

University of Wisconsin Madison



CT Contrast Agents and Enhancement Principles

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CT EDUCATION AND COLLABORATION COLLECTIVE



CONFLICT OF INTEREST

No Conflict of interest to declare.

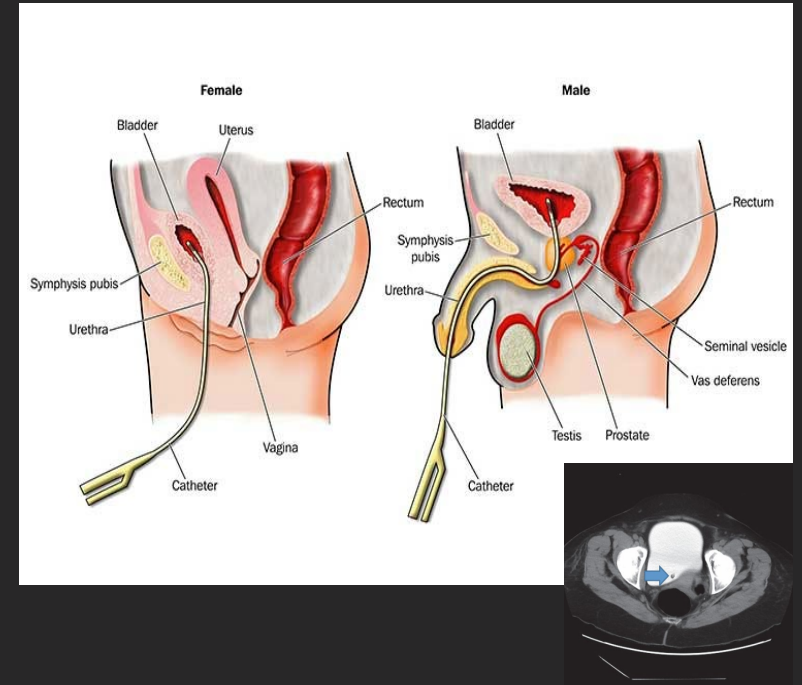
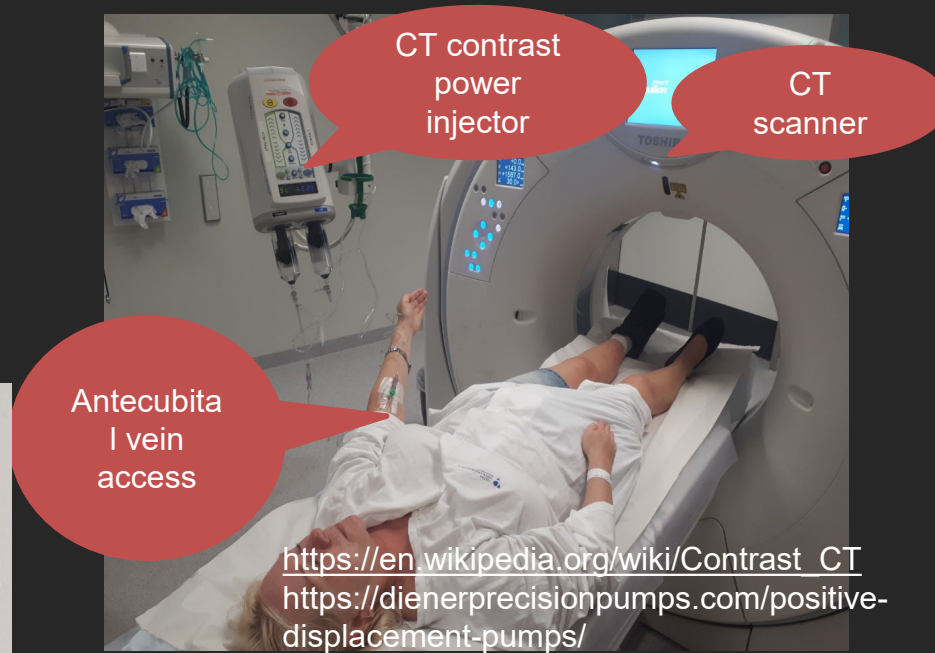
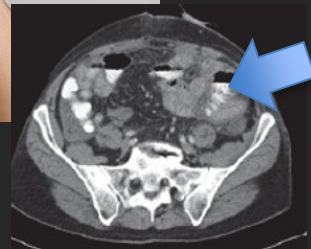


TEACHING POINTS

1. Learn about the major types of contrast agents used in CT: why they work and their clinical applications
2. Understand the route IV contrast agents take through the body: speed of travel, changes in enhancement, and commonly used imaging phases
3. Review the factors that influence CT contrast agent enhancement

