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REVIEW ARTICLE

Low radiation dose in computed tomography: the role of iodine

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ABSTRACT

Recent approaches to reducing radiation exposure during CT examinations typically utilize automated dose modulation strategies on the basis of lower tube voltage combined with iterative reconstruction and other dose-saving techniques. Less clearly appreciated is the potentially substantial role that iodinated contrast media (CM) can play in low-radiation-dose CT examinations. Herein we discuss the role of iodinated CM in low-radiation-dose examinations and describe approaches for the optimization of CM administration protocols to further reduce radiation dose and/or CM dose while maintaining image quality for accurate diagnosis. Similar to the higher iodine attenuation obtained at low-tube-voltage settings, high-iodine-signal protocols may permit radiation dose reduction by permitting a lowering of mAs while maintaining the signal-to-noise ratio. This is particularly feasible in first pass examinations where high iodine signal can be achieved by injecting iodine more rapidly. The combination of low kV and IR can also be used to reduce the iodine dose. Here, in optimum contrast injection protocols, the volume of CM administered rather than the iodine concentration should be reduced, since with high-iodine-concentration CM further reductions of iodine dose are achievable for modern first pass examinations. Moreover, higher concentrations of CM more readily allow reductions of both flow rate and volume, thereby improving the tolerability of contrast administration.

INTRODUCTION

CT is an indispensable diagnostic imaging technique whose use and range of applications have increased dramatically in recent years, primarily due to its widespread availability, ease-of-use and cost-effectiveness relative to other diagnostic procedures.[1] However, while rapid, ongoing technical innovations have led to marked improvements in image quality and diagnostic performance, the increasing utilization of CT has raised considerable concern over the risks associated with exposure to ionizing radiation, particularly with regard to the risk of radiation-induced cancer.[2–11] Overall, radiation exposure from CT examinations in Europe accounts for roughly 60% of the total radiation dose from all radiographic procedures[12] while the Lifetime Attributable Risk of radiation-induced cancer from CT scanning has been estimated to range from around 0.7%[3] to 1.5–2.0%.[4]

Although the "as low as reasonably achievable"[13,14] or, more appropriately for radiographic procedures, the "as low as diagnostically acceptable" principle is the widely invoked "rule-of-thumb" approach to minimize patient exposure to radiation, it is, as the term indicates, merely a principle rather than a scientific or technical innovation. In looking to reduce radiation exposure to patients, manufacturers of scanners have introduced various automated dose modulation strategies on the basis of lower tube voltage (kVp) and/or tube current (mAs) combined with iterative reconstruction (IR) and other dose-saving approaches to image acquisition.[1] Such techniques have been shown to permit considerable radiation dose savings.

Less clearly appreciated is the potentially substantial role that iodinated contrast media (CM) can play in low-radiation-dose CT examinations. The relative attenuation of iodinated contrast material is increased at lower kVp,[15] resulting in higher contrast enhancement than that obtained at higher kVp for a similar amount of administered CM. Several studies across a range of applications have exploited this increased attenuation at low kVp to emphasize the possibilities for reducing both CM dose and radiation dose when utilizing low-kVp protocols.[16–22] However, very few studies have focused on the possibilities for further radiation dose reduction using optimized CM injection protocols. Moreover, considerable debate exists as to the optimal approach to lowering the CM dose when utilizing low-kVp protocols.

Herein we discuss the role of iodinated CM in low-radiation-dose examinations and describe approaches for the optimization of CM administration protocols to further reduce radiation dose and/or CM dose while maintaining image quality for accurate diagnosis.

