Contrast enhancement in MDCT coronary angiography

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Introduction

Multidetector (MD) technology has created new dimensions in spatial and temporal resolution in computed tomography (CT) scanning. Multislice CT scanners allow non-invasive coronary angiography within a single breath hold by use of faster gantry rotation times and sophisticated algorithms for retrospective electrocardiographic gating [1].

Four-row CT scanners have shown promising results [2], even with a scan time of approximately 40 s and suboptimal spatial and temporal resolution. Owing to the increased number of detector rows and faster gantry rotation, the introduction of 16-row scanners has decreased the time needed for imaging the entire heart to approximately 20 s and, thus, enabled consistent images of the coronary arteries to be obtained at CT angiography. An improved sensitivity of this technique in the detection of significant coronary artery stenoses has been reported [3,4].

A prerequisite for successful CT angiography is prominent vascular enhancement. In order to achieve this, the injection parameters must be accurately chosen and associated with synchronization protocols between the arterial passage of the contrast agent and CT data acquisition. The introduction of MD row CT technology requires even further optimization and synchronization, due to the shorter acquisition times [5].

Modality of contrast material administration (parameters affecting bolus geometry)

The pattern of arterial enhancement (bolus geometry) in a patient is influenced in the first instance by parameters such as their age, body weight and cardiac output, which are not operator controlled. Other parameters affecting the bolus geometry, such as the volume, injection rate and iodine concentration, are related to the modality of the contrast material administration and, thus, are operator controlled [6,7].

Contrast material volume

Ideally, a volume of contrast material normalized for a patient’s body weight will result in a predictable degree of arterial enhancement. On the other hand, it is conceivable that an increase in the contrast material volume will produce a proportional increase in arterial enhancement. A fixed amount of contrast material is generally applied in clinical practice [8]. Since it is mandatory to obtain good coronary artery enhancement for the whole duration of the CT scan, an injection volume of approximately 100 ml at 4 ml/s will take approximately 25 s to be administered, that is to say just a little longer than the average scan time of a 16-row CT imager [6].

In order to contain the dose of iodine and the risk of contrast material nephropathy, combined methods of a contrast material bolus followed by a saline solution flush have been applied to coronary CT angiography.

Contrast enhancement in coronary CT angiography

The pattern of enhancement in a given vessel of interest can be described as a curve obtained by plotting attenuation values within the vessel against the time after intravascular injection of the contrast material. This curve is also known as the bolus geometry and its shape resembles the temporal changes in attenuation within the vessel (see Fig. 3.1). As it is observed with a fixed injection rate in clinical practice, this curve typically has a quite low upslope, a delay in reaching a plateau, rather than a peak and, eventually, a slow decrease in the enhancement. Being aware of the attenuation changes in time is not trivial, since CT angiography is based on the fast acquisition of data during the arterial phase of contrast passage.

In order to image coronary arteries optimally, the timing and duration of CT scanning should be synchronized to the timing and duration of the actual enhancement curve, in particular to the portion resembling high and relatively homogenous attenuation.

Fig. 3.1. Attenuation–time curves after contrast agent injection in CT coronary angiography. (a) In ideal settings the bolus geometry and dynamics (dotted line, 1) have a rectangular shape and overlap the CT imaging window (light grey rectangle). The actual enhancement curve (continuous line, 2) has a steep upslope, a rounded peak and a washout downslope. Portions of all the three enhancement phases are imaged. PME, time to the peak of maximum enhancement; PME, the peak of maximum enhancement. (b) The contrast material volume, injection rate and concentration affect the bolus geometry by elevating the peak of enhancement. The time to peak is delayed by an increase in volume and is obtained earlier by an increase in concentration, whereas it stays unaffected by changes in the iodine concentration. Source: Cademartiri et al. (2003) [9].
angiography. Previous studies in the literature have described the injection of a saline solution in patients undergoing thoracic CT in order to push a decreased volume of contrast material, which allowed a 20% decrease in the contrast material volume with a similar degree of tissue enhancement \(^{(10)}\). More recently, the use of a saline solution injected intravenously immediately after the contrast material main bolus, which is known as a bolus chaser, has been tested in non-invasive 16-row CT coronary angiography and has been compared to conventional contrast material protocols without a bolus chaser \(^{(11)}\). The ‘low-volume’ protocol with a bolus chaser showed comparable enhancement at the level of the coronary arteries with a 35% decrease in the contrast material volume.

