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Contrast Medium Injection Technique

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Corresponding Author:	D. Fleischmann, MD UNITED STATES
First Author:	D. Fleischmann, MD
Order of Authors:	D. Fleischmann, MD
	Richard Hallett, MD
Abstract:	The general goal of intravenous contrast medium (CM) delivery in computed tomography (CT) is to achieve adequate enhancement of the organ or vessels within the anatomic territory of interest, synchronized with the CT acquisition. This apparently simple goal is increasingly difficult to achieve with rapidly and continuously evolving multiple detector-row CT (MDCT) technology. Given that acquisition times have substantially decreased with each new generation of MDCT scanners, correct scan timing and tailoring clinical injection protocols is ever more challenging and less forgiving. Thus, a working understanding of early contrast medium dynamics has become a prerequisite for the rational design of current and future injection strategies. The selection of CM type, CM iodine concentration, considerations regarding the interrelated effects of injection flow rates, CM injection duration and injection volume, new injection devices, and individual patient factors all have to be integrated to optimize acquisition of a diagnostically meaningful MDCT examination. The purpose of this chapter is to provide the reader with the basic tools for designing rational contrast medium injection protocols for various applications of thoracic MDCT. This will encompass a review of physiologic and pharmacokinetic principles, as well as a discussion of contrast media properties, injection devices and tools for accurate scan timing. Topics of current interest, including CM strategies for patients with chronic kidney disease (CKD) and low kVp image acquisition, will be discussed. In addition, practical examples of injection protocols will be provided. Keywords: Contrast media, Iodinated contrast, CT technique, CT angiography, catheters, safety, CT, chest imaging

4 Contrast Medium Injection Technique

D. FLEISCHMANN AND R. HALLETT*

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INTRODUCTION

The general goal of intravenous contrast medium (CM) delivery in computed tomography (CT) is to achieve adequate enhancement of the organ or vessels within the anatomic territory of interest, synchronized with the CT acquisition. This apparently simple goal is increasingly difficult to achieve with rapidly and

- DOMINIK FLEISCHMANN, MD. Professor of Radiology, Chief of Cardiovascular Imaging, Director – Computed Tomography, Department of Radiology, Stanford University School of Medicine, Stanford CA, USA

- RICHARD L. HALLETT, MD. Chief, Cardiovascular Imaging, Northwest Radiology Network, Indianapolis IN. Clinical Assistant Professor of Radiology, Division of Cardiovascular Imaging, Department of Radiology, Stanford University School of Medicine, Stanford CA, USA.

continuously evolving multiple detector-row CT (MDCT) technology. Given that acquisition times have substantially decreased with each new generation of MDCT scanners, correct scan timing and tailoring clinical injection protocols is ever more challenging and less forgiving. Thus, a working understanding of early contrast medium dynamics has become a prerequisite for the rational design of current and future injection strategies. The selection of CM type, CM iodine concentration, considerations regarding the interrelated effects of injection flow rates, CM injection duration and injection volume, new injection devices, and individual patient factors all have to be integrated to optimize acquisition of a diagnostically meaningful MDCT examination.

The purpose of this chapter is to provide the reader with the basic tools for designing rational contrast medium injection protocols for various applications of thoracic MDCT. This will encompass a review of physiologic and pharmacokinetic principles, as well as a discussion of contrast media properties, injection devices and tools for accurate scan timing. Topics of current interest, including CM strategies for patients with chronic kidney disease (CKD) and low kVp data acquisition, will be discussed. In addition, practical examples of injection protocols will be provided.

4.1 Contrast Media for Multiple Detector-Row CT

All currently used angiographic x-ray CM are water-soluble derivates of symmetrically iodinated benzene. They are either negatively charged ionic molecules (ionic CM) or nonionic molecules (non-ionic CM). The diagnostic use of x-ray contrast media is based on the physical ability of iodine to absorb x-rays, not on pharmacological effects, and is similar for all angiographic CM. Although small differences have been demonstrated in the rate of diffusion of different contrast media into organ parenchyma, the magnitude of these differences is not such as to affect the choice of CM in practice.

The selection of intravenous contrast medium for MDCT is not so much governed by physicochemical properties such as osmotic pressure, viscosity and electrical charge, but primarily by safety considerations and rate of expected adverse reactions. Non-ionic CM are generally safer than ionic contrast media, with fewer adverse reactions (KATAYAMA et al. 1990). In addition, CM delivery for MDCT requires the use of a power injector and comparably high injection rates – notably for CT angiography. Injection rates greater than 2.0-2.5ml/s have a greater potential to cause acute nausea and vomiting, and – as a result – motion, if ionic CM are used. Furthermore, extravasation of ionic CM is less well tolerated than non-ionic CM. Therefore, non-ionic CM are probably the best choice for contrast enhanced MDCT in general (HOPPER 1996).

Because of the unique anatomy of large vessels in the chest and the complexity of early contrast medium dynamics, an increased awareness towards the iodine concentration of the contrast agent is critical in thoracic MDCT applications.

4.2 Pharmacokinetic and Physiologic Principles

From a pharmacokinetic point of view, all angiographic x-ray contrast media represent extracellular fluid markers. After intravenous administration these agents are rapidly distributed between the vascular and interstitial spaces (DAWSON and BLOMLEY 1996a). The volume of distribution is about 0.25 l/kg bodyweight, which typically represents the extracellular fluid space. The main process of elimination is renal glomerular filtration. In general, kinetics were found to be linear or proportional to the dose. Because relative CT attenuation values (ΔHU – Δ Hounsfield Units),

derived by subtracting background attenuation before administration of contrast medium, are linearly related to the concentration of contrast medium (iodine), contrast medium dynamics may be expressed in these units (DAWSON and BLOMLEY 1996b, 1996a).

Pharmacokinetic studies on CM have typically concentrated on the phase of elimination (following CM injection) rather than on the very early phase of CM distribution (during CM administration). For thoracic CTA, however, it is the particularly complex phase of early contrast medium dynamics, which determines vascular enhancement, perivenous artifacts, and, to a lesser degree, parenchymal enhancement.

It is important to recognize that early vascular enhancement and subsquent tissue enhancement phases utilized in MDCT are affected by different pharmaco-kinetics, which will be reflected in the timing and composition of injection techniques. Early vascular enhancement is essentially determined by the relationship between iodine administration per unit of time (mg I/s) versus blood flow per unit of time (i.e. cardiac output [l/min]). Parenchymal enhancement is governed by the relationship of total iodine dose (mg I) versus total volume of distribution (i.e. body weight [kg]).

4.2.1 Early Contrast Medium Dynamics in the Chest

The sequence of early vascular enhancement effects in the thorax following intravenous administration of CM is particularly complex, because it differs between the great veins, the heart, the pulmonary and systemic arteries. This is illustrated in Figure 4.1. Figure 4.1a shows a series of non-incremental dynamic images obtained every two seconds at the level of the pulmonary artery during the injection of a small test-bolus. CM appears 4 seconds after the begin of the injection, relatively undiluted and incompletely mixed, in the superior vena cava (which collects approximately one third [~25ml/s] of the cardiac output [~80 ml/s]). This causes both bright enhancement but also perivenous streak artifacts. The subsequent enhancement of the pulmonary arteries and of the thoracic aorta is less strong, because it has mixed in the right atrium and ventricle with blood from the inferior vena cava and coronary sinus. The magnitude (in HU) and the time course (in seconds) of opacification for each vascular territory is plotted in Figure 4.1c. Note, that pulmonary arterial enhancement begins immediately (2s) after enhancement of the superior vena cava. The bolus, which is subsequently delayed and broadened in the pulmonary circulation and left heart chambers, appears in the thoracic aorta after another ten seconds (14 s after initiation of the injection). Figure 4.1d integrates the relative enhancement effects (in ΔHU, above baseline) for a prolonged injection of 20 seconds for each vessel, respectively. Note, that the enhancement events overlap in time. During a prolonged MDCT acquisition of e.g. 20 seconds, the enhancement is expected to be substantially greater in the superior vena cava than in the pulmonary vasculature and in the aorta (Figure 4.1b). With respect to perivenous artifacts, it is pertinent that the time window, which shows maximum pulmonary arterial and aortic enhancement without dense opacification of the superior vena cava is particularly narrow.

4.2.2 Early Arterial Contrast Medium Dynamics

Early contrast medium dynamics for a given vascular territory such as the pulmonary or systemic arteries have gained substantial interest because of their implications for CT angiography. Whereas time attenuation responses to intravenously injected CM vary widely between vascular territories and across

individuals (as discussed below), some basic principles apply to all arterial (pulmonary and systemic) vessels.

Figure 4.2 schematically illustrates the early arterial contrast medium dynamics as observed in the supra-celiac abdominal aorta: When a 16 ml testbolus of contrast medium is injected intravenously, it causes an arterial enhancement response in the aorta. The time interval needed for the contrast medium to arrive in the arterial territory of interest is referred to as the contrast medium transit time (t_{CMT}). The first peak in the enhancement response is also referred to as the "*first pass*" effect. For a given individual and vascular territory, the enhancement response is proportional to the iodine injection rate.

After the CM is distributed throughout the intravascular and interstitial fluid compartments of the body, a certain proportion of CM reenters the right heart ("*recirculation*"). It is important to realize that within the time-frame relevant to MDCT acquisiton one will not only observe the *first pass* of contrast material but also its *recirculation*. As shown in Figure 4.2, a larger (128 mL), prolonged (32 s) bolus of CM can be viewed as the sum of eight subsequent injections of small "testbolusses" of 16 mL each. Each of these eight "testbolusses" has its own effect on arterial enhancement, respectively. Under the assumption of a time-invariant linear system, the cumulative enhancement response to the entire 128 mL injection equals the sum (time integral) of each enhancement response to their respective eight testbolusses (FLEISCHMANN 2002). Note, that the recirculation effects of the earlier testbolusses overlap (and thus sum up) with the first pass effects of later testbolusses.

In other words, when contrast medium is injected intravenously over a prolonged period of time (e.g. over 15 to 40s), the arterial enhancement will continuously increase over time, before it decreases rapidly after the end of the injection. This well documented effect is particularly important for CTA injection protocols, because it refutes the widely held misconception, that continuous-rate prolonged injections lead to an arterial enhancement plateau. Biphasic (or multiphasic) injections with high initial and lower continuing flow rates lead to a more favorable plateau-like arterial enhancement (FLEISCHMANN et al. 2000).

From the erroneous assumption that constant-rate injections cause a constant plateau enhancement comes another widely held misconception. One might intuitively assume, that the average arterial enhancement from a 30 s CTA acquisition achieved with a 30 s contrast medium injection is identical to the average enhancement from a 15 s CTA acquisition achieved with a 15 s injection duration. Again, it is apparent from Figure 4.2, that if only 50% of contrast medium was injected (corresponding to the first four of eight "test bolusses"), the cumulative enhancement (the sum of the first four test-enhancement curves) is substantially less compared to the cumulative enhancement from the total dose (eight "test bolusses"). It follows, that if one wants to achieve the same level of enhancement with shorter injection times the injection flow rate and/or the iodine concentration of the agent has to be increased. Alternatively, the injection delay may be increased relative to the t_{CMT}. This relative increase of the delay plus the scan time should equal the injection duration (see section 4.5).