DIFFERENT TYPES OF CONTRAST AGENTS IN CT

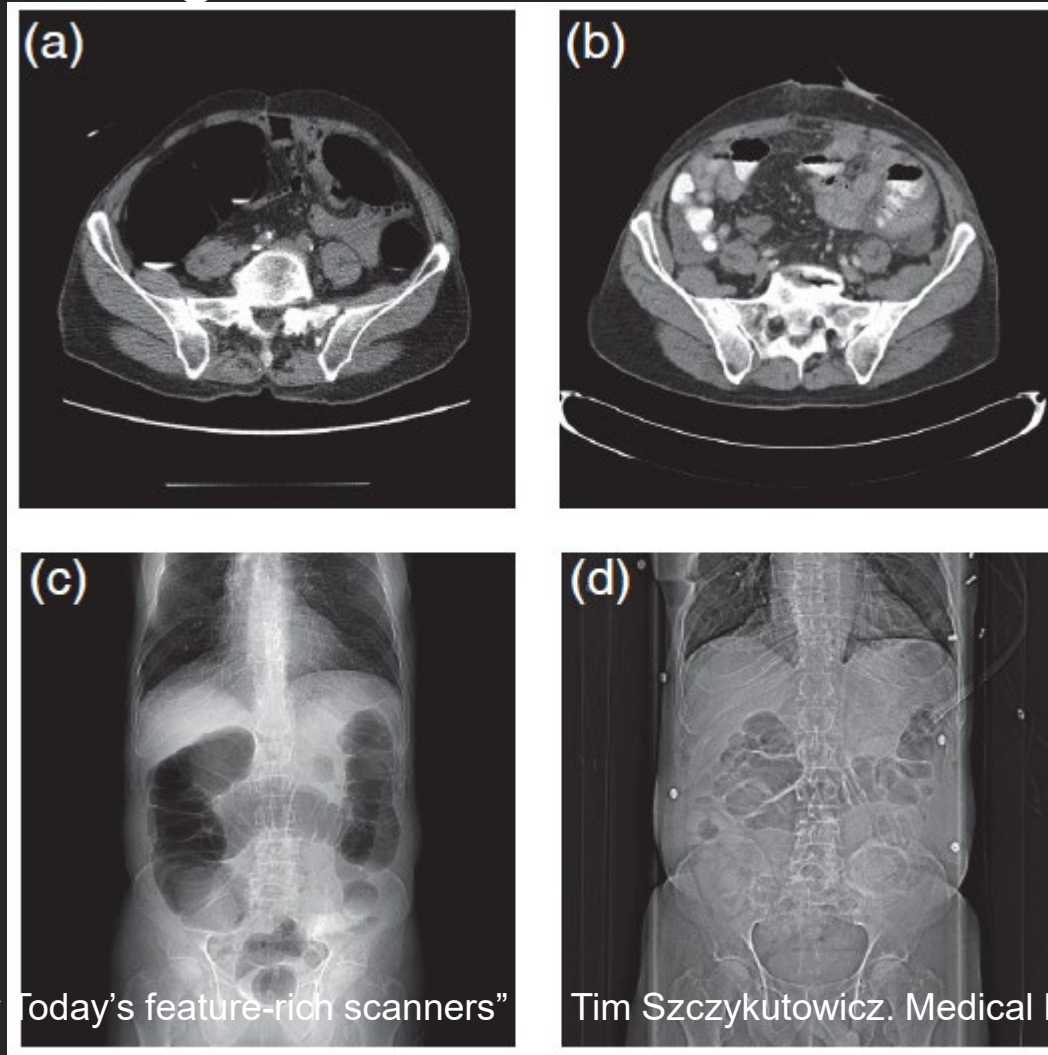
CT contrast agents make soft tissue contrast in CT



CT CONTRAST 101-NEGATIVE AGENTS

CO2 gas contrast
agent

Same pt no
CO2



Both scans
have
positive oral
agent

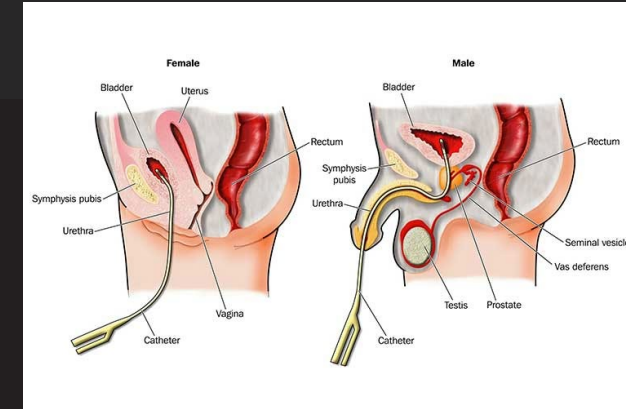
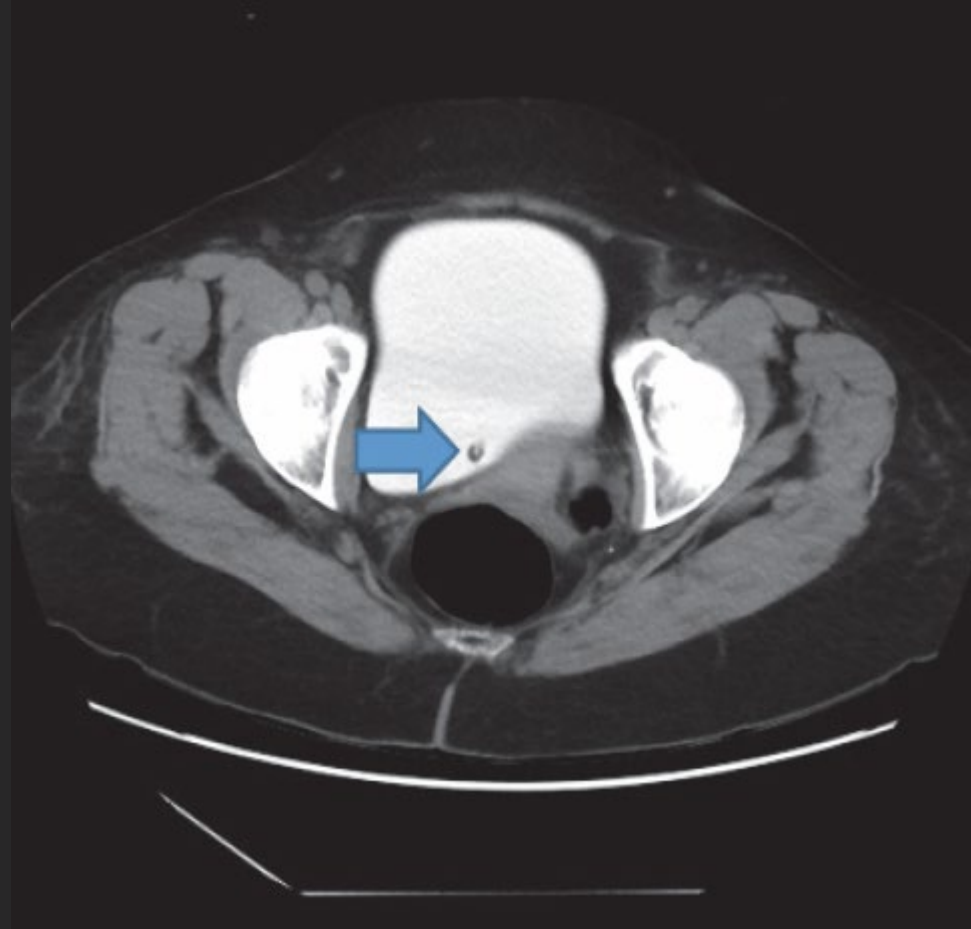
Note: the
localizers
even show
the CO2