Fundamentals of low-tube-voltage examinations in CT

The number of X-ray photons delivered in CT depends on the tube current (mA) and exposure time (s) and increases linearly with increasing mAs. The number of photons is directly proportional to the applied radiation dose.[23] Conversely, the kVp determines the energy of the photons delivered. A common misconception is that the lower energy of the delivered photons is the reason for the radiation dose reduction potential of low-kVp examinations in CT. However, according to the recommendations of the International Commission on Radiological Protection, the weighting factor given to all sparsely ionizing radiations is equivalent (*i.e.* scored as "one"), implying that the biological effect of X-ray photons is independent of their energy. Moreover, the absorption of the low-energy photons typically delivered in medical examinations is higher than that of higher energy photons, especially in superficial body regions, meaning that the radiation dose applied to a patient should be even higher at low kVp. Softer X-rays are potentially more biologically damaging and thus have a larger radiation risk than hard X-rays because lower energy X-rays deposit a larger proportion of the dose in the body in the form of track-end electrons.[23] The actual reason the radiation dose is lower at low kVp is that the number of photons generated by the CT tube is considerably lower at low kVp than at higher kVp when the same mAs value is used.[24] This is primarily for technical reasons, such as the lower effectiveness of the tube at low kV (the X-ray tube output is proportional to kVp^2 and thus a reduction from 120 to 100 kVp will result in $(100/120)^2 = 0.69$, *i.e.* about 69% of the photons compared with that emitted at 120 kVp) and stronger filtering of low-kV photons.

Knowing this, it is evident that increased image noise (N) is a consequence of imaging at low kVp. Image noise is proportional to the denominator of the square root of the number of X-ray photons ($\#p$) and is thus directly dependent on the number of photons delivered:[24]

$$N \sim 1\Big/\sqrt{\#p} = 1\Big/\sqrt{\text{mAs}} \qquad (1)$$

The lower the number of photons delivered, the greater the image noise. Thus, protocols that utilize a low-kVp setting with unchanged mAs will deliver a reduced radiation dose but will suffer from increased image noise. A compensatory increase in mAs is thus required to overcome the greater noise. However, quantifying the optimum increase in mAs for an individual patient can be challenging. The resulting low practicability and lack of standardized guidelines may have been reasons for the reluctance among radiologists to use low-kVp protocols.[25]

In practice, approaches to mAs compensation in low-kVp examinations focus on maintaining either a constant image noise (N) or a constant signal-to-noise ratio (SNR).

Constant image noise

If the approach chosen is to maintain a constant N, then the potential for radiation dose reduction at lower tube potentials is limited or non-existent.[26] This has been demonstrated in studies on phantoms in which noise was shown to increase substantially on low-kV images, especially for phantoms with larger diameters.[27] Moreover, significant photon-starvation artefacts appear due to the decreased penetration capability of the lower energy photons and electronic noise. Even for a 25-cm phantom which represents the attenuation of a very small adult, a 29% increase in dose [relative volume CT dose index ($CTDI_{vol}$)] was required at 80-kV examination in order to match the noise of a 120-kV examination.[26] In other words, the required mAs compensation would have to be high even in small adults so as to swamp any perceived benefit of reduced kV if mAs compensation is based on matching image noise. For this reason, image reconstruction techniques such as IR have been developed to compensate for image noise.

Constant signal-to-noise ratio

The alternative approach is to maintain a constant SNR, in which the signal S is defined as the signal from the iodinated CM in the body. The X-ray absorption of iodine increases with decreasing effective kVp as long as the effective energy remains above the κ-edge (33.2 KeV) of iodine.[15] Thus, the signal S will be higher in low-kV CT examinations with the same amount of contrast applied. This is one of the fundamental roles of iodine in low-radiation-dose examinations. Owing to this higher signal, higher noise can also be accepted when maintaining a constant SNR because:

$$\text{SNR} = S/N \sim S \cdot \sqrt{\text{mAs}} \qquad (2)$$

Thus, when the SNR is kept constant at reduced kVp, only a moderate compensatory increase in mAs is needed. However, the indication and size of the patient should still be considered. Phantom measurements have shown that the $CTDI_{vol}$ needed for identical SNR relative to that at 120 kV is 46% at 80 kV and 62% at 100 kV for a small adult phantom. This implies a tremendous reduction in radiation dose. However, for a large patient (45-cm diameter phantom), 18% more dose ($CTDI_{vol}$) is needed at 80 kV relative to that at 120 kV in order to match the iodine SNR.[15] Thus, even when the choice is to maintain a constant SNR, a low-kV protocol may not be feasible for radiation dose reduction in all patients (Figure 1). Importantly, these considerations apply not only to single-energy low-kVp examinations but also to dual-energy or spectral imaging examinations.

