Exhibit Number: PHEE-23

Factors Affecting Contrast Enhancement In Computed Tomography Imaging

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Building Intelligent Connections

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Disclosures

- G.V. Toia: Canon Medical Systems.
- S.D. Rose: Imalogix, GE Healthcare and Qaelum.
- T.P. *Szczykutowicz:* Canon Medical Systems, GE, Alara Imaging, Imalogix, Aidoc, Medical Physics Publishing, Qaelum, RadUnity.
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- R.R. Bladorn: No disclosures
- C.R. Bartels: No disclosures

Teaching points

- Improper contrast enhancement is a leading motivator for repeated CT examinations.

- Many interacting factors influence contrast enhancement including physics-based, patient-related and contrast protocol related.

- Three physics (beam energy, beam hardening, scan duration), two patient (blood volume, cardiac output), and five contrast prescriptions (contrast volume, injection rate, iodine concentration, scan delay, saline flush) related factors will be described giving the reader the ability to quantify the change in contrast enhancement when performing CT protocol optimization and to achieve optimal contrast enhancement.

Iodinated contrast media (ICM)

Injection of ICM is widely used in computed tomography (CT) to increase anatomic enhancement and visualization. ICM increases contrast to noise ratio of structures containing ICM across the imaged anatomic field of view.

Without contrast

Put your ICM glasses on 😉

With contrast

Chambers and vessels of the heart and mediastinum are better visualized after ICM injection

Liver parenchyma and abdominal vessels are better visualized after ICM injection

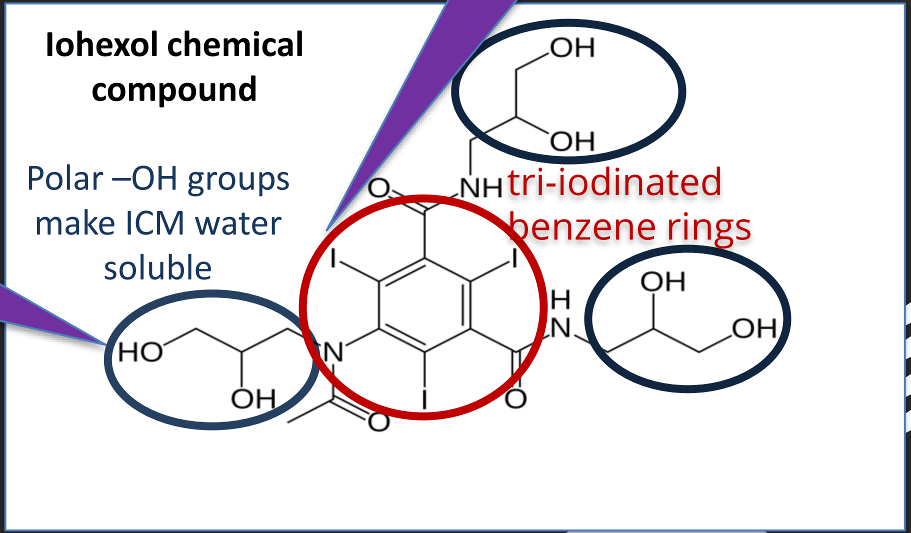
Iodinated contrast media (ICM)

Contrast materials used in diagnostic imaging:

- ❑ iopamidol
- ❑ iohexol
- ❑ iopromide
- ❑ ioversol
- ❑ ioxilan
- ❑ iodixanol (the same osmolality as serum)

3 Iodine atoms per contrast molecule

These parts of the molecule make it water soluble



Iohexol is a common CT ICM and is available in different concentrations (milligram of iodine per milliliter of contrast).

Common concentrations of ICM used for diagnostic CT in the USA is 300-370 mgI/ml.

Examples of good and poor contrast enhancement

174 kg patient received 96 ml volume of ICM→ poor enhancement

Same patient repeated with 159 ml volume of ICM→ good enhancement

Larger volume of ICM results in higher contrast enhancement so why not give more ICM!?

ICM can cause **acute adverse** effects like allergic reactions and physiologic reactions (i.e., cardiac arrhythmias, depressed myocardial contractility, etc.) and **delayed effects** (e.g., cutaneous reactions)

While rare, **contrast-induced acute kidney injury (CI-AKI)** or contrast-indued nephropathy can happen which is a sudden deterioration in renal function that is caused by the intravascular administration of iodinated contrast medium. CI-AKI may be proportional to dose for cardiac angiography

That is why cannot just give a very large amount of contrast volume to the patients!!!

Contrast optimization is important!!!

1. ACR manual on contrast media, 2024

Factors affecting contrast

To optimize contrast volume, we first need to have a decent knowledge of what factors and how affect contrast enhancement. Following is a list of factors affecting iodine contrast enhancement in CT:

- Beam energy
- Beam hardening
- Scan duration

Physics-based factors

- Blood volume
- Cardiac output

Patient-related factors

- Contrast volume
- Injection rate
- Iodine concentration
- Scan timing (scan delay)
- Saline flush

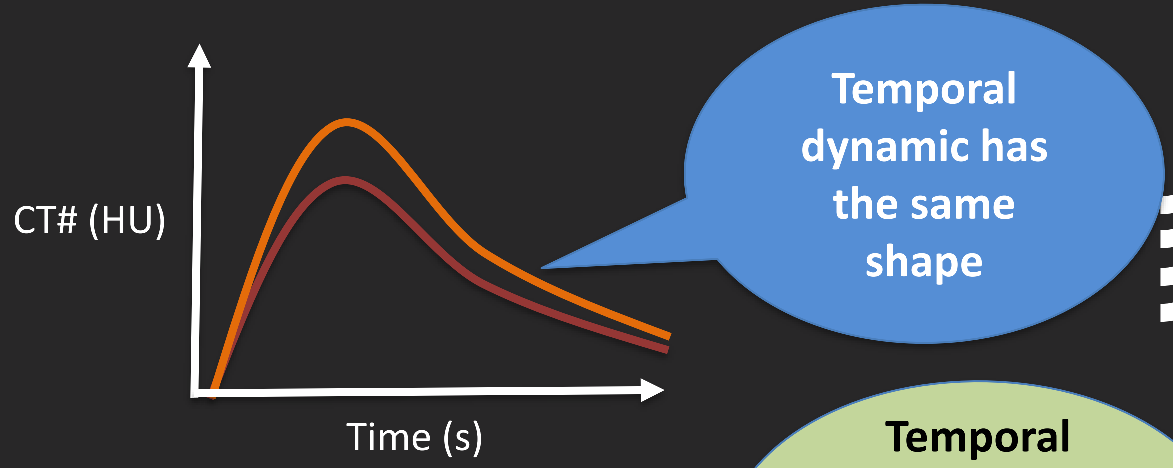
Contrast Protocol-based factors

Interacting factors affecting magnitude and temporal dynamics of enhancement

Interacting factors affecting iodine contrast enhancement can be further divided into two general types based on whether they influence enhancement magnitude or dynamics

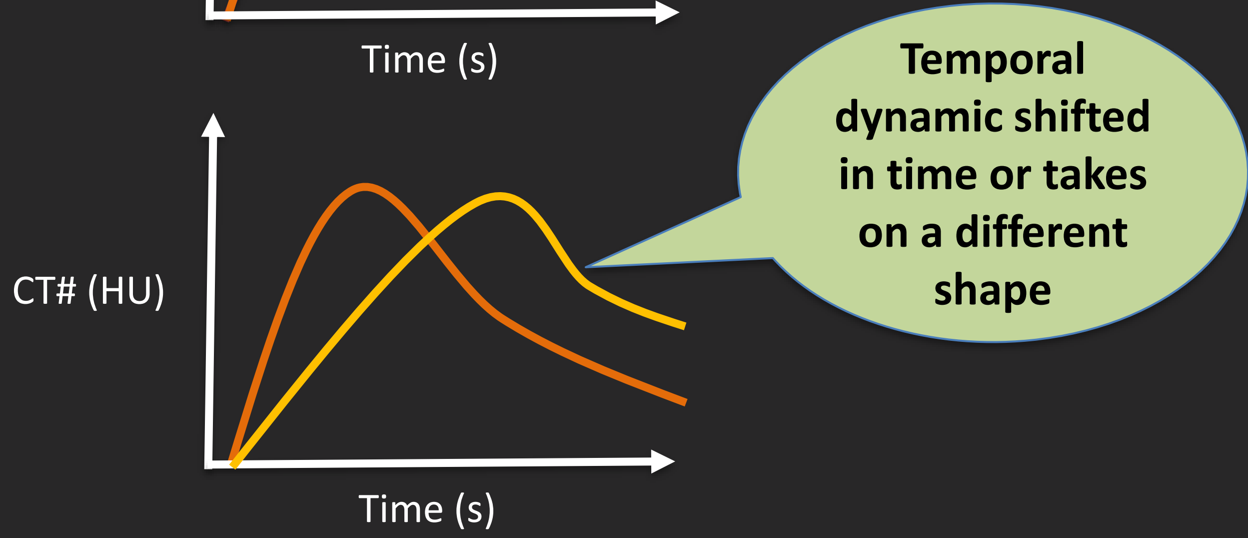
Scalar Factors

Factors that change the magnitude of enhancement by a fixed amount over all time (e.g., changing kV)



Temporal Factors

Factors that modify the temporal dynamics of contrast enhancement (e.g., shifting peak)

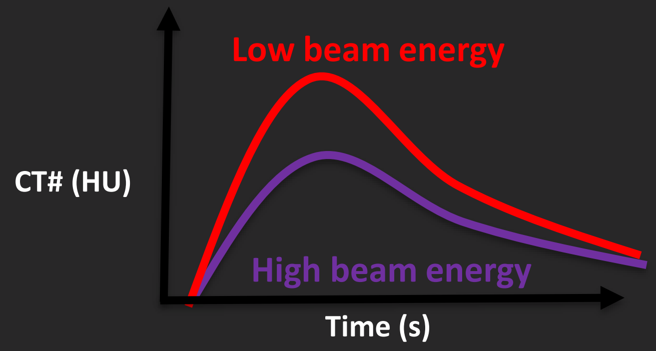


Some factors can be both scalar and temporal.

Physics-based factors affecting contrast:
1. Beam energy (kV)

Scalar factor

No effect on peak enhancement time



Linear attenuation coefficient (μ) in CT is given by the summation of Photoelectric (PE) and Compton contributions

$$\mu(\vec{X},E)=\boldsymbol{\tau}_{PE}(\vec{X},E)+\boldsymbol{\sigma}_{Compton}(\vec{X},E)$$

$$=K\boldsymbol{\rho}_e(\vec{X})\frac{Z^3(\vec{X})}{E^3}+\boldsymbol{\rho}_e(\vec{X})f_{KN}(E)$$

$\boldsymbol{\rho}_e$ = electron density
Z= atomic number
E= beam energy
f_{KN} =Klein-Nishina factor

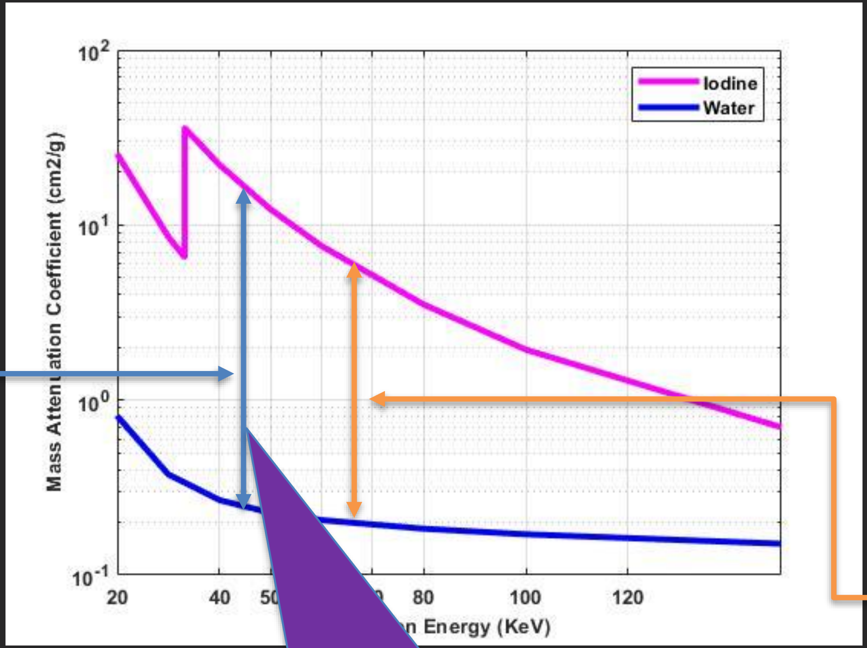
Linear attenuation coefficient is inversely proportional to the cube of beam energy.

1. Jiang, Hsieh. "Computed tomography: principles, design, artifacts, and recent advances." Bellingham, Washington USA (Published by SPIE and John Wiley & Sons, Inc.): SPIE 2009: 39-44.
2. Szczykutowicz T. The CT handbook: optimizing protocols for today's feature-rich scanners. Medical Physics Publishing, Madison WI. 2020: 282-289.

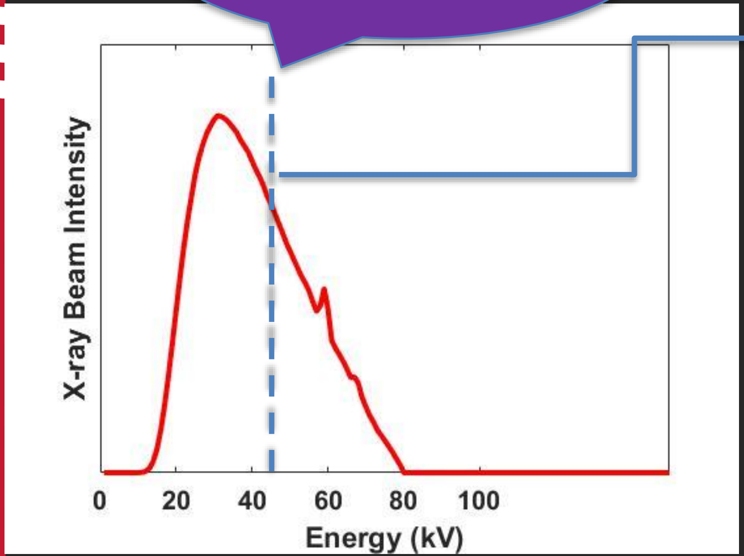
Physics-based factors affecting contrast:
1. Beam energy (kV)

$$CT\ number = \frac{\mu_I - \mu_W}{\mu_W} \times 1000$$

The distance between these curves at each beam energy (difference between linear attenuation coefficients of water and iodine) is iodine contrast



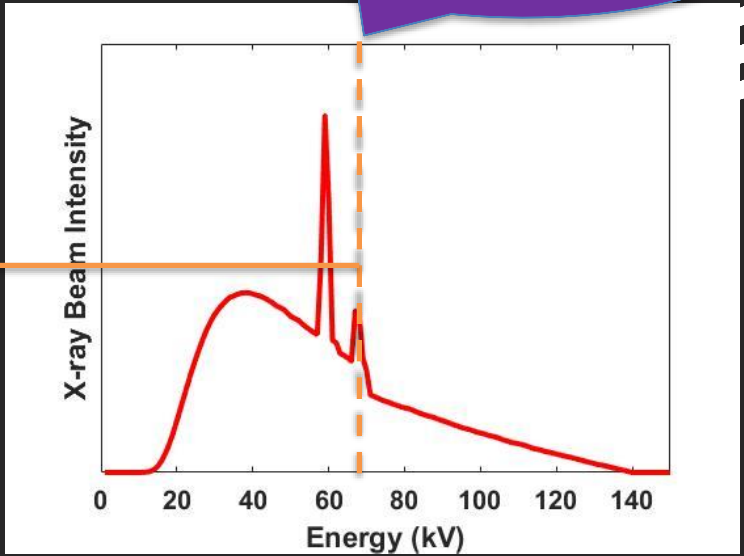
Mean effective energy = 45 keV



80 kV acquisition X-ray spectrum

Larger difference between mass attenuation coefficient of Iodine and water at 80 kV (lower energy)→ <u>**Increased contrast**</u>

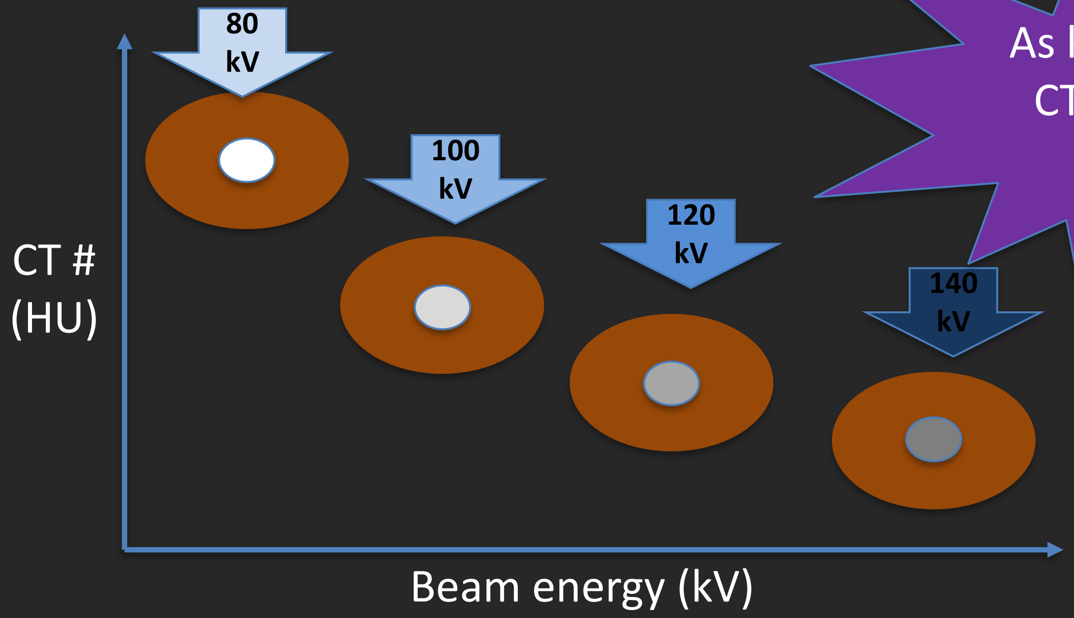
Mean effective energy = 67 keV



140 kV acquisition X-ray spectrum

1. Jiang, Hsieh. "Computed tomography: principles, design, artifacts, and recent advances." Bellingham, Washington USA (Published by SPIE and John Wiley & Sons, Inc.): SPIE 2009: 39-44.
2. Szczykutowicz T. The CT handbook: optimizing protocols for today's feature-rich scanners. Medical Physics Publishing, Madison WI. 2020: 282-289.

