Contrast Medium Delivery Strategies and Radiation Dose Parameters Affecting Renal CT Angiography: Literature Review

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Learning objectives

Renal Computed Tomography Angiography has become the examination of choice for evaluating renal vasculature. It has challenged the role of conventional angiography as it offers improved temporal and spatial resolution at reduced radiation dose. New challenges in contrast administration have emerged with faster scan acquisition times demanding synchronization between scanner and contrast administration.

This literature review entails an overview of:

- The parameters affecting vascular opacification during renal CTA.
- The current protocol strategies used in contrast medium delivery in renal CTA.
- Quick overview of Radiation dose Parameters in CTA in general.

Background

Introduction:

The rapid evolution of computed tomography (CT) technology over the past two decades with the introduction of multi-detector CT (MDCT) together with improved image processing have broadened the applications of CT angiography (CTA) to include the entire vascular territories (1). Renal CTA has become the examination of choice over other imaging modalities for evaluating the renal vasculature. Although conventional angiography is still the gold standard, renal CTA is highly regarded as a valuable imaging tool since it is minimally invasive, offers high spatial and temporal resolutions, short scan and examination times at reduced radiation dose (2, 3).

Renal CTA is clinically indicated to rule out suspected renovascular hypertension by quantifying renal artery stenosis. Other indications include renal transplant recipient and donor evaluation, arteriovenous communications, renal artery aneurysm, renal parenchymal or vascular calcifications and renal manifestations of a systemic disease (e.g., vasculitis, thromboembolic disease)(4, 5).

The major disadvantages of CTA are the exposure of patients to ionizing radiation and the use of iodinated contrast agents that 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 prolonged hospital stay and increased medical costs (6-8). This has raised awareness in the need to optimize Contrast medium (CM) administration, since it was found that there is significant correlation between increased CM volume administration and the risk of CIN i.e. higher volumes of CM increase the risk of CIN, however, contrast volume of less than 30 ml can be safely given in patients with renal dysfunction (9-13).

Optimization of CM delivery was relatively overlooked since the contention of CT technology was determined by faster tube rotations, greater slice coverage, and lower radiation dose solutions. However, several studies proposed different methods for optimization of CM dose and delivery strategies offering reduction of CM volume and exposure to radiation with optimal enhancement (14, 15).

PARAMETERS AFFECTING CONTRAST ENHANCEMENT AND SCAN TIMING:

Contrast enhancement is affected by several factors that falls into three categories: patient characteristics, contrast parameters and scanner parameters (16) (Fig.1).

PATIENT CHARACTERISTICS:

Patient body size (weight and height) and cardiac output (cardiovascular circulation time) are the two most significant patient-related factors affecting the contrast enhancement. Supplementary influential factors such as age, sex, venous access, renal function, and various other pathologic conditions are less significant (16-18).

A. Patient's body weight:

- It has inverse proportional relationship to the magnitude of contrast enhancement in a nearly one-to-one ratio (16-20).
- This is explained by the fact that larger patients have larger blood volumes which leads to greater dilution of CM in blood of these patients, thus; requiring higher CM dose or rates than smaller patients for the same degree of contrast enhancement (21).
- Multiple methods have been proposed to calculate the optimal CM required according to body size:
  1. The first method was based on total body weight (TBW) using 1:1 linear scale by doubling the iodine mass when the patient's body weight doubles (18). However, this method has its limitation since it was found to
overestimate the CM required for obese patients. Therefore, other complex methods were employed using other body size indices to calculate CM volume such as lean body weight (LBW) (22-28), body surface area (BSA) (26, 27, 29, 30) and body mass index (BMI) (27, 29).

2. **Lean body weight:** calculation of CM dose is formulated on the basis of LBW with the exclusion of adipose tissue. The method was found by several studies to be better index than the total body weight as it achieves a greater consistent enhancement with reduced patient-to-patient variability (22-28). However, complex algorithms pose a difficulty in translating these into the clinical environment.

3. **Body surface area:** It was proposed as an alternative of using body weight as it is less associated with excessive body fat. BSA was also found to achieve more a more consistent enhancement with reduced patient-to-patient variability (27, 29, 30). Current investigation suggests its superiority over the LBW method owing to the simplicity of BSA calculation (26).

4. **Body mass index:** is a body factor associated with contrast enhancement. BMI is not an index for body size but it's a method to assess adiposity and should not be used alone in calculation of CM volume. Therefore it should be incorporated with other body size indices such BW and BSA (16).

**B. Cardiac output and cardiovascular circulation:**

- Cardiac output is directly proportional to the contrast bolus arrival time and the time to peak (TTP) but it is inversely related to the extent of maximal arterial peak enhancement (31).

