Contrast medium administration and image acquisition parameters in renal CT angiography: what radiologists need to know

ABSTRACT
Over the last decade, exponential advances in computed tomography (CT) technology have resulted in improved spatial and temporal resolution. Faster image acquisition enabled renal CT angiography to become a viable and effective noninvasive alternative in diagnosing renal vascular pathologies. However, with these advances, new challenges in contrast media administration have emerged. Poor synchronization between scanner and contrast media administration have reduced the consistency in image quality with poor spatial and contrast resolution. Comprehensive understanding of contrast media dynamics is essential in the design and implementation of contrast administration and image acquisition protocols. This review includes an overview of the parameters affecting renal artery opacification and current protocol strategies to achieve optimal image quality during renal CT angiography with iodinated contrast media, with current safety issues highlighted.

Personality medicine is a popular topic in radiology today. Scientists are flooding academic journals, conference proceedings, and book chapters with arguments about radiation reduction strategies with a personalized approach. However, contrast media (CM) dose reduction has been overlooked, which is of great concern. As such, 3% of all patients admitted for renal dialysis are a direct result of excessive CM volume delivered during radiologic imaging in the course of their hospital stay (1).

Studies suggest that CM volumes employed during renal computed tomography (CT) angiography (CTA) range from 30–120 mL (2–4). This wide array of CM dose has different effects on scanner parameters. For example, employing 30 mL CM volume with a tube current selection of 80 kVp renders acceptable image quality. However, image quality can either be quantitative or qualitative in nature, which increase the subjectivity of good versus acceptable image quality with desired CM doses. Therefore, judging optimal image quality is determined by the amount of noise and vascular opacification of the renal arteries.

Vascular opacification that is too low may compromise the visualization of small renal vasculature and underestimate plaque formation and stenosis (5). Previous studies on contrast injection protocols for renal CTA suggested that the adequate attenuation value for the arteries is greater than 211 Hounsfield units (HU) (6). However, attenuation values of the renal arteries have reached as high as 435±48 HU, while those of the renal veins have reached 277±29 HU (7).

The sensitivity and specificity for diagnosing greater than 50% renal artery stenosis during renal CTA range from 67%–100% and 77%–98%, respectively (8). Renal magnetic resonance angiography (MRA) has sensitivity and specificity of 88%–100% and 70%–100% with low interobserver variability, especially for severe stenosis greater than 70% (9).

Renal CTA provides accurate, noninvasive, and time-efficient diagnostic evaluation for medical management of renal arterial disease as well as creating a roadmap prior to surgical intervention. Such clinical questions arise when a hypertensive individual has renal CTA to exclude renal artery stenosis, fibromuscular dysplasia, or dissection. Pathology-specific renal CTA examinations include determining if vasculitis involves the renal arteries or the extent of renal aneurysmal changes. Preoperative renal CTA planning can be useful for nephron-sparing surgery prior to resection of renal masses or as post-procedural follow-up of renal stenting or surgical revascularization. Finally, renal CTA is also employed in the evaluation of the kidney donor and recipient prior to transplantation.
Large volumes of CM greater than 100 mL could potentially lead to contrast-induced nephropathy (CIN). CIN is the third leading cause of hospital-acquired acute renal failure, accounting for 11% of all cases, contributing to a prolonged hospital stay and increased medical costs (10). It has raised awareness of the need to optimize CM administration. There is a significant correlation between increased CM volume administration and the risk of CIN, i.e., higher doses of CM increase the risk of CIN (11–13). Additionally, CM doses less than 30 mL can be safely given in patients with chronic renal failure (14).

Factors affecting vascular opacification and pharmacokinetic relationships of blood flow during renal CTA

In the majority of people, each kidney is supplied by a single renal artery arising from the abdominal aorta at the level of L1-L2; renal arteries are usually 4–6 cm in length and 5–6 mm in diameter (15). Accessory renal arteries are present in about one-third of individuals; they arise from the aorta or the iliac arteries. Upper and lower accessory renal arteries supply the kidney, which tend to be smaller in caliber than the main renal arteries.