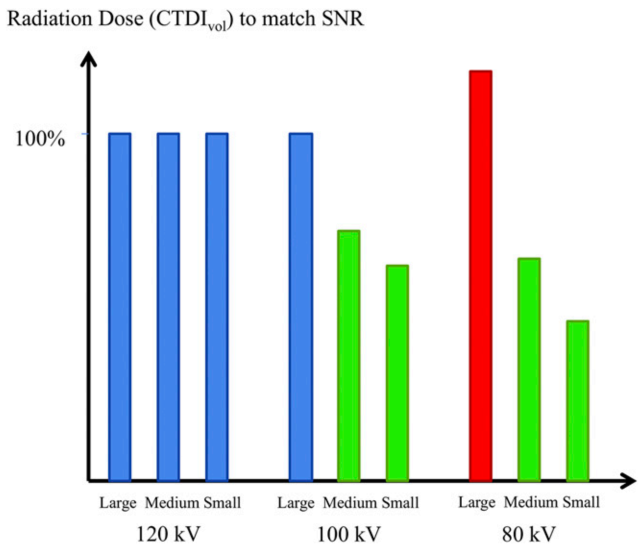
One option to optimizing tube potential is to use patient weight or size-based kV-mAs tables and to manually adjust values for a specific patient. However, a less complex approach is automated kVp selection in which radiation exposure is individually determined on the basis of effective attenuation values measured by the scanner.[28]

The appropriate choice of kV is invariably determined by the clinical task to be performed. For the evaluation of highly iodine-enhanced vessels or structures, the iodine contrast-to-noise ratio (CNR) may be the most appropriate metric to use. Thus, the potential of low-kVp protocols for radiation dose reduction is highest for indications such as CT angiography (CTA) and acquisitions during the arterial phase (*e.g.* for detection of arterially vascularized liver tumours). For these indications, low kVp and higher iodine signal not only have the potential to reduce radiation dose but also to improve image quality. This applies similarly to all organs with considerable parenchymal enhancement in the portal-venous phase such as in the liver, kidney and pancreas. Zamboni et al[29] found a higher conspicuity of pancreatic adenocarcinoma when using low kVp, whereas Ramgren et al[30] used highly concentrated CM and low kVp to improve image quality in intracranial CTA.

On the other hand, for non-enhancing or poorly enhancing soft-tissue structures, matching noise may be more appropriate. Since iodine does not provide a higher signal in these cases, dose reduction with low kV is generally limited. Many diagnostic tasks, such as routine contrast-enhanced abdominal CT examinations, fall somewhere between these two scenarios. Image quality indices such as the "noise-constrained iodine CNR" have been proposed to quantify different levels of image quality for different diagnostic tasks.[31] AutokV tools (*e.g.* CarekV; Siemens Healthcare) employ these principles; the strength of the setting "noise *vs* CNR constraints" for an individual examination is defined by the user (settings from non-enhanced CT to highly iodine-enhanced CT, *e.g.* in CTA) and the software automatically determines the optimal kVp and adapted mAs based on a fixed-reference mAs.

In summary, the role of iodine in radiation dose reduction using low kVp is fundamental. Iodine attenuation is higher at low kVp, and thus SNR can be kept constant with reduced radiation exposure. The greatest potential of low kVp for reducing exposure is mainly limited to highly iodine-enhancing examinations such as CTA or arterial phase imaging.

