fig. 8), unless the injection duration is shortened to match the reduced scan duration.

For the majority of pulmonary CTA studies, well-designed fixed scan delays (typically 15 s) are usually adequate because contrast enhancement in the pulmonary arteries increases rapidly with fast injections of contrast medium. However, precise timing in pulmonary CTA is crucial when a "tight" contrast bolus is used with fast MDCT because pulmonary artery enhancement can be delayed considerably in patients with cardiac dysfunction, pulmonary artery hypertension, or compromised central or peripheral venous flow [50, 51]. The need to individualize the scan delay for cardiac and coronary artery CTA is well recognized. For peripheral run-off CTA, it is crucial that the scan delay is long enough that the scan does not outpace the contrast bolus but is completed when the bolus reaches the pedal arteries. One approach is to reduce scan speed and to use a longer injection to match scan duration; this may be particularly appropriate for imaging diseased peripheral vessels [52].

Our proposed approach to determining a scan delay involves: (1) estimating time-to-peak contrast enhancement from injection duration and *Tarr*, and (2) calculating scan delay by subtracting one-half of the scan duration from the estimated peak enhancement time (Table 1, Fig. 9). Time-to-peak enhancement may be estimated using either a "variable" approach, in which *Tarr* is estimated assuming normal circulation, or a "circulation-adjusted" approach, in which *Tarr* is measured using a test-bolus or bolus-tracking technique.

For the variable scan delay approach, time-to-peak aortic enhancement is determined as "injection duration + (x s)," in which "x" is larger for shorter injection durations but is typically a number between 0 and 10 [23]. For example, for a 30-s injection, the peak aortic enhancement would occur at "30+5=35" s (a 5-s additional delay is used in this example because a 30-s injection is considered to be of intermediate duration). Using this estimated peak time, scan delay for the arterial phase for a 20-s scan would be calculated as "35 – 20/2=25" s. Likewise, the scan delay for a 10-s scan would be "35 – 10/2=30" s.

For the circulation-adjusted delay approach, either a test-bolus or a bolus-tracking technique is used to measure *Tarr*. If 15 s is taken as the normal default value for *Tarr* (i.e., a typical value in a patient with normal circulation), time-to-peak aortic enhancement corresponds to "injection duration + (*Tarr* – 15)+(0 to 10 s)" or " injection duration + *Tarr* – (5 to 15 s)." Thus, at *Tarr* = 15, the circulation-adjusted and variable delay approaches are equivalent. The scan delay can be computed from this equation using the same steps as for the variable delay approach: for example, for a 10-s scan with a 30-s injection, the scan delay would be "30 + (*Tarr* – 15)+(5) – (10/2)" or "*Tarr* +15." Thus, when a test-bolus method is used, the scan delay is determined by adding 15 s to the measured *Tarr*. On the other hand, when a bolus-tracking method is used, *Tarr* is not estimated prior to the injection of a full bolus of contrast medium. In this case, the scan will start at "*Tarr* + 15": i.e., after 15 s of additional "diagnostic delay" once the 50-HU enhancement threshold is reached [53].

Practical Tips

1. Three factors should be considered when determining a scan delay for CTA: (1) contrast

Table 1. Contrast enhancement times and proposed scan delays in different applications

	Pulmonary CTA	Coronary thoracic aorta CTA	Abdominal aorta/peripheral runoff	Hepatic parenchyma/portal vein
Contrast arrival time (s)[a]	*Tarr* = 7–10	*Tarr* = 12–15	*Tarr* = 15–18	30–40 (*Tarr* = 15–18)
Peak time (s)[a]	From 15 to ID (peak reaches a plateau rapidly)	ID + (0 to 5)[b]	ID + (5 to 10)[b]	ID + (25 to 40)[b]
Fixed scan delay (s)	15 (20 for slow injection)	20	30 (20-25 for slow scan)	60–70
Variable scan delay (s)	15 (20 for slow injection)	ID + 5 – SD/2	ID + 5 – SD/2	ID + 35 – SD/2
Circulation-adjusted delay	*Tarr* + 5	ID + (*Tarr* – 10) – SD/2	ID + (*Tarr* – 10) – SD/2	ID + (*Tarr*×2+5) – SD/2