The kidneys are relatively small organs; yet, they receive up to 25% of the cardiac output. The vascular pattern of the kidney is complex, and the distribution of renal blood flow is nonhomogeneous in each kidney (16). Therefore, the amount of blood volume and CM injection during CTA is proportional to the renal blood flow. After intravascular administration, CM molecules move across the renal capillary membranes into the interstitial, extracellular space. CM is continuously eliminated through the glomeruli, since it has very short transit time through the renal circulation—only six seconds between the initial arterial and venous opacification (17). Less than 1% is excreted in patients with normal renal function (18). Following intravascular administration in patients with normal renal function, the elimination half-life is approximately two hours and 75% of the administered dose is excreted in the urine within four hours. Approximately 98% of the injected CM is excreted by 24 hours (19).

The velocity of the plasma volume and the plasma CM concentration in the kidneys determine the urinary excretion rate of CM in the body. The rate of CM loss from the blood circulation does not correlate with the velocity of emergence in the urinary tract. Independent of the number of compartments, renal clearance is defined as the ratio of the urine excretion rate to the plasma concentration. Its value for renal substance excretion, such as iodinated CM, for healthy individuals is on the order of 1.76 mL min\(^{-1}\) kg\(^{-1}\) (20). Understanding CM delivery strategies and nonhomogeneous blood flow distribution in the renal arteries during renal CTA is paramount to achieve superior arterial opacification and image quality. CM opacification in the renal arteries is affected by several factors that are divided into three main categories: patient characteristics, contrast parameters, and scanner parameters (Fig. 1) (21).

Patient characteristics

Patient body size (weight and height) and cardiac output (cardiovascular circulation time) are essential patient-related factors that affect both vascular and parenchymal enhancement. Additional influential factors such as age, sex, venous access, renal function, and various other pathologic conditions contribute to blood flow circulation variables (21).

Patient’s body weight is an important patient-related factor affecting the degree of vascular and parenchymal enhancement. It is inversely proportional to the magnitude of contrast enhancement by an approximately one-to-one ratio (21). Larger patients have larger blood volumes that result in greater dilution of CM in their blood. Therefore, to reduce the dilution of CM, higher CM doses or faster injection rates are necessary to achieve optimal vascular and parenchymal enhancement. It is therefore recommended that 30 mL be used for pediatric patients, 50 mL for adult patients below 80 kg, 80 mL between 80–100 kg, and 100 mL for patients greater than 120 kg (22).
**Lean body weight.** Obese patients have large amounts of adipose tissue, which is less perfused with blood and contributes little to the dilution of the CM in the blood. As a result, CM volume can be calculated on the basis of lean body weight with the omission of adipose tissue. The method was found by several studies to be a superior index than the total body weight since it achieved increased vascular and organ enhancement with reduced patient-to-patient variability (23, 24). However, such complex algorithms pose a difficulty in translation into the clinical environment.

**Body surface area** is routinely employed in clinical practice to calculate drug dosage. It was proposed as an alternative to using body weight since it is less associated with excessive body fat. Body surface area was also found to achieve consistent vascular opacification with reduced patient-to-patient variability (25). Current studies support body surface area as a superior calculation method than lean body weight (26).

**Body mass index (BMI)** (weight in kilograms divided by the height in meters squared) is a body factor associated with contrast enhancement. BMI is not an index for body size, but it is a method to assess adiposity and should not be used alone in calculation of CM volume. As an example, a small baby with high BMI would require less CM volume than a thin adult with low BMI. Nevertheless, it should be incorporated with other body size indices such as lean body weight and body surface area (21).

**Cardiac output and cardiovascular circulation time** are the most important patient-related factors affecting vascular opacification. Cardiac output is directly proportional to the contrast bolus arrival time known as the time-to-peak (TTP). However, it is inversely related to the extent of maximal vascular enhancement. When the cardiac output decreases, the circulation time increases, which leads to a delay in TTP and increased vascular contrast opacification due to the slower clearance of CM volume. Whereas, in patients with high cardiac output, contrast bolus arrives faster at reduced vascular enhancement. This is true for all organs of the body (27). Therefore, when calculating the scan acquisition time, individualizing scan delay for each organ by using a test-bolus or bolus-tracking technique to eliminate variation in cardiac output between patients and the uptake of the blood of each organ is essential.

**Contrast media parameters**

Contrast-related factors include vascular access site, injection duration, injection rate, CM volume, concentration, bolus shape, and use of saline chaser.

**Vascular access site.** The intravenous access site will affect TTP. Ideally, the location of choice is the antecubital vein, as it will always have less dilution of contrast with the blood since the distance to the heart is reduced compared with palmer surface location. Also, to further reduce dilution, a right-sided injection site may be preferred for a shorter route to the superior vena cava via the brachiocephalic vein compared with the left side.