**Injection rate**

In order to evaluate the relative effect of the injection rate in vascular and hepatic enhancement during CT, some authors have performed simultaneous and dynamic measurements of aortic, portal and hepatic attenuation in animal models and concluded that a higher injection rate has prominent effects on arterial enhancement without a consistent effect on venous and parenchymal (i.e. liver) enhancement \(^{(12)}\). Claussen et al. \(^{(13)}\) reported that, in a patient population and with a peripheral injection site, below a threshold of 8 ml/s the peak aortic enhancement depends mainly on the rate of injection, so that the elevation of the injection rate leads to a proportional increase in arterial enhancement regardless of the iodine concentration and injection volume \(^{(14)}\).

The higher risk of renal dysfunction associated with a higher iodine load led to the development of strategies for improving the homogeneity of arterial enhancement to fit the imaging window, so that the overall amount of contrast material to be injected could be reduced. In particular, multiphasic protocols have been tested in which the injection rate is decreased during the contrast injection \(^{(15-17)}\). A higher injection rate at the beginning of the injection and a lower rate in the second part of the injection produce a prolongation of the plateau of enhancement. Such a change in the bolus geometry was meant to allow the collection of the CT data set from the entire field of view with a constant level of arterial enhancement while less contrast material volume is administered. The use of a multiphasic protocol for the administration of contrast material in 16-row coronary CT angiography does not provide significant advantages over a monophasic protocol in terms of vessel attenuation \(^{(18)}\), since the faster scan time (faster gantry rotation plus an increased number of detector rows) makes the potential benefit for data acquisition of a longer plateau of enhancement worthless.

The injection rates used in clinical coronary CT angiography range between 4 and 5 ml/s \(^{(6)}\). A large and proximal antecubital vein is commonly used in CT coronary angiography and 18–20-gauge cannulas allow the injection rate to be achieved without complications.

**Iodine concentration**

Mathematical models for the description of contrast enhancement of blood vessels have been developed based on physiological data and pharmacokinetic rules. According to these approaches contrast enhancement of blood vessels follows the rules of a one-compartment model and depends on the volume of the vessel compartment, the flow rate within the vessel, the contrast material concentration and the time \(^{(19)}\).

In animal series with a given injection rate and volume, changes in the contrast material concentration proved to have a prominent effect on arterial enhancement, whereas venous and parenchymal (i.e. liver) enhancement were affected much less prominently \(^{(12,14)}\).

Fenchel et al. \(^{(20)}\) determined the influence of two different iodine concentrations of contrast material (400 mg/ml versus 300 mg/ml) on contrast enhancement in abdominal multislice CT in a study performed on a patient population. According to these authors the early enhancement of the aorta, coeliac trunk and superior mesenteric artery was significantly higher when the 400 mg/ml contrast material was used, thus allowing an excellent evaluability of the splanchnic arteries \(^{(20,21)}\). Similarly, there is clinical consent that effective opacification of the thoracic aorta is better achieved by injecting high-concentration contrast materials at injection rates of 3 ml/s or more \(^{(22)}\). The ideal iodine concentration for high vascular enhancement in coronary CT angiography is reported to be 350–400 mg/ml \(^{(6)}\).

**CT scan synchronization (prediction of bolus geometry)**

Synchronization of the scan with maximum enhancement of the vessels under investigation (imaging window) is the ultimate step required, in order to perform robust coronary CT angiography.

Optimal acquisition timing is even more crucial when evaluation of the patency of an in-stent coronary artery lumen is attempted on the basis of measured contrast enhancement, as reported in early papers \(^{(23,24)}\).

In general, for helical CT or MD row helical CT, the most frequently used bolus-timing techniques are a fixed-delay technique, bolus tracking and determination of the transit time by means of a test bolus injection.

**Fixed-delay technique**

Although the synchronization of contrast material administration is becoming increasingly important secondary to the introduction of faster MDCT scanners, controversies still remain about the opportunity for using these techniques. On the basis
of experience and related to angiographic data, a fixed delay of 25 s was used for imaging the abdominal aorta after intravenous injection of 150 ml of contrast material. In such series, 98% of the attenuation measurements were judged adequate for angiographic evaluation [25].

**Bolus-tracking technique**

This technique is based on real-time monitoring of the angiographic bolus with the acquisition of a series of dynamic low-dose monitoring scans at the level of the vessel of interest during injection. It is possible to start the main scanning manually or automatically with a trigger threshold.

The advantages of tracking the contrast agent bolus over the use of a fixed scan delay were assessed at dual-phase helical CT of the liver by Kopka et al. [26]. Heavy and severely diseased patients represent the only limitation to this approach in that the attenuation threshold in tissues is often not achieved [27].