- When calculating the scan acquisition time, it is paramount to individualize scan delay for each organ by using a test-bolus or bolus-tracking technique due to the variation in cardiac output between patients and the uptake of blood of each organ (31, 32).

- Renal parenchyma enhancement is affected by the cardiac output due to it dense capillary network which allows significant corticomedullay enhancement.

**CONTRAST PARAMETERS:**

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

**A. Vascular Access Site:**

- CM arrival time and peak enhancement will be affected by the intravenous access site.
• It is more ideal to use the right side as it has shorter route to the superior vena cava and with less dispersion of CM (33, 34).

B. Injection Duration:

• It is defined as total CM volume divided by the injection rate (16).
• It affects both the peak time and extent of contrast enhancement.
• Longer injection durations (with keeping the injection rate constant) increase the extent of contrast enhancement as more CM administered.
• Slower injections rates combined with longer injection durations results in delayed TTP and vice versa (21, 35-37).
• The ideal injection duration is determined by the scanning conditions and the clinical objectives of the examination:
  1. In single detector CTA, the rule of thumb (the injection duration equals scan duration) was used for setting the injection duration (38),
  2. This rule can't be applied with faster CT scanners (MDCT) where scan is acquired in a few seconds, as employing this rule will lead to inadequate enhancement.
• Scan duration does not correlate with injection duration, it is closely associated with a combination of scanner, patient and contrast variables that demonstrate individualized protocols that provide optimal vascular opacification during CTA (39-41).

C. Injection Rate:

• TTP and the degree of enhancement of CM are also affected by the injection rate:
  1. When keeping both the volume and iodine concentration of the CM constant, an increase in rate will increase the extent of the contrast enhancement while reducing TTP and arterial enhancement duration.
  2. When keeping the volume and iodine concentration constant, a decrease in rate will reduce the extent of contrast enhancement while increasing the TTP and arterial opacification duration (41).
• Faster injection rates produce greater vascular opacification but reduce the temporal window during CT acquisitions.
• Increased injection rate has its limitations, increasing the rate more than 8-10ml/s does not improve the enhancement, 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 (42).
• Injection rates used in renal CTA are usually between 4-6 mL/s, using faster rates with faster scanners (2, 4, 15).

D. Contrast Bolus Shaping:

• Shaping the CM bolus is vital in formulating optimal opacification in the vessel of interest while minimizing perivenous.

• There are several methods to shape bolus delivery:

1. The first of which was the uniphasic-rate injections, delivered by injecting CM at a constant rate, enhancement pattern produced by this method is known as the "peaked" or "hump" enhancement (16).

2. The second method is the biphasic-rate injection, starting with constant injection rate followed by a slower constant rate, this method is helpful for slower CT scanners as it prolongs the injection duration thus prolonging the contrast enhancement duration without increasing in the volume of CM (43), Fleischmann et al. reports optimal opacification of the renal arteries using the biphasic-rate injection method (15).

3. A variation of biphasic contrast injection methods, begins with injecting CM followed by a saline, this technique is achieved by introducing the dual-syringe power injector.

4. Multiphasic exponentially decelerated contrast injection is a relatively new method introduced by Bae et al. (44), as the name implies, this method starts with injecting at given rate that exponentially decelerated to the end of the injection, they concluded that uniform vascular enhancement and reduced CM volume can be achieved with this method.

E. Saline Chaser:

• It allows better utilization of CM that would have been remained unused within the injection tubing and peripheral as Saline chaser pushes the tail of the injected contrast bolus into the central circulation.

• It decreases the amount of needed contrast volume without affecting the level of contrast enhancement (45-50).

• Saline chaser was found to increase the extent of peak arterial enhancement (47, 49-51).

F. Contrast Concentration:

• The opacification in the artery of interest is significantly correlated to the extent of iodine delivery.

• Adjusting iodine delivery is usually performed either by changing the rate or the concentration of the administered CM.
• Higher iodine concentration with constant injection rate, volume and injection duration leads to higher vessel opacification but TTP remains unaffected.

• It was found that injecting a small volume of high concentration CM at fixed rate will lead to early peak but shorter duration of contrast enhancement (52).

• Employing high concentration CM is usually preferred in renal CTA (2, 15, 53, 54).

• High concentration CM has higher viscosity which might have a higher risk of medullary hypoxic injury or direct toxicity to the renal tubular cells resulting in CIN than a CM with a lower viscosity (14, 55, 56).