4.2.3 Physiologic Parameters Affecting Vascular Enhancement

The vascular enhancement response to intravenously injected CM is characteristic for a given vascular territory and for a given patient. It is determined by individual physiologic parameters, and beyond the control of the observer. The contrast material transit time (t_{CMT}) from the injection site to the vascular territory of interest depends on the anatomic distance between them, and also on the encountered

physiologic flow rates between these landmarks. Except for the veins used for intravenous access, injection flow rates hardly affect the t_{CMT}. For systemic arteries, the t_{CMT} is primarily controlled by cardiac output. Cardiac output also accounts for most of the wide interindividual variability of the t_{CMT}. Low cardiac output prolongs, and high cardiac output decreases the t_{CMT}. Obviously, the t_{CMT} can be substantially delayed in patients with venous obstructions downstream from the injection site.

The degree of arterial enhancement following the same intravenous contrast medium injection is also highly variable between individuals ("patient effect"). Even in patients considerd to have normal cardiac output, mid aortic enhancement may range from 140 HU to 440 HU (a factor of three) between patients (SHEIMAN et al. 1996). Even if body weight is taken into account, the average aortic enhancement ranges from 92 to 196 HU/ml/kg (a factor of two) (HITTMAIR and FLEISCHMANN 2001). Adjusting the contrast medium volume (and injection rates) to body weight will therefore reduce interindividual differences of arterial enhancement, but will not completely eliminate them. The key physiologic parameters affecting individual arterial enhancement are cardiac output and the central blood volume.

Cardiac output is inversely related to the degree of arterial enhancement, particularly in first pass dynamics (BAE et al. 1998b): If more blood is ejected per unit of time, the contrast medium injected per unit of time will be more diluted. Hence, arterial enhancement is lower in patients with high cardiac output, but it is stronger in patients with low cardiac output (despite the increased t_{CMT} in the latter). This effect is illustrated in two patients with chronic thromboembolic pulmonary hypertension, in whom cardiac output was known from invasive measurements (Figure 4.3).

Central blood volume is also inversely related to arterial enhancement – but presumably affects recirculation and tissue enhancement rather than the first pass effect. (DAWSON and BLOMLEY 1996a) Central blood volume correlates with body weight. If total contrast medium volumes are chosen relative to body weight, then 1.5 to 2.0 mL/kg bodyweight (450-600 mg I / kg) are a reasonable quantity for arterial CTA.

Other physiologic factors which affect the t_{CMT} but also pulmonary as well as arterial enhancement is a temporarily diminished venous return caused by a forced Valsalva maneuver of the patient in an attempt to hold his or her breath. In patients with known but also in previously undiagnosed asymptomatic individuals with a patent foramen ovale, such a maneuver may also cause a temporary right-to-left shunt with early arterial enhancement.

4.2.4 Physiologic Parameters Affecting Tissue Enhancement

Parenchymal and soft tissue enhancement also diverges between different organs and tissues (LEGGETT and WILLIAMS 1995). Arterial blood flow, the relative proportions of intravascular to interstitial fluid compartments and diffusion coefficients between compartments all play a role. Highly perfused tissue such as the renal cortex and the spleen, as well as hypervascular neoplasms, exhibit a similar but somewhat delayed enhancement course (e.g. 10 to 15 s delay relative to arterial enhancement for hypervascular liver lesions. Maximum lesion-to-background contrast between many other moderately enhancing pathological lesions (inflammatory or neoplastic) occurs 60s or longer following CM administration (FOLEY 2002). It is again noted that such attenuation differences are generally dose dependent, and less affected by the injection flow rate.

4.2.5 Perivenous 'Streak' Artifacts

Streak artifacts arising from densely opacified brachiocephalic veins or the superior vena cava during CM administration are a well-known problem in thoracic CT. Streak artifacts may obscure neighboring structures and pathology, or lead to spurious abnormalities, such as a pseudo-intimal flap suggestive of aortic dissection. Similarly, artifacts arising from the right atrium and ventricle of the heart may obscure the right coronary artery in coronary CT angiography.

In technical terms, these artifacts are caused by beam hardening (e.g. in the vicinity of subclavian and brachiocephalic veins) or by the acquisition of inconsistent projection data (views) collected during the time window needed for the reconstruction of a given CT cross sectional image. The latter situation occurs when densely opacified blood is incompletely mixed with unopacified blood and swirls within the superior vena cava during data acquisition.

Streak artifacts can therefore be reduced or completely avoided, if the CT acquisition is performed after contrast material is already removed from the large veins. This can be accomplished by flushing the venous system with saline immediately after the CM injection (HOPPER et al. 1997; HAAGE et al. 2000). Hand exercising during CM administration has also been reported to exhibit this effect (NAKAYAMA et al. 2000). It is important to keep in mind, though, that the time window exhibiting strong pulmonary and systemic arterial but minimal venous enhancement is remarkably short. Artifacts can also be reduced, if the attenuation difference between newly injected swirling contrast medium and blood is minimized (FLEISCHMANN et al. 1997). This can be accomplished by using lower injection flow rates and less concentrated contrast medium (RUBIN et al. 1996), and / or by scanning during a recirculation phase. Diminished arterial opacification is a potential trade-off when such a strategy is used.

Double-piston (“dual head”) power injectors, which allow automated saline flushing and online variation of CM concentration may be the most versatile tools for CM administration, while also minimizing streak artifacts at the same time during fast MDCT acquisitions.

4.2.6 Mathematical Modeling

Accurate prediction and controlling of time dependent arterial enhancement is highly desirable for MDCT, particularly with faster scanners and for CTA. Ideally, one wants to predict and control the time course and the degree of vascular enhancement in each individual – independent of an individual’s underlying physiology. Two mathematical techniques addressing this issue have been developed.

The first is a sophisticated *compartmental model*, which predicts vascular and parenchymal enhancement using a system of more than 100 differential equations to describe the transport of contrast medium between intravascular and interstitial fluid compartments of the body (BAE et al. 1998a). For CT angiography, this model suggests multiphasic injections to achieve uniform vascular enhancement. The injection flow rate is maximum at the beginning of the injection followed by a continuous, exponential decrease of the injection rate (BAE et al. 1998b).

The second *black-box model* approach is based on the mathematical analysis of a patient's characteristic time-attenuation response to a small test-bolus injection (FLEISCHMANN and HITTMAIR 1999). Assuming a time-invariant linear system, one can mathematically extract and describe each individual's response to intravenously injected contrast medium ("patient factor") and use this information to individually tailor biphasic injection protocols to achieve uniform, prolonged arterial enhancement

at a predefined level. The principle of this technique is outlined in Figure 4. The method is robust and has been successfully used in clinical practice.

Mathematical models utilizing both the “compartmental” and “black-box” models have recenty been incorporated into commercial CM power injector systems. The greatest value of these systems, however, may come from the gained insights into early contrast medium dynamics for the time frame relevant for current and future CT technology, which allows rational design and implementation of empiric and routinely applicable injection techniques.

4.3 Instrumentation and Technique

4.3.1 Intravenous Access

Adequate intravenous CM administration for MDCT requires the use of a mechanical, programmable power injector. A large cubital or antebrachial vein is the most favorable injection site. For a given vein the largest diameter peripheral catheter, which accommodates the desired injection rate is selected. Whereas cannula lumen diameters as small as 22g (0.71 mm) may suffice for routine thoracic MDCT, diameters up to 17g (1.47 mm) have been used for dedicated CTA of the thoracic aorta. If high injection flow rates are desired, a fast manual saline injection with the patient's arms in scanning position (usually above the head) before mechanical CM delivery is recommended to assure correct peripheral catheter position. Injections through a central venous catheter reduce the contrast medium transit time (t_{CMT}), injections in a peripheral vein at the dorsum of the hand slightly prolong the t_{CMT}. In both instances, the flow rates may need to be adapted in order to prevent CM extravasation or catheter rupture.

Advances in IV cannula design, including the addition of sideholes/ fenestrations, have resulted in lower shear force on the cannula, reduced venous wall stress, and less pressure drop across the cannulas. Radial velocities are more uniform and exiting velocity of CM from the cannula is reduced. These devices allow delivery of CM at higher flow rates at each guage size than previously available (WEBER, et al. 2009). This allows use of smaller gauage cannulas with preservation of high flow rates and decreased incidence of extravasation (JOHNSON, et al. 2014).

4.3.2 Power Injectors and Safety Issues

The use of CM in MDCT carries the same risk of idiosyncratic (non dose-dependent) adverse reactions as in other CM applications. These allergy-like effects are well described (KATAYAMA et al. 1990) and their discussion is beyond the scope of this chapter. Because MDCT requires faster injections and the use of a power injector, dose-dependent (non-idiosyncratic) adverse effects, and the risk of CM extravasation have recently regained interest.

Dose dependent adverse reactions include nausea, vomiting, arrhythmia, pulmonary edema, and cardiovascular collapse. Based on clinical and experimental evidence for ionic CM, one might naturally assume that rapid injections would be less well tolerated than slower injections (DAWSON 1998). However, at least for injection flow rates up to 4 ml/s, there seems to be no correlation between injection rate and the overall rate of adverse reactions (JACOBS et al. 1998).

The rate of CM extravasation during the intravenous administration of CM with power injectors is low, ranging from 0.2 to 0.6% (BELLIN et al. 2002). Whereas this is presumably higher when compared to hand-injection and drip infusion technique, no correlation was found between extravasation frequency and injection rates up to 4 ml/s (JACOBS et al. 1998). Most extravasations involve only small volumes and result in minimal to mild symptoms if non-ionic CM is used.

Large volumes of CM may be involved, however, in non-communicative patients such as infants and children, elderly, or unconscious patients. Monitoring of the injection site during CM administration is recommended for these patients, because severe extravasation injuries could occur without the usual patient complaints. Such extravasations have occasionally been reported, and guidelines for managament of extravasation injuries should be at available (BELLIN et al. 2002). Recently an automated CM extravasation device has been developed, which interrupts the mechanical injection when a skin-impedance change due to fluid extravasation is detected (NELSON et al. 1998). Such a device might prove useful in high-flow-rate MDCT applications (BIRNBAUM et al. 1999). Newer IV cannula design may also decrease extravasation rate (JOHNSON, et al. 2014).

4.3.3 Saline Flushing of the Veins

Flushing the venous system with saline immediately after CM injection pushes the CM column from the veins into the circulation. This has two desirable effects in thoracic MDCT.

First, because the CM which would otherwise remain in the arm veins after the end of the injection contributes to vascular enhancement, opacification of intrathoracic vessels is improved. This effect can also be exploited to reduce the total CM volume in routine thoracic MDCT (HOPPER et al. 1997; HAAGE et al. 2000). Second, because saline flushing removes CM from the brachiocephalic veins and the superior vena cave, it reduces perivenous streak artifacts in thoracic and cardiac CT.