Figure 1. The volume CT dose index ($CTDI_{vol}$) values needed to match the signal-to-noise ratio (SNR) obtained in water phantoms with three tube potentials and three phantom sizes (25-, 35- and 45-cm diameter). Unlike at 120 kV, 80 and 100 kV allow for a radiation dose reduction in small- and medium-size phantoms. However, with the large-size phantom, 80 kV would require a higher radiation dose to match SNR than 120 kV (based on values provided by Yu[26]).

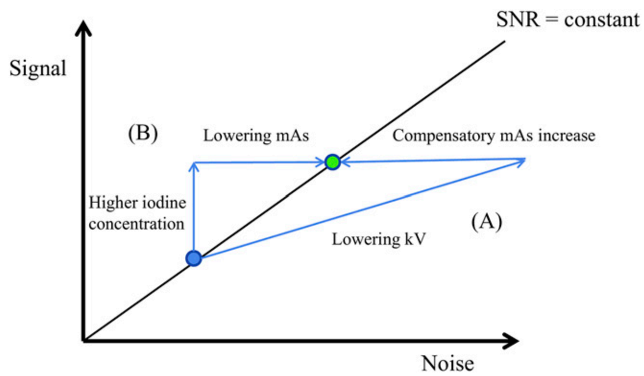


AN ADDITIONAL OPTION TO REDUCE RADIATION DOSE WITH IODINE

An alternative and supplemental approach to reducing the radiation dose in CT is through increasing the iodine concentration in the target structures to be examined. Based on a similar SNR = constant approach to that utilized in low-kV examinations, the use of a higher iodine concentration means that higher noise can be accepted due to the higher iodine signal. The increased noise in this scenario is realized by lowering the mAs which in turn implies reduced radiation dose (Figure 2). To note, however, is that this approach is different from and in addition to the approaches utilized in the automated tube current modulation tools that are provided for CT scanners. These tools can further reduce the overall applied radiation dose by modifying a reference mAs over scanning time and space[32] while the "high iodine concentration—low mAs" concept allows an overall lowering of the reference mAs.

Despite the fact that this concept seems simple and straightforward, awareness of and experience with this approach to

Figure 2. Two options to reduce the radiation dose while keeping a constant signal-to-noise ratio (SNR). (A) Low-tube-voltage approach: lowering kV increases iodine signal but at the same time increases noise; a compensatory increase in mAs is needed to achieve the same SNR (green dot); (B) starting from the same standard examination (standard kV, blue dot), increasing the local iodine concentration provides higher signal and allows for a reduction of the mAs to match the SNR at the identical level.



radiation dose reduction is somewhat limited. Nevertheless, several studies have demonstrated its validity. Szucs-Farkas et al[33] demonstrated its potential in chest phantom studies, noting that a similar CNR to that achieved with a 300-mg-iodine/ml CM concentration could be achieved with a 400-mg-iodine/ml CM concentration but at 18–40% lower $CTDI_{vol}$ depending on the phantom size and applied kVp.

In clinical studies, this benefit has been demonstrated for CTA of the aorta, the pulmonary arteries and myocardial perfusion CT.[34–38] One advantage is that the limitations associated with low-kVp examinations do not apply to this approach. Thus, large body habitus, for which a low-kVp protocol is typically not a feasible approach to reduce radiation dose (Figure 1), is generally not a limitation for the high iodine concentration–low mAs concept. Furthermore, low kV is a limitation in some other applications since the maximum tube output (mAs) is technically limited at lower kVp. The required compensatory mAs increase for low kV may thus not always be feasible. This is especially the case at high helical pitch. Therefore, when a fast scanning speed and a short scan time are desired, a low tube potential may not be appropriate, even for small patients.[26] The high iodine concentration–low mAs approach, however, would again not be a limitation in these cases.

The low kV and "low mAs–high iodine concentration" options can be combined to maximize the radiation dose reduction potential. Iezzi et al[34] showed that the radiation dose could be reduced by as much as 74% when reducing kVp from 120 to 80, at the same time increasing the iodine signal by using 400 mg iodine/ml concentration instead of 300 mg iodine/ml. It can also be combined with automatic kVp selection tools. In this case, the reference mAs should be set at a lower level when using a contrast injection protocol that provides higher signal. Schwarz et al[35] demonstrated that autokV tools can work more effectively in choosing the lower kVp option more frequently when high iodine concentration (IC)/low mAs is used.