CT PARAMETERS:

In addition to patient characteristics and contrast parameters, CT scanning parameters affect image quality. CT related factors include CT tube voltage, scan duration, contrast bolus arrival time and scan delay in relation to contrast injection.

A. Scan direction:

• Scan usually performed at the same direction of CM bolus propagation.

• Craniocaudal direction is commonly used with scan starting at the upstream of contrast opacification and moving downstream with contrast bolus direction at the same rate. This result in an effective use of CM.

• Recent studies suggests that scan direction does not affect contrast opacification in the abdominal vasculature (40).

B. Scan Timing or 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. There are two methods for setting scan delay; either using fixed delay or an optimized delay according to three parameters (contrast bolus arrival time, injection duration and scan duration).

1. Fixed scan delay

• It is a preprogrammed delay between CM injection and the start of the CTA acquisition without monitoring the desired region of interest (ROI).

• Tsuge et al. (57) studied scan delay in renal CTA using fixed injection duration (30 seconds) with contrast volume of 2ml/kg and found the optimal
scan delay for renal CTA to be 25-30 seconds from the start of contrast injection.

- Fixed scan delay method doesn't take in consideration the difference in contrast bolus arrival time between individuals (depending on cardiovascular dynamics and body habitus) or the short acquisition durations provided by the faster CT scanner generations. Thus, it could lead to missing of the bolus if the delay is not properly chosen (41).

2. Optimized Scan Delay:

- It depends on the determination of the contrast bolus arrival time to the targeted region of interest.

- Contrast bolus arrival time is closely related to the cardiovascular circulation time and shows considerable variance ranging from 8 to as long as 40 seconds in patients with cardiovascular disease.

- Two techniques have evolved for determining of the contrast arrival time which are test bolus technique and bolus tracking technique (17):

i. Test bolus technique:

- It is performed by injecting small amount of CM (10-20 mL), ROI is placed inside the lumen of the target vessel which is usually the abdominal aorta in renal CTA at the level of diaphragm or supra-renal artery (Fig. 2).

- Series of low radiation dose scans is then initiated at the level of ROI.

- Changes of enhancement (measured in HU) within ROI are plotted in a time-enhancement curve.

- TTP of the test bolus is determined and is used to estimate scan delay for the full bolus diagnostic CT.

ii. Bolus tracking technique:

- Enhancement changes over ROI is performed in real time while injecting the full bolus of CM.

- A predetermined enhancement threshold is set at the ROI (50 - 150 HU).

- Series of low radiation dose scans are taken, and when the enhancement threshold at ROI is reached, diagnostic scanning starts manually or after a preprogrammed scan delay.

The contrast bolus arrival time determined by test bolus or bolus tracking techniques should not be used as scan delay. Bolus arrival time is merely a factor used for individualizing the scan delay relative to it by including additional delay before starting diagnostic scanning. Other factors that should be incorporated with bolus arrival time for
optimizing the scan delay are scan duration and injection duration. (35, 58). For the single detector CT scanners, bolus arrival time was usually used as a scan delay (38, 59), but with the faster acquisition times provided with MDCT, longer additional delay is preferred because it will be closer to the time of maximum enhancement (35, 58). Injection duration has also important role in determining the scan delay as shorter injection durations leads to early TTP of contrast and therefore require shorter scan delays (35, 36, 60, 61).

C. Tube Voltage:

- Low tube voltage increases the contrast enhancement, as with lower voltage, x-ray photon energy gets nearer to the k-edge of iodine (62, 63).
- Low tube voltage doesn't only improves enhancement, it also reduces the CM needed (64) and the radiation dose administered to the body (65-67).
- Benefits of low voltage have been recognized in pediatric, thin individuals and CTA applications (14, 65-70).
- This has been tested on renal CTA and results demonstrated greater contrast enhancement with lower contrast and radiation dose when using lower tube voltages (14, 66).
- However, despite increased image noise with low tube voltages, it was found that low tube voltage increases the contrast to noise ratio (CNR) (65, 67). And moreover it was found that it also improves Image quality (14, 65).
- Recently, a new technology for automated voltage and current selection was introduced, in this technology, a software tool optimizes the tube voltage and current for each patient on the basis of patient attenuation measured from scout image and the user-specified CT study task, it was found that using this technology reduces radiation dose while maintaining image quality and CNR (71, 72).