Saline flushing has been performed (a) manually - using a three-way valve – or (b) by layering saline above contrast in the syringe of a power injector, or (c) by using two interconnected power injectors. The former techniques, however, are impractical for routine CT, because the manual technique may expose the radiologist or technologist to radiation, and the layering technique is time consuming and poses a risk for contamination.

The most convenient technique for routine saline flushing after CM injection are new programmable double piston power injectors (one syringe for contrast material, one for saline) similar to those used in MR angiography. Furthermore, these devices may not only allow variation in CM injection rates, but also the ability to vary the contrast material concentration during a single injection (through saline admixture). Such a strategy might allow to achieve the desired enhancement profile by initially injecting non-diluted contrast medium, followed by a phase of diluted contrast medium injection, with subsequent saline flushing to avoid artifacts.

4.3.4 Scanning Delay & Automated Bolus Triggering

A fixed, empiric injection-to-scan delay may be adequate for many routine thoracic and abdominal CT acquisitions, particularly if maximum vessel opacification is not of critical importance. The greatest advantage of fixed-delay protocols is

obviously ease of use. As early contrast medium dynamics in patients without cardiocirculatory disease are within a comparable range, and as it is easier to achieve good opacification in the pulmonary arteries compared to more distant systemic arteries, fixed scanning delays have also been employed successfully for pulmonary CTA acquisitions.

For dedicated arterial or organ (liver) MDCT imaging studies a fixed scanning delay cannot be recommended, because the arterial CM transit time (t_{CMT}) is prohibitively variable between individual patients – ranging from 8 to as long as 40 seconds in patients with cardiovascular diseases. One might completely miss the bolus with a fast MDCT acquisition if the delay is not properly chosen.

In vascular MDCT, therefore the delay needs to be timed relative to the contrast transit time (t_{CMT}). It is important to realize that with the possibility of very fast MDCT acquisitions the t_{CMT} itself does not necessarily serve as the scanning delay, but rather as a means of individualizing the delay relative to it. Depending on the vessels or organ of interest an additional delay relative to the t_{CMT} needs to be selected. In CTA, this additional delay may be as short as 0 to 2 seconds added to the t_{CMT} ("t_{CMT} + 2s"). For visualizing hypervascular liver lesions this additional delay may be 10 to 15 seconds ("t_{CMT} + 15s"). Transit times can be easily determined using either a test-bolus injection or an automatic bolus triggering technique.

Test Bolus: The injection of a small test-bolus (15 – 20 mL) while acquiring a low-dose dynamic (non-incremental) CT acquisition is a reliable means to determine the t_{CMT} from the intravenous injection site to the arterial territory of interest (VAN HOE et al. 1995). The t_{CMT} equals the time-to-peak enhancement interval measured in a region-of-interest (ROI) placed within a reference vessel. Furthermore, time attenuation curves obtained from one or more regions of interest can be used for individual bolus shaping techniques using one of the previously described mathematical models. A test-bolus is particularly useful to determine the t_{CMT} if unusual CM injection sites need to be used (e.g., lower extremity veins).

Bolus Triggering: Many CT scanners have this feature built into their system. A circular region-of-interest (ROI) is placed into the target vessel on a non-enhanced image. While contrast medium is injected, a series of low-dose non-incremental scans are obtained, while the attenuation within a ROI is monitored or inspected visually. The t_{CMT} equals the time when a predefined enhancement threshold ("trigger level") is reached (e.g. 100 ΔHU) or observed by the person performing the scan. The minimal trigger delay to initiate the MDCT acquisition after the threshold has been reached ("trigger delay") depends on the scanner model and on the longitudinal distance between the monitoring-series and the starting position of the actual MDCT series. The minimal "trigger delay" before a scan can be initiated after the trigger threshold is reached is currently between 2 and 8 seconds. Bolus triggering is a very robust and practical technique for routine use and has the added advantage that it does not require an additional test-bolus injection.

4.3.5 Contrast Medium Concentration

Vascular enhancement (over time) is proportional to the number of iodine molecules administered (over time). This *iodine administration rate* can therefore be increased either by increasing the injection flow rate, by increasing the iodine concentration of the contrast medium used (Figure 4.4), or both. Thus, to achieve a certain iodine administration rate (e.g. 1.2 g/s), a faster (e.g. 4 mL/s) injection flow

rate will be needed with standard (300 mg I/mL) CM, compared to a slower (e.g. 3 mL/s) flow rate with high-concentration (400 mg I/mL) CM. Very high iodine administration rates, up to 2.4 g/s or more can be safely injected with a 400 mg I /mL solution at 6 mL/s, whereas an injection flow rate of 8 mL/s would be required using standard (300mg I / mL) solution. High iodine administration rates are useful in CTA, notably in patients with low enhancement response due to underlying cardiocirculatory disease, and for avoiding high injection flow rates. Furthermore, high iodine administration rates are also desirable for specific non-vascular imaging purposes e.g. for detecting hypervascular liver lesions, or in organ perfusion studies.

Low concentration contrast media, on the other hand, have the advantage that they cause less perivenous artifacts at the level of the brachiocephalic veins and the superior vena cava in thoracic MDCT, particularly if no saline-flushing of the veins is employed (RUBIN et al. 1996).

4.4 Clinical Contrast Medium Injection Protocols

The following section provides an overview of clinically applicable CM injection protocols for various thoracic MDCT applications. The suggested protocols are based on pharmacokinetic considerations, published clinical and experimental data, mathematical approximations and practical experience. An attempt is made to provide both, a universal approach to injection strategies as well as specific examples of injection protocols.

Because of the wide variation among available MDCT scanner types (ranging from dual-channel to 320-slice MDCT systems, with subtantial variation in rotation times and selectable table increments) the protocols are tabulated according to the acquisition times. Abbreviations for temporal variables are indexed as follows: t_{SCAN} = acquisition time; t_{INJ} = injection duration.

The actual CM injection protocols should be adjusted to match the suggested iodine doses and administration rates. CM doses and injection rates should also be adjusted (±20%) in patients with a body weight smaller than 60kg and greater than 90kg bodyweight.

Given the availablility of wide area-detector CT and systems with very rapid gantry rotation times, scan acquisition times may be very short- for example, one gantry rotation for coronary imaging and < 2 s for the entire chest, abdomen, and pelvis. One may be tempted to use very short CM injection protocols as well, however, caution should be exercised. As discussed above, since observed enhancement continually increases during continued injection, a very short injection duration will lead to lower level vascular enhancement. A very short injection duration will essentially serve as a “test bolus” with a narrow enhancement peak and little benefit of recirculation effects. One can compensate, to some degree, by increasing the CM injection flow rate. However, at programmed flow rates above 8 mL/sec there is no observed benefit over slower injection rates, but the risk of CM extravasation can be higher. Further, since the bolus is very short and bolus triggering includes some 3-8 sec of added delays, the bolus could be easily missed, resulting in an inadequate exam. A very short injection duration also increases the likelihood of outrunning the CM bolus completely, especially if the scanner is operated at high pitch over long distances, such as peripheral runoff CTA. Finally, it is important to remember that in general at least 7 seconds of CM injection time is needed to assure complete filling of most vascular territories.

4.4.1 Routine Thoracic and Mediastinal MDCT

Indications: Evaluation of various systemic or thoracic diseases; staging/follow up malignancies (lymphoma, bronchogenic carcinoma).
Objectives: Opacification of thoracic vessels for better delineation of mediastinal and hilar structures.
Strategy: A small to moderate amount of iodine (20-35g I) CM (60-120ml of 300mgI/ml CM) delivered at a slow injection rate (1.5 to 3.0 ml/s) and comparably long injection duration (> 30s) results in sufficient opacification of thoracic vessels. Low concentration agents or saline flushing are favorable to reduce perivenous artifacts. A fixed delay is adequate and should be determined so that the injection ends 5 seconds earlier than the MDCT acquisition (Delay = t_{INJ} + 5s – t_{SCAN}). This minimizes perivenous artifacts, particularly when a saline flush and a caudocranial scanning direction is used. Examples are shown in Table 4.1a-c.

4.4.2 Pulmonary Arteries

Indications: Acute pulmonary embolism, chronic thrombo-embolic pulmonary hypertension (CTEPH), pulmonary arteriovenous malformations (AVM), pulmonary artery aneurysms and arteriovenous fistulas.
Objectives: High opacification of pulmonary arteries, in order to detect vascular abnormalities – notably filling defects or mural thrombus.
Strategy: Moderate to large amount of iodine is required to allow distinction between opacified blood and intraluminal abnormalities. A larger amount of iodine is necessary if an additional, delayed (approx. 2 min) acquisition of the lower extremity veins (CT venography) is desired. Moderate to high injection flow rates (3.0 to 4.0 ml/s) are required with a standard concentration agent, if a higher concentration agent is used, flow rates can be slower. Saline flushing is recommended. A fixed delay is adequate in the majority of patients, and should again be determined so that the injection ends 3 seconds earlier than the end of MDCT acquisition (Delay = t_{INJ} + 3s – t_{SCAN}). For patients with severely compromised cardiocirculatory distress (CTEPH), slower injection rates suffice (because diminished cardiac output leads to brighter enhancement). Image quality is more consistent if the delay is timed relative to the contrast medium transit time. (Table 4.2a,b)

4.4.3 Thoracic and Coronary CT-Angiography

Indications: Aneurysms and dissection of the thoracic aorta and its branches, atherosclerotic or inflammatory (arteritis) arterial stenosis or occlusion, thoracic outlet syndrome, chest trauma. Coronary CT angiography.
Objectives: High opacification of systemic and/or coronary arteries.
Strategy: For fast acquisitions ($\geq$ 64-channel MDCT), moderate amounts of iodine at high iodine administration rates are required (i.e. high injection flow rates and/or high iodine concentration agent). For slower acquisitions, larger total CM volumes (with longer injection durations and preferably biphasic injections) are optimal. Individual scan timing relative to the t_{CMT} is mandatory. Saline flushing is beneficial in thoracic outlet and coronary CTA in order to reduce artifacts in the vicinity of large veins, the right heart. (Table 4.3a,b)

4.4.4 Thoracic Veins

Indications: Assessment of venous thrombosis, obstruction or occlusion.

Objective: Delineation of venous anatomy and pathology for treatment planning
Strategy A: Intravenous CM injection into the contralateral (non-diseased) arm requires large iodine doses (e.g. 100-150 ml) at slow to moderate injection rates in order to visualize the diseased venous territory during a recirculation phase. A long delay (end of MDCT acquisition should be approx. 15s after the end of the injection) and saline flushing are recommended. This strategy also allows assessment of systemic arteries.
Strategy B: 200 ml of diluted CM (1:10 to 1:20 diluted with normal saline) injected into the diseased arm (or both arms using a Y-connector) at a slow injection rate (2 – 4 ml/s) are sufficient to directly opacify the thoracic veins.