CT CONTRAST 101-POSITIVE AGENTS

Positive agents are Iodinated contrast media (ICM)

Positive oral contrast
introduced via Foley
catheter

(arrow shows catheter,
don't confuse this with
an artifact)



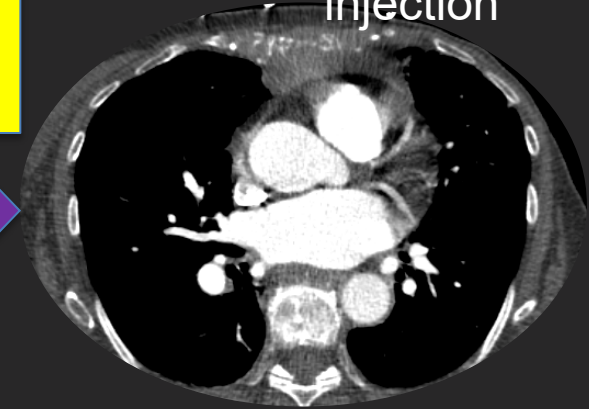
<https://www.ausmed.com/cpd/articles/urinary-catheter>

CT CONTRAST 101

Positive **IV** contrast
(**ICM**) introduced
through intravenous
injection



Put your ICM
glasses on 😊



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

Most common application of ICM in CT is vascular (e.g. CT angiography) and visceral enhancement (e.g. parenchymal scan)

Pre ICM injection
(Unenhanced)

Post ICM injection in
healthy individual

Post ICM injection in patient
with pulmonary embolism

A segment of the pulmonary artery remains unopacified due to pulmonary embolism, clearly visible following ICM injection.

Post ICM injection in
patient with HCC

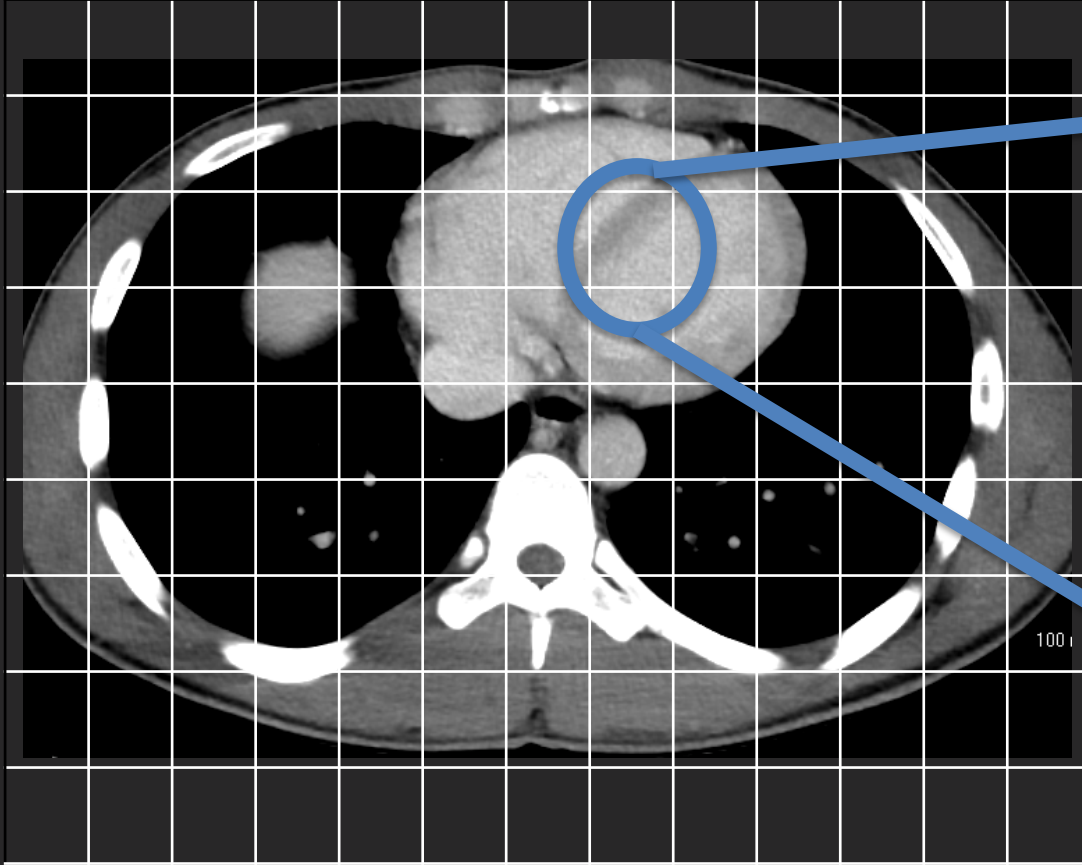
Hepatocellular carcinoma is detectable only after ICM injection