Limitations of both the low-kV and low-mAs/high-iodine-signal approaches—especially when both approaches are combined—are that streaking and dark shadow artefacts are potentially more prevalent in high-signal structures.[26] On the other hand, broadening the window width can compensate for image noise and thus further improve image quality at high-contrast examinations.[39,40]

THE IMPORTANCE OF IODINE DELIVERY RATE

The "low-mAs/high-iodine-signal" approach requires a higher iodine concentration in the relevant body structures to be examined. Two injection parameters influence iodine enhancement in CT: the total iodine dose (D) and the iodine delivery rate (IDR).[41–43]

$$D[\text{g iodine}] = \text{Volume}[\text{ml}] \times \text{iodine concentration}[\text{g iodine/ml}] \quad (3)$$

$$\text{IDR}[\text{g iodine/s}] = \text{flow rate}[\text{ml/s}] \times \text{iodine concentration}[\text{g iodine/ml}] \quad (4)$$

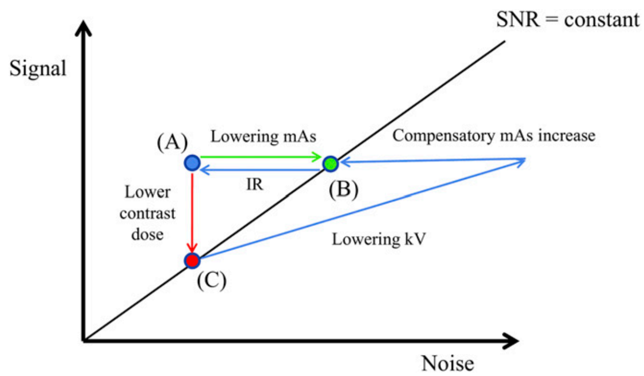
Dose D is the relevant parameter that determines maximum enhancement in venous phase examinations while the IDR crucially influences the maximum enhancement in first pass examinations such as CTA, arterial phase imaging and perfusion CT.[41–43] It also has benefits in parenchymal phases although to a lesser degree.[44] Since first pass examinations are precisely the highly iodine-enhancing examinations in which the potential for radiation dose reduction is the greatest, when designing optimum contrast injection protocols for radiation dose reduction, it is the IDR that is the most crucial parameter. This has been borne out by several studies that have utilized optimized contrast injection protocols using high flow rates and high iodine concentrations to increase IDR in the context of radiation dose reduction.[34–38] Crucially, it is important to bear in mind that such protocols do not imply the injection of more iodine but merely that a faster IDR is needed.[43]

On the other hand, an increase in iodine dose is potentially an option for radiation dose reduction in venous phase examinations, although in these low-iodine-enhancing examinations, the potential to reduce radiation dose using the SNR = constant approach (either by lowering kVp or by high IC/low mAs) is more limited. Nevertheless, lower radiation exposure and improved image quality using the "high IC/low mAs" concept has been demonstrated for portal-venous phase abdominal CT.[45]

CONTRIBUTION OF ITERATIVE RECONSTRUCTION

IR is a technique for reducing radiation exposure that utilizes an alternative image reconstruction algorithm to filtered back projection to reduce noise without impairing signal.[46–51] The combination of low kVp and IR is now an established approach in modern CT. Importantly, IR can be combined with the high IC/low mAs approach and other techniques to further reduce radiation dose. In principle, IR has three potential benefits (Figure 3).

Figure 3. Three options when combining iterative reconstruction (IR) and low kVp. (A) Increased image quality due to a higher signal-to-noise ratio (SNR) (all blue arrows, end at blue dot). (B) Additional reduction in radiation dose by lowering mAs (green arrow to green dot, to match SNR of that obtained at low kV if no IR was used). (C) Contrast dose reduction to obtain signal, image noise and SNR as before (red arrow to red dot; identical situation compared with standard).