4.4.5 Thoraco-Abdominal MDCT

Indications: Assessment of thoracoabdomial diseases, such as staging of lymphoma.
Objectives: Delineation of hilar and mediastinal structures, combined with adequate parenchymal enhancement of abdominal and pelvic organs.
Strategy: Since delineation of thoracic vessels is relatively easily achieved, CM delivery is weighted towards adequate parenchymal and soft-tissue enhancement. Large iodine doses (0.5 to 0.6g of iodine / kg BW) corresponding to approximately 100 to 150 ml (depending on the iodine concentration and on the patient's body weight) are required. Injection rates can be moderate to slow, the scan delay should be long enough to allow tissue enhancement (≥ 60 s).
Dedicated biphasic acquisitions (with high iodine administration rates) are also possible with MDCT, where the first acquisition includes the thorax and upper abdomen, the second acquisition includes the abdomen and pelvis (other sequences are also possible if the MDCT scanner technology permits). Timing is optimized for biphasic abdominal imaging, i.e. the first acquisition should include the liver in a late arterial phase (Delay =t_{CMT}+10s, or Delay ≅ 25 s), the second acquisition is obtained during a hepatic parenchymal phase (Delay =t_{CMT}+40s, or Delay ≅ 60 s).

4.5 Advanced Contrast Medium Considerations

4.5.1 Contrast Medium Considerations in Patients with Chronic Kidney Disease

Chronic kidney disease (CKD) is defined as either the presence of kidney damage, or glomerular filtration rate (GFR) measurement < 60 mL/min/1.73 m2 for more than 3 months. CKD can be divided into stages of renal dysfunction based on GFR:

STAGE	*DESCRIPTION*	*GFR (mL/min/1.73m2)*
I	Kidney damage with normal or increased eGFR	≥90
II	Mild CKD	60-89
III	Moderate CKD	30-59

IV	Severe CKD	15-29
V	Kidney Failure	<15 (or dialysis)

Direct measurement of GFR is time consuming and may be clinically impractical. As a result, renal function is typically estimated based on laboratory tests and other variables such as age. The result is an estimated GFR (eGFR). An easy online calculator that follows the National Kidney Foundation DKD-EPI guidelines (http://www.kidney.org/professionals/KDOQI/gfr_calculator) (LEVEY, 2009) is our standard method for eGFR determination. Of note, the calculator utilizes serum creatinine, age, sex, and race and calculates results in ml/min/1.73m^2 BSA. This result is useful to directly compare renal function between individuals. However, to directly calculate the most appropriate CM dose, the result will need to be corrected for body weight.

Larger numbers of cardiovascular CT procedures are being performed today, including greater utilization of CT in patients with underlying CKD. Pre-existing CKD has been recognized as a risk factor for contrast-induced nephropathy (CIN). The degree of potential deleterious impact from CM administration in patients with CKD remains controversial (MCDONALD, et al. 2014), but the need to protect renal parenchymal function is not. There is good pharmacokinetic and clinical evidence that the ratio of the volume of CM administered to the underlying degree of renal dysfunction can predict the subsequent risk of CIN (ALTMANN 1997, GURM 2011, LASKEY 2007, NYMAN 2008, SHERWIN 2005). Specifically, a CM-to-eGFR ratio of 3.7 has been found to offer optimum discrimination between patients who will develop CIN and those who will not (LASKEY 2007). On a practical clinical level, a ratio of <2.0 has shown no significant increased risk of CIN (GURM, 2011). As such, these findings can be used to design a rational strategy for CM injection tailored to the patient's renal function and the clinical scan parameters.

In patients with CKD, lower concentration CM (300 mgI-/mL) can be utilized. The total CM volume is calculated at two times the eGFR, corrected for body weight (e.g. CM vol = 2 x eGFR x (body wt kg/75). For example, for eGFR = 30, standard sized (75kg) patient would receive: 2 x 30 x 75/75 = 60 mL CM for injection.

Table 2 lists sample calculations for three different patient sizes, all with the same eGFR of 30 mL/min/1.73m^2:

Patient Body Weight (kg)	eGFR based CM volume (2x eGFR)	Adjustment for BW (BW/75)	Final CM volume available (mL)
50	2 x 30 = 60 mL	50/75 = 0.67	40
75	2 x 30 = 60 mL	75/75 = 1.00	60
100	2 x 30 = 60 mL	100/75 = 1.33	80
Generic	(2 x eGFR)	BW/75	= total volume

Clinical decision-making:

Once the maximal CM volume has been calculated, it is imperative to then decide whether the clinical question can be answered by utilizing only the available amount of CM. Chest CT imaging, where scan times for most applications are <10 sec, lends itself well to smaller CM volume administration protocols. Other vascular territories, such as lower extremity CTA, require longer injection profiles (FLEISCHMANN, et al. 2006) and may not be feasible to assess at very small CM volumes.

One instance deserves special mention: in the acute setting and when dealing with life-threatening emergent conditions, the risk of CIN can be outweighed by the urgent need to obtain relevant information to guide life-saving treatment decision-making. In these instances, standard doses and rates of CM should be utilized, irrespective of renal function status.

4.5.2 Low Energy / Low Contrast Imaging

Utilization of of lower peak tube voltage (kVp) can be employed in selected patients to help maximize signal from available CM, decrease patient radiation dose, and/or provide greater arterial enhancement (Figure 4.5) . Among others, these techniques are valuable for pediatric, smaller body-size adult patients, and patients with CKD. Current generation CT scanners allow scanning at tube potentials lower than the standard 120 kVp (e.g. 100 kVp, 80 kVp). At lower kVp, the proportional absorption of x-rays by iodine increases as the energy approaches iodine's k-edge of 33.2 keV. This phenomenon translates into higher observed attenuation values of CM-enhanced structures (NEWTON, 1981) However, a greater fraction of these (lower-energy) x-ray photons are also absorbed in tissue; therefore tube current (milli-Ampere, mA) must increase to offset the increase in image noise. It is possible, especially with older scanners, that tube current output may be insufficient alone to prevent high image noise acquisitions. Current generation scanners are best suited to acquire high mA exams. In older scanners, however, either slowing the pitch or gantry rotation time (e.g. to 0.5 sec) has the effect of increasing photon flux per tube rotation and limiting noise (at the expense of greater patient dose).

In general, attenuation of iodine increases by 25% from 120 kVp to 100 kVp, and another 25% from 100 kVp to 80 kVp (Table 1). Thus, by decreasing the tube voltage from 120 kVp to 80 kVp, one should observe approximately 50% increased iodine attenuation. Conversely, increasing the tube voltage from 120 kVp to 140 kVp will decrease iodine attenuation by approximately 25%. Although image noise also decreases at high kVP imaging, attenuation also decreases, with resultant limited benefit to signal-to-noise ratio (SNR) at the expense of higher patient dose.

	140 kVp	120 kVp	100 kVp	80 kVp	70 kVp

Iodine Attenuation Compared to 120 kVp:	- 25% attenuation	-	+ 25% attenuation	+ 50% attenuation	+ 70% attenuation

Table 1: Iodine attenuation at different kVp imaging.

The observed effects of lower kVp imaging can be leveraged to predict arterial enhancement at lower kVp and to subsequently modify CM injection protocols to obtain adequate diagnostic quality at lower CM injection rates. Using this strategy, the injection duration, scan-time, and any scan delays should be kept constant. The tube current (mAs) should be increased by 30-50% for each "step" down in kVp. Then, for each step down in kVp (e.g. 120 to 100 kVp, and 100 to 80 kVp), an increase in attenuation should allow a reduction in CM volume by 25%. To maintain similar noise levels when manually selecting mA, depending on vendor, one could either select the same noise level on the scanner (auto/smart mA), or try to match the CTDI of the new (low kVp) protocol to the original (120 kVp) protocol.

Disadvantages of low kVp imaging

The expected signal gain from CM administration may not be realized if small volumes (flow rates) of CM are administered, either by design (for low kVp imaging) or as a result of CM extravasation. Partial volume effects may also limit the iodine concentration in a given voxel. These phenomena, in addition to potentially higher image noise at lower tube voltages, can lead to significant SNR reduction if appropriate corrections are not applied.

The increased mA required for lower kVp imaging also requires a larger x-ray focal spot size, resulting in focal spot blooming beyond nominal size, which decreases spatial resolution (OH, et al. 2014). In some situations where accurate measurements are essential (e.g. TAVR planning), accuracy and inter-observer agreement could be adversely affected. Newest generation scanner technology advances may also help address this phenomenon (OH, et al 2014 and SOLOMON, et al 2015).

Other limitations are also observed. At lower kVp, the "signal" from calcium is also increased, the blooming effect of vascular calcifications and metal (valve prostheses, wires, etc.) is more pronounced, and beam-hardening artifacts may appear worse. The iodine concentration in small vessels and along the periphery of vessels is also less than in the center of large vessels. Further, cardiovascular CT is usually reviewed interactively at a 3D workstation. Many of the 3D/4D post-processing and visualization techniques utilized in clinical practice, such as maximum-intensity projection (MIP), inherently amplify (or sum) image noise across the slab thickness. In this scenario, small vessels can be completely obscured by surrounding image noise.

Iterative Reconstruction Techniques

Recent advances in computing processor speed and image reconstruction algorithms have allowed use of iterative reconstruction (IR) techniques to improve CT image quality. A full discussion of these techniques is beyond the scope of this chapter, however, brighter vessels and borders may be more sharply defined with IR techniques, which could be a benefit for smaller vessel assessement. Poorly opacified vessels, however, may be more difficult to define or distorted by artifacts. Use of IR techniques have yielded images with lower noise to be acquired at lower patient dose (LEIPSIC, 2010). Newer model-based IR (MBIR) techniques allow even more substantial patient dose and noise savings while maintaining diagnostic image quality (KATSURA, 2012).

4.6 Conclusion

A basic understanding of early contrast medium dynamics provides the foundation for the design of current and future CM injection protocols for various clinical applications of thoracic MDCT. Additionally, a thorough knowledge of the technical and safety aspects of the injection equipment and CM used is necessary. Special considerations in patients with chronic kidney disease can be employed to optimize image quality and promote patient safety. Recent advances in scanner technology and image reconstruction algorithms allow further refinement of image quality and patient radiation dose. With these tools at hand, CM utilization can be optimized towards the clinical necessities while exploiting the full capabilities of latest and continuously evolving MDCT technology.

4.7 References

Altmann DB, Zwas D, Spatz A, Bergman G, Spokojny A, Riva S, Sanborn TA. Use of the contrast volume to estimated creatinine clearance ratio to predict renal failure after angiography. *Journal of Interventional Cardiology*. 1997;10:113-119

Bae KT, Heiken JP, Brink JA (1998a). Aortic and hepatic contrast medium enhancement at CT. Part I. Prediction with a computer model. Radiology 207: 647-55.

Bae KT, Heiken JP, Brink JA (1998b). Aortic and hepatic contrast medium enhancement at CT. Part II. Effect of reduced cardiac output in a porcine model. Radiology 207: 657-62.

Bellin MF, Jakobsen JA, Tomassin I, et al. (2002). Contrast medium extravasation injury: guidelines for prevention and management. Eur Radiol 12: 2807-12.

Birnbaum BA, Nelson RC, Chezmar JL, et al. (1999). Extravasation detection accessory: clinical evaluation in 500 patients. Radiology 212: 431-8.