Put your ICM
glasses on 😊



Usually, it will always be diluted by blood (IVC administration) or water (oral) or urine (catheter injection)

WHY CONTRAST AGENTS WORK?



$$CT\ number = \frac{\mu - \mu_w}{\mu_w} \times 1000$$

linear attenuation coefficient of each voxel normalized by linear attenuation coefficient of water

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.

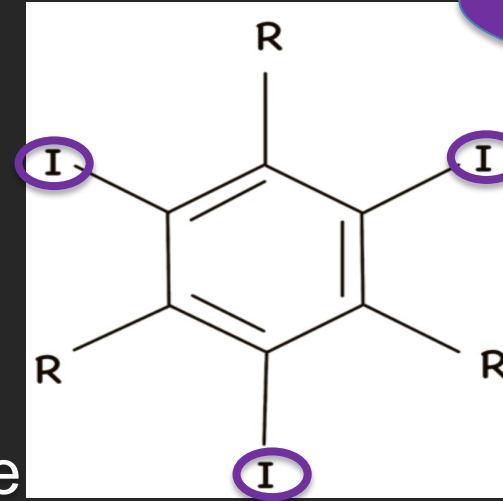
Positive ICM agent:

- $\mu(\vec{X}, E) = \tau_{PE}(\vec{X}, E) + \sigma_{Compton}(\vec{X}, E)$
- $= K \rho_e(\vec{X}) \frac{Z^3(\vec{X})}{E^3} + \rho_e(\vec{X}) f_{KN}(E)$

$$Z_I = 53$$

$$Z_{\text{eff of water}} = 7.42$$

Increased CT number when voxel contains iodine



3 Iodine atoms per contrast molecule



Negative gas agent:

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

Decreased CT number when voxel contains CO₂ due to low mass density and electron density

Iohexol is a common CT ICM and in different concentrations

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

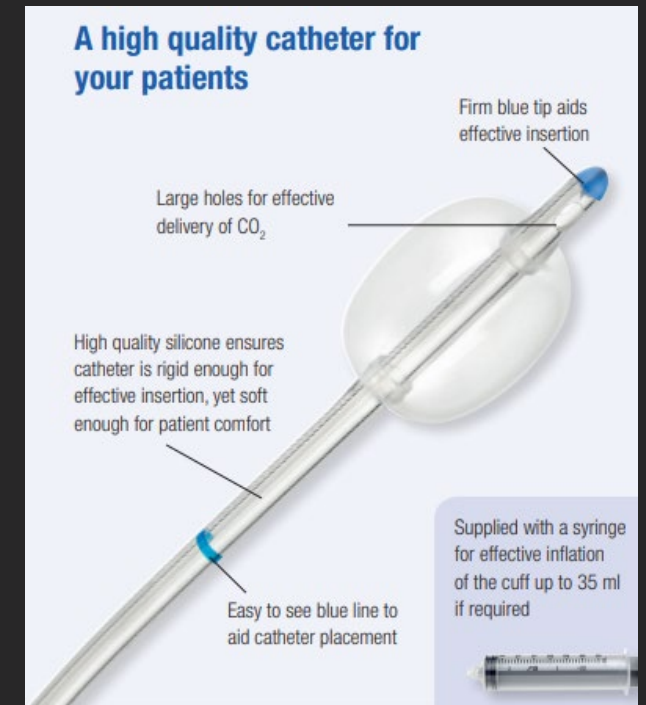
Most common application of CO₂ in CT is patients with allergy to ICM and poor renal function used in both arteriography and venography



Air/CO₂

Generates CT number
~-1000, “usually
doesn’t get diluted”