**Injection duration** is defined as total CM volume divided by the injection rate (21). It affects both TTP and the extent of vascular enhancement. Longer injection durations (keeping the injection rate constant) increase the extent of vascular and parenchymal enhancement as increased CM dose is administered. Longer injection periods delay the maximum deposit of CM, which results in a delayed TTP and vice versa (28). The ideal injection duration is determined by the scanning conditions and the clinical objectives of the examination. In single-detector CTA, the rule of thumb is that the injection duration equals scan duration; but this rule cannot be applied with faster CT scanners, since the image is acquired in just a few seconds and employing this rule would lead to inadequate vascular enhancement. Although scan duration does not correlate with injection duration, it is closely associated with a combination of scanner, patient, and contrast variables; thus, individualized protocols provide optimal vascular opacification during CTA (29).

**Injection rate.** TTP and the degree of vascular enhancement are closely affected by the injection rate. When keeping both the volume and the iodine concentration of the CM constant, an increase in injection rate will increase the extent of vascular opacification while reducing TTP at reduced vascular enhancement duration. However, when keeping the volume and the iodine concentration constant, a decrease in the injection rate will reduce the extent of vascular enhancement while increasing the TTP and the duration of vascular opacification. So faster injection rates provide greater vascular opacification, but reduce the temporal window during CTA. However, fast injection rates have their limitations; increasing the rate more than 8–10 mL/s does not increase the vascular enhancement of the arterial tree, possibly because of pooling in the central venous system with reflux into the inferior vena cava. Faster injection rates have been known to increase the risk of extravasation (30). Injection rates used in renal CTA range between 4–6 mL/s since faster injection rates are necessary with faster scanners.

**Contrast media volume.** Continual efforts have been made to provide patient-specific contrast administration. The work of Bae et al. (31), Fleischmann (32), and Fleischmann and Hittmair (33) demonstrated the feasibility and benefit of individually customized contrast protocols based on additional factors beyond weight, such as procedure information, patient characteristics, and data from test-bolus injections, allowing individualization of scan delay computation. These volume calculations were much more elaborate than the commonly used 1:1 linear calculation method, where 1 mL of CM volume is used for every 1 kg of patient’s weight. Numeric simulations based on previous work involve detailed analysis and sophisticated manipulation of test bolus data with the ability to further reduce cardiovascular variability. However, complex algorithms have been difficult to translate into routine clinical practice and, therefore, are rarely used.

**Contrast bolus shaping.** Shaping the CM bolus is vital in formulating optimal vascular opacification in the vessel of interest while minimizing perivenous artifacts that could potentially reduce image quality. There are several methods to shape bolus delivery, the first of which is the uniphasic-rate injection, where CM is injected at a constant rate. Enhancement pattern produced by this method is known as the “peaked” or “hump” enhancement. As time enhancement curve progressively increases, it peaks shortly after the completion of the injection and is followed by a relatively rapid decline in opacification, lacking true plateau of peak enhancement (21) (Fig. 2a–2c). The second method is the biphasic-rate injection, where injection is started at a constant rate and followed by a slower constant rate. This method is helpful for slower CT scanners as it prolongs the contrast enhancement by prolonging the injection duration without increasing the volume of CM (34). Fleischmann et al. (35) reports optimal opacification of the renal arteries using the biphasic-rate injection method. A variation of biphasic injection technique
is the biphasic-concentration injection, starting with injecting undiluted CM followed by a diluted CM. This technique is achieved by introducing the dual-syringe power injector, which simultaneously inject the undiluted CM and saline. Bae et al. (36) introduced a unique injection shaping method, the multiphasic exponentially decelerated contrast injection. As the name implies, this method starts by injecting at a given rate that exponentially decelerates towards the end of the injection. They concluded that uniform vascular enhancement and reduced CM dose can be achieved with this method.