Dawson P (1998). Does Injection rate affect the tolerance? Contrast media in practice : questions and answers. Dawson PH and Clauss W. New York, Springer Verlag: 135-6.

Dawson P, Blomley MJ (1996a). Contrast agent pharmacokinetics revisited: I. Reformulation. Academic Radiology 3 Suppl 2: S261-3.

Dawson P, Blomley MJ (1996b). Contrast media as extracellular fluid space markers: adaptation of the central volume theorem. British Journal of Radiology 69: 717-22.

Fleischmann D (2002). Present and future trends in multiple detector-row CT applications: CT angiography. Europ Radiol 12: S11-S16.

Fleischmann D, Hittmair K (1999). Mathematical analysis of arterial enhancement and optimization of bolus geometry for CT angiography using the discrete fourier transform. J Comput Assist Tomogr 23: 474-84.

Fleischmann D, Ringl H, Nowotny R, et al. (1997). Streak artifacts arising from the superior vena cava in contrast enhanced CT: qualitative and quantitative assessment. European Radiology 7: 285.

Fleischmann D, Rubin GD, Bankier AA, et al. (2000). Improved uniformity of aortic enhancement with customized contrast medium injection protocols at CT angiography. Radiology 214: 363-71.

Fleischmann, D., Hallett, R. L., & Rubin, G. D. (2006). CT angiography of peripheral arterial disease. *Journal of Vascular and Interventional Radiology : JVIR*, *17*(1), 3–26.

Foley WD (2002). Special focus session: multidetector CT: abdominal visceral imaging. Radiographics 22: 701-19.

Gurm HS, Dixon SR, Smith DE, Share D, Lalonde T, Greenbaum A, Moscucci M. Renal function-based contrast dosing to define safe limits of radiographic contrast media in patients undergoing percutaneous coronary interventions. *J Am Coll Cardiol*. 2011;58:907-914

Haage P, Schmitz-Rode T, Hubner D, et al. (2000). Reduction of contrast material dose and artifacts by a saline flush using a double power injector in helical CT of the thorax. AJR Am J Roentgenol 174: 1049-53.

Hittmair K, Fleischmann D (2001). Accuracy of predicting and controlling time-dependent aortic enhancement from a test bolus injection. J Comput Assist Tomogr 25: 287-94.

Hopper KD (1996). With helical CT, is nonionic contrast a better choice than ionic contrast for rapid and large IV bolus injections? AJR Am J Roentgenol 166: 715.

Hopper KD, Mosher TJ, Kasales CJ, et al. (1997). Thoracic spiral CT: delivery of contrast material pushed with injectable saline solution in a power injector. Radiology 205: 269-71.

Jacobs JE, Birnbaum BA, Langlotz CP (1998). Contrast media reactions and extravasation: relationship to intravenous injection rates. Radiology 209: 411-6.

Johnson, PT, Johnson GM, and Fishman EK. IV Contrast Administration With Dual Source 128-MDCT: A Randomized Controlled Study Comparing 18-Gauge Nonfenestrated and 20-Gauge Fenestrated Catheters for Catheter Placement Success, Infusion Rate, Image Quality, and Complications AJR 2014; 202:1166-1170.

Katayama H, Yamaguchi K, Kozuka T, et al. (1990). Adverse reactions to ionic and nonionic contrast media. A report from the Japanese Committee on the Safety of Contrast Media. Radiology 175: 621-8.

Laskey WK, Jenkins C, Selzer F, Marroquin OC, Wilensky RL, Glaser R, Cohen HA, Holmes DR, Jr. Volume-to-creatinine clearance ratio: A pharmacokinetically based risk factor for prediction of early creatinine increase after percutaneous coronary intervention. *J Am Coll Cardiol*. 2007;50:584-590

Leggett RW, Williams LR (1995). A proposed blood circulation model for reference man. Health Physics 69: 187-201.

Leipsic J, Ngueyn G, Brown J, et al. (2010). A Prospective Evaluation of Dose Reduction and Image Quality in Chest CT Using Adaptive Statistical Iterative Reconstruction. AJR Am J Roentgenol 194(1), 191-9.

Katsura M, Matsuda I, Akahane M, et al. (2012). Model-based iterative reconstruction technique for radiation dose reduction in chest CT: comparison with the adaptive statistical iterative reconstruction technique. Eur Radiol 22(8)1613-23.

Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF, 3rd, Feldman HI, Kusek JW, Eggers P, Van Lente F, Greene T, Coresh J, Ckd EPI. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150:604-612

McDonald JS, McDonald RJ, Carter RE, Katzberg RW, Kallmes DF, Williamson EE. (2014). Risk of intravenous contrast material-mediated acute kidney injury: a propensity score-matched study stratified by baseline-estimated glomerular filtration rate. Radiology 271:65–73.

Nakayama M, Yamashita Y, Oyama Y, et al. (2000). Hand exercise during contrast medium delivery at thoracic helical CT: a simple method to minimize perivenous artifact. J Comput Assist Tomogr 24: 432-6.

Nelson RC, Anderson FA, Jr., Birnbaum BA, et al. (1998). Contrast media extravasation during dynamic CT: detection with an extravasation detection accessory. Radiology 209: 837-43.

Newton TH, authors rc. One of the titles. In: Newton TH, Potts DG, eds. *Radiology of the skull and brain: Technical aspects of computed tomography*. Saint Louis,: Mosby; 1981.

Nyman U, Bjork J, Aspelin P, Marenzi G. Contrast medium dose-to-gfr ratio: A measure of systemic exposure to predict contrast-induced nephropathy after percutaneous coronary intervention. *Acta radiologica*. 2008;49:658-667

Oh LC, Lau KK, Devapalasundaram A, Buchan K, Ardley N, Huynh M. Efficacy of 'fine' focal spot imaging in ct abdominal angiography. *Eur Radiol*. 2014;24:3010-3016

Rubin GD, Lane MJ, Bloch DA, et al. (1996). Optimization of thoracic spiral CT: effects of iodinated contrast medium concentration. Radiology 201: 785-91.

Sheiman RG, Raptopoulos V, Caruso P, et al. (1996). Comparison of tailored and empiric scan delays for CT angiography of the abdomen. Ajr. American Journal of Roentgenology 167: 725-9.

Sherwin PF, Cambron R, Johnson JA, Pierro JA. Contrast dose-to-creatinine clearance ratio as a potential indicator of risk for radiocontrast-induced nephropathy: Correlation of d/crcl with area under the contrast concentration-time curve using iodixanol. *Invest Radiol*. 2005;40:598-603

Van Hoe L, Marchal G, Baert AL, et al. (1995). Determination of scan delay-time in spiral CT-angiography : utility of a test bolus injection. J Comput Assist Tomogr 19: 216-220.

Weber PW, Coursey CA, Howle LE, Nelson RC, Nichols EB, Schindera ST. Modifying peripheral IV catheters with side holes and side slits results in favorable changes in fluid dynamic properties during the injection of iodinated contrast material. *AJR* 2009; 193:970–977

Table 4.1a: Routine Thoracic MDCT

Acquisition time (s)	Scanning delay (s)	Iodine dose (g)	Iodine administrtion rate (g/s)	CM Volume (ml) [a]	Injection rate (ml/s) [a]	Injection Duration (s)
20	25	30	.75	100	2.5	40
15	30	30	.75	100	2.5	40
10	28	30	.90	100	3	33
5	33	30	.90	100	3	33

[a] Volume and flow rate calculated for 300 mg I / ml concentration CM.

Table 4.1b: Routine Thoracic MDCT, High CM Dose Protocol [a]

Acquisition time (s)	Scanning delay (s)	Iodine dose (g)	Iodine administrtion rate (g/s)	CM Volume (ml) [b]	Injection rate (ml/s) [b]	Injection Duration (s)
20	25	36	.90	120	3	40
15	30	36	.90	120	3	40
10	25	36	1.20	120	4	30
5	30	36	1.20	120	4	30

[a] applicable if soft tissue enhancement (e.g., chest wall) is also desired; provides good pulmonary and systemic arterial enhancement as well. Patients with >90kg BW.
[b] Volume and flow rate calculated for 300 mg I / ml concentration CM.

Table 4.1c: Thoracic MDCT, Minimum Dose Protocol [a]

Acquisition time (s)	Scanning delay (s)	Iodine dose (g)	Iodine administrtion rate (g/s)	CM Volume (ml) [b]	Injection rate (ml/s) [b]	Injection Duration (s)
20	25	18	.90	60	1.5	40
15	30	18	.90	60	1.5	40
10	25	18	1.20	60	2	30
5	20	18	1.20	60	2	30

[a] suffices for vessel delineation, if saline flush is used. Saline flushing is strongly recommended.
[b] Volume and flow rate calculated for 300 mg I / ml concentration CM.

Commented [D1]: I think the tables are a bit outdated;

Nobody scans a chest in 30s;
Maybe just delete the 30 and 25 s rows (even maybe the 20s), ….

Table 4.2a: Pulmonary Artery CTA, fixed Delay

Acquisition time (s)	Scanning delay (s)	Iodine dose (g)	Iodine administrtion rate (g/s)	CM Volume (ml) [a]	Injection rate (ml/s) [a]	Injection Duration (s)
20	23	36	.90	120	3	40
15	18	36	1.20	120	4	30
10	23	36	1.20	120	4	30
5	28	36	1.20	120	4	30

[a] Volume and flow rate calculated for 300 mg I / ml concentration CM.

Table 4.2b: Pulmonary Artery CTA, with Individual Timing

Acquisition time (s)	Scanning delay (s)	Iodine dose (g)	Iodine administrtion rate (g/s)	CM Volume (ml) [a]	Injection rate (ml/s) [a]	Injection Duration (s)
20	t_{CMT}+8	30	.90	100	3	33
15	t_{CMT}+10	27	1.20	90	4	30
10	t_{CMT}+15	27	1.20	90	4	30
5	t_{CMT}+20	27	1.20	90	4	30

Note – t_{CMT} = contrast medium transit time, as established with a test-bolus or bolus triggering technique.

[a] Volume and flow rate calculated for 300 mg I / ml concentration CM.

Table 4.3a: Thoracic CTA, Uniphasic Injection

		Iodine		300mg I/ml CM	400mg I /ml CM
Acquisition time (s)	Scanning delay (s)	Dose (g)	Administration rate (g/s)	CM Volume @ Inj.Rate (ml@ml/s) [a]	CM Volume @ Inj.Rate (ml@ml/s) [b]
20	t_{CMT}+8	39	1.2	130 @ 3	100 @ 3
15	t_{CMT}+8	36	1.5	120 @ 5	90 @ 3.8
10	t_{CMT}+8	33	1.8	110 @ 6	85 @ 4.5
5	t_{CMT}+12	27	1.8	90 @ 6	70 @ 4.5

Note – t_{CMT} = contrast medium transit time, as established with a test-bolus or bolus triggering technique.

[a] Volume and flow rate calculated for 300 mg I / ml concentration CM.

[b] Volume and flow rate calculated for 400 mg I / ml concentration CM.