CTA computed tomography angiography, *Tarr* contrast arrival time, *ID* injection duration (s), *SD* scan duration (s)
For CTA, ID = "15 s + $^1/_2$ SD" (with saline flush) or "20 s + $^1/_2$ SD" (without saline flush) is suggested with the injection rate of 4 ml/s
For the liver, ID is determined by considering the total iodine load of 0.5 gI/kg
Peak time increases by 3–5 s with the use of saline flush
Tarr: **a** for pulmonary CTA, 100 HU threshold over the pulmonary artery with the first scan at 10 s after the start of the injection; **b** for aorta and hepatic phases, 50 HU threshold over the aorta with the first scan at 10 s after the start of the injection
[a]Assuming normal cardiac circulation, body weight of 60–80 kg, and the injection rate of 3–5 ml/s via the antecubital vein
[b]A larger number is used for a shorter injection duration

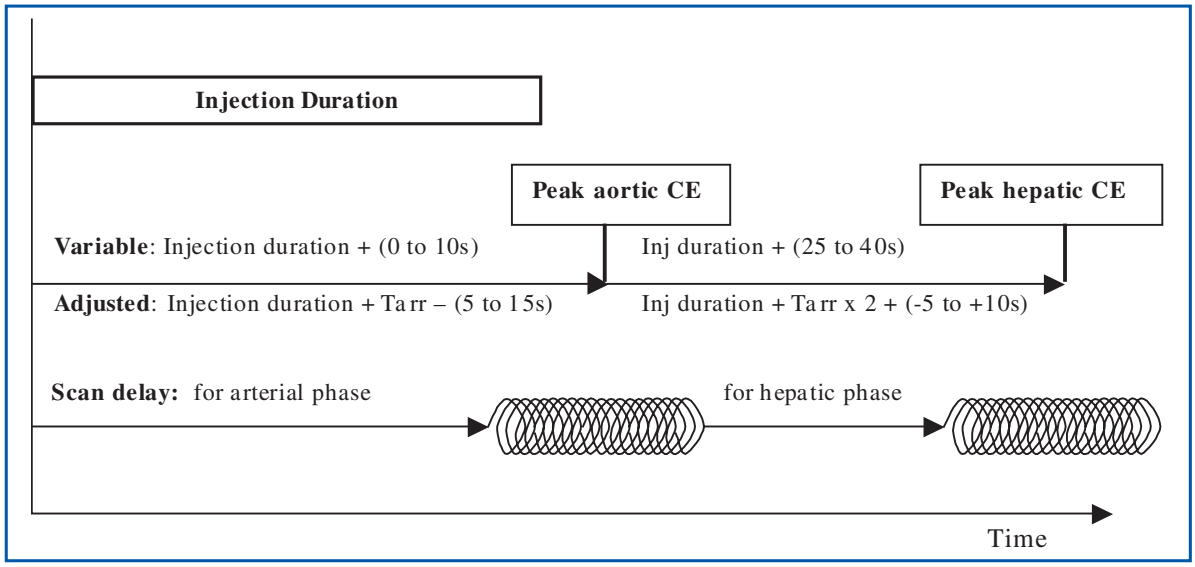

Fig. 9. Schematic diagram describing the times-to-peak aortic and hepatic enhancement and associated scan delays for a given injection duration. Times-to-peak enhancement of the arterial and hepatic phases are estimated from injection durations and contrast arrival times. We propose two approaches of estimating time-to-peak enhancement: variable (contrast arrival time is empirically estimated assuming normal circulation) and circulation-adjusted (contrast arrival time is measured using a test-bolus or bolus-tracking technique). From estimated peak time, scan delay can be calculated by subtracting one-half of the scan duration

medium injection duration, (2) *Tarr*, and (3) scan duration.

2. Traditionally, for slow CTA studies, the scan delay was chosen to equal a patient's *Tarr*. Because this approach does not provide precise scan timing with faster MDCT scanners and shorter injection durations, an additional diagnostic delay must be included to determine the appropriate scan delay.
3. The shorter the scan duration, the longer the additional delay needed to ensure that imaging takes place during the peak of aortic enhancement.
4. The scan delay can be calculated by subtracting

one-half of the scan duration from time-to-peak enhancement time. The time-to-peak enhancement in turn is estimated from the injection duration and *Tarr* using either a variable approach or a circulation-adjusted approach.

Hepatic Imaging

Among the many clinical applications for MDCT in hepatic imaging are: detection and characterization of primary or metastatic hepatic lesions, diagnosis of diffuse liver diseases, assessment of vascular and biliary patency or obstruction, tumor staging, monitoring treatment response, and preoperative evaluation for surgical resection. The high temporal resolution of MDCT permits the liver to be imaged during multiple precisely defined phases of contrast enhancement.