Saline chase. Another technique for optimizing contrast bolus delivery is by injecting a saline chaser or (saline flush) immediately after the CM. Saline chaser pushes the tail of the injected contrast bolus into the central circulation, allowing better utilization of CM that would have remained redundant within the injection tubing and peripheral veins (Fig. 2c). Saline decreases the amount of required CM volume without affecting the level of vascular opacification (37). Moreover, saline chaser was found to increase the extent of peak arterial opacification (38). The rate of saline chaser injection in relation to the rate of CM injection plays a vital role in adjusting the contrast opacification, as injecting saline at faster rates could result in higher opacification whilst injecting at slower rates can result in prolonged lower opacification (39). However, a recent study suggested that faster saline chaser rates may not result in further increases in the degree of contrast opacification (38). As a result, employing 100 mL saline chaser increases vascular opacification during renal CTA.

Contrast concentration. Vascular opacification in the artery of interest is correlated to the extent of iodine delivery. Adjusting iodine delivery is usually performed either by changing the contrast injection rate or the concentration of the CM (Fig. 3). Furthermore, keeping the injection rate, volume, and injection duration of CM constant, vessel opacification increases with higher iodine concentration, but the TTP is unaffected since the duration and rate of injection remain fixed. Conversely, when the iodine mass and injection rate are kept constant, the volume and duration will vary with iodine concentration; the volume of higher concentration CM will be smaller than the volume of lower concentration CM. It was found that injecting a small volume of high concentration CM at fixed rate leads to early peak but shorter duration of contrast enhancement (40). Several studies have investigated the difference between high and low concentration CM. However, higher iodine concentrations (> 350 mg/L iodine) yielded greater vascular opacification during CTA (41). Employing high concentration CM is usually preferred in renal CTA (42). However, the greater the concentration of CM, the greater the viscosity, which may increase the risk of medullary hypoxic injury or direct toxicity to the renal tubular cells resulting in CIN (43).

CT parameters
In addition to patient characteristics and contrast parameters, CT scanning parame-
CT is an important tool in diagnostic imaging. The choice of tube voltage affects image quality. CT-related factors include scan duration, direction, contrast bolus arrival time, scan delay with respect to contrast injection, and CT tube voltage.

**Scan duration and direction** are essential scanning parameters that play a critical role in formulating the CM injection protocol. Usually, long scan durations necessitate long injection times and short scan durations can be performed with short injection times. The shorter scans provided by the new CT scanners (scan duration of <5 s) present a challenge, as the injection duration cannot be reduced due to scan duration being faster than physiologic blood circulation, resulting in inadequate vascular opacification. Adjusting CM delivery to have the entire vascular tree of interest opacified is vital since faster CT scanners can cover longer ranges at shorter scan times. On the other hand, scan direction has no impact on renal CTA. Therefore, the shortest possible scan duration (pitch value less than 0.9 mm/rot) is an important variable that needs to be considered when designing CTA protocols.

**Scan delay.** To obtain high-quality images, it is essential to set scan timing at the peak contrast enhancement in the targeted region of interest (ROI). There are two methods for setting the scan delay: either a fixed delay or an optimized delay according to three parameters (contrast bolus arrival time, injection duration, and scan duration) can be used.

**Fixed scan delay** is calculated based on experience with CTA. It is a preprogrammed delay between CM injection and the start of the CTA acquisition without monitoring the desired ROI. Tsuge et al. (44) studied scan delay in renal CTA using fixed injection duration (30 s) with CM volume of 2 mL/kg and found the optimal scan delay for renal CTA to be 25–30 s from the start of contrast injection. The fixed scan delay method is unable to adjust for cardiovascular circulation time variation between individuals. Short acquisition times provided by the faster CT scanners could lead to early or late vascular opacification if the bolus delivery is not predetermined accurately (45).

**Tube voltage.** X-ray energy is an important parameter affecting CM enhancement. Vascular opacification is directly proportional to iodine delivery to the ROI. This proportionality increases with decreasing CT tube voltage, leading to increased vascular opacification, as x-ray photon energy gets closer to the k-edge of iodine at lower voltages (46) (Fig. 4). Low voltage not only improves vascular opacification, but it also reduces the volume and concentration of CM needed (47) and the radiation dose administered to the body (48). Both 80 kVp and 100 kVp techniques have been researched during renal CTA and results demonstrated greater vascular opacification with lower contrast and radiation dose compared with 120 kVp (43). A disadvantage of low tube voltage is the increased image noise in patients with large body habitus (49). It is therefore recommended that 80 kVp tube voltage be used for pediatric patients, while adult patients below 80 kg should be scanned at 100 kVp, patients between 80–100 kg at 100 kVp, and finally patients greater than 120 kg at 140 kVp (22).