Physics-based factors affecting contrast:
1. Beam energy (kV)

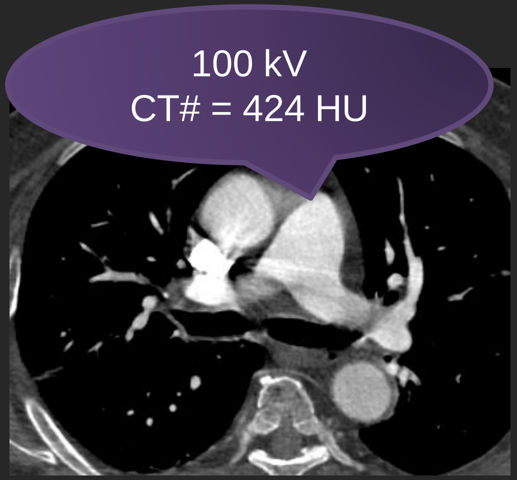


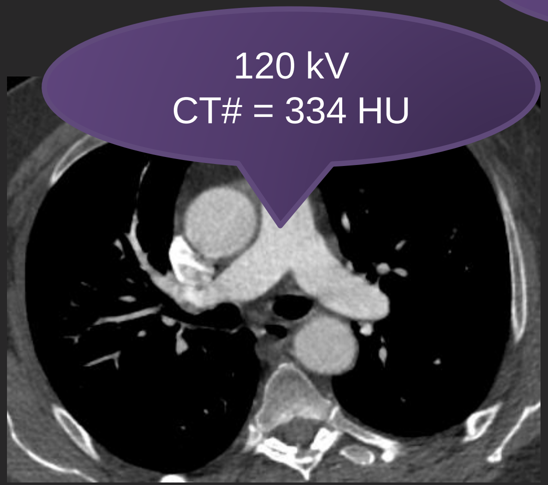
As kV increases, CT# drops for Iodine

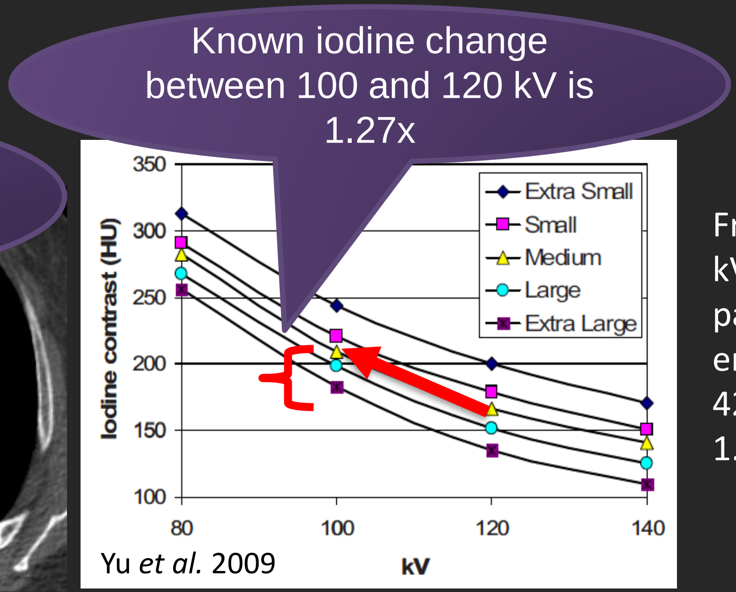
Beam energy (kV)	Relative iodine enhancement (to a reference beam energy=120 kV)
80	1.68
100	1.27
120	1
140	0.826

Everything fixed between these two images except **beam energy**

Weight: 92 kg
Contrast Volume= 86 ml
Saline flush= 20 ml
Injection rate= 5 ml/s
Iodine concentration= 350 mgI/ml





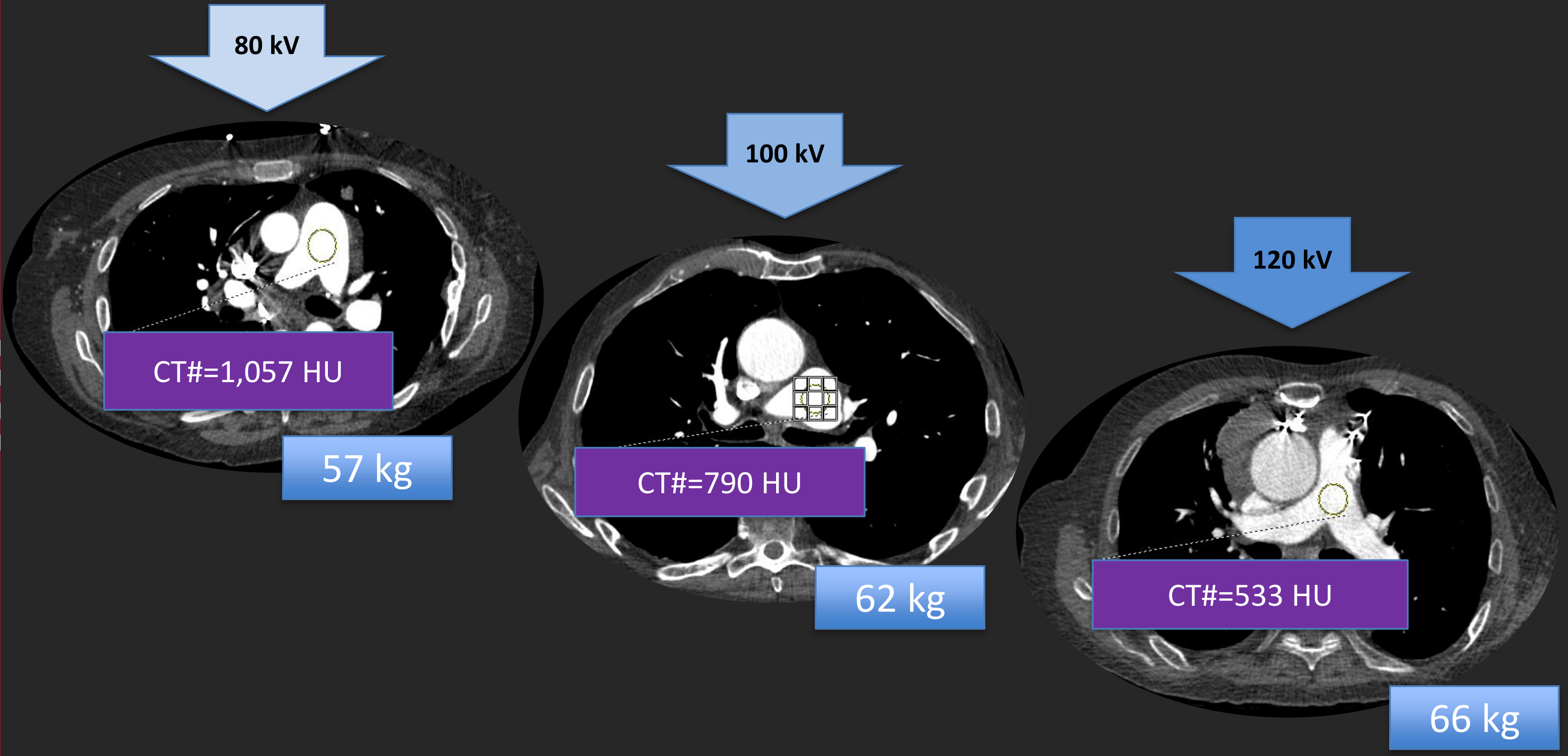


Yu *et al.* 2009

From 100 kV to 120 kV ratio of measured patient iodine enhancement was 424HU/334HU = 1.27

1. Szczykutowicz T. The CT handbook: optimizing protocols for today's feature-rich scanners, 2020.
2. Yu L, Li H, Fletcher JG, McCollough CH. Automatic selection of tube potential for radiation dose reduction in CT: a general strategy. Medical physics. 2010 Jan;37(1):234-43.

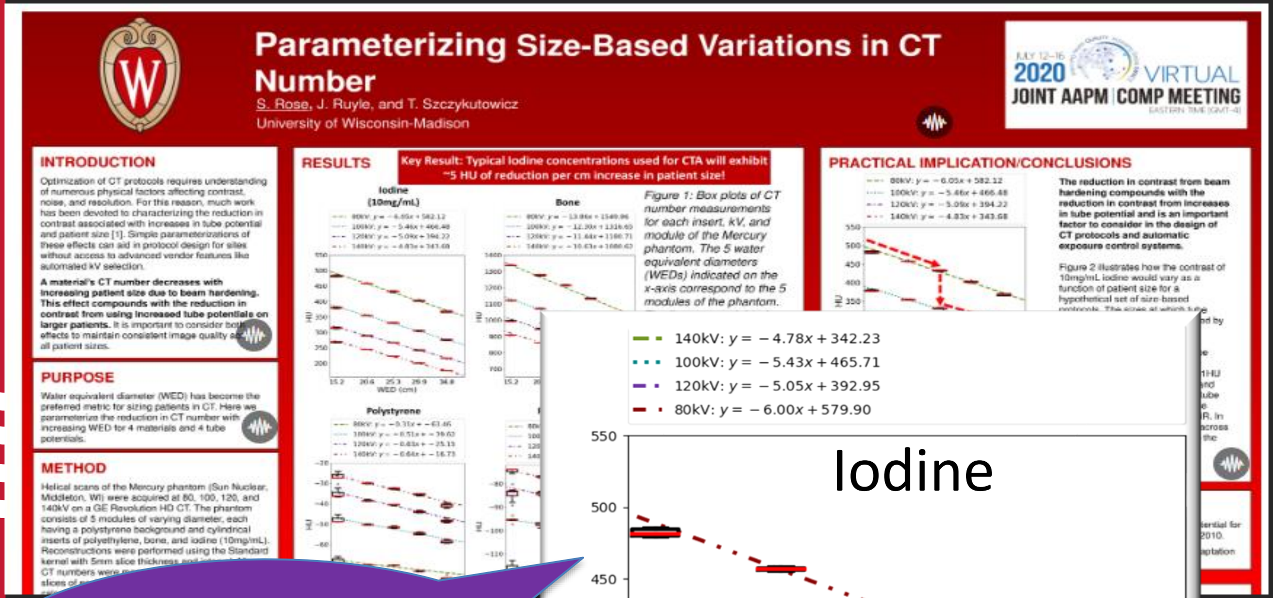
Physics-based factors affecting contrast:
1. Beam energy (kV), clinical example

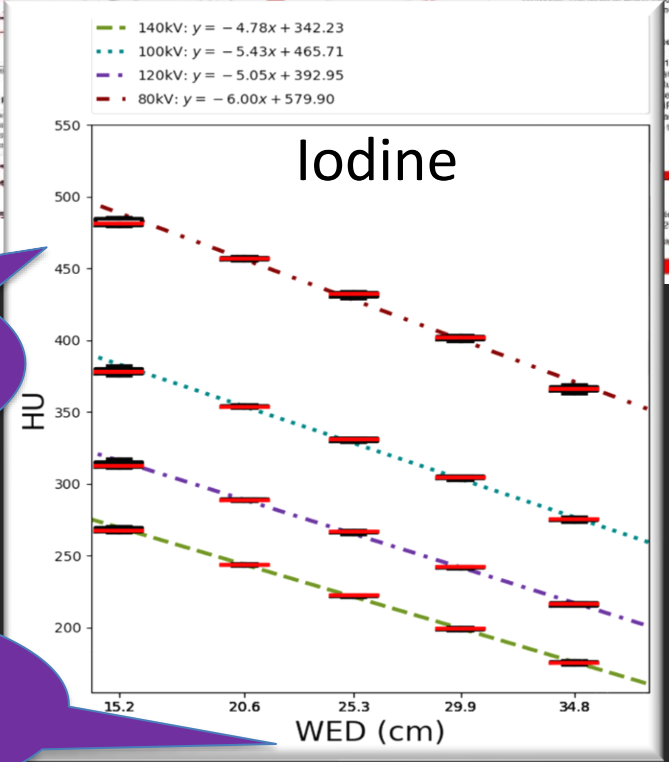


For the same iodine concentration, CT number drops with acquisition energy.

Three patients, all with similar weights, contrast volumes, and contrast administration parameters.

Physics-based factors affecting contrast:
2. beam hardening (BH) related to patient size



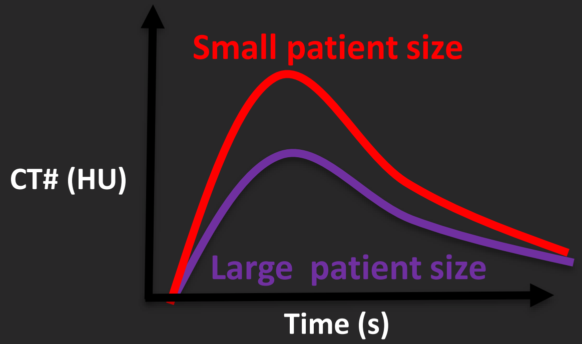


Huge reduction in CT# with changing patient size

WED = water equivalent diameter → a surrogate for patient size

Scalar factor

No effect on peak enhancement time



Same Iodine concentration + Different patient sizes = Different CT# values!

WHY ?

1. **Parameterizing Size-Based Variations in CT Number** AAPM ePosterLibrary. Rose S. 07/12/20; 302594; BReP-SNAP-I-36 Topic: Multi-detector CT

Physics-based factors affecting contrast:
2. beam hardening (BH) related to patient size

CT Number Accuracy and Association With Object Size: A Phantom Study Comparing Energy-Integrating Detector CT an Deep Silicon Photon-Counting Detector CT

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Multispecialty · Original Research

Keywords
CT number, energy integrating, photon counting, quantitative imaging, x-ray CT

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S. D. Rose receives royalties from Qaelum related to intellectual property. P. J. Pickhardt is an advisor to Bracco, Nanox, and GE Healthcare, is a consultant to Zebra Medical, and has stock and stock options from Cellectar, Elucent, and Shine. M. G. Lubner is a consultant to Farcast Biosciences, and her spouse has received previous grant funding from Philips and Ethicon. G. V. Toia is a consultant to GE Healthcare and Canon Medical Systems. R. Bujila, Z. Yin, and S. Slavic are employees of GE Healthcare. T. P. Szczykutowicz receives research support from Canon Medical Systems and GE Healthcare; receives consulting fees from Alara Imaging, Imalogix, Aidoc, and Asto CT/Leo Cancer Care; receives royalties from Medical Physics Publishing; receives royalties related to intellectual property from Qaelum; and is a founder of RadUnity. The remaining

BACKGROUND. Variable beam harden g based on patient size causes variation in CT numbers for energy-integrating de ctor (EID) CT. Photon-counting detector (PCD) CT more accurately determines eff ctive beam energy, potentially improving CT number reliability.