Multiphasic Hepatic Imaging

Approximately 20% of the blood supply to the liver derives from the hepatic artery while the remaining 80% derives from the portal vein. Injected contrast medium initially reaches the liver via the hepatic artery; in patients with normal circulation, the typical hepatic artery arrival time is approximately 15 s after the start of the injection. During the next 10–20 s, contrast medium from the splanchnic venous return enters the portal vein and hepatic parenchyma. However, whereas contrast medium from the splenic and pancreatic circulation arrives in the portal vein earlier than that from the intestinal circulation, the contribution of the portal vein to hepatic enhancement is usually very small within the first 30 s after initiation of the contrast injection [54, 55].

For routine abdominal CT or as part of a thoraco-abdominal and pelvic imaging survey, the liver is scanned once during the hepatic phase, i.e., during the phase of maximal liver parenchyma enhancement. However, to detect hypervascular liver lesions or to evaluate the hepatic vascular anatomy, it is highly desirable to scan during at least one phase prior to the hepatic phase. When optimizing multiphasic hepatic imaging, the goal is to scan during maximal enhancement for each phase and to minimize the influence of other enhancement phases.

For dedicated hepatic CT imaging, the three contrast-enhancement phases of interest are early arterial phase, late arterial/portal vein inflow phase, and hepatic parenchymal phase [56]. The early arterial phase begins with the arrival of contrast medium in the hepatic artery and ends prior to portal vein enhancement. The diagnostically useful early arterial phase begins about 10 s after contrast arrival and lasts for approximately 10 s (20–30 s from the start of contrast medium injection with a typical injection protocol and normal circulation). Prior to this, at the time of earliest contrast arrival in the hepatic artery, enhancement is too weak for adequate early arterial phase imaging. The late arterial/portal vein inflow phase (referred to simply as the late arterial phase in this chapter) corresponds to the time of maximum aortic enhancement. This occurs shortly (typically 0–10 s) after completion of injection, with the optimal temporal window lasting approximately 10 s. The hepatic parenchymal phase occurs when the peak contrast bolus has traveled through the splanchnic circulation and has returned to the portal venous system. This occurs typically at 25–40 s after completion of the injection and corresponds to the phase of maximum hepatic parenchyma enhancement.

The early arterial phase of enhancement is useful primarily for acquisition of a pure arterial data set for CTA and has only a limited role in imaging the liver. For detection of hypervascular primary or metastatic neoplasms, the late arterial phase is the preferred imaging phase [25, 57–67]. During this phase, hypervascular hepatic lesions enhance maximally while the hepatic parenchyma remains relatively unenhanced, commensurate with the relatively small contribution of the hepatic artery to the total hepatic blood supply. The hepatic parenchymal phase, the period of peak hepatic enhancement, is the phase used for routine abdominal CT imaging. Most hepatic lesions, including most metastases, are hypovascular and are therefore best depicted against the maximally enhanced hepatic parenchyma during this phase. The delayed imaging phase (>3 min after the start of contrast injection) is useful for detecting and characterizing some hepatocellular carcinomas [68] and for characterizing cholangiocarcinomas [69]. During this phase, hepatocellular carcinomas typically appear hypoattenuating whereas cholangiocarcinomas often demonstrate delayed contrast enhancement relative to the background hepatic parenchyma.

Contrast Enhancement Magnitude

The magnitude of hepatic enhancement is affected by numerous factors, such as contrast medium volume and concentration, rate and type of injection, scan delay time, and body weight [2, 7–10, 13–15, 22, 23, 25, 32, 33, 70–78]. The magnitude of hepatic parenchymal enhancement is directly and almost linearly related to the amount of total iodine mass administered (i.e., total contrast medium volume × concentration) [2, 8, 10, 15, 22, 23, 70–73, 75, 77, 78] (Fig. 3b). The most important patient-related

factor affecting the magnitude of hepatic enhancement is body weight, which demonstrates a linear inverse relationship with the magnitude of enhancement: as body weight increases, the magnitude of hepatic parenchymal enhancement decreases [1, 2, 73] (Fig. 1b). As a consequence, the total iodine load should be increased when imaging large patients in order to achieve a constant degree of hepatic enhancement. The iodine load can be increased by increasing contrast medium concentration, volume injected, or injection rate [13, 23, 78].