RADIATION DOSE:

- There are multiple scan parameters affecting the radiation dose administered to the body during CT, including body size, tube current, tube voltage, pitch, scan range, number of scans and scan modes.
- Many efforts have been made to reduce the radiation dose by modifying these different scan parameters, but the challenge was to reduce the radiation dose while achieving optimal image quality.
- Various patient size indices have been used to create body size optimized CT protocols with lower radiation dose, these protocols were mainly tested in pediatric patients and some adult CT applications to spare them unnecessary exposure to high radiation (68, 69):
1. Body weight and BMI (73, 74) were the first to be used.
2. Cross-sectional dimensions found to yield a better results (75, 76).

- Optimizing CT protocols for lower radiation according to body size is usually done by adjusting tube voltage, as radiation dose varies with the square of the tube potential (63), and as was discussed earlier lower tube voltages resulted in reduced radiation doses (64, 65, 77).

**RENAL CTA RELATED FACTORS:**

**A. Renal Vascular Anatomy:**

Commonly, 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 (4). Accessory renal arteries are present in approximately one third of individuals; they arise from the aorta or the iliac arteries. Accessory renal arteries usually supplies the upper or the lower poles of the kidney and they tend to be smaller than the main renal arteries (4, 78) Majority of people have one renal vein arising from each kidney, about 15% of healthy population have multiple renal veins.

**B. Renal Dynamics:**

The kidneys are relatively small organs but receive up to 25% of cardiac output, thus receive the same percentage of CM injected. CM has very short transit time through the renal circulation, with 6 seconds between the initial arterial and venous opacification (Fig. 3,4) (79). Renal enhancement can be divided into 4 phases: arterial phase, combined venous/angionephrogram phase, nephrogram phase and excretory phase; with these phases occurring at 15-25 seconds, 30-40 seconds, 80-120 seconds and 180-300 seconds, respectively after injection of CM (78).

**Images for this section:**
Fig. 1: Overview of Parameters Affecting Contrast Enhancement and Scan Timing

- **Patient Characteristics:**
  - Magnitude: Weight, height, cardiac output, age, sex.
  - Timing: Cardiac Output, venous access.
  - Others: Breath-hold, diseases, renal function

- **CT Parameters:**
  - Magnitude: scan duration, scan delay.
  - Timing: scan delay, scan duration.
  - Others: Radiation dose, scan phases.

- **Contrast Parameters:**
  - Magnitude: Iodine concentration and volume, injection rate, bolus shape.
  - Timing: injection duration (volume, rate)
  - Others: injection protocol
Fig. 2: Determination of contrast bolus transit time using test-bolus injection. Region of interest is placed inside abdominal aorta (red circle). Resulting enhancement curves display time needed to reach peak of maximum contrast enhancement for test bolus.
Fig. 3: Renal CTA in 3D volume-rendering view, right renal artery aneurysm (Arrow). Reduced perfusion of the upper segment of the right kidney due to the large renal artery aneurysm (arrowhead).
**Fig. 4:** Renal CTA in 3D volume-rendering view, Renal Cell Carcinoma in the right kidney (arrow).
Findings and procedure details

Renal CTA Technique:

Scan Range: the optimal anatomic coverage for renal CTA ranges between the celiac arteries to the aortic bifurcation, additionally, it is recommended that the range of CTA should include 2 cm above the renal organ to the aortic bifurcation in order not to miss renal artery anomalies. However, scan range modification should be done in patients with ectopic or transplanted kidneys.

Pre contrast scan: a low dose unenhanced imaging is usually performed. It is advised to do pre contrast scans prior to CTA because it helps identification of renal hemorrhage, vascular calcifications, calculi and renal masses (5).

Renal CTA scan: there are several protocols in the literature summarized Table 1 & 2.

Table 1:

Overview of Renal CTA Contrast Delivery Protocols by different authors.

<table>
<thead>
<tr>
<th>Author</th>
<th>Bolus shaping</th>
<th>CT Type</th>
<th>Scan Time (Second)</th>
<th>Contrast Volume (mL)</th>
<th>Rate (mL/second)</th>
<th>Concentration (mgI/ml)</th>
<th>Scan timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fleischman et al.</td>
<td>Uniphasic</td>
<td>4 MDCT</td>
<td>27 s</td>
<td>120</td>
<td>4</td>
<td>300</td>
<td>tCMT +2 s</td>
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<tr>
<td></td>
<td>Injection</td>
<td></td>
<td></td>
<td>90</td>
<td>3</td>
<td>400</td>
<td>tCMT +2 s</td>
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<td></td>
<td></td>
<td>4 MDCT</td>
<td>21 s</td>
<td>105</td>
<td>5</td>
<td>400</td>
<td>tCMT +5 s</td>
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<td>3.8</td>
<td>300</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>8 MDCT</td>
<td>7.5 s</td>
<td>80</td>
<td>6</td>
<td>400</td>
<td>tCMT +2 s</td>
</tr>
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<td></td>
<td>70</td>
<td>4.5</td>
<td>400</td>
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</tr>
<tr>
<td>Fleischman et al.</td>
<td>Biphasic</td>
<td>4 MDCT</td>
<td>27 s</td>
<td>I = 30, II = 80</td>
<td>I = 6, II = 3.5</td>
<td>300</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Injection</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td>I = 22.5, II = 60.5</td>
<td>I = 4.5 II = 2.6</td>
<td>400</td>
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I = 30, II = 80