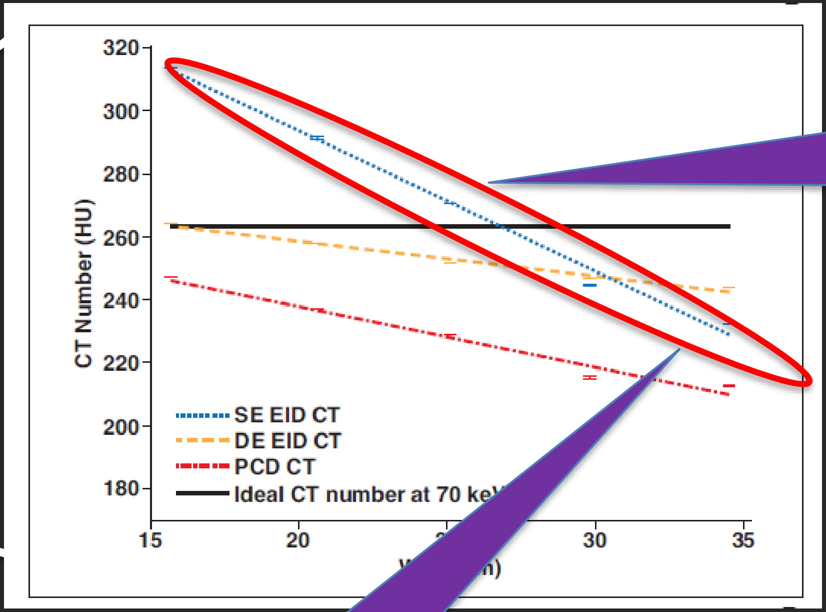
OBJECTIVE. The purp of the present study was to compare EID CT and deep silicon PCD CT in terms o oth the effect of changes in object size on CT number and the overall accuracy of numbers.

METHODS phantom with polyethylene rings of varying sizes (mimicking patient sizes) as w as inserts of different materials was scanned on an EID CT scanner in single-en (SE) mode (120-kV images) and in rapid-kilovoltage-switching dual-energy (DE) mode (70- ages) and on a prototype deep silicon PCD CT scanner (70-keV images). ROIs were placed to re the CT numbers of the materials. Slopes of CT number as a function of object size were puted. Materials' ideal CT number at 70 keV was computed using the National Institute of rds and Technology XCOM Photon Cross Sections Database. The root mean square error ( ) between measured and ideal numbers was calculated across object sizes.

RESULTS. Slope (expressed as Hounsfield units per centimeter) was sign ntly closer to zero (i.e., less variation in CT number as a function of size) for PCD CT than for SE EID CT for air (1.2 vs 2.4 HU/cm), water (−0.3 vs −1.0 HU/cm), iodine (−1.1 vs −4.5 HU/cm), and bone (−2.5 vs −10.1 HU/cm) and for PCD CT than for DE EID CT for air (1.2 vs 2.8 HU/cm), water (−0.3 vs −1.0 HU/cm), polystyrene (−0.2 vs −0.9 HU/cm), iodine (−1.1 vs −1.9 HU/cm), and bone (−2.5 vs −6.2 HU/cm) ($p < .05$). For all tested materials, PCD CT had the smallest RMSE, indicating CT numbers closest to ideal numbers; specifically, RMSE (expressed as Hounsfield units) for SE EID CT, DE EID CT, and PCD CT was 32, 44, and 17 HU for air; 7, 8, and 3 HU for water; 9, 10, and 4 HU for polystyrene; 31, 37, and 13 HU for iodine; and 69, 81, and 20 HU for bone, respectively.

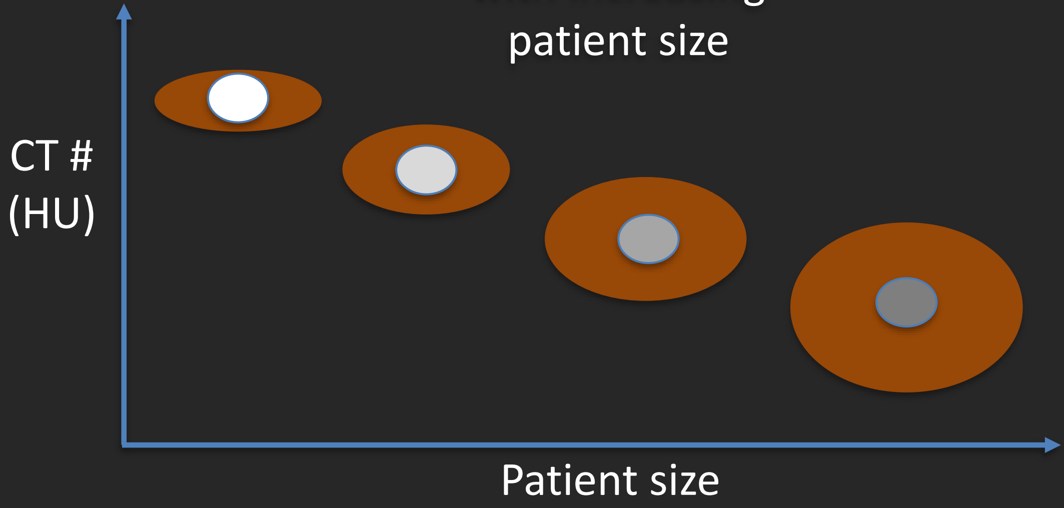
CONCLUSION. For numerous materials, deep silicon PCD CT, in comparison with SE EID CT and DE EID CT, showed lower CT number variability as a function of size and CT numbers closer to ideal numbers.

CLINICAL IMPACT. Greater reliability of CT numbers for PCD CT is important given the dependence of diagnostic pathways on CT numbers.



Great variability on iodine CT# with increasing water equivalent diameter (WED) of patients.

CT # decreases with increasing patient size

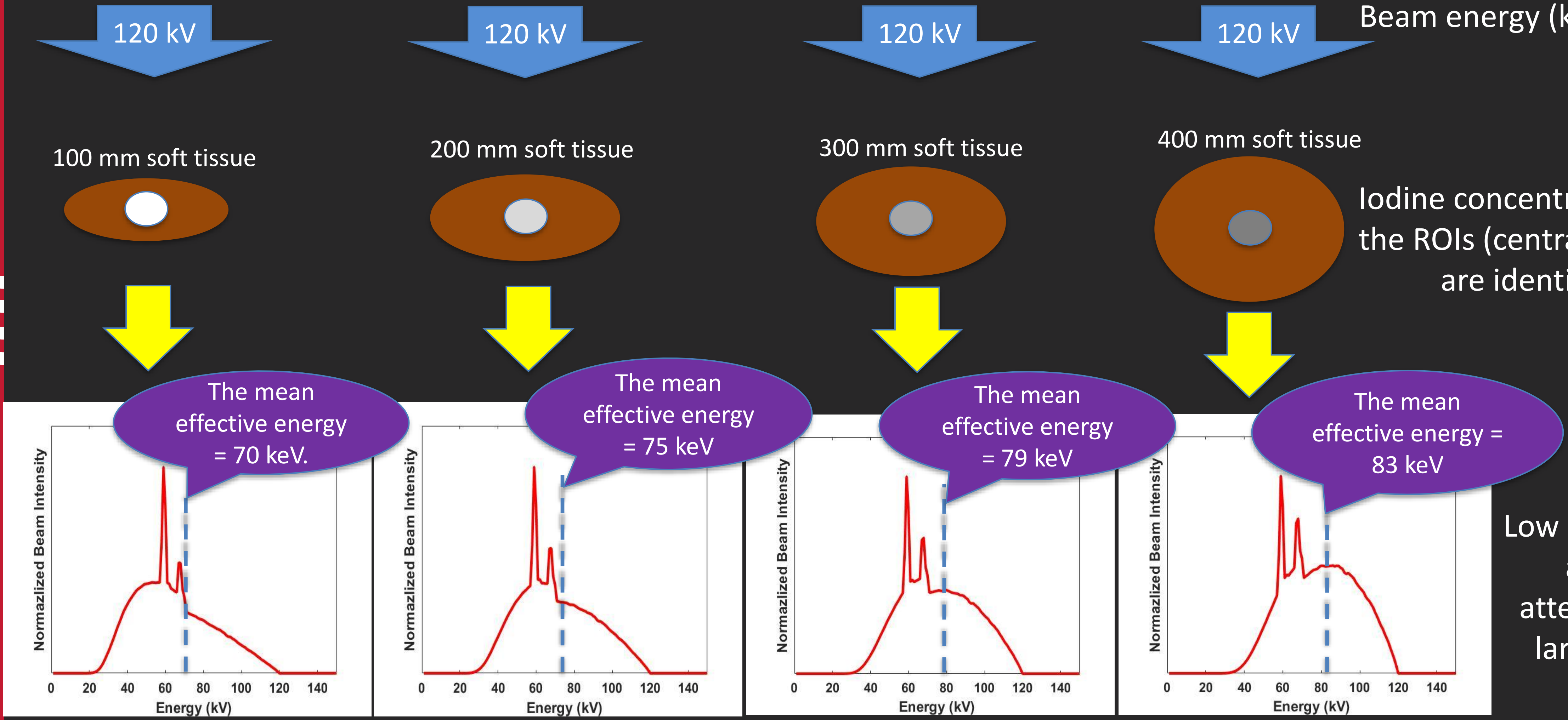


At 120 kV, "rule of thumb" iodine contrast goes down by 4.5 HU per cm of WED

1. Salyapongse AM, Rose SD, Pickhardt PJ, et al. CT Number Accuracy and Association With Object Size: A Phantom Study Comparing Energy-Integrating Detector CT and Deep Silicon Photon-Counting Detector CT. AJR 2023; 221(4):539-47.

Physics-based factors affecting contrast: 2. beam hardening (BH) related to patient size

Beam energy (kV) is identical



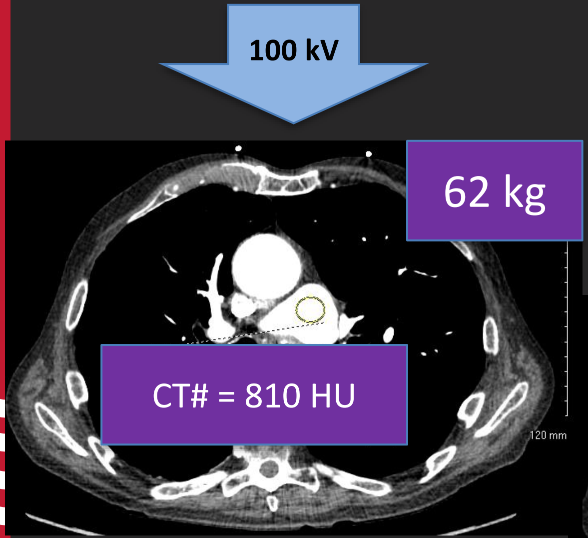
Iodine concentrations in the ROIs (central circles) are identical

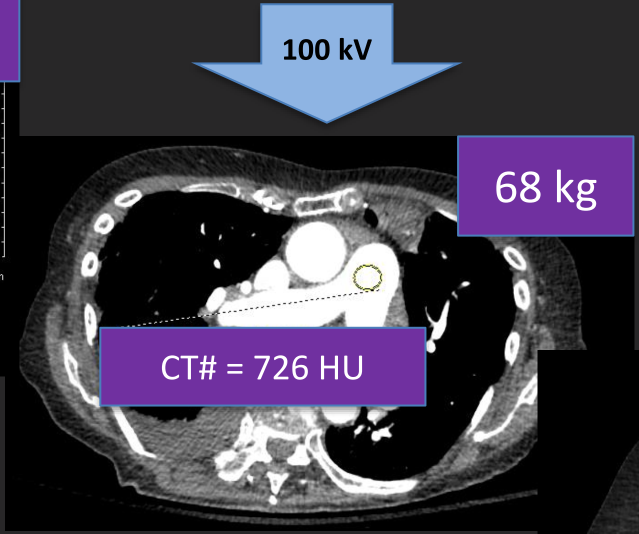
Low energy X-rays are more attenuated by a larger patient

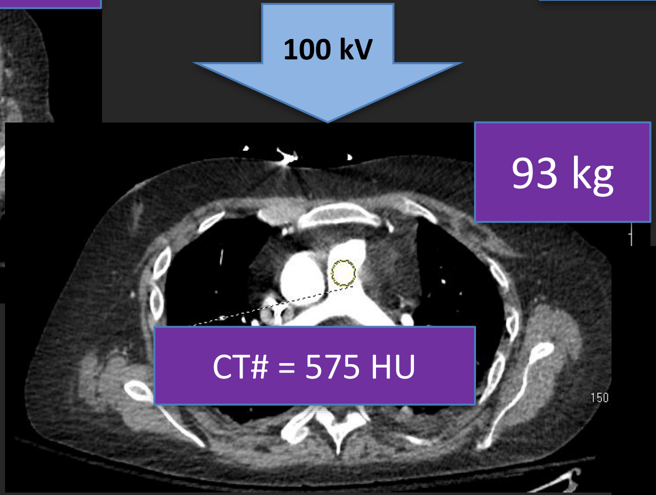
Beam hardening: the gradual increase of average x-ray beam energy as it passes through more patient tissue.

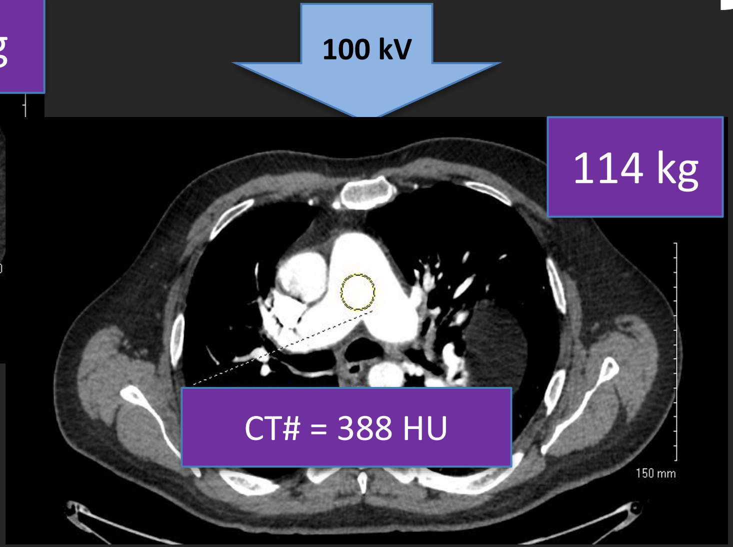
1. Schindera ST, Tock I, Marin D, et al. Effect of beam hardening on arterial enhancement in thoracoabdominal CT angiography with increasing patient size: an in vitro and in vivo study. Radiology 2010; 256(2):528-35

Physics-based factors affecting contrast:
2. beam hardening (BH) related to patient size, clinical example









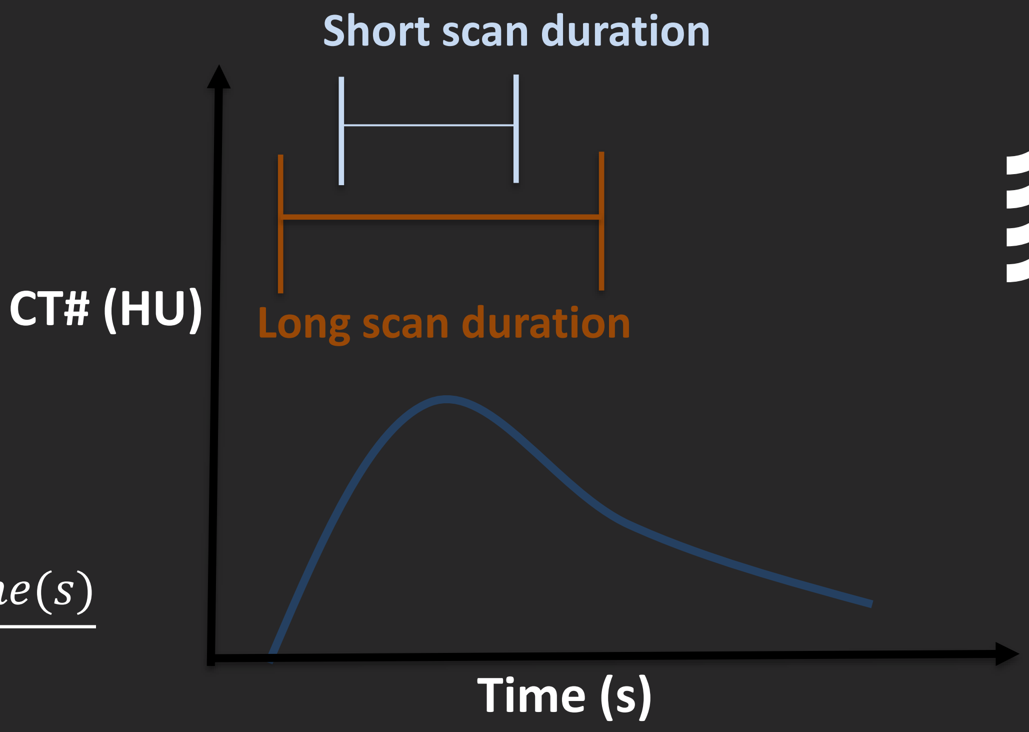
For the same iodine concentration, CT number drops with patient size.