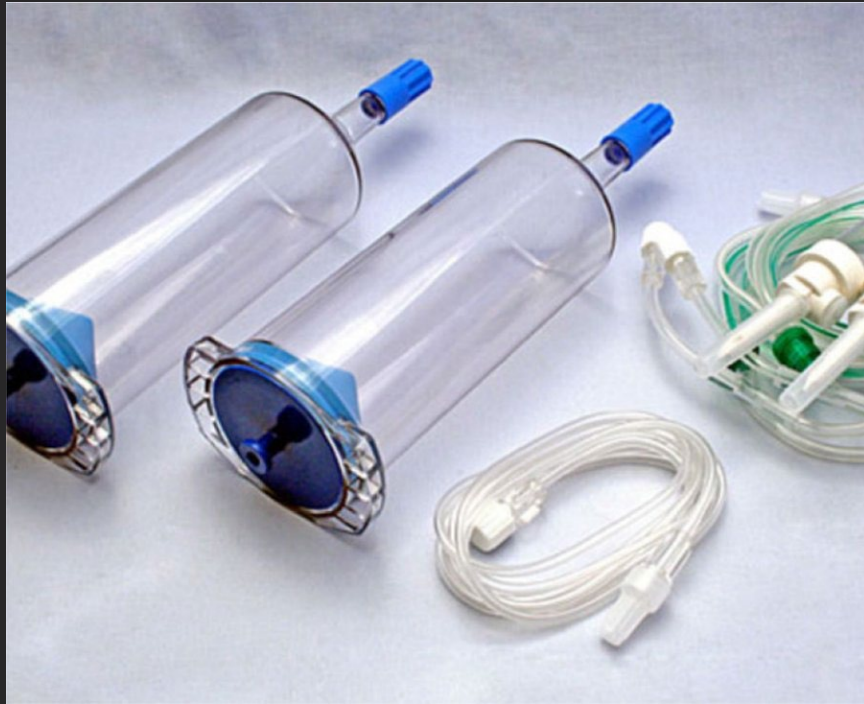
Used for CTC



IV INJECTION OF ICM

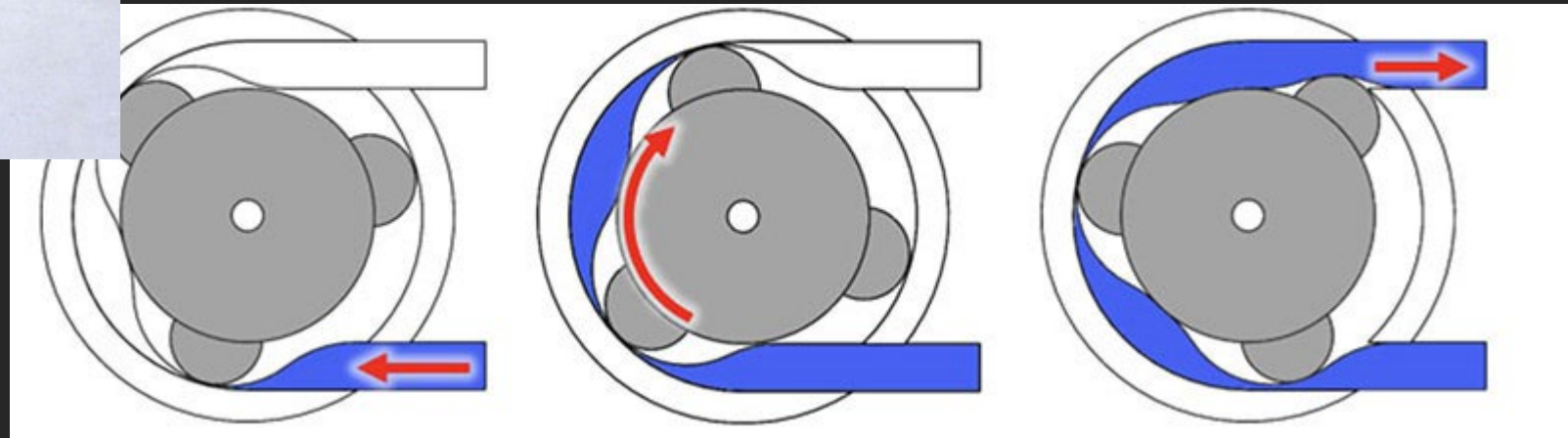


CT CONTRAST 101



Piston based pump... simple, the plunger pushes the agent out

Peristaltic pump, the rotating action pushes agent along a flexible tube



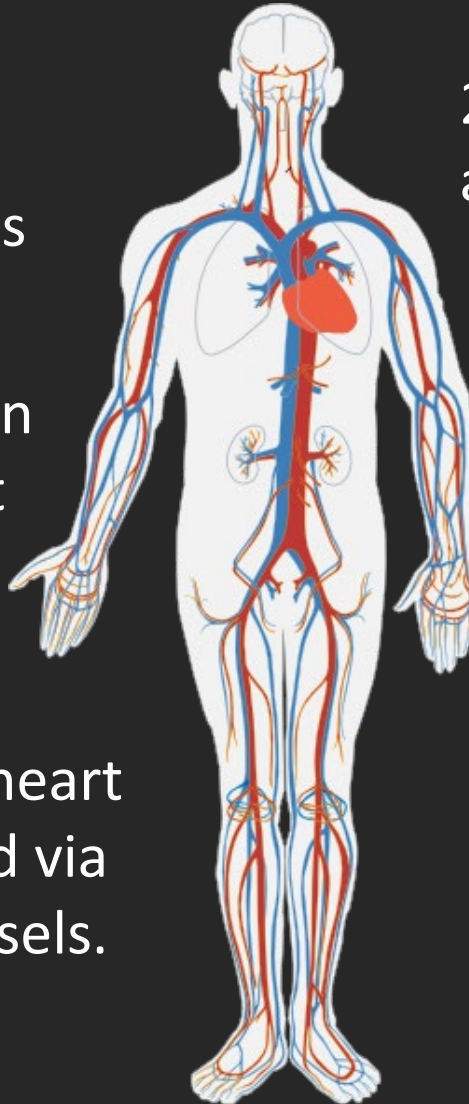
<https://dienerprecisionpumps.com/positive-displacement-pumps/>