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<table>
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<tr>
<th>Study</th>
<th>Injection Type</th>
<th>MDCT</th>
<th>Duration</th>
<th>tCMT</th>
<th>Additional Details</th>
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<tr>
<td>Eklof et al. 2006 (80)</td>
<td>Uniphasic</td>
<td>16</td>
<td>96±13</td>
<td>3-4</td>
<td>300 tCMT +4s</td>
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<td>Rau et al. 2007 (54)</td>
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<td>300mg/5</td>
<td>5</td>
<td>300 tCMT +7s</td>
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<td>Goshima et al. 2007 (81)</td>
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<td>8</td>
<td>2 mL/kg 4</td>
<td>300</td>
<td>Optimal at tCMT +5-10s</td>
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<td>Tsuge et al. 2009 (57)</td>
<td>Uniphasic</td>
<td>8</td>
<td>2ml/kg, mean 107</td>
<td>300</td>
<td>Optimal at 25-30 s</td>
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<td>Budoff et al. 2010 (82)</td>
<td>Uniphasic</td>
<td>16 or 64</td>
<td>35-70</td>
<td>4</td>
<td>300-370</td>
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<tr>
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<td>100</td>
<td>4</td>
<td>300-400 tCMT +4-5 s</td>
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<tr>
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<td>Biphasic</td>
<td>64</td>
<td>110</td>
<td>5</td>
<td>370</td>
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</table>

tCMT: contrast bolus arrival, determined either by test bolus technique or bolus tracking technique.
Table 2:

Overview of Renal CTA Scanning Parameters by different authors. KVP: Tube Voltage, mA: Tube Current

<table>
<thead>
<tr>
<th>Author</th>
<th>MDCT Type</th>
<th>KVP</th>
<th>mA</th>
<th>Rotation Time</th>
<th>Collimation Section Thickness</th>
<th>Pitch</th>
<th>Reconstruction Interval</th>
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<td>1.25</td>
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<td></td>
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<td></td>
<td></td>
<td>0.5-s</td>
<td>1.25</td>
<td>1.5</td>
<td>0.7</td>
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<td></td>
<td></td>
<td></td>
<td>0.5-s</td>
<td>2 x 1.25</td>
<td>1.675</td>
<td>0.8</td>
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<tr>
<td>Eklof et al. 2006 (80)</td>
<td>16-Channel MDCT</td>
<td>120</td>
<td>16 x 1</td>
<td>0.5-s</td>
<td>1.25</td>
<td>1</td>
<td>0.7</td>
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<td>Rau et al. 2007 (54)</td>
<td>16-Channel MDCT</td>
<td>120</td>
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<td>0.5-s</td>
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<td>0.938</td>
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<td>Goshima et al. 2007 (81)</td>
<td>8-Channel MDCT</td>
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<td>16 x 1</td>
<td>0.5-s</td>
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<td>Tsuge et al. 2009 (57)</td>
<td>8-Channel MDCT</td>
<td>Auto mA</td>
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<td>0.5-s</td>
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<td>0.625</td>
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Conclusion

Although CT technology has evolved rapidly over the past two decades, the synchronization between scanning and CM delivery have not advanced at the same rate. Nonetheless, there have been some promising innovations in the field of CM delivery, targeting optimal arterial enhancement at reduced CM volumes and radiation dose. Body habitus has been found to be an important factor in tailoring CM volume. Knowledge of Cardiovascular Dynamics and anatomical variation is crucial in renal CTA. Current trends in renal CTA favors high injection rates and high iodine concentrations with the use of MDCT. Image quality depends on multiple factors such as optimal scan acquisition time at peak arterial contrast enhancement. This is achieved with bolus shaping accompanied with calculating bolus arrival time with either bolus tracking technique or test bolus technique. New effective methods evolved to reduce radiation dose including the use of body habitus indices and the automated tube voltage and current. Despite all of these new techniques in and scanning protocols and CM delivery, none, has been universally applied in renal CTA.

Personal information

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Decelerated Contrast Material Injection Method