A method of interactive determination of the scanning delay in MDCT imaging of abdominal aortic aneurisms has also been published [28]. Low-radiation monitoring images were acquired in a single transverse section cephalad to the body region under investigation. The diagnostic portion of the scan was triggered manually and the power injector stopped as soon as contrast enhancement in the monitoring section could be qualitatively assessed. According to this study, a 29% decrease in contrast agent dose could be achieved with no enhancement loss at the level of the aorto-iliac arteries [28].

A protocol for optimal visualization of the pulmonary arteries in the diagnosis of pulmonary embolism was developed with the injection of a small bolus at a slow injection rate, the passage of which was monitored at the level of the pulmonary veins and triggered the injection of the main bolus [29]. This was meant to reduce high-density artefacts arising from pooling of the contrast agent in the right sections of the heart and allow better evaluation of the pulmonary arteries.

In a recent study, the efficacy of the bolus-tracking technique was compared to that of a test bolus in coronary CT angiography [8]. The authors reported that the bolus-tracking group had more homogenous and steady enhancement compared with the test bolus group.

**Test bolus technique**

This technique is based on the calculation of the scan delay time by means of the intravenous injection of a small amount of contrast material (20 ml or 15–20% of the main bolus) during the acquisition of a series of dynamic, low-dose monitoring scans at the level of the vessel of interest [6]. The calculated delay time is eventually exerted between the commencement of the contrast main bolus injection and the start of CT data acquisition. Bolus tracking was revealed to be superior to the test bolus technique in optimizing coronary artery opacification in 16-detector row CT coronary angiography [8].

**Conclusion**

A quick overview of the literature attempting to optimize the contrast injection parameters and scanning synchronisation techniques is reported in Table 3.1. Some authors have focused on CT angiography in patient populations. Although others have experimented on animals or have primarily considered parenchymal (i.e. liver and pancreas) enhancement patterns, data on aortic enhancement are nevertheless available from these studies.

Being aware of the X-ray attenuation changes in time within the vessels under investigation is not trivial, since CT angiography is strictly based on the fast acquisition of data during the arterial phase of contrast passage and most of these works have tested and expressed their efforts at optimizing contrast enhancement for CT angiography by means of measurements of vascular attenuation over time. The attenuation values sampled are distributed and described according to the bolus geometry (and its changes).

The bolus geometry and dynamics resemble the temporal changes in contrast enhancement within the vessels of interest (Fig. 3.1a). A rectangular profile that overlaps the imaging window is an ideal setting for the bolus geometry. In practice, the enhancement curve has an upslope, a smooth peak resembling a plateau and a washout portion. The shape of the bolus geometry can be manipulated in order to provide adequate contrast enhancement, both in terms of peak height and duration. The volumes, injection rate and iodine concentration of the contrast material are the parameters that should be adjusted in order to optimize the attenuation of vessels. Such an effort can

### Table 3.1 Summary of the literature on the parameters affecting the bolus geometry and techniques of CT scanning synchronisation

<table>
<thead>
<tr>
<th>Volume</th>
<th>Injection rate (ml/s)</th>
<th>Concentration (mg I/ml)</th>
<th>Measured mean peak aortic attenuation (HU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yamashita et al. [30]</td>
<td>1.5 ml/kg*</td>
<td>3.0</td>
<td>300</td>
</tr>
<tr>
<td>Han et al. [14]</td>
<td>2.5 ml/kg*</td>
<td>0.5*</td>
<td>300</td>
</tr>
<tr>
<td>Haage et al. [31]</td>
<td>2.0 ml/kg*</td>
<td>2.0*</td>
<td>280</td>
</tr>
<tr>
<td>Garcia et al. [12]</td>
<td>1.5 ml/kg*</td>
<td>6.0*</td>
<td>388</td>
</tr>
<tr>
<td>Cademartiri et al. [5]</td>
<td>2.0 ml/kg*</td>
<td>3.0*</td>
<td>288</td>
</tr>
<tr>
<td>Ho et al. [28]</td>
<td>20 + 100 ml test bolus*</td>
<td>4.0</td>
<td>320</td>
</tr>
<tr>
<td>Haage et al. [31]</td>
<td>100 ml bolus tracking*</td>
<td>4.0</td>
<td>300</td>
</tr>
<tr>
<td>Cademartiri et al. [11]</td>
<td>107 ± 20 ml*</td>
<td>4.0</td>
<td>285</td>
</tr>
<tr>
<td>150 ml*</td>
<td>3.0</td>
<td>370</td>
<td></td>
</tr>
<tr>
<td>60 + 30 ml saline*</td>
<td>4.0</td>
<td>320</td>
<td></td>
</tr>
<tr>
<td>100 + 40 ml saline*</td>
<td>4.0</td>
<td>327</td>
<td></td>
</tr>
</tbody>
</table>

Changes in the peak aortic attenuation are reported.
* Parameters tested in each study.
† Interactive delay protocol.
neglect neither the technical performance of the imager, such as the gantry rotation time and number of detector rows (i.e. the scanning time), nor the size of the vascular territory to be imaged, since synchronization of the data acquisition with robust enhancement in the entire field of view must be achieved.