Table 4.3b: Thoracic CTA, Biphasic Injection

		Iodine		300mg I / ml CM		400mg I / ml CM	
Acquisition time (s)	Scanning delay (s)	Total dose (g)	Biphasic administration (g @ g/s)	Total volume (ml) [a]	Biphasic injections (ml@ml/s) [a]	Total volume (ml) [b]	Biphasic injections (ml@ml/s) [b]
20	t_{CMT}+8	34	9 @ 1.8 + 25 @ 1.4	115	30 @ 6 + 85 @ 4.5	90	23 @ 4.5 + 67 @ 3.4
15	t_{CMT}+8	32	9 @ 1.8 + 23 @ 1.4	105	30 @ 6 + 75 @ 4.5	80	23 @ 4.5 + 57 @ 3.4
10	t_{CMT}+8	29	9 @ 1.8 + 20 @ 1.5	95	30 @ 6 + 65 @ 5	75	23 @ 4.5 + 52 @ 3.8
5	t_{CMT}+12	24	9 @ 1.8 + 15 @ 1.5	80	30 @ 6 + 50 @ 5	65	23 @ 4.5 + 42 @ 3.8

Note – t_{CMT} = contrast medium transit time, as established with a test-bolus or bolus triggering technique.

[a] Volume and flow rate calculated for 300 mg I / ml concentration CM.

[b] Volume and flow rate calculated for 400 mg I / ml concentration CM.

Figure Legends:

Figure 4.1: Early Contrast Medium Dynamics in the Chest
(a) Sequence of vascular enhancement observed in a non-incremental dynamic CT acquisition following the intravenous injection of a small test-bolus are shown (see text for details). (b) Maximum intensity projection of a MDCT pulmonary angiogram shows extensive opacification of the left brachicephalic vein and SVC. As densely opacified blood is mixed with unenhanced blood from the inferior vena cava in the right atrium and ventricle, the pulmonary arterial enhancement is substantially smaller than the enhancement in the SVC. Aortic enhancement is again slightly less than PA enhancement.Analysis of the time attenuation curves from a 4s test-injection (c) allows to predict the time attenuation curves for a prolonged, 20s injection (d). Note, that the time window of maximum aortic enhancement without SVC enhancement is particularly narrow.
SVC = superior vena cava; PA = pulmonary artery; AO = thoracic aorta.

Figure 4.2: Simple "additive model" illustrates the relationship between contrast medium injection (a, c) and cumulative arterial enhancement (b, d).
Note that due to the asymmetric shape of the test-enhancement curve (b) and recirculation effects (the "tail" in the test-enhancement), arterial enhancement (the "time integral of 8 testbolusses") increases continuously over time (d). There is no enhancement plateau (adapted from FLEISCHMANN 2002).

Figure 4.3: Cardiac Output and Pulmonary Arterial Enhancement
(a) Two patients with chronic thrombo-embolic pulmonary hypertension (CTEPH) are compared. PAP = pulmonary arterial pressure [systolic/diastolic (mean)]; CO = cardiac output. (b) Following a small test-bolus injection (16 ml @ 4ml/s), the time-attenuation response measured in the pulmonary artery is smaller in the patient with greater cardiac output.
(c) Corresponding thin-slab volume rendered images of pulmonary vessels.

Figure 4.4: Iodine Administration Rates and CM Concentration
For a given CM concentration, the Iodine administration rate (g/s) can be varied by selection of the injection flow rate (in mL/s). High-concentration agents permit greater iodine administration rates at the same injection rates.

Figure 4.5. Use Of Low Kvp Scanning To Decrease Patient Dose With Preserved Image Quality
A 54 kg female patient with chest pain presented for CCTA. 80 kVp tube voltage was utilized, with prospective ECG synchronization and iterative reconstruction techniques. Patient dose was 0.4 mSv. High degree of vessel enhancement with relatively little background image noise is noted on both curved-planar reconstructions (upper row) and slice through images (lower row).

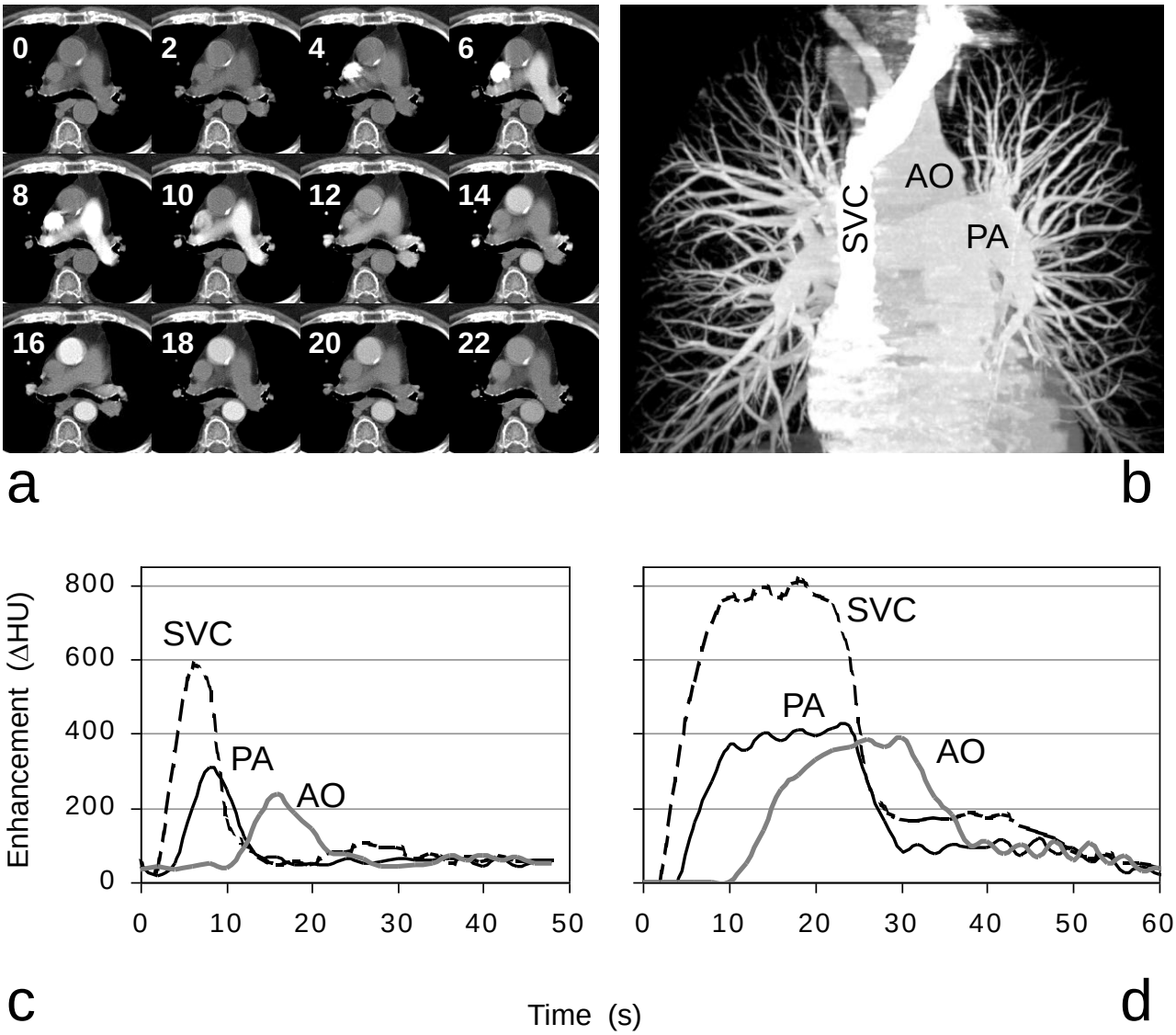


Figure 4.1: Early Contrast Medium Dynamics in the Chest

(a) Sequence of vascular enhancement observed in a non-incremental dynamic CT acquisition following the intravenous injection of a small test-bolus are shown (see text for details). (b) Maximum intensity projection of a MDCT pulmonary angiogram shows extensive opacification of the left brachicephalic vein and SVC. As densely opacified blood is mixed with unenhanced blood from the inferior vena cava in the right atrium and ventricle, the pulmonary arterial enhancement is substantially smaller than the enhancement in the SVC. Aortic enhancement is again slightly less than PA enhancement.
Analysis of the time attenuation curves from a 4s test-injection (c) allows to predict the time attenuation curves for a prolonged, 20s injection (d). Note, that the time window of maximum aortic enhancement without SVC enhancement is particularly narrow.
SVC = superior vena cava; PA = pulmonary artery; AO = thoracic aorta.