Improved image quality

Without any modification, the higher SNR can be used to improve image quality and the visualization of small enhancing structures (*e.g.* small vessels in CTA or arterially enhancing lesions) (Figure 3a). Studies have shown that low kVp in the absence of IR can lead to an increase in image quality.[29,30] Clearly, if IR were to be utilized, a further reduction of noise and thus an increase in SNR would be possible, resulting in increased image quality.

Lowered radiation exposure

The mAs can be further reduced to obtain a SNR that is similar to that which would otherwise have been obtained had low kV been used without IR (Figure 3b), thus IR is used to additionally reduce radiation dose, giving SNR values that are similar to the above-mentioned "low kV alone" and low-mAs/high-iodine-signal approaches (Figure 2). This has been demonstrated in several studies.[52–55]

Reduced iodine dose

The third option is to reduce the contrast dose to obtain the same signal S, the same noise N and the same SNR as with the standard kV and without IR (Figure 3c). Numerous studies addressing low contrast volume and low iodine concentration suggest that this approach is widely used.[16–22,56–73]

Of note, these three options can be combined to give a low kV + IR CT protocol that provides a lower radiation dose but which keeps the SNR higher than that of standard protocols, thereby combining radiation dose reduction with image quality improvement. The limitations of the constant SNR approach in low-iodine-enhancing examinations (*e.g.* routine venous phase abdominal CT) do not apply in this setting since the noise is also kept low. However, strong kVp reductions may still be susceptible to photon-starvation artefacts, especially in larger patients.

In general, the relative benefits of increased image quality, lower radiation exposure, and contrast dose reduction have to be weighed against each other, especially in first pass examinations where all options are feasible. The decision should depend on the individual clinical situation. Although radiation dose reduction may be more important in younger, healthier patients, the opposite may be true for contrast dose reduction. Safety and tolerability of contrast injections thus become part of the decision-making process.

HOW TO REDUCE CONTRAST DOSE

As evident from Equation (3) above, a reduction of contrast volume and/or a reduction of the iodine concentration will result in a reduced iodine dose. However, although several studies have focused on the potential value of reduced iodine concentration in conjunction with low-kV settings,[56–68] numerous factors clearly favour reduced contrast volume rather than lower concentration as a means to reduce the total administered contrast dose.[16–23,69–73]

The CT applications with the highest potential for low-kV/low-radiation-dose protocols are CTA and perfusion imaging in which the signal during the first pass of CM is crucially influenced by the IDR. As noted above, the potential for iodine reduction in a low-kVp setting derives from the considerably higher attenuation of iodine at low kV (Figure 4a,b). However, a drawback of reducing the iodine concentration for these applications is that the IDR would also be reduced for a similar given injection rate. Although this would result in a lower CM dose, both the contrast bolus shape and maximum enhancement would remain essentially unchanged (Figure 4c), meaning that the opportunity for further contrast (or radiation) dose reduction is lost. A benefit of maintaining a high iodine concentration and reducing only the volume administered for the same injection rate is that the IDR remains high resulting in greater enhancement (Figure 4d) and potentially improved image quality. An additional benefit is that the contrast and/or radiation dose can be reduced still further (*i.e.* by further reductions in administered CM volume or mAs, respectively).

To note is that the injection duration is shorter when the volume administered is reduced. For most first pass examinations using newer scanner technologies, this is an additional benefit because the bolus duration should mimic the scanning duration.[73] An unnecessarily long injection leads to a waste of CM[41] because the CM administered after the acquisition of data does not contribute to data acquisition. Unfortunately, this principle is often overlooked in clinical practice. Multidetector CT has dramatically short image acquisition times, typically of just a few seconds.[74,75] Therefore, the necessarily higher volumes associated with administration of CM containing lower concentrations of iodine are increasingly inappropriate. The use of low iodine concentration to reduce iodine dose does not utilize the potential for contrast injection optimization (Figure 4a,c), whereas the use of high iodine concentration and lower volume more practically permits the optimization of injection protocols (Figure 4d,e).