An increase in the contrast material volume increases arterial enhancement and delays the maximum enhancement peak (Fig. 3.1b).

A higher injection rate also produces an increase in arterial enhancement. On the other hand, the enhancement peak will be earlier regardless of whether such a change in contrast injection is accomplished (Fig. 3.1b). Both of these latest features are desirable in coronary CT angiography, such that high injection rates are used. Nevertheless, in clinical practice such effects are limited by a higher risk of contrast material extravasation. Theoretically, administering the injection at decreasing rates acts on the bolus geometry and prolongs the plateau phase, which is the imaging phase and allows the contrast agent dose to be reduced by minimizing the vessel enhancement in non-diagnostic phases. With the advent and widespread diffusion of 16-detector row CT scanners this strategy is not even required any more, owing to the faster coverage of the body region to be imaged at maximum enhancement, which automatically contains the contrast dose needed.

The attenuation accomplished in the vessels is also proportional to the iodine concentration of the contrast agent, whereas the time to the peak remains unaffected by changes in the concentration (Fig. 3.1b). Thus, the use of high-concentration contrast agents is preferred over the use of low-concentration ones. Conversely, one has to be aware that the influx of contrast of a very high concentration may cause a combination of motion and high-density artefacts when imaged in CT. Moreover, it is well known that viscosity increases with iodine concentration and decreases with rising temperatures. Hence, high-concentration contrast materials (monomeric 2350 mg/ml or dimeric 320 mg/ml) should be administered only after appropriate heating at 38°C. It has been pointed out that the contrast material volume shares the effect of elevating the peak of enhancement with the other injection parameters. Nevertheless, at a fixed concentration and injection rate, a very high contrast volume would also increase the overall iodine load. In clinical practice adequate enhancement during the imaging window is generally fulfilled through the use of fixed amounts of contrast material according to the temporal performance of the CT imager. In our experience, provided that an adequate concentration and injection rate are feasible for robust CT angiography in the first instance, the latter parameter is ultimately adjusted to a trade-off depending on the diagnostic question and patient habits. For example, a larger field of view and a longer scan time are usually required for full coverage of bypass graft surgery. In these circumstances, no deterioration in image diagnostic accuracy occurs with a slight reduction in the injection rate. A larger blood pool and a higher X-ray attenuation may be partly associated with poorer vascular enhancement in heavier patients. As a rule of thumb, if the patient’s weight is over 90 kg, a 20% increase in contrast material volume might be advisable.

Optimizing the bolus geometry ultimately means tailoring the enhancement within the vessels under study (which is a dynamic effect of contrast material administration) to the acquisition performance of the CT imager. Once the injection parameters have been adjusted and robust enhancement is predictable in the vascular bed, the CT data acquisition must be accurately synchronized to the most homogenous phase of enhancement. In other words, it would be worthless to obtain good contrast enhancement that does not correspond to the imaging window.

To this purpose, several options are available. The imaging delay can be calculated by means of the test bolus technique by detecting the time for a small test bolus injection to travel to the vessels under study.

Bolus tracking is a synchronization technique in which, after one single contrast injection, a monitoring acquisition phase triggers the diagnostic acquisition phase as soon as the attenuation in the territory to be imaged reaches a threshold, which is visually or automatically assessed. Both a test bolus and bolus tracking can be advantageously applied to coronary CT angiography. A recent paper by Cademartiri et al. tested the efficiency of both methods in 16-detector row CT and assessed a more homogenous and steady enhancement with the bolus-tracking technique, in particular at the level of left coronary branches. The analysis of the aortic bolus geometry revealed that the scan was performed during the plateau of enhancement in this group. In contrast, since the calculated scan delay was slightly shorter in the test bolus group, such patients were imaged when the contrast material in the ascending aorta was still increasing (upslope of the attenuation–time curve). Regardless of whether a four-detector row CT imager should be used for performing coronary angiography, hyperventilation may be necessary prior to the start of the data acquisition, owing to the relatively long scanning time. The wide respiratory movements in hyperventilation may not allow a reliable monitoring sequence for bolus tracking at the level of the ascending aorta. In these settings, the choice of a bolus test over bolus tracking may be mandatory.

References