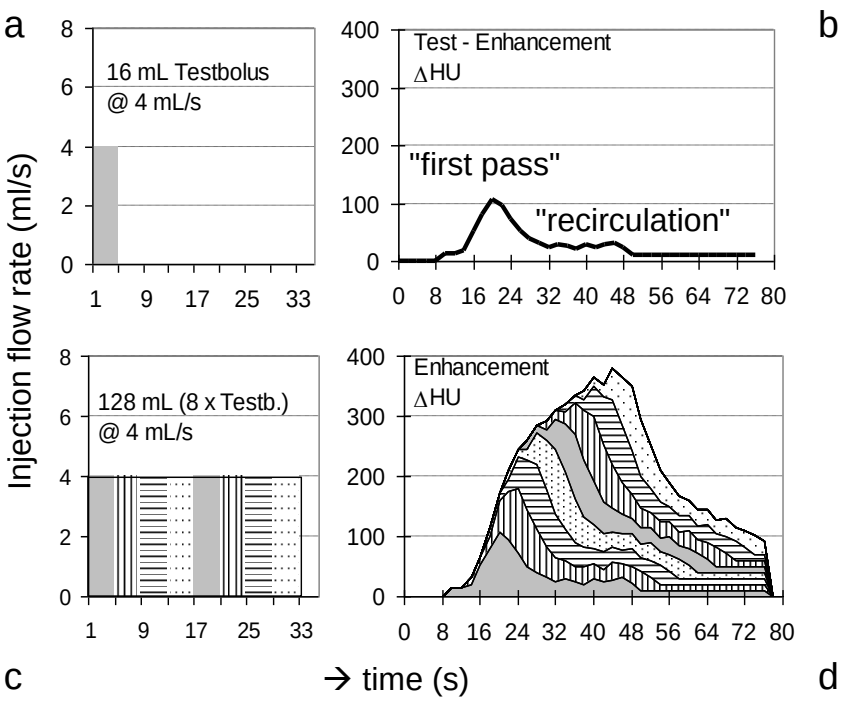
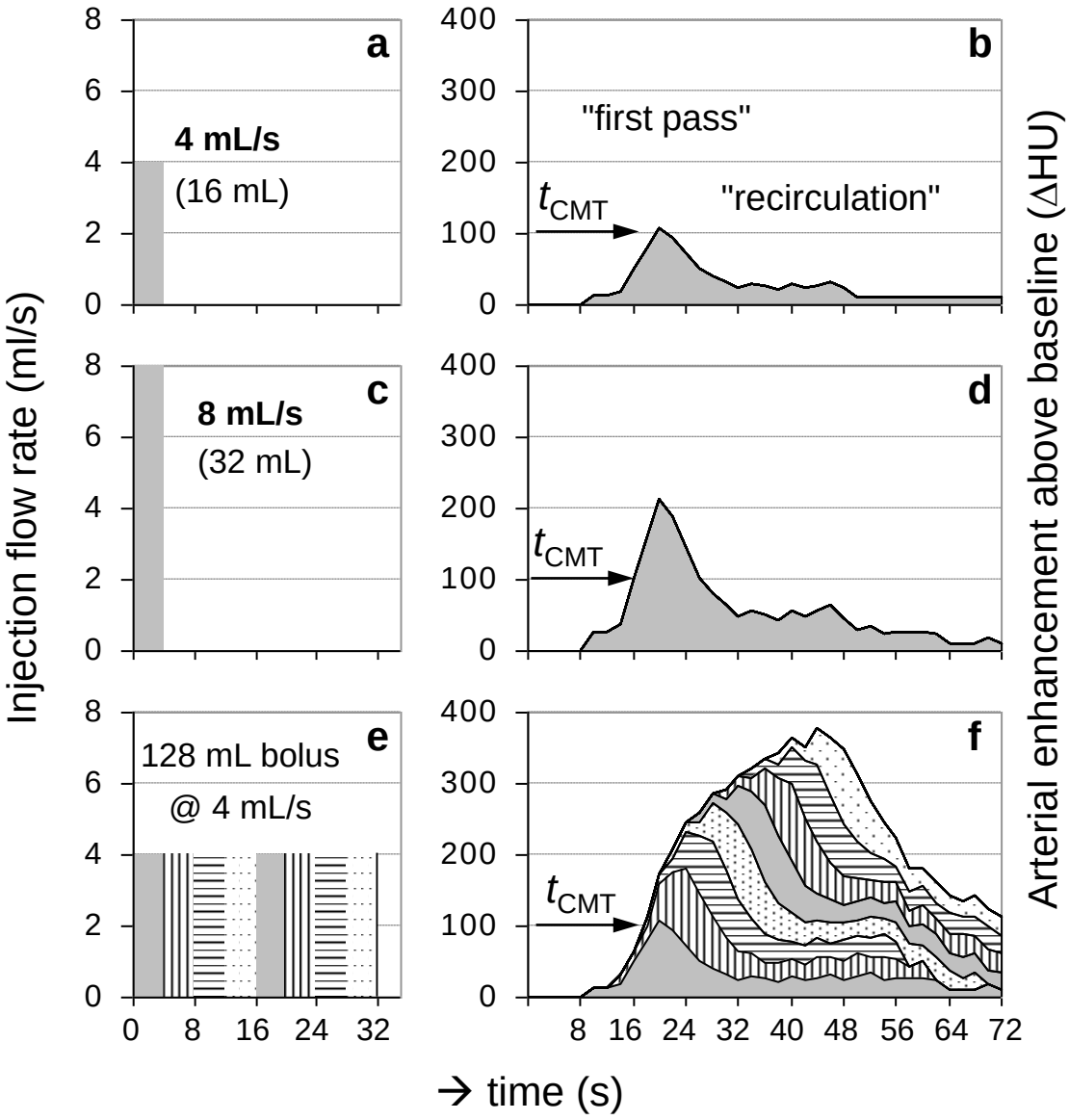


Figure 4.2: Simple "additive model" illustrates the relationship between contrast medium injection (a, c) and cumulative arterial enhancement (b, d).

Note that due to the asymmetric shape of the test-enhancement curve (b) and recirculation effects (the "tail" in the test-enhancement), arterial enhancement (the "time integral of 8 testbolusses") increases continuously over time (d). There is no enhancement plateau (adapted from FLEISCHMANN 2002).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b
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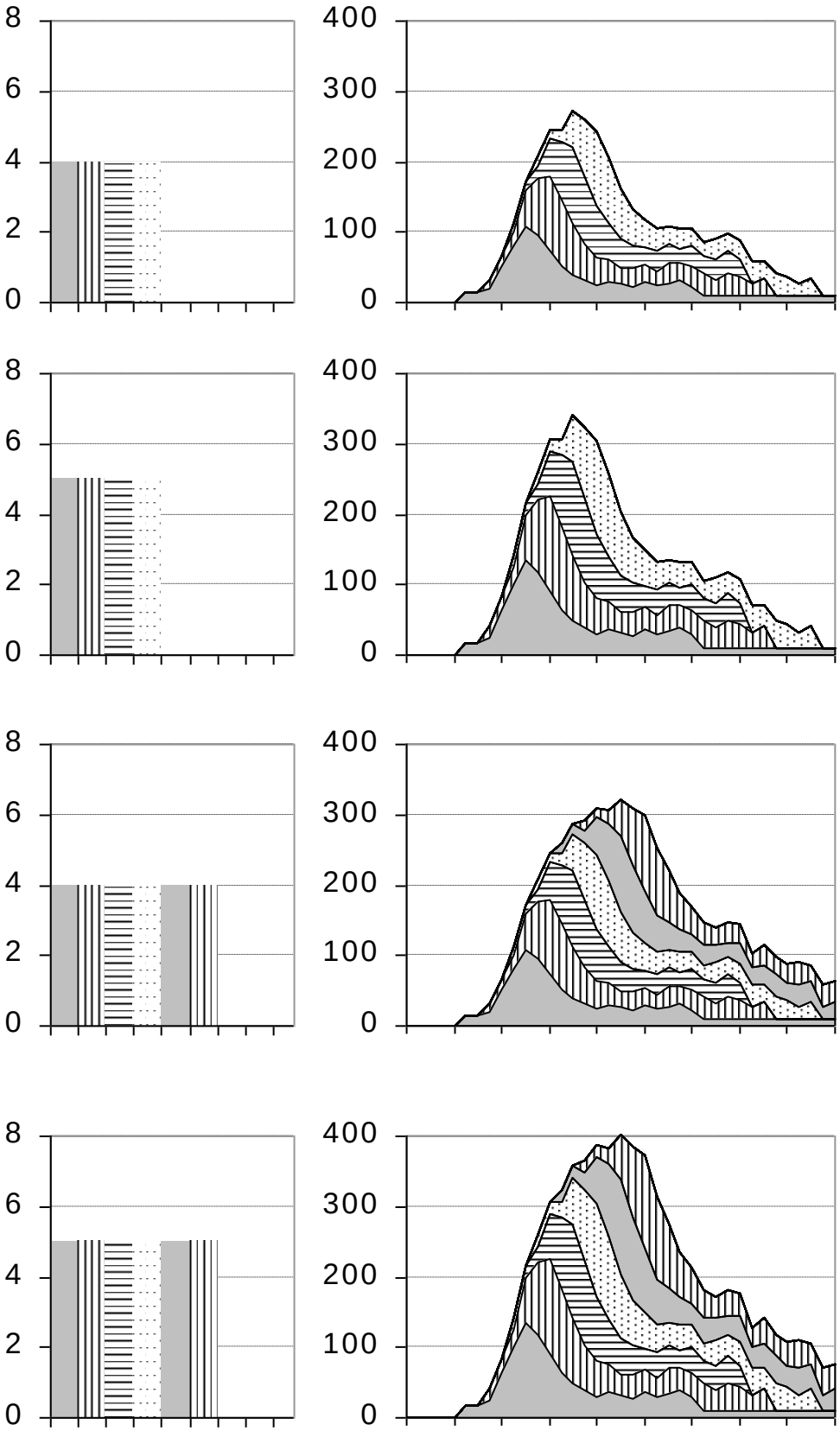
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2
0
400
300
200
100
0

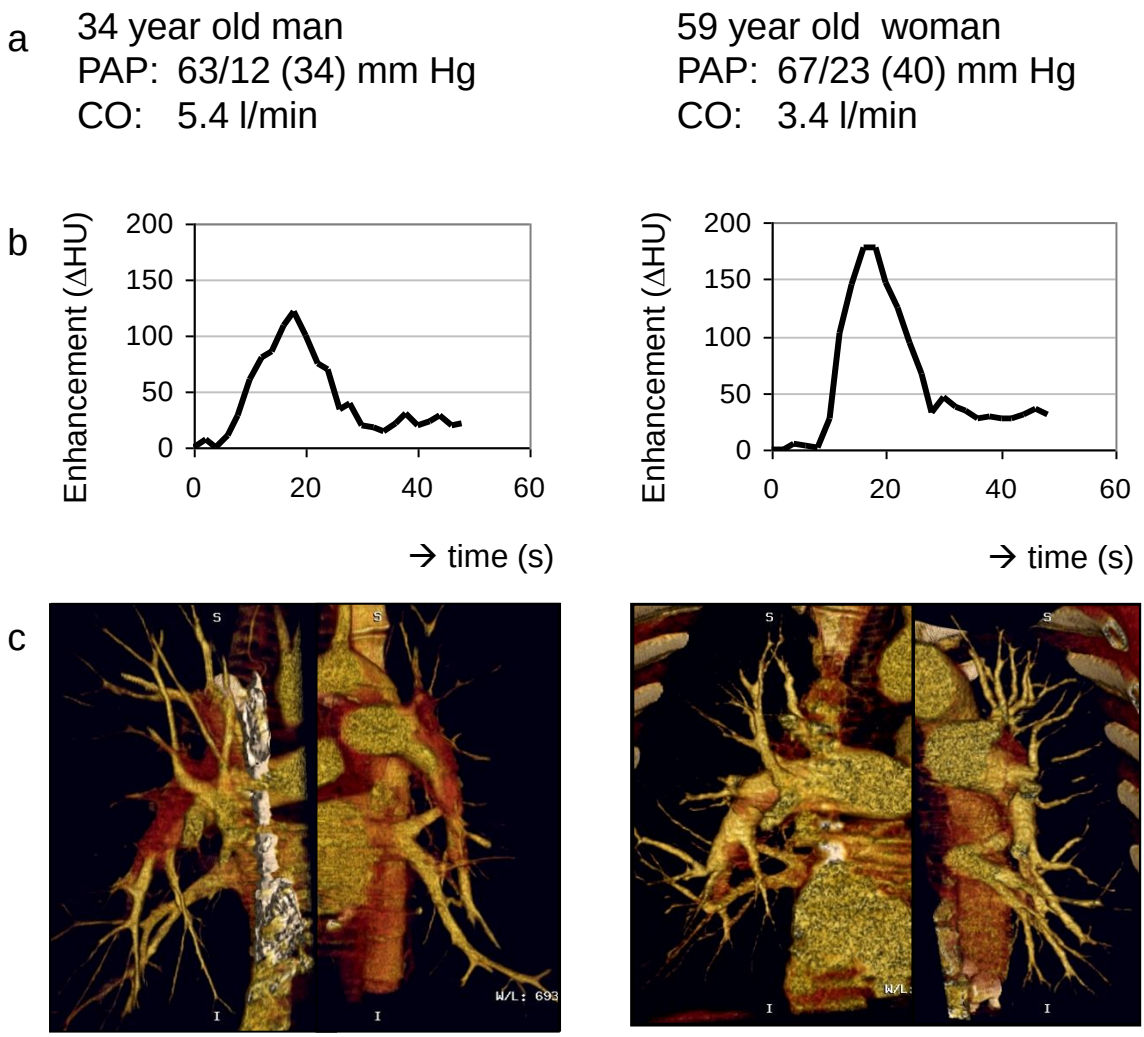

Figure 4.3: Cardiac Output and Pulmonary Arterial Enhancement

(a) Two patients with chronic thrombo-embolic pulmonary hypertension (CTEPH) are compared. PAP = pulmonary arterial pressure [systolic/diastolic (mean)]; CO = cardiac output.
(b) Following a small test-bolus injection (16 ml @ 4ml/s), the time-attenuation response measured in the pulmonary artery is smaller in the patient with greater cardiac output.
(c) Corresponding thin-slab volume rendered images of pulmonary vessels.