Three patients with similar contrast volumes and contrast administration parameters.

Physics-based factors affecting contrast:
3. Scan duration

Scan duration doesn't change the form or scaling of the contrast enhancement curve, it changes how we sample it.

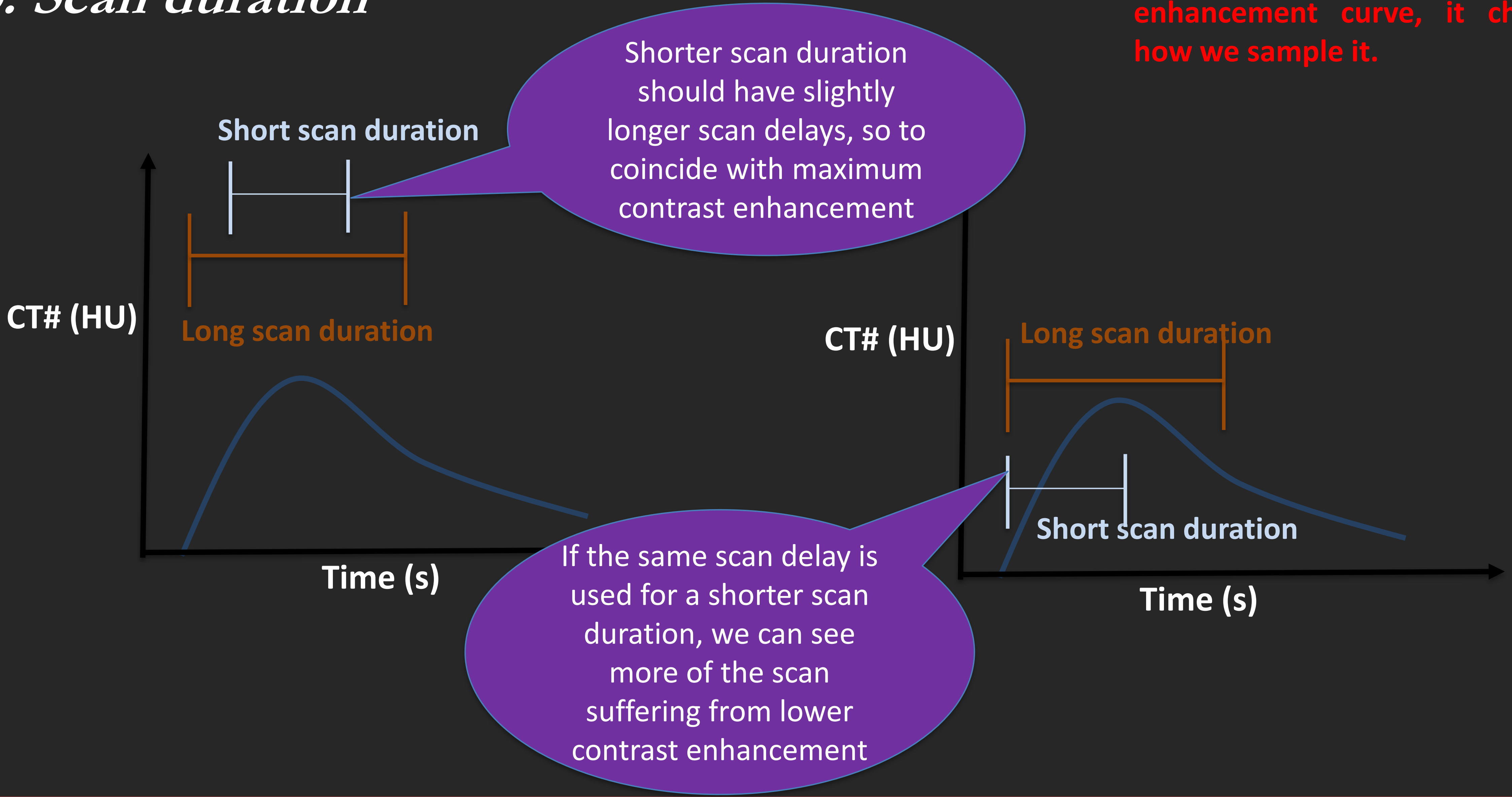
$$\text{Scan Duration(s)} = \frac{Scan\ Range(mm) * Rotation\ time(s)}{Pitch * Collimation\ (mm)}$$



1. Szczykutowicz T. The CT handbook: optimizing protocols for today's feature-rich scanners, 2020
2. Bae KT. Intravenous contrast medium administration and scan timing at CT: considerations and approaches. Radiology. 2010 Jul;256(1):32-61

Physics-based factors affecting contrast: 3. Scan duration

Scan duration doesn't change the form or scaling of the contrast enhancement curve, it changes how we sample it.



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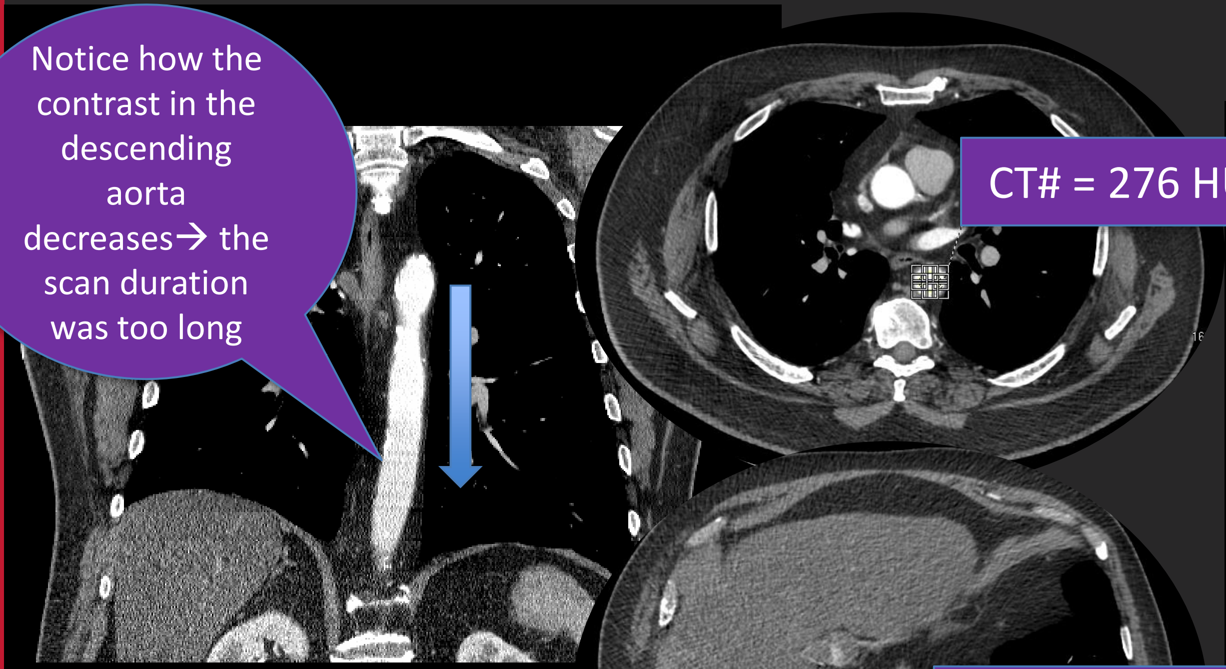
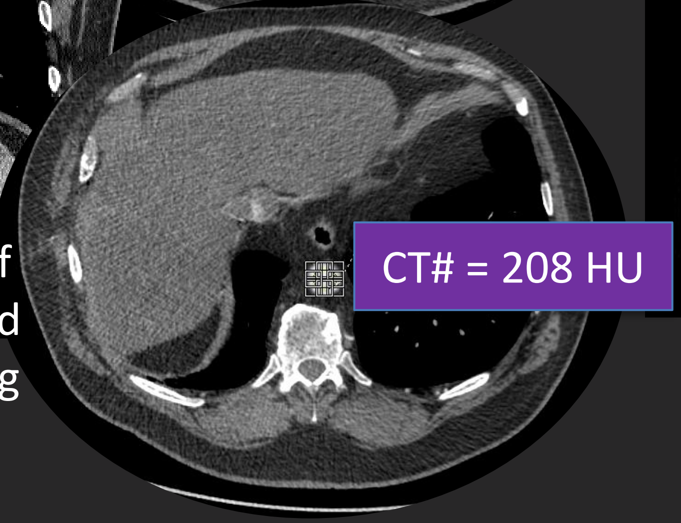
2. Bae KT. Intravenous contrast medium administration and scan timing at CT: considerations and approaches. Radiology. 2010 Jul;256(1):32-61

Physics-based factors affecting contrast:
3. Scan duration, clinical example

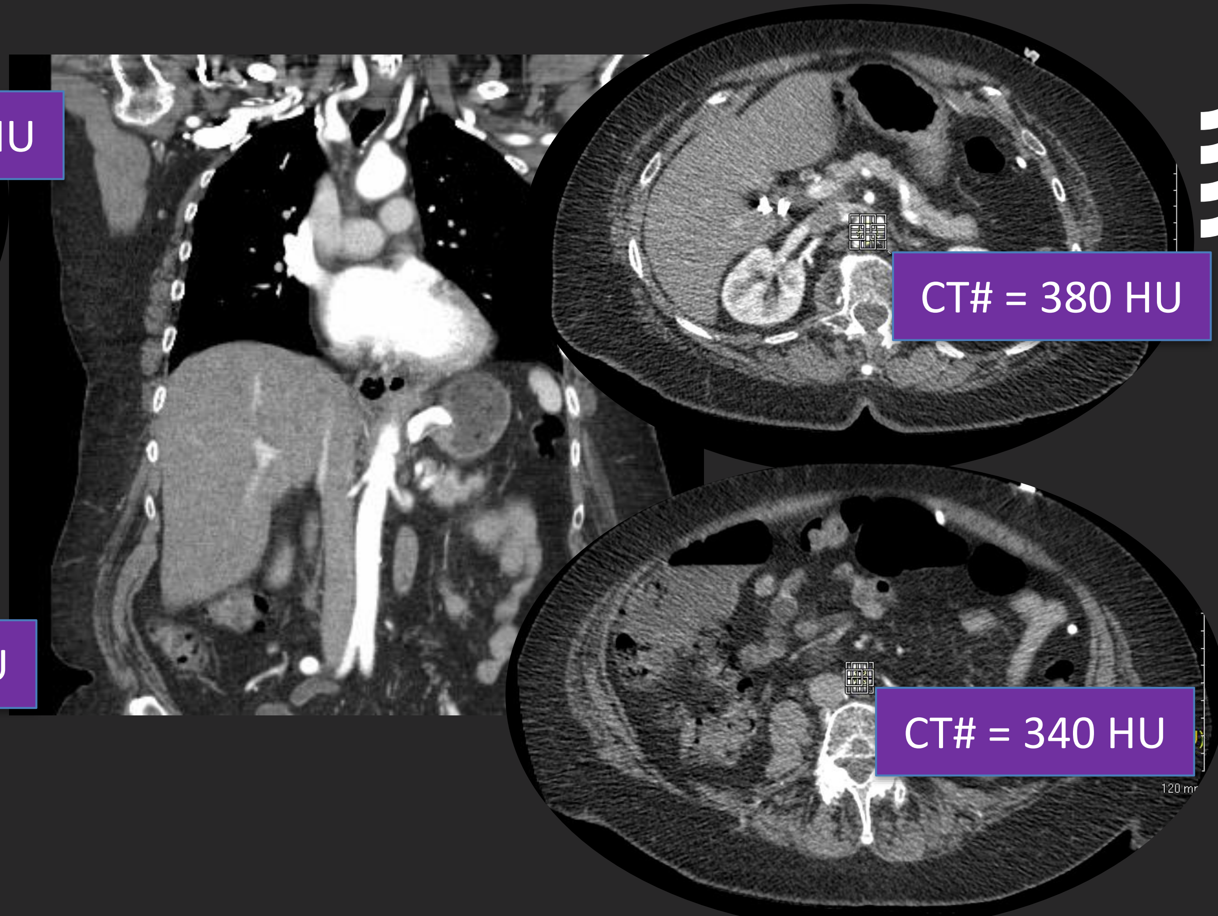
In this retrospective gated chest/abdomen exam, the scan duration was too long and eventually the contrast enhancement decreased, as shown



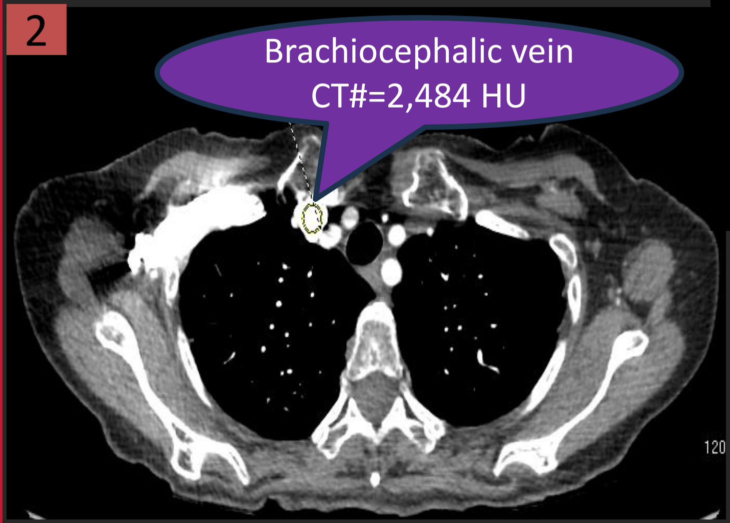


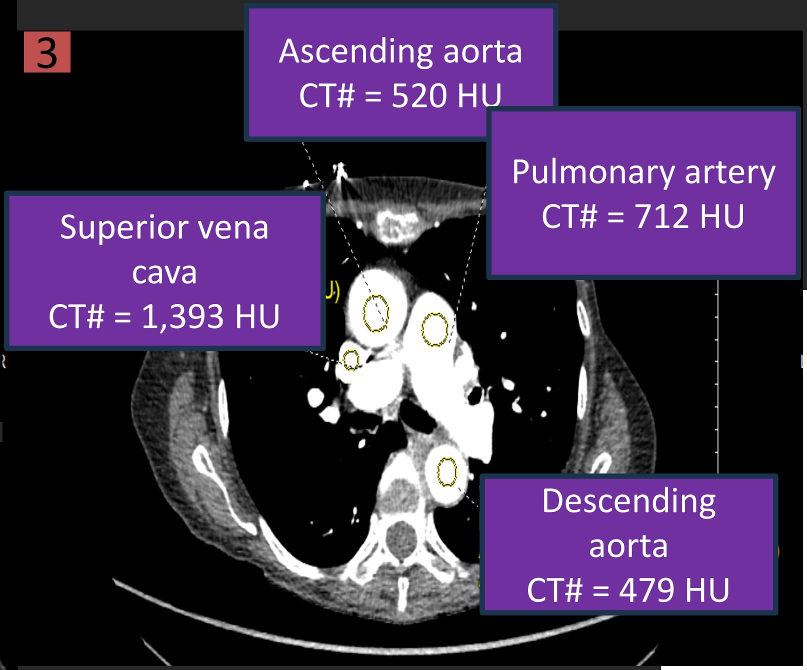
Blue arrow shows direction of scan (i.e., increasing time) and you can appreciate decreasing enhancement shown in descending aorta