THE ROUTE OF IV CONTRAST AGENTS

3. Blood goes to right ventricle and goes out pulmonary artery to lungs

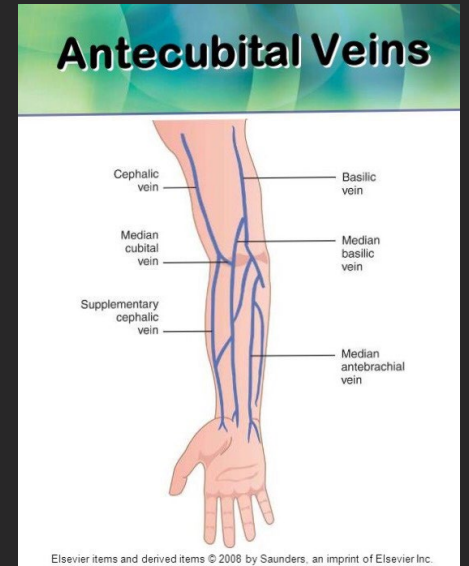
4. Returns via pulmonary vein and goes to left side of heart to be pushed out aorta via left ventricle.

5. First stop is supplying heart via coronaries. Then head via carotid and vertebral vessels.

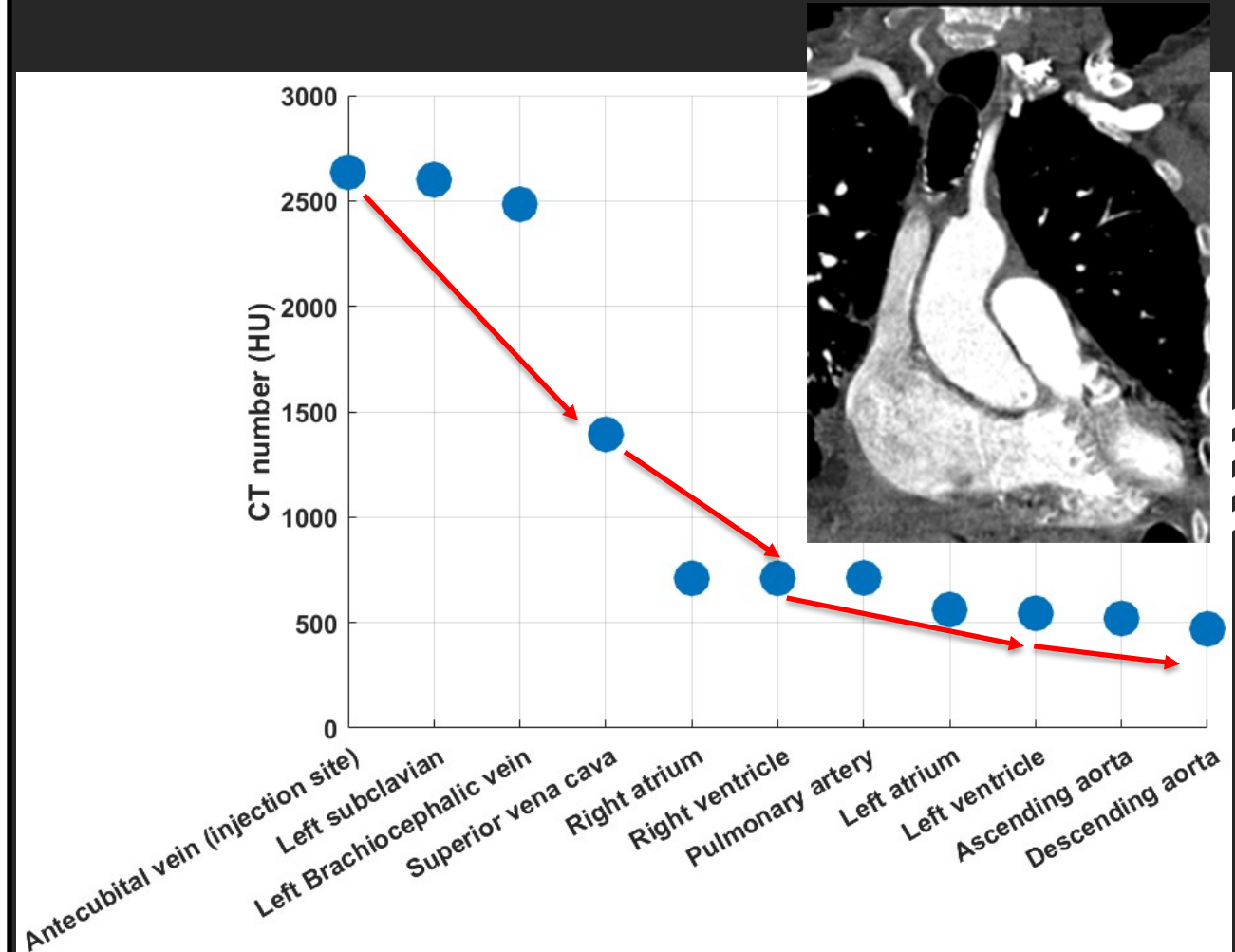
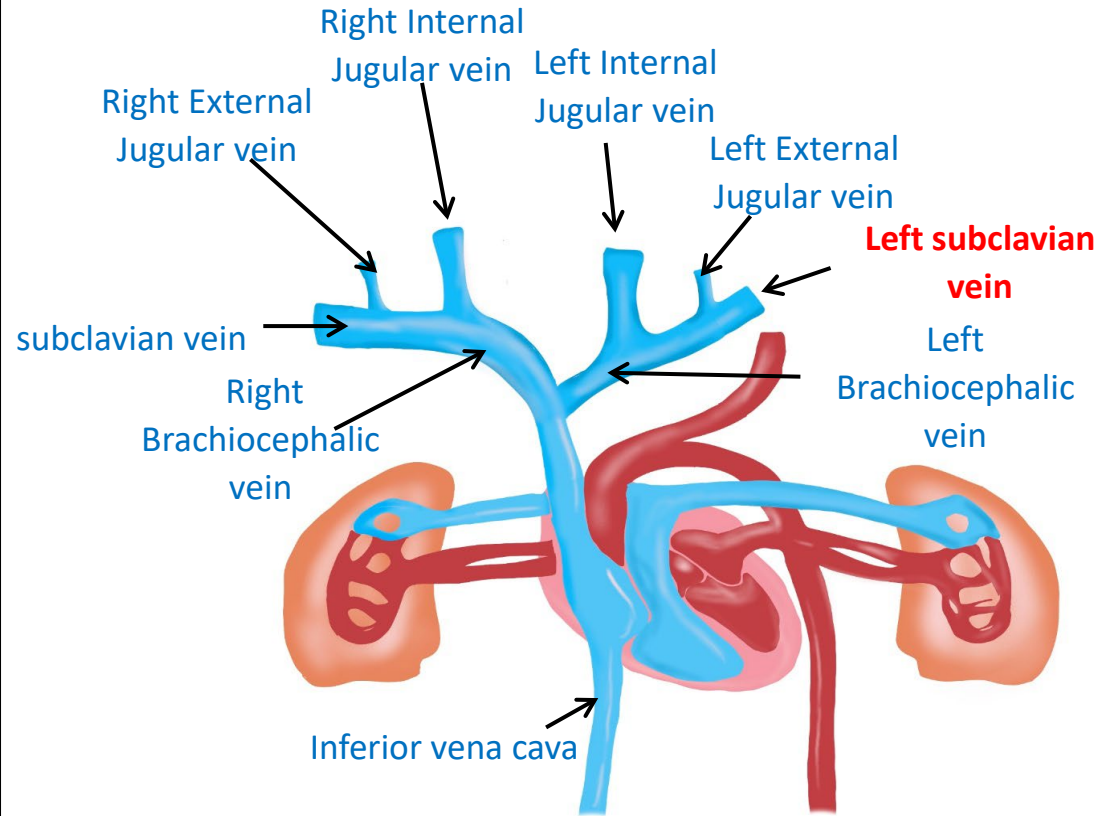