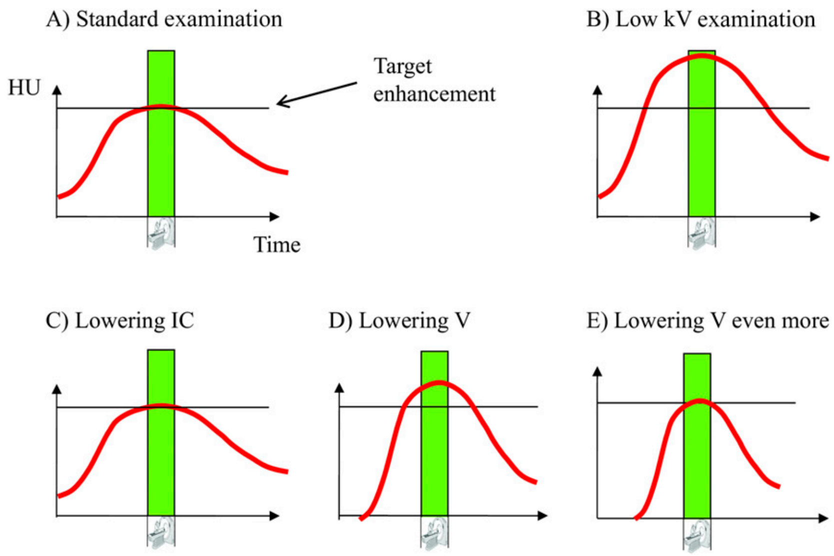
First pass examinations which cover large body areas such as peripheral CTA not only require that the width of the contrast bolus matches the acquisition over time but also that it matches over space. Otherwise, the bolus may be overridden if the acquisition time is too fast or venous overlay may occur if the scan is too slow.[75] Since the individual variation in bolus "transportation" can be considerable and may not be known a priori, a relatively slow table speed and broadening of the contrast bolus is required. In such situations, the above-mentioned option to optimize the bolus geometry is limited.

SAFETY AND TOLERABILITY ASPECTS OF IODINATED CONTRAST ADMINISTRATION IN CT

For all CT examinations, a reduction of the iodine concentration generally means that the injected volume and flow rate will be higher than if a higher iodine concentration is used at the same contrast dose and IDR. This touches on issues related to tolerability and safety.

Apart from serious allergoid or anaphylactoid reactions, which can occur after administration of only small amounts of any CM,[76] the most relevant side effect of iodinated CM which possibly has a correlation with dose is contrast-induced nephropathy,[77] more recently referred to as contrast-induced acute

Figure 4. Illustration of contrast dose reduction in first pass CT examinations. (a) Contrast enhancement over time compared with acquisition time (green bar) in a standard setting. (b) Use of low kV increases iodine enhancement when the same injection protocol is used. (c) Iodine concentration (IC) is reduced to obtain the same enhancement level as in the standard examination. (d) When volume V is reduced instead of IC, a sharper contrast bolus will be injected (due to higher IDR); with the same amount of contrast dose reduction compared with (c) (in grams of iodine), a higher enhancement level is obtained. (e) Thus, more contrast dose reduction is feasible when lowering volume V instead of IC when targeting the same enhancement level. HU, Hounsfield unit.



kidney injury. Although the existence of contrast-induced nephropathy/contrast-induced acute kidney injury in contrast-enhanced CT is currently a matter of debate,[78–84] patients with renal impairment or an elevated risk of renal impairment are nevertheless still likely to benefit most from a reduction of contrast dose.[77]

Apart from iodine dose, also injection volume and flow rate can influence safety and tolerability. Although maintaining a high flow rate is beneficial in terms of IDR and the potential for radiation and/or CM dose reduction, for many patients, particularly elderly patients or patients with poor venous condition, a high flow rate may be difficult to achieve, inappropriate or potentially harmful. In such cases, administration of a higher concentration CM at a reduced flow rate is potentially advantageous in reducing intolerability while maintaining a sufficiently high IDR.[43] Likewise, a reduced total volume of administered CM is beneficial in terms of lowered cardiac preload, a factor that may be especially crucial in critically ill patients.