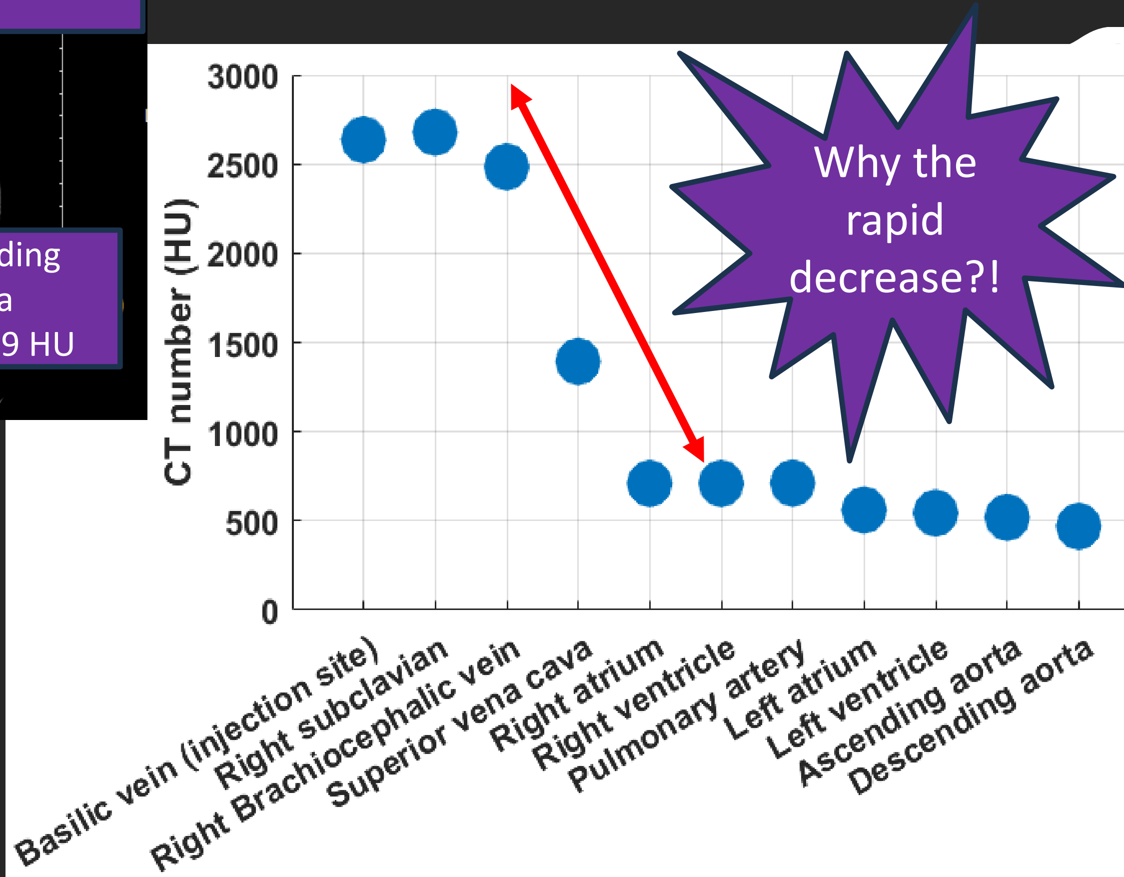
In this retrospective gated chest/abdomen exam, the scan duration was appropriate for the bolus duration. The contrast enhancement was constant through the aorta as shown



Patient-related factors affecting contrast: 1. Blood volume







Patient-related factors affecting contrast:
1. Blood volume

CT enhancement is linear with iodine concentration

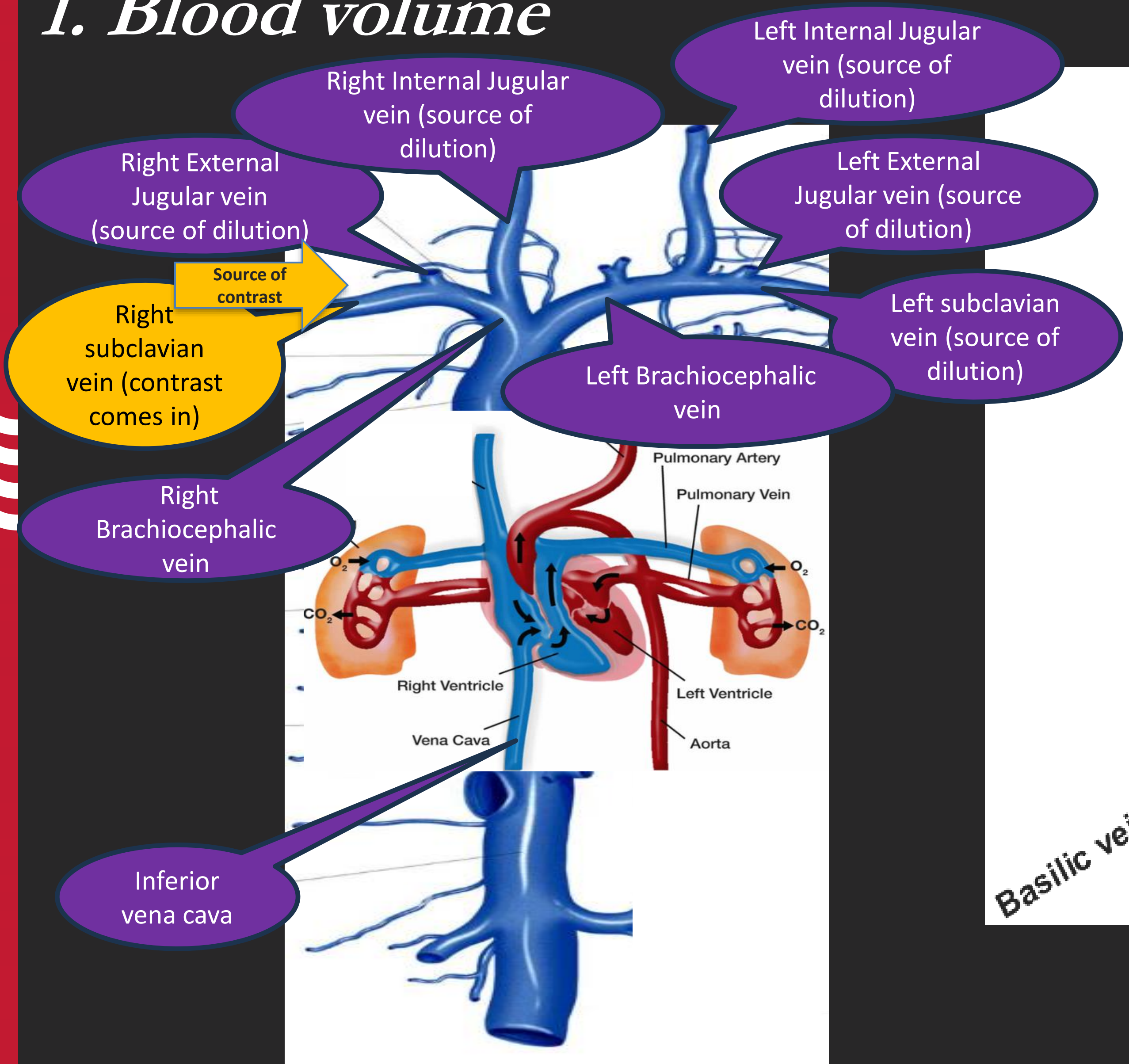
+

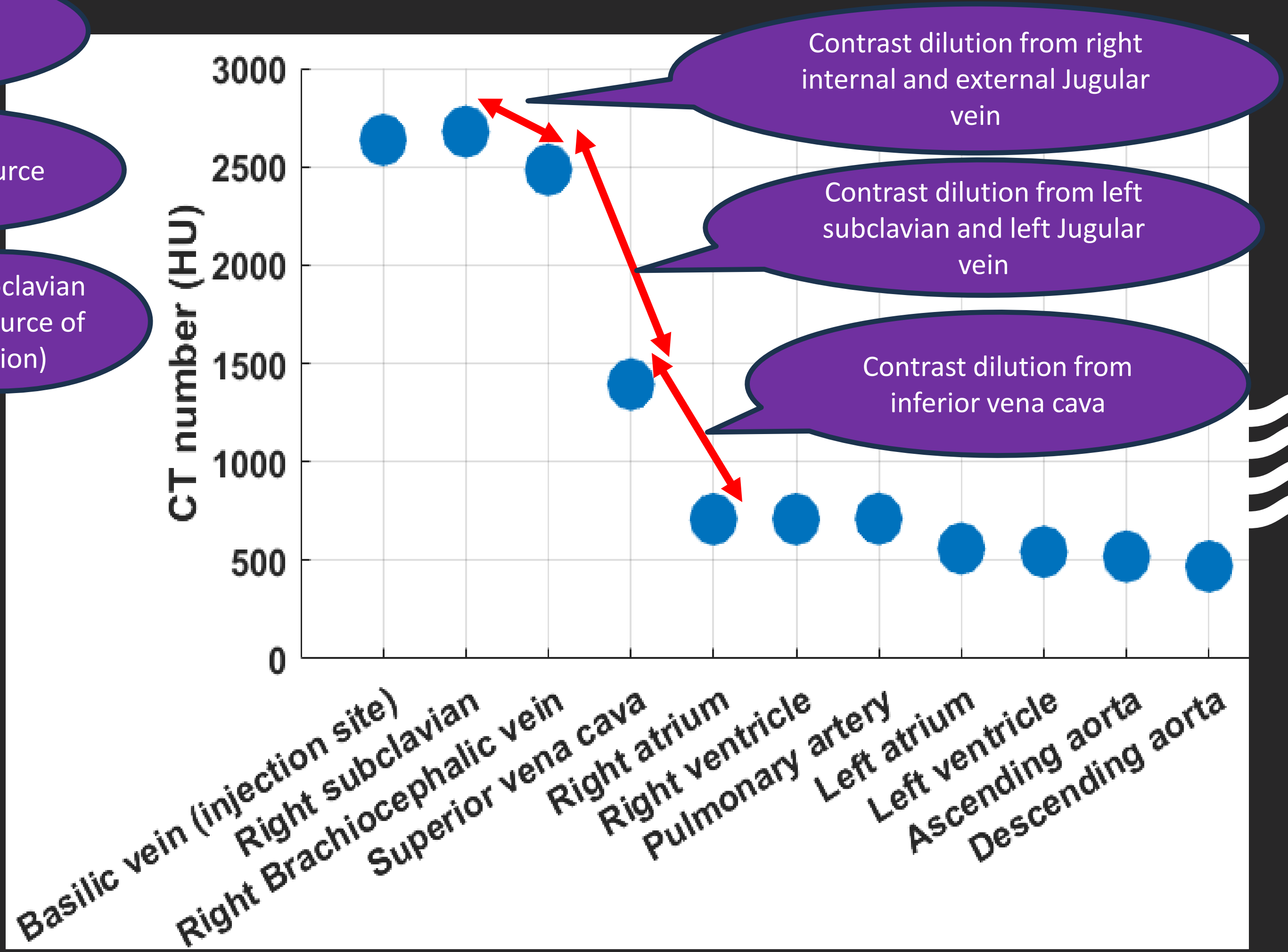
As contrast travels from injection site (e.g., antecubital vein) to the right side of the heart it gets diluted from other veins also heading into the right atrium

=

We see a large decrease in CT enhancement as contrast moves from the injection site through the heart and lungs.
Additionally, contrast gets diluted when entering organ parenchyma.

Patient-related factors affecting contrast:
1. Blood volume





1. Feldschuh J, Enson Y. Prediction of the normal blood volume. Relation of blood volume to body habitus. Circulation. 1977 Oct;56(4):605-12.
2. Ho LM, Nelson RC, DeLong DM. Determining contrast medium dose and rate on basis of lean body weight: does this strategy improve patient-to-patient uniformity of hepatic enhancement during multi–detector row CT?. Radiology. 2007 May;243(2):431-7.

Patient-related factors affecting contrast:
1. Blood volume

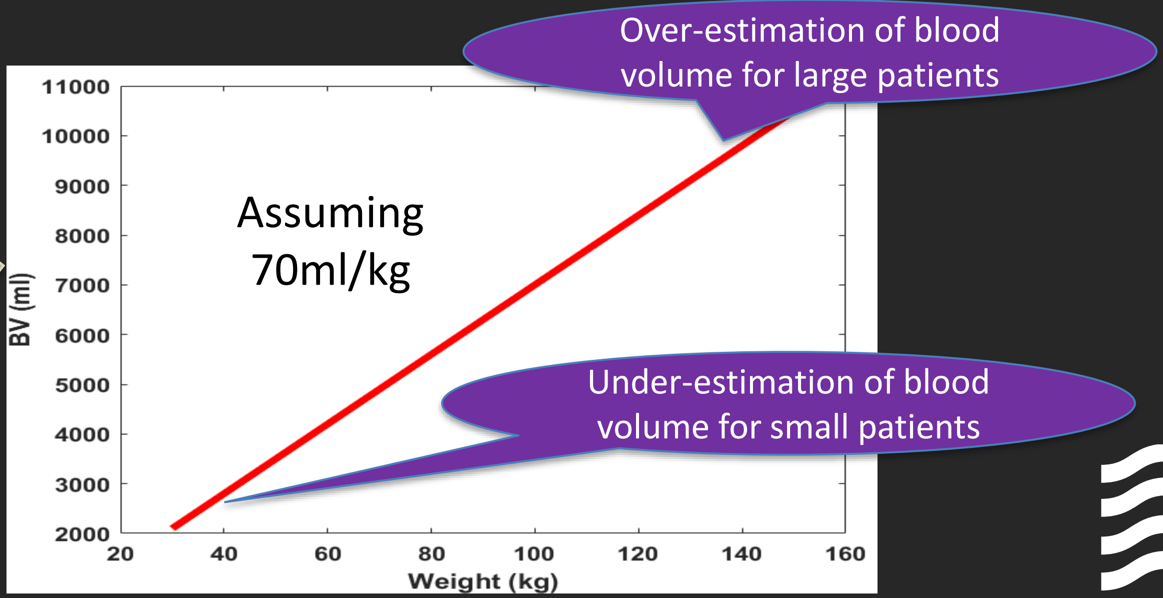
Total blood volume increases with body weight primarily because larger Lean body mass and organ size require a greater volume of blood to ensure proper circulation and oxygen delivery to tissues.

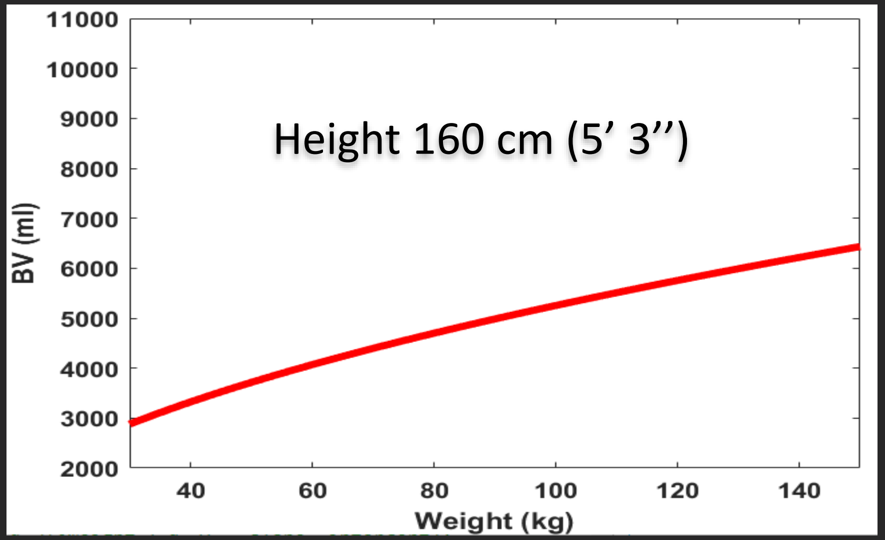
BV is not related by a constant ratio to weight alone. This undoubtedly reflects variations in body composition which are not included by absolute weight. organ/fat/muscle/bone ratio (all of which have different vascular and interstitial space in the tissue and thus contributes differently to dispersing or diluting the contrast material) is not equal with patient weight.