Insufficient hepatic parenchymal enhancement results in diminished lesion conspicuity [16, 17, 73]. The minimum level of hepatic enhancement acceptable for adequate liver imaging has variously been reported to be 30 HU [79], 40 HU [80–82], or 50 HU [9, 33, 74, 77, 83, 84]. In a multicenter study, Megibow et al. [19] found that 30 HU was the lowest limit of acceptable hepatic enhancement and that no definite clinical gain was achieved with hepatic enhancement greater than 50 HU. The iodine mass required to achieve this enhancement can be estimated on the basis of patient weight [2, 77]. In this regard, Heiken et al. [2] found that the maximum hepatic enhancement calculated as a function of patient weight was 96±19 HU per gram of iodine per kilogram of body weight. Thus, approximately 0.5 gI/kg is needed to achieve the maximum hepatic enhancement of 50 HU; i.e., 35 gI for a 70-kg patient. A similar weight-adjusted dose conversion ratio was reported in later studies [37, 67, 73, 78, 85].

Hepatic parenchymal enhancement increases mildly with an increase in injection rate although this is apparent only at relatively low injection rates (<3 ml/s) [22, 23, 74] (Figs. 4 and 5). Although the magnitude of hepatic parenchymal enhancement may not increase substantially at high injection rates (e.g., 4– 6 ml/s) compared with intermediate injection rates (e.g., 2–3 ml/s), a fast injection rate increases the magnitude of hepatic arterial enhancement and thus better separates the peaks of hepatic arterial and hepatic parenchymal enhancement [23, 62, 86]. As a result, fast injection rates are desirable in multiphase hepatic imaging and for detection of hypervascular liver masses [62, 73–75, 86, 87] (Fig. 6). Likewise, recent studies [25, 33, 35, 37, 38] that compared contrast media with different iodine concentrations for dual-phase MDCT liver imaging found that high-concentration contrast medium increases detection of hypervascular lesions by increasing the iodine delivery rate (Fig. 7a).

Practical Tips

1. The magnitude of hepatic parenchymal enhancement is directly and almost linearly related to the total administered iodine mass per body weight. When imaging large patients, the total iodine load should be increased to achieve a constant degree of hepatic enhancement.
2. Approximately 0.5 gI/kg is needed to achieve the maximum hepatic enhancement of 50 HU; i.e., 35 gI for a 70-kg patient.
3. Although increasing the delivery rate of iodine (i.e., use of high injection rate or high concentration contrast medium) may not substantially increase the magnitude of hepatic parenchymal enhancement, it is desirable in multiphase hepatic imaging and for detection of hypervascular liver masses because it increases the magnitude of hepatic arterial enhancement and better separates the peaks of hepatic arterial and hepatic parenchymal enhancement.

Scan Timing

Fixed scan delays from the initiation of contrast medium injection are commonly used for hepatic imaging. The typical scan delay for arterial phase imaging for a 30-s contrast medium injection is 20–30 s for SDCT [58] and 30–35 s for MDCT. For both SDCT and MDCT, the scan delay for hepatic parenchymal phase imaging is approximately 55–70 s. Note that the scan delay required for arterial phase imaging on MDCT is longer than that on SDCT because the shorter image acquisition time of MDCT permits scanning to be performed more closely to the peak of aortic enhancement.

Whereas the hepatic enhancement phase lasts 20–30 s, with gradual changes in enhancement, the arterial phase lasts for only 10-15 s, with abrupt changes in enhancement [88]. Thus, it is more critical to accurately determine the scan delay for the arterial phase. The time to aortic contrast arrival varies widely, from 10–36 s [64, 66, 86, 89], due to interindividual variations in circulation time. It is therefore necessary to use a test-bolus or bolus-tracking technique to acquire images during individualized enhancement phases.

Both test-bolus [13, 25, 37, 64, 66, 78] and bolus-tracking methods [11, 32, 34, 86, 89–92] have been used to determine the arterial phase scan delay for dual-phase hepatic imaging studies. Typically, an ROI is placed over the descending thoracic aorta just above the diaphragmatic dome at the same level as the start of the diagnostic scan. *Tarr* in the aorta is measured from the peak timing of a test bolus (15–20 ml of contrast) or, when using a bolus-tracking program, from the time to reach a contrast enhancement threshold of 50–100 HU above baseline attenuation. In order to avoid the early arterial phase and to scan during the late arterial phase, a further 5- to 15-s delay is added to determine scan delay. As discussed above, the magnitude of this additional delay depends on injection duration and scan speed.