2. Blood goes into SVC and then into right atrium

1. Inject via antecubital vein



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SPEED OF ICM TRAVEL

Contrast time of arrival will vary from person to person, but assuming an antecubital injection, values will generally be in the range of

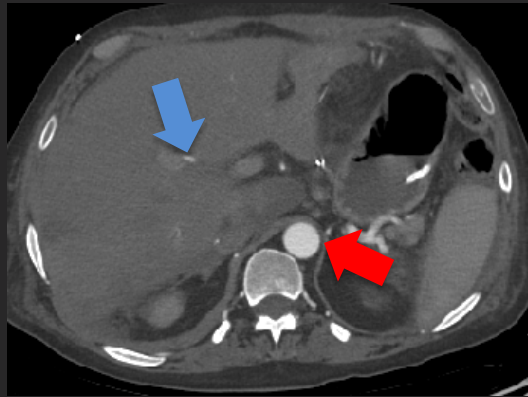
7 to 10 seconds for the pulmonary artery,
12 to 15 seconds for the ascending aorta,
15 to 18 seconds for the abdominal aorta,
and 30 to 40 seconds for hepatic parenchyma.

Text copied from "The CT Handbook: Optimizing Protocols for Today's feature-rich scanners" By Tim Szczykutowicz. Medical Physics Publishing 2020

Another reference Bae, K. T., J. P. Heiken, and J. A. Brink. (1998). "Aortic and hepatic contrast medium enhancement at CT. part i. prediction with a computer model." *Radiology* 207(3):647–55.