Estimation of blood volume (mk/kg) over a wide range of patient body weight was made possible by Lemmens and Brodsky equation:

$$BV_{In}\left(\frac{ml}{kg}\right) = \frac{70}{\sqrt{\frac{BMI}{22}}}$$

$$\text{Total BV}(ml) = \frac{70}{\sqrt{\frac{BMI}{22}}} * \text{Weight (kg)}$$





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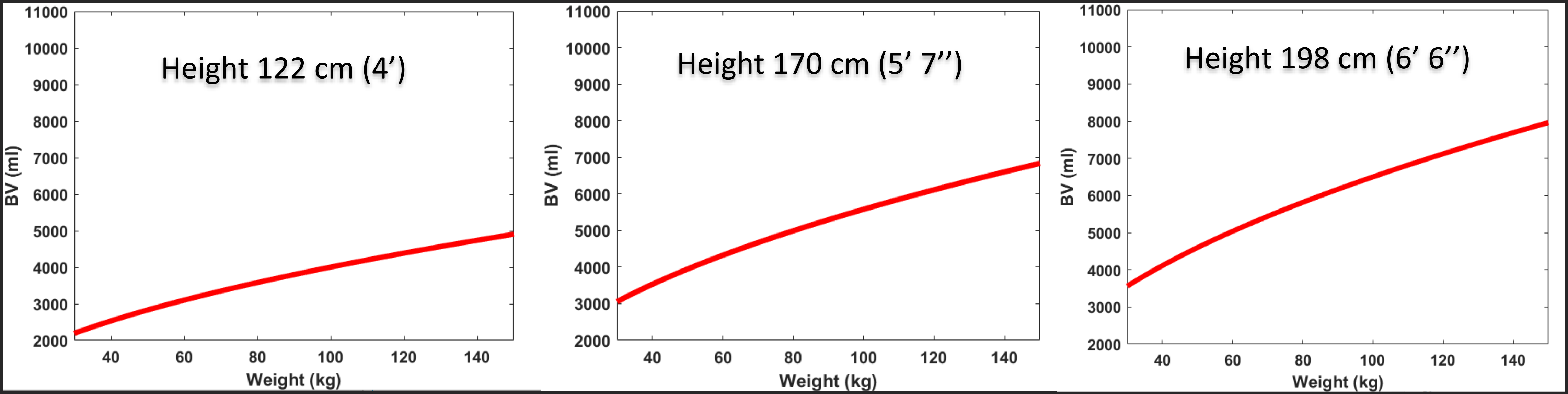
Patient-related factors affecting contrast:
1. Blood volume

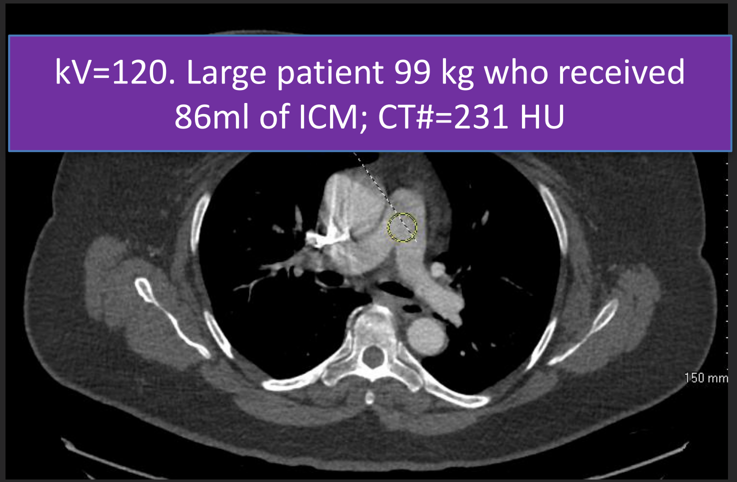


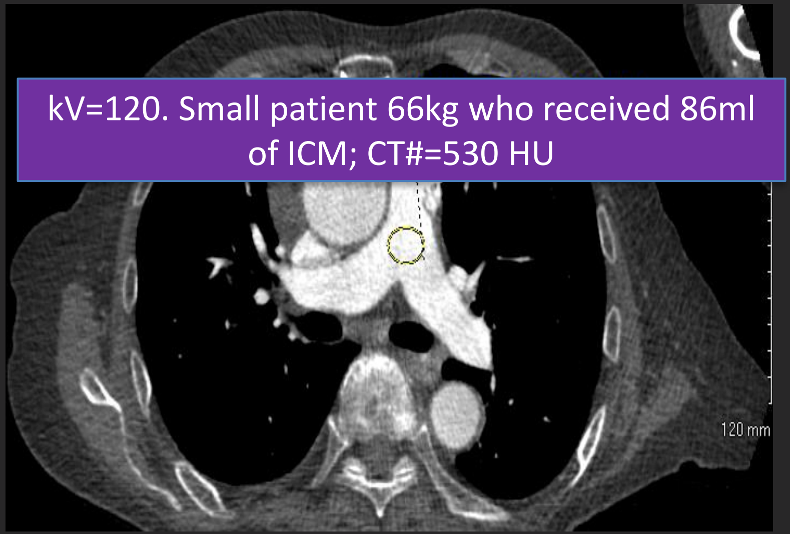
BMI is not a comprehensive measure for contrast agent dilution. As height increases for the same weight, BMI decreases, but blood volume increases (i.e., contrast dilution).

Patient-related factors affecting contrast:
1. Blood volume

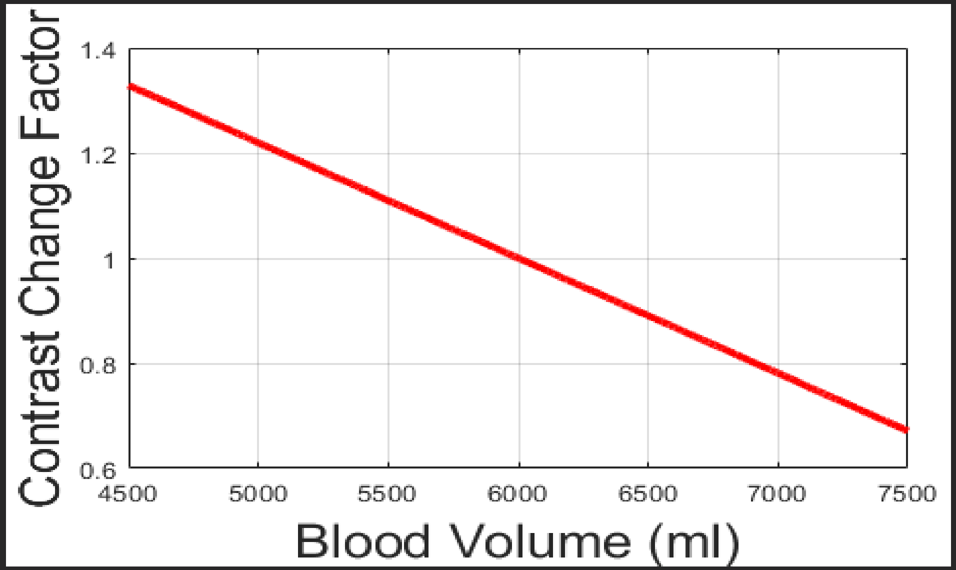
Scalar factor

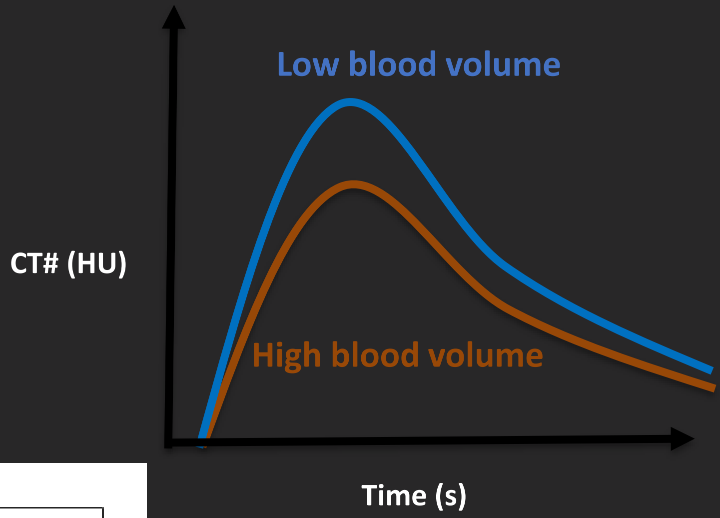
No effect on peak enhancement time





Effect of blood volume on contrast enhancement is derived from Schoellnast *et al.* 2006 shown below



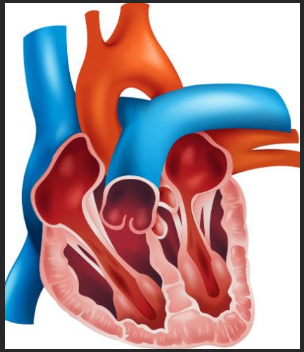


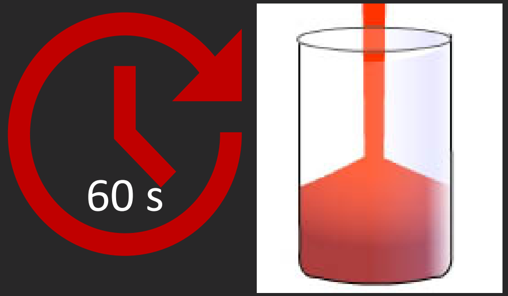
1. Schoellnast H, Deutschmann HA, Berghold A, Fritz GA, Schaffler GJ, Tillich M. MDCT angiography of the pulmonary arteries: influence of body weight, body mass index, and scan length on arterial enhancement at different iodine flow rates. American journal of roentgenology. 2006 Oct;187(4):1074-8

Patient-related factors affecting contrast: 2. Cardiac output

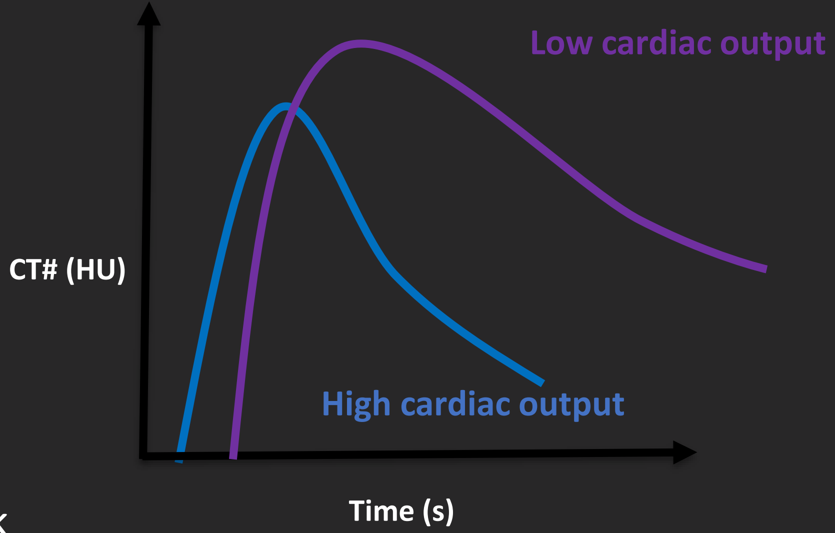
Temporal factor affecting contrast

Cardiac output: the volume of blood pumped by the heart in a 60 s interval.





Cardiac output (ml)=heart rate (BPM)*stroke volume (amount of blood ejected from the ventricle during one heartbeat)



Low cardiac output → circulation of ICM slows, ICM arrives and clears slowly → delayed time to peak enhancement

Low cardiac output → slower clearance of ICM → higher and prolonged peak aortic and parenchymal enhancement

Low cardiac output → Contrast enhancement increases because less un-opacified blood mixes with ICM when the cardiac output is low

No specific model

Understanding the other variables presented helps interpret cardiac output's effect on enhancement.

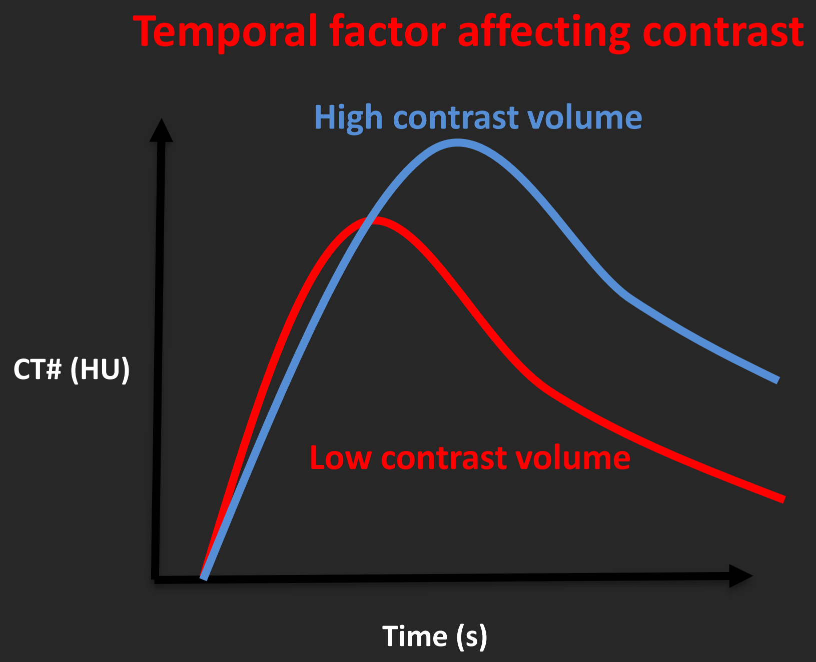
1. Bae KT. Intravenous contrast medium administration and scan timing at CT: considerations and approaches. Radiology. 2010 Jul;256(1):32-61

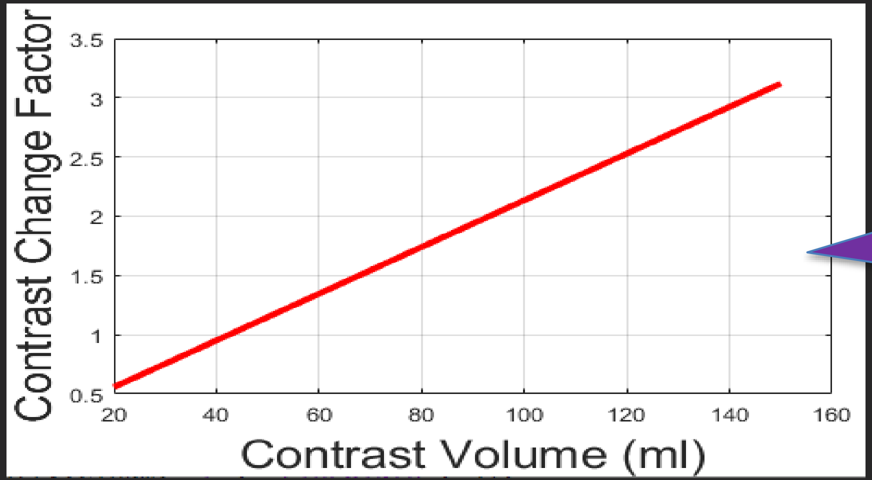
Contrast Protocol-based factors affecting contrast:
1. Contrast volume

High contrast volume→ high peak arterial enhancement

High contrast volume with fixed injection rate→ increased time to peak enhancement

As contrast volume increases, the injection duration (i.e., bolus length) increases linearly