Determination of the contrast bolus arrival time to the targeted ROI is critical for calculating the optimal scan delay. Contrast bolus arrival time is closely related to the cardiovascular circulation time and, therefore, shows considerable variance ranging from 8 s to as long as 40 s in patients with cardiovascular disease. Two techniques have evolved to predict accurately the contrast arrival time, namely, the test bolus technique and the bolus tracking technique (32).

**Test bolus technique** is performed by injecting a small amount of CM (10 mL) with saline flush (30 mL). The ROI is placed inside the lumen of interest, which is usually at the level of the diaphragm or suprarenal artery. A series of low radiation dose scans are initiated at the level of ROI. Changes in the opacification (measured in HU) within ROI are plotted in a time-enhancement curve and TTP of the test bolus is determined and used to estimate scan delay for the CTA acquisition.

**Bolus tracking technique**, measuring enhancement changes over ROI, is performed in real-time, while injecting the full bolus of CM. A predetermined enhancement threshold is set at the level of ROI (50–150 HU), a series of low radiation dose scans are taken, and when the enhancement threshold at the ROI is reached, diagnostic scanning is started automatically after a preprogrammed scan delay. Ideally, predetermined thresholds at 100 HU provide peak arterial opacification in the renal arteries and low venous opacification in the renal veins when thresholds at this level are chosen. However, changes in breath-hold can significantly alter the cardiovascular dynamics resulting in venous opacification of the renal veins due to Valsalva (Fig. 2d).

Which of those two techniques provides optimal opacification is a cause for debate. Some studies suggest bolus tracking for its practicality and because it is more efficient in CM use than the test bolus technique (50), whilst others prefer test bolus technique because it provides a test for the...
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venous access before the actual exam and provides mathematical modeling of an individual’s cardiovascular circulation time and CM pharmacokinetic response, which can then be used to predetermine the CM volume during CTA (51).

The contrast bolus arrival time determined by test bolus or bolus-tracking techniques should not be used as the only factor to determine the scan delay. Bolus arrival time is merely a factor used for individualizing the scan delay. Other factors that should be incorporated with bolus arrival time for optimizing the scan delay are scan duration and injection duration. (52). For single-detector CT scanners, bolus arrival time is usually used as a scan delay (53), but with faster acquisition times provided by new generation CT scanners, longer additional delay is preferred because it will be closer to the time of peak vascular opacification (52). Injection duration also has an important role in determining the scan delay, as shorter injection durations lead to early TTP of contrast, which requires shorter scan delays (54) (Figs. 5–7). Goshima et al. (55) conducted a study to determine the optimal scan delay at different renal enhancement phases including the renal arterial phase; 2 mL/kg of CM was administered at a rate of 4 mL/s and using 8-row CT, optimal scan delay for arterial phase was 5–10 s after the bolus-tracking trigger at 50 HU.

Contrast media safety

There is no universally agreed upon threshold of serum creatinine elevation (or degree of renal dysfunction) beyond which intravascular iodinated contrast medium should not be administered. Laboratory tests may be used to estimate the risk of CIN prior to administering CM. Serum creatinine concentration is the most commonly used measure of renal function (<1.4 mg/dL), but it has limitations as an accurate measure of glomerular filtration. Serum creatinine is influenced considerably by the patient’s gender, muscle mass, nutritional status, and age. Impaired renal function can exist when the serum creatinine is “normal.” Normal serum creatinine is maintained until the glomerular filtration rate (GFR) —at least as reflected in creatinine clearance— is reduced by nearly 50%. Normal GFR clearance for healthy women and men is 88–128 mL/min and 97–137 mL/min, respectively (normal levels may vary slightly between labs).

Increasing CM volume can increase the radiation dose to radiosensitive organs such as breast glandular tissue and liver parenchyma during renal CTA. Additionally, researchers have identified predisposing risk factors for the development of CIN. The most significant predictor of CIN is history.
Table 1. Scanner, contrast, and filtered back projection reconstruction parameters

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Contrast bolus geometry

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Contrast parameters

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FBP, filtered back projection.

Table 2. Scanner, contrast, and iterative reconstruction parameters

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Contrast parameters

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IR, iterative construction.
Conflict of interest disclosure
The authors declared no conflicts of interest.

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37. Fleischmann D. Multiple detector-row CT angiography of the renal and mesenteric vessels. Eur J Radiol 2003; 45:579–587. [CrossRef]