Scan delays for both the arterial and hepatic phases can be determined by considering injection duration, *Tarr*, and scan duration. The time-to-peak enhancement of the arterial and hepatic phases can be estimated from injection duration and arterial *Tarr* (Table 1, Fig. 9). The scan delay can be calculated from the estimated peak enhancement time by subtracting one-half of the scan duration. Again, both variable and circulation-adjusted approaches can be used.

Time-to-peak aortic enhancement is estimated as described previously in the section on CTA. For the variable scan delay approach, using an estimated peak time derived as "injection duration + (0 to 10 s)" [23], the scan delay for the arterial phase for a 20-s scan with a 30-s injection would be "30+5 – 20/2=25" s, while that for a 10-s scan would be "30+5 – 10/2=30" s. For the circulation-adjusted scan delay approach, the time-to-peak aortic enhancement corresponds to "injection duration + (*Tarr* – 15)+(0 to 10 s)" or "injection duration + *Tarr* – (5 to 15 s)." For a 10-s scan with a 30-s injection, the scan delay would be "30 + (*Tarr* – 15)+(5) – (10/2)" or "*Tarr* +15." When a bolus-tracking method is used, the scan will start at "*Tarr* + 15," i.e., after 15 s of additional diagnostic delay once the 50 HU enhancement threshold is reached [53].

Time-to-peak hepatic enhancement for the variable scan delay approach is estimated as "injection duration + (25 to 40 s)" [23, 73, 93]. Again, a longer additional delay is added for injections of shorter duration. For example, for a 30-s injection, peak hepatic enhancement would occur at "30 + 35 = 65" s. The scan delay for the hepatic phase for a 20-s scan would then be "65 – 20/2=55" s, while that for a 10-s scan would be "65 – 10/2=60" s. Using arterial *Tarr* measured over the abdominal aorta, for the circulation-adjusted scan delay approach, time-to-peak hepatic enhancement can be estimated as "injection duration + *Tarr*×2+(–5 to +10 s)." When *Tarr* is 15 s, this equation is again identical to that of a delay determined using the variable approach. For a 10-s scan with 30-s injection, the scan delay would be "30 + *Tarr*×2+(5) – (10/2)" s, or "*Tarr*×2+30" s. At a *Tarr* of 15 s, the scan delay for the hepatic phase would be 60 s.

Practical Tips

1. Three factors should be considered when determining scan delays for hepatic imaging: (1) contrast medium injection duration, (2) *Tarr*, and (3) scan duration.
2. For multiphase hepatic imaging, it is more critical to accurately determine the scan delay for the arterial phase than for the hepatic phase. A test-bolus or bolus-tracking technique is used to acquire images during individualized enhancement phases.
3. Time-to-peak enhancement of the arterial and hepatic phases can be estimated from injection duration and arterial *Tarr*. From the estimated peak enhancement time, the scan delay can be calculated by subtracting one-half of the scan duration. Just as with CTA, both the variable and circulation-adjusted approaches to estimating the times-to-peak enhancement are possible for hepatic imaging.

Summary

A variety of patient-related and injection-related factors can affect the magnitude and timing of intravenous contrast medium enhancement. Although these factors are interrelated, some (body size, contrast volume and iodine concentration, saline flush) have more of an effect on enhancement magnitude while others (cardiac output, contrast injection duration, contrast injection rate) have more of an effect on the temporal pattern of contrast enhancement.

MDCT, with its dramatically shorter image acquisition times, permits images with high spatial resolution to be acquired at multiple, precisely defined phases of contrast enhancement. However, to make full use of the benefits that MDCT provides, protocols for contrast administration and scan timing must be modified to take into account the specific objectives of each clinical imaging application and the different MDCT scanners available. For example, a faster injection rate or a contrast medium with high iodine concentration may be desirable for many MDCT applications to improve arterial enhancement and tumor-to-parenchyma attenuation difference during the hepatic arterial phase. Injection duration should be considered for determinations of scan delay because it critically affects time-to-peak enhancement. Individualized scan delay is more critical with MDCT than with SDCT. The contrast arrival time (*Tarr*) measured using test-bolus or bolus-tracking techniques can be integrated with injection duration to predict peak enhancement time. The scan delay is then estimated such that the center of the scan is timed to the peak of contrast enhancement.

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