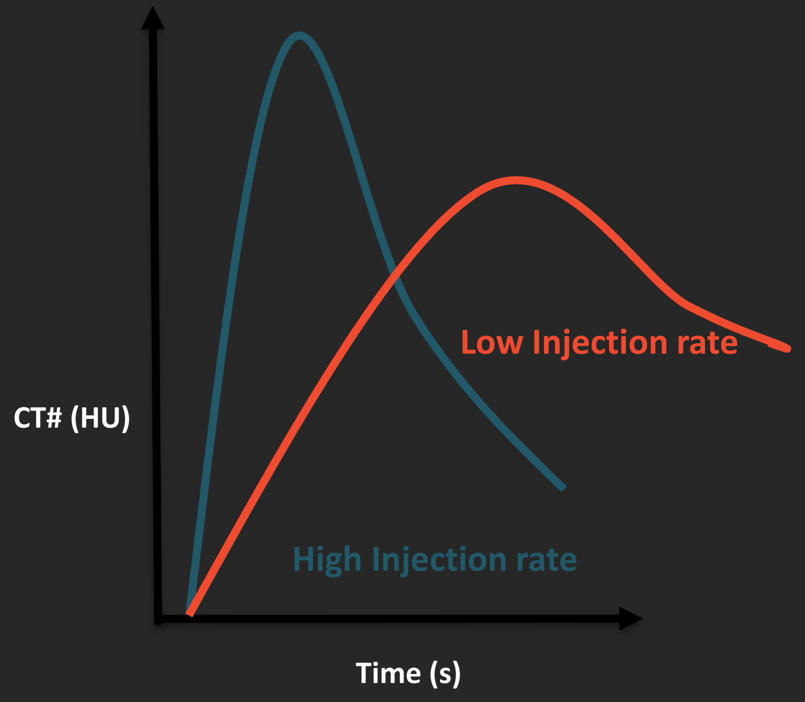
For a fixed patient size, we see a roughly linear increase in enhancement with contrast volume

1. Holmquist F, Hansson K, Pasquariello F, Björk J, Nyman U. Minimizing contrast medium doses to diagnose pulmonary embolism with 80-kVp multidetector computed tomography in azotemic patients. Acta radiologica. 2009 Jan 1;50(2):181-93

Contrast Protocol-based factors affecting contrast:

2. Injection rate

Temporal factor affecting contrast

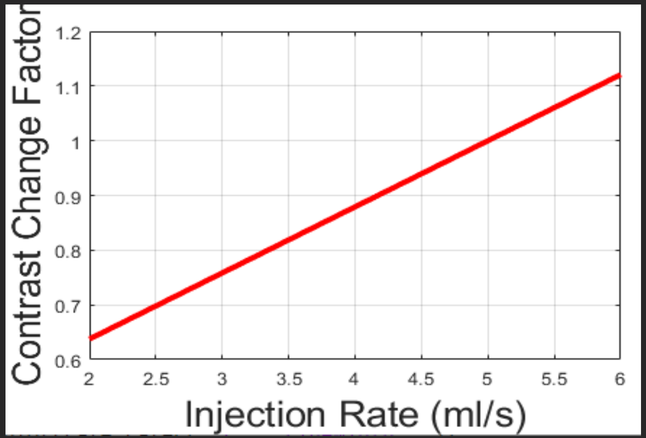


High injection rate → Increased peak arterial enhancement

High injection rate → Decreased time to peak arterial enhancement.

Higher injection rate → Reduces potential temporal window for CT scanning (i.e., peak of contrast plateau is shorter)

For delayed phases, injection rate has little to no effect on enhancement



we see a roughly linear increase in peak arterial enhancement with injection rate

1. Kim T, Murakami T, Takahashi S, Tsuda K, Tomoda K, Narumi Y, Oi H, Nakamura H. Effects of injection rates of contrast material on arterial phase hepatic CT. AJR. American journal of roentgenology. 1998 Aug;171(2):429-32

Contrast Protocol-based factors affecting contrast: 3. Iodine concentration

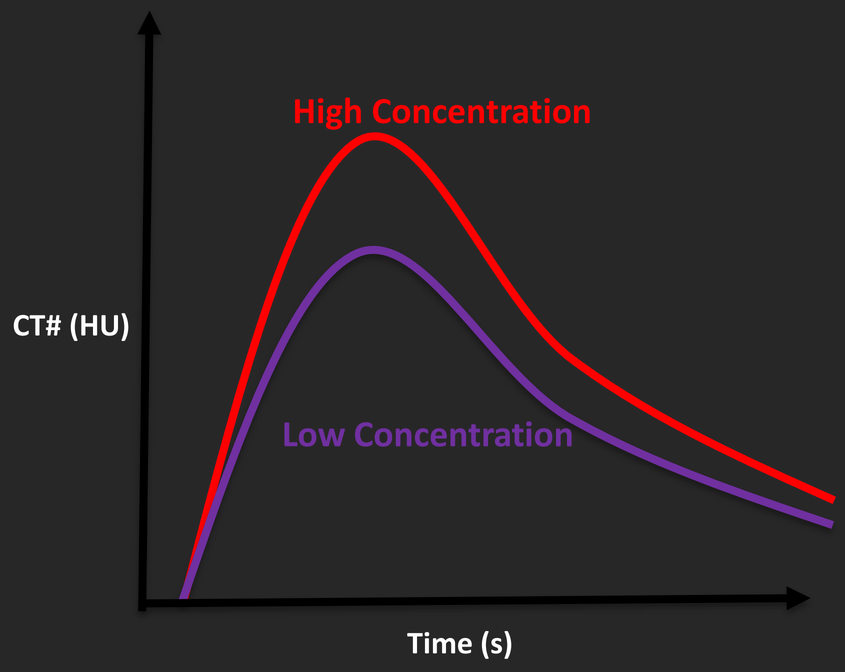
We usually use higher concentration ICM for arterial studies.

Change in enhancement is equal to the ratio of the change in contrast agent concentration if everything else is held fixed and total iodine mass changes in proportion to ICM concentration.

For example, if a patient ROI measures 100 HU when using 300 mgI/ml and we keep everything the same and repeat the scan using 370 mgI/ml, we would measure an enhancement of 100 HU * 370/300 = 123 HU

If we change ICM concentration and keep the volume fixed, the total iodine mass to the patient changes proportional to the change in ICM concentration.

Scalar factor affecting contrast



1. Bae KT. Intravenous contrast medium administration and scan timing at CT: considerations and approaches. Radiology. 2010 Jul;256(1):32-61

Contrast Protocol-based factors affecting contrast: 3. Iodine concentration

To keep total iodine mass constant when changing ICM concentration:

$$\text{New ICM volume (ml)} = \frac{Original\ ICM\ Volume(ml) * Original\ ICM\ Conc.(mgI/ml)}{New\ ICM\ Conc.(mgI/ml)}$$

Change in ICM concentration	
Keep total iodine mass prescription fixed (i.e., total mass of iodine in mg)	Allow iodine mass to change in proportion to ICM concentration
Time to peak enhancement is decreased/increased when ICM concentration increases/decreases	No effect on peak enhancement time with fixed volume, rate and injection duration.

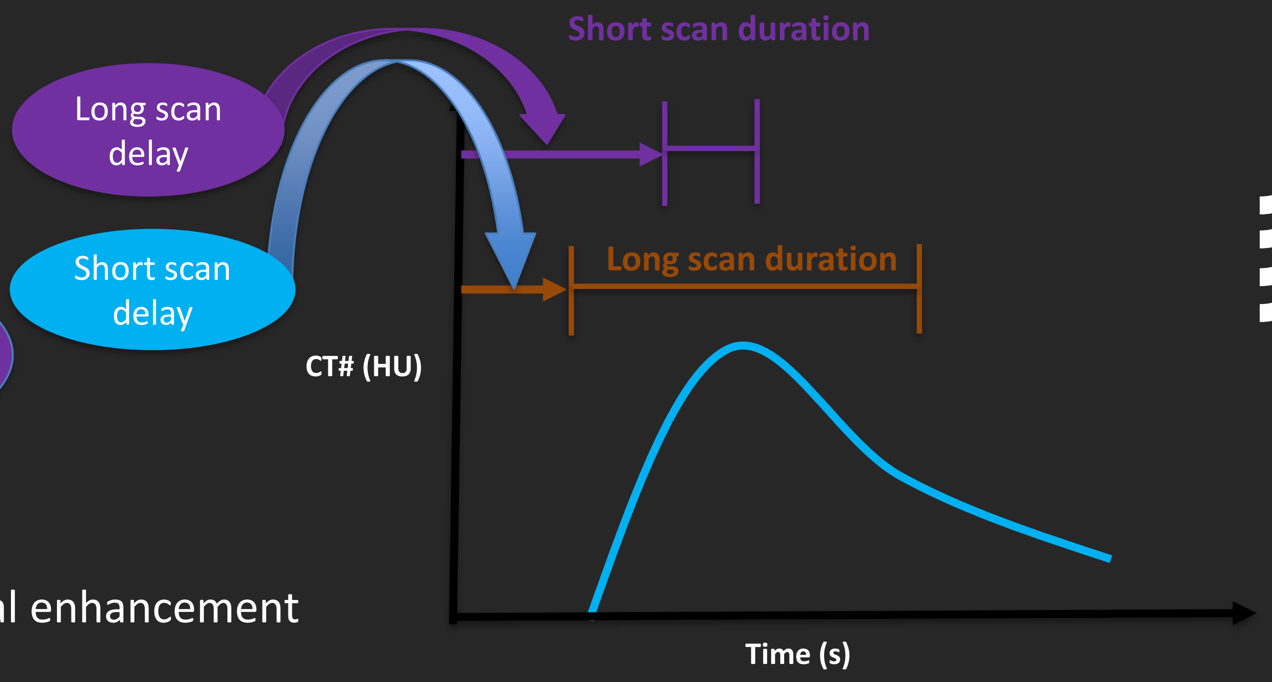
1. Bae KT. Intravenous contrast medium administration and scan timing at CT: considerations and approaches. Radiology. 2010 Jul;256(1):32-61

Contrast Protocol-based factors affecting contrast:
4. Scan delay

Scan delay doesn't change the form or scaling of the contrast enhancement curve, it changes how we sample it.

$$\text{Optimal Scan Delay} = T_{Peak} - \frac{1}{2}T_{scan\ duration}$$

Anatomy and indication specific (i.e., for abdominal CTA this may be from an ROI in the aorta, for parenchymal liver it would be an ROI in liver)



Peak enhancement need to be optimized based on optimal enhancement time and scan duration

If scan delay is not set properly, peak enhancement can be missed.

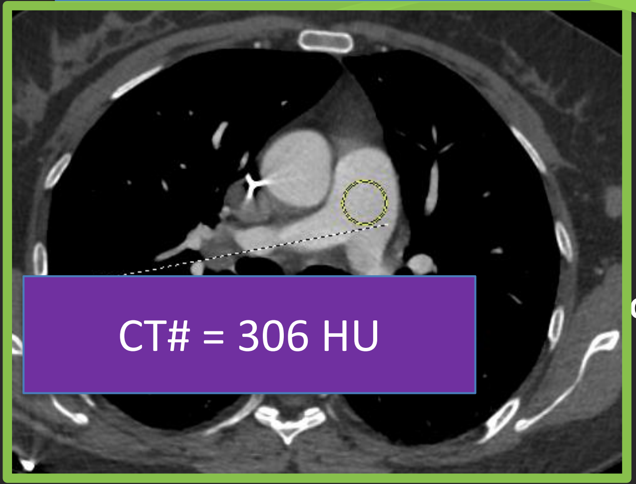
1. Bae KT. Intravenous contrast medium administration and scan timing at CT: considerations and approaches. Radiology. 2010 Jul;256(1):32-61

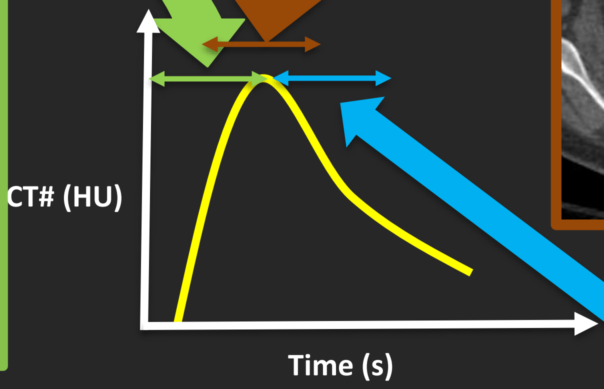
2. Szczykutowicz T. The CT handbook: optimizing protocols for today's feature-rich scanners, 2020

Contrast Protocol-based factors affecting contrast:
4. Scan delay

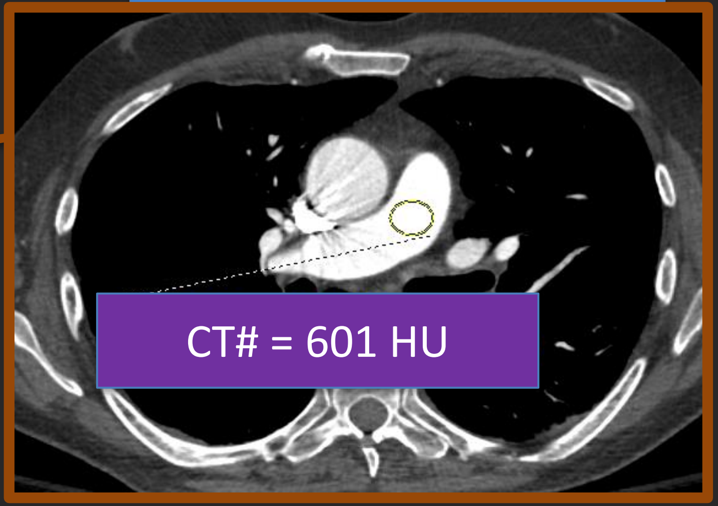
Everything fixed between these three images except **scan delay**

CT pulmonary angiography was performed **too early**

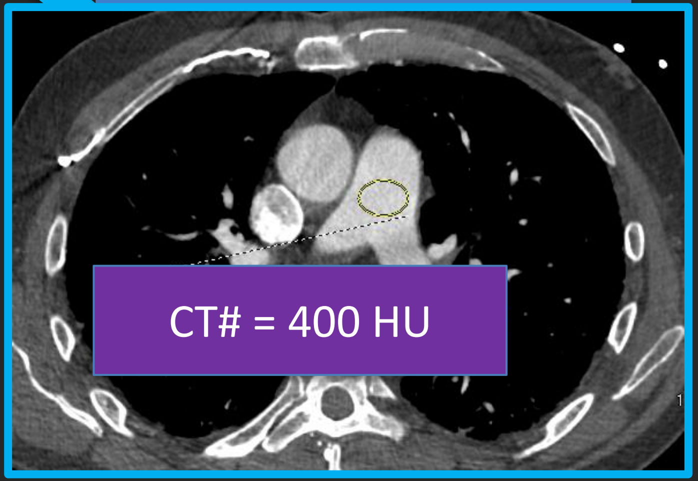




Well-timed CT pulmonary angiography



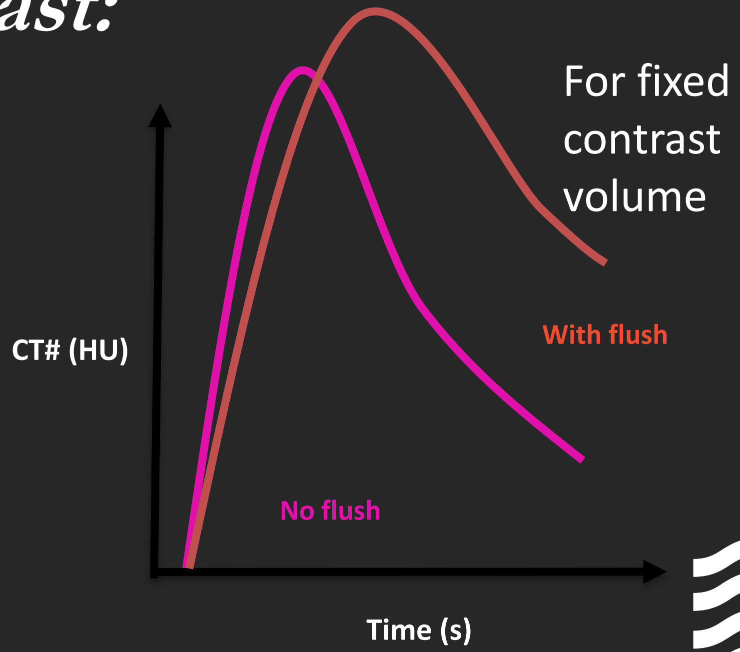
CT pulmonary angiography was performed **too late**



Beam energy = 80 kV
Weight: ~57 kg
Contrast Volume = 86 ml
Saline flush = 20 ml
Injection rate = 5 ml/s
Iodine concentration= 350 mgI/ml

Contrast Protocol-based factors affecting contrast: 5. Saline flush

Temporal factor affecting contrast



Saline flush (aka "chaser") is a saline injection immediately following a contrast injection.