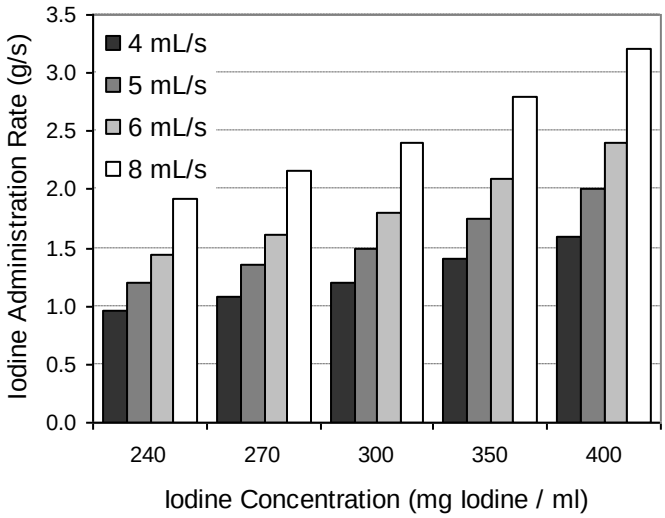

Figure 4.4: Iodine Administration Rates and CM Concentration

For a given CM concentration, the Iodine administration rate (g/s) can be varied by selection of the injection flow rate (in mL/s). High-concentration agents permit greater iodine administration rates at the same injection rates.

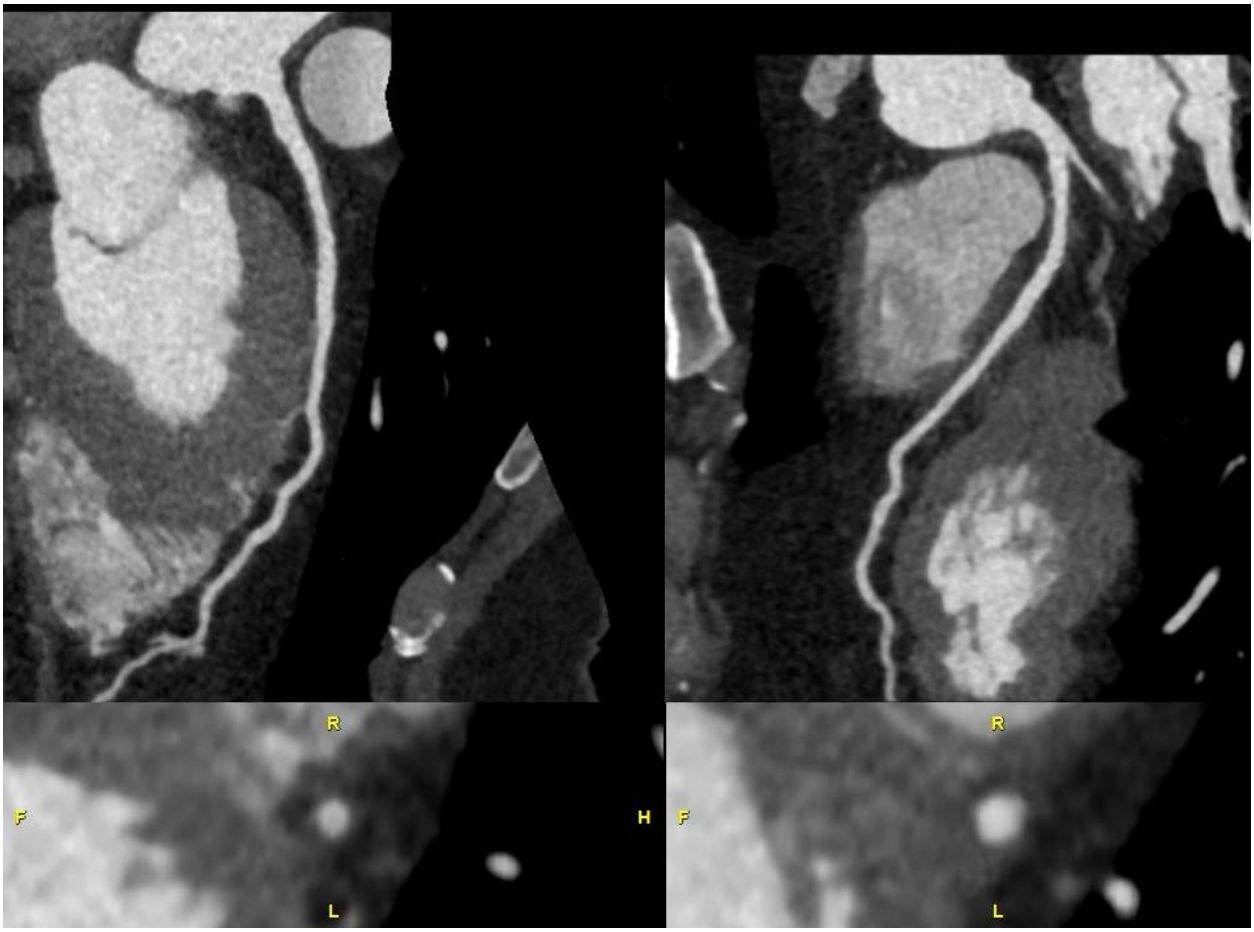

Figure 4.5. Use of low kVp scanning to decrease patient dose with preserved image quality.

A 54 kg female patient with chest pain presented for CCTA. 80 kVp tube voltage was utilized, with prospective ECG synchronization and iterative reconstruction techniques. Patient dose was 0.4 mSv. High degree of vessel enhancement with relatively little background image noise is noted on both curved-planar reconstructions (upper row) and slice through images (lower row).

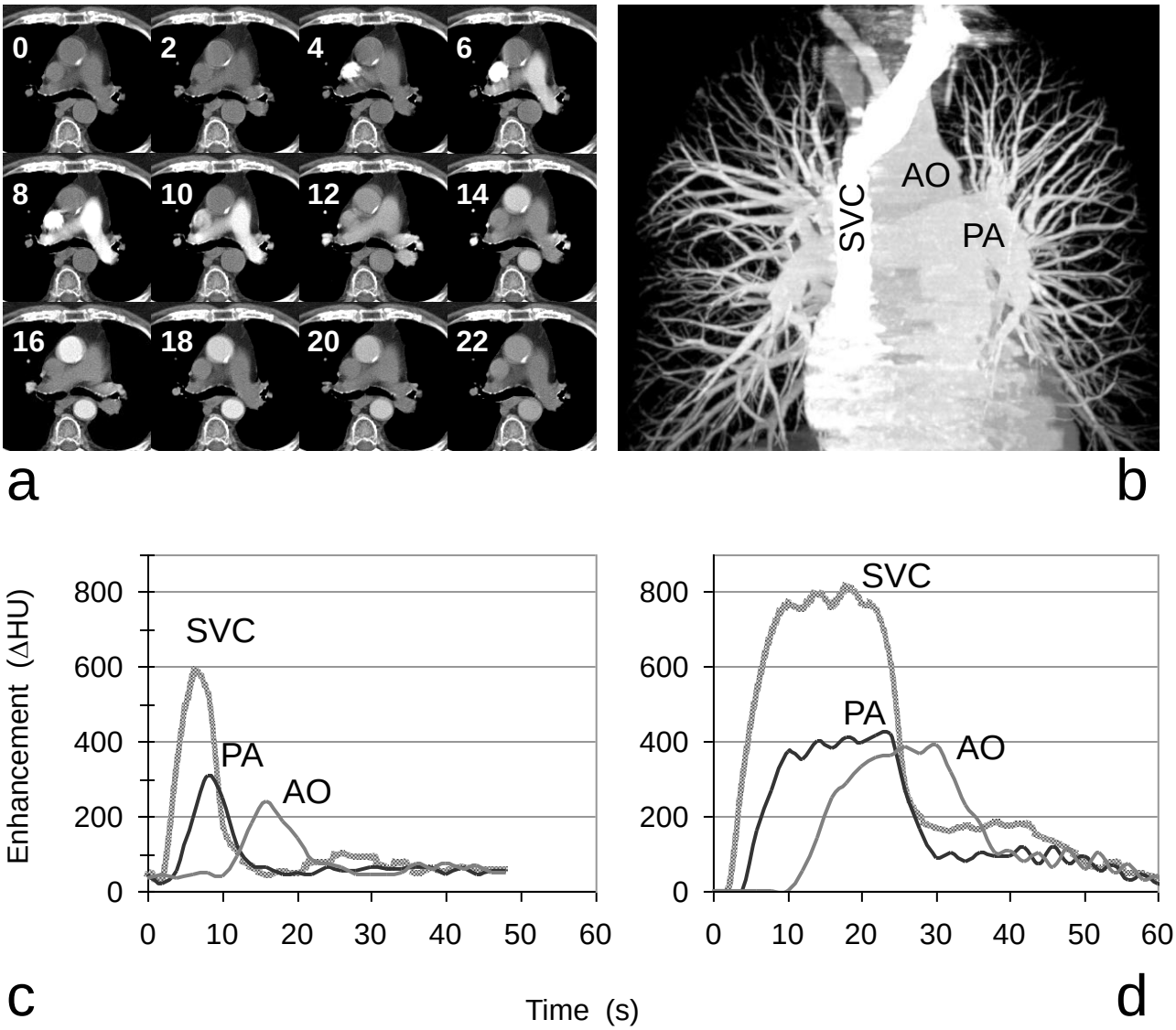

Figure 4.1: Early Contrast Medium Dynamics in the Chest

(a) Sequence of vascular enhancement observed in a non-incremental dynamic CT acquisition following the intravenous injection of a small test-bolus are shown (see text for details). (b) Maximum intensity projection of a MDCT pulmonary angiogram shows extensive opacification of the left brachicephalic vein and SVC. As densely opacified blood is mixed with unenhanced blood from the inferior vena cava in the right atrium and ventricle, the pulmonary arterial enhancement is substantially smaller than the enhancement in the SVC. Aortic enhancement is again slightly less than PA enhancement.
Analysis of the time attenuation curves from a 4s test-injection (c) allows to predict the time attenuation curves for a prolonged, 20s injection (d). Note, that the time window of maximum aortic enhancement without SVC enhancement is particularly narrow.
SVC = superior vena cava; PA = pulmonary artery; AO = thoracic aorta.