It has been stated that high IC and newer scanner generations are mutually compatible and that sporadic failure would be unpreventable if using low IC due to the fact that, in most cases, a patient's cardiac output is not known prior to scan initiation.[84] Studies have confirmed this suggestion. A study comparing low- and high-concentration CM at identical flow rate (*i.e.* resulting in a higher IDR with the high iodine concentration) found no differences in the rate of adverse events.[85] Conversely, at identical IDR, Mühlenbruch[86] found a significantly higher rate of general patient discomfort when using a lower iodine concentration. Specifically, significantly greater patient discomfort was noted with a CM containing 300 mgI/ml than with CM containing 370 or 400 mgI/ml despite relatively moderate injection rates.

The possibility that high flow rate is associated with greater patient discomfort was reinforced by Andreini et al[87] who demonstrated increased heat sensation, higher post-examination heart rate and an increased number of premature heartbeats for an identical volume (80 ml) of iodixanol-320 injected at 6.2 ml s^{-1} compared with 5.0 ml s^{-1}. Again, these findings suggest that the possibility to lower the injection rate while maintaining a sufficiently high IDR for diagnosis is a potential advantage for high-concentration CM over low-concentration CM in terms of patient tolerability.

A potentially confounding factor is that solution viscosity increases when the iodine concentration is increased. However, there is no evidence that a higher viscosity of the contrast agent formulation reduces tolerability or safety.[86,87] On the other hand, high viscosity can be a technical challenge since the required injection pressure increases with viscosity. With the highest iodine concentration (400 mg I/ml) flow rates of up to 6 ml s^{-1} are feasible using commercially available injectors.[88] Of note, administration of CM containing 300 mg I/ml does not deliver a higher maximum IDR since 8 ml s^{-1} was the maximum injection rate achievable with this lower iodine concentration giving the same maximum IDR of 2.4 gI/s. Warming the CM reduces viscosity, and therefore allows for higher injection rates. Clinical observation suggests that patients are often more comfortable if the CM is warmed before administration.[89]

More relevant than CM formulation viscosity is the viscosity of the iodinated molecules themselves, and it is important not to confuse the two. Contrast agents formulated at high iodine concentrations have, by definition, minimally viscous molecules because it is their low viscosity that facilitates the preparation of more highly concentrated formulations.[90] Conversely, the more viscous molecules (*e.g.* molecular dimers such as iodixanol which have the highest viscosity of all non-ionic products) cannot be formulated at high concentrations. Any considerations or concerns regarding the viscosity of the ingredients should therefore not impact the choice of the iodine concentration but rather the choice of the contrast agent product itself.

CONCLUSION

The role of iodine is fundamental in low-radiation-dose CT. The higher iodine attenuation obtained at low-kVp settings allows for a reduction in radiation exposure while maintaining SNR. Similarly, high-iodine-signal protocols may permit radiation dose reduction by permitting a lowering of mAs. This is particularly feasible in first pass examinations where high-iodine signal can be achieved by injecting iodine more rapidly. The combination of recent technical developments, principally relating to low kV and IR, permits further reductions of radiation exposure, increases diagnostic image quality and/or allows for a reduction of the iodine dose. In an optimum contrast injection protocol, the volume of CM administered rather than the iodine concentration should be reduced, as with high-iodine-concentration CM further reductions of iodine dose are achievable for modern first pass examinations. Moreover, when necessary (*e.g.* in elderly patients), higher concentration CM more readily permit a reduction of flow rate and volume, thereby improving the tolerability of contrast administration.

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