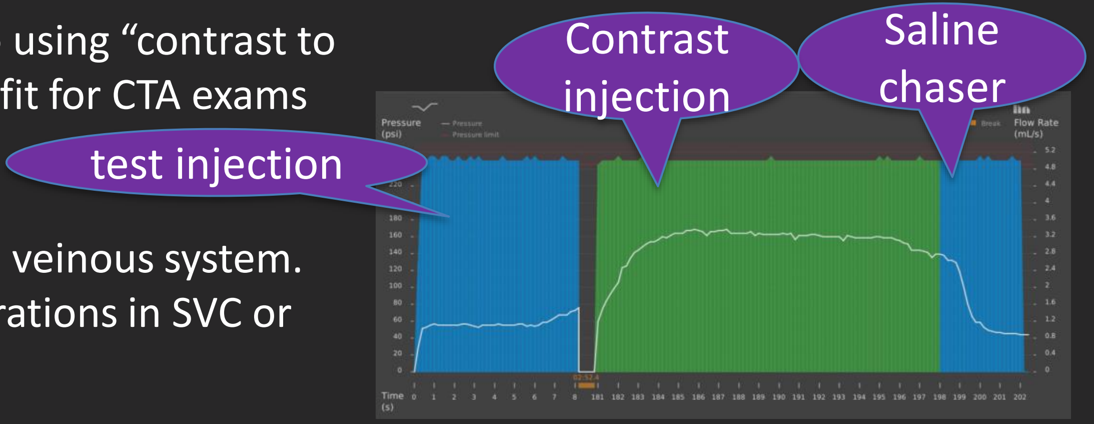
When we use a flush, we see a prolonged time to peak arterial HU compared to non-flush.

Use of 20-30 ml of saline flush leads to a 5-10% increase in peak arterial enhancement.

Contrast can be reduced with use of a flush. For volumes up to ~30 ml, contrast agent can be traded with saline volume to keep peak arterial enhancement constant.

We can think of the flush as “saline pushing the contrast” as opposed to using “contrast to push the contrast” from injector to the heart. This is why we see a benefit for CTA exams and little benefit for parenchymal phase exams.

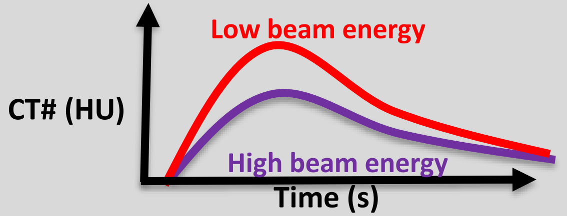
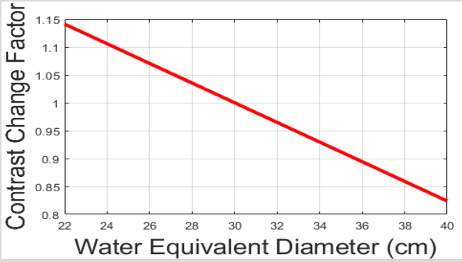
Usually used on CTA exams to make sure iodine is not wasted and left in veinous system. It can reduce ICM streak artifact issues when ICM is left in high concentrations in SVC or other vessels in a patient’s arm or upper thorax.

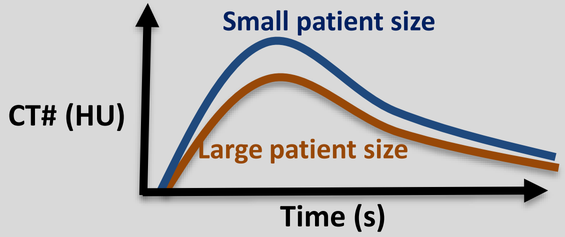
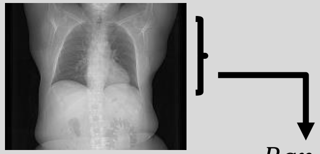
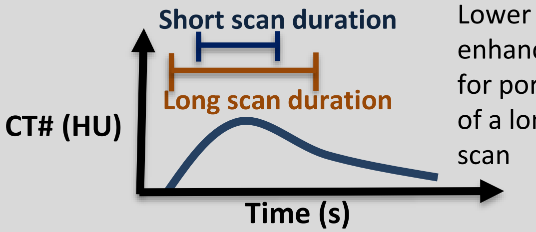


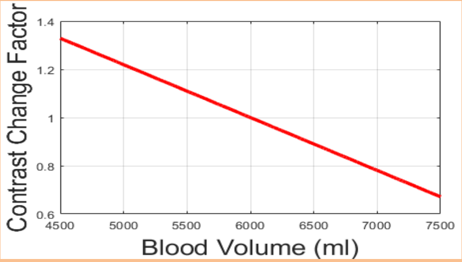
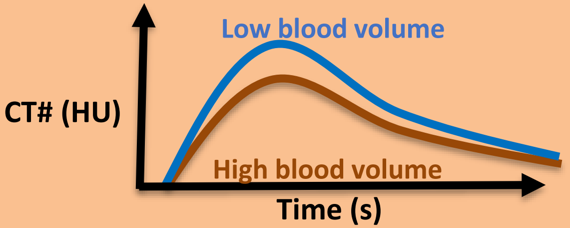
1. Bae KT. Intravenous contrast medium administration and scan timing at CT: considerations and approaches. Radiology. 2010 Jul;256(1):32-61.

2. Lee CH, Goo JM, Bae KT, Lee HJ, Kim KG, Chun EJ, Park CM, Im JG. CTA contrast enhancement of the aorta and pulmonary artery: the effect of saline chase injected at two different rates in a canine experimental model. Investigative radiology. 2007 Jul 1;42(7):486-90

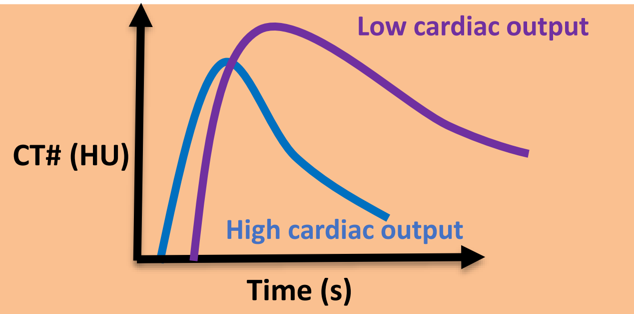
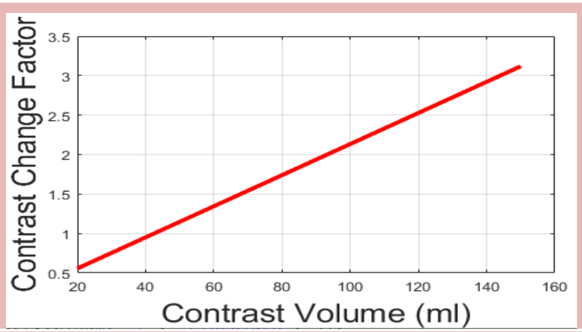
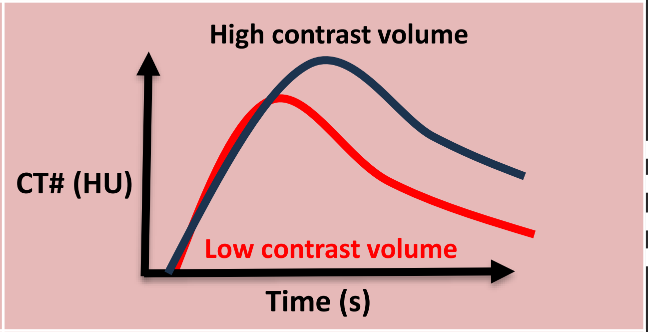
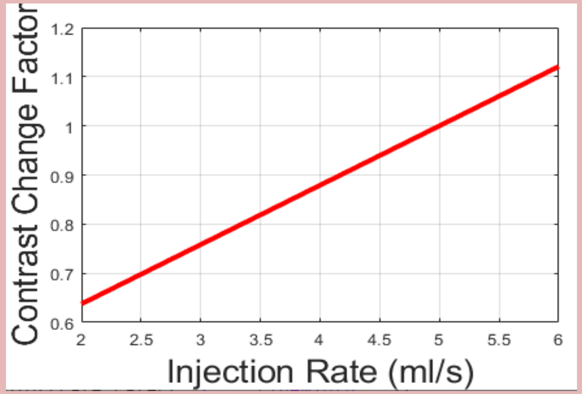
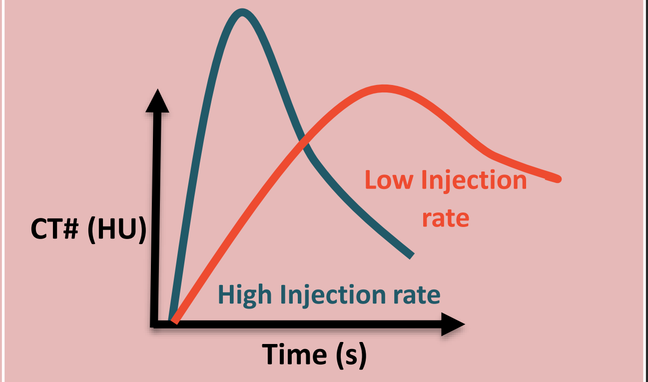
3. Behrendt FF, Bruners P, Keil S, Plumhans C, Mahnken AH, Das M, Ackermann D, Günther RW, Mühlenbruch G. Effect of different saline chaser volumes and flow rates on intravascular contrast enhancement in CT using a circulation phantom. European journal of radiology. 2010 Mar 1;73(3):688-93

<table>
<tr><th>Parameter</th><th>Effect on Enhancement</th><th>Effect on Peak Enhancement Time</th><th>Model</th><th>Model Curve of Attenuation Vs. Time.</th></tr>
<tr><td>Physics-Based:
Beam energy[1,2]
(kV)</td><td>enhancement increases when beam energy decreases</td><td>No effect on peak enhancement time.
Affects the threshold in bolus tracking series (happens faster or later depending on beam energy).</td><td><table><tr><th>kV</th><th>Relative iodine HU to 120 kV</th></tr><tr><td>80</td><td>1.68</td></tr><tr><td>100</td><td>1.27</td></tr><tr><td>120</td><td>1</td></tr><tr><td>140</td><td>0.826</td></tr></table></td><td>
</td></tr>
<tr><td>Physics-Based:
Beam hardening[3]
(BH) related to patient size</td><td>enhancement increases when patient's weight decreases</td><td>No effect on peak enhancement time.
Affects the threshold in bolus tracking series (happens faster or later depending on beam energy).</td><td>

Shown for 120 kV normalized to a 300 mm sized patient: correction amount needed to undo beam hardening</td><td>
</td></tr>
<tr><td>Physics Based:
Scan duration[1,4]</td><td>Needs to be optimized based on contrast medium injection duration</td><td>Needs to be optimized based on contrast medium injection duration</td><td>
$$\text{Scan Duration} = \frac{Range * Rotation\ time}{Pitch * Collimation}$$</td><td>

Lower enhancement for portions of a longer scan</td></tr>
<tr><td>Patient-Based:
Blood volume[5]</td><td>enhancement increases when blood volume decreases</td><td>No effect on peak enhancement time.
Affects the threshold in bolus tracking series (happens faster or later depending on beam energy).</td><td>
</td><td>
</td></tr>
</table>

1. Szczykutowicz T. The CT handbook: optimizing protocols for today's feature-rich scanners, 2020.
2. Yu L, Li H, Fletcher JG, McCollough CH. Automatic selection of tube potential for radiation dose reduction in CT: a general strategy. Medical physics. 2010 Jan;37(1):234-43.
3. Salyapongse AM, Rose SD, Pickhardt PJ, Lubner MG, Toia GV, Bujila R, Yin Z, Slavic S, Szczykutowicz TP. CT Number Accuracy and Association With Object Size: A Phantom Study Comparing Energy-Integrating Detector CT and Deep Silicon Photon-Counting Detector CT. American Journal of Roentgenology. 2023 May 31.
4. Bae KT. Intravenous contrast medium administration and scan timing at CT: considerations and approaches. Radiology. 2010 Jul;256(1):32-61.
5. Schoellnast H, Deutschmann HA, Berghold A, Fritz GA, Schaffler GJ, Tillich M. MDCT angiography of the pulmonary arteries: influence of body weight, body mass index, and scan length on arterial enhancement at different iodine flow rates. American journal of roentgenology. 2006 Oct;187(4):1074-8.

Parameter	Effect on Enhancement	Effect on Peak Enhancement Time	Model	Model Curve of Attenuation Vs. Time.
Patient-Based: **Cardiac output**[1]	Reduced cardiac output increases the magnitude of peak aortic and parenchymal enhancement.	Delayed peak arterial and parenchymal enhancement. Contrast material arrives slowly and clears slowly.	No specific model Understanding the other variables presented helps interpret cardiac output's effect on enhancement.	
Contrast Protocol- Based: **Contrast volume**[2]	enhancement increases when contrast volume increases for all phases	Higher contrast volume with fixed injection rate increases time to peak enhancement.		
Contrast Protocol- Based: **Injection rate**[3]	Peak arterial enhancement increases when injection rate increases. Much smaller affect on parenchymal phases, no effect on delayed phases.	Peak arterial enhancement happens earlier with higher injection rate. Higher injection rate reduces potential temporal window (width of enhancement curve peak gets smaller) for CT scanning.		

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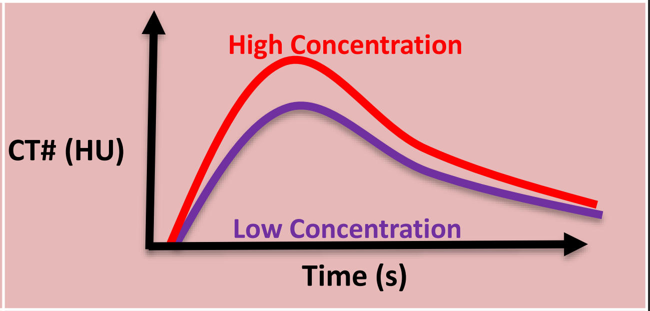
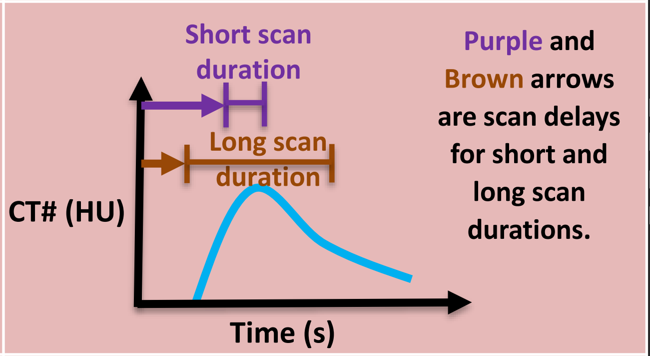
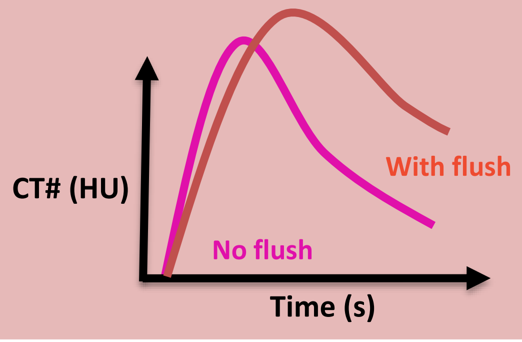
Parameter	Effect on Enhancement	Effect on Peak Enhancement Time		Model	Model Curve of Attenuation Vs. Time.
Contrast Protocol-Based: **Iodine Concentration**[1]	All phases increase enhancement when ICM concentration increases and total iodine mass increases.	No effect on peak enhancement time with fixed volume, rate and injection duration.	Increasing concentration decreases time to peak enhancement time with fixed total iodine mass.	Change in enhancement is equal to the ratio of the change in contrast agent concentration	
Contrast Protocol-Based: **Scan delay**[1,2]	Need to be optimized based on optimal enhancement time and scan duration.	If scan delay is not set properly, peak enhancement can be missed.		Scan Delay $= T_{Peak} - \frac{1}{2} T_{scan\ duration}$	
Contrast Protocol-Based: **Saline Flush**[1,3,4]	Use of 20-30 ml of saline flush leads to a 5-10% increase in peak arterial enhancement.	Prolonged time to peak arterial HU compared to non-flush.		Contrast can be reduced with use of a flush. For volumes up to ~30 ml, contrast agent can be traded with saline volume to keep peak arterial enhancement constant.	

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