COMMONLY USED IMAGING PHASES

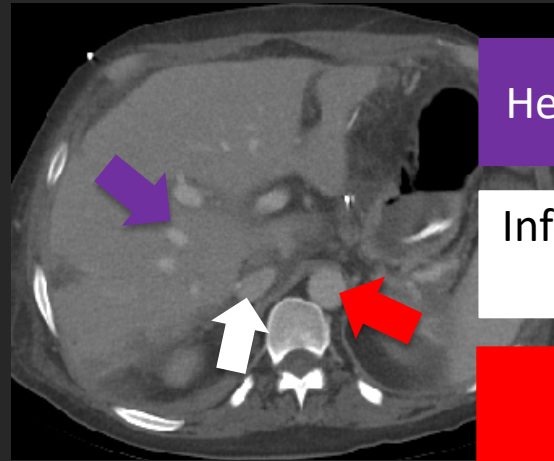
Arterial phase



Intrahepatic
artery

Aorta

Venous phase

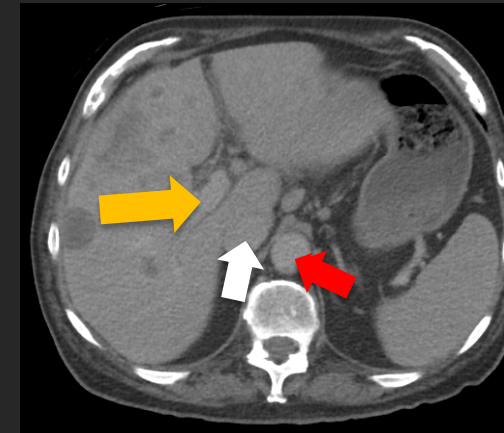


Hepatic vein

Inferior vena
cava

Aorta

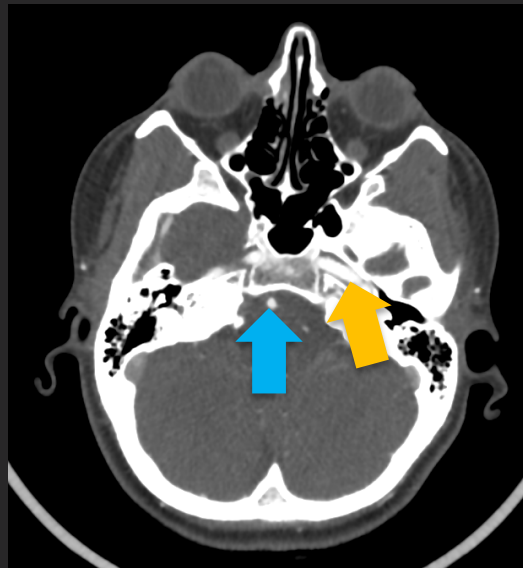
Delayed phase



Portal vein

Inferior vena
cava

Aorta



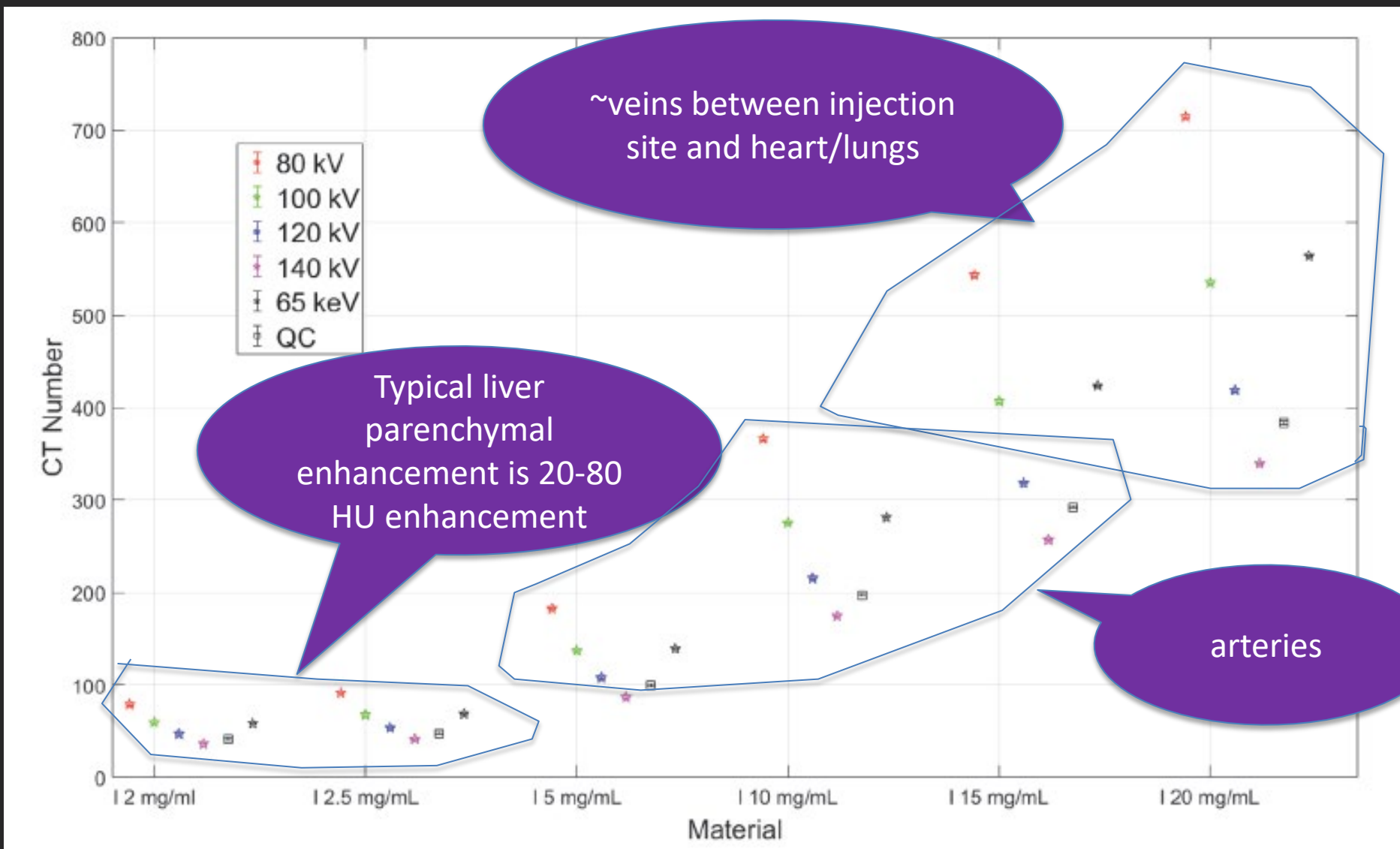
Basilar
artery

Carotid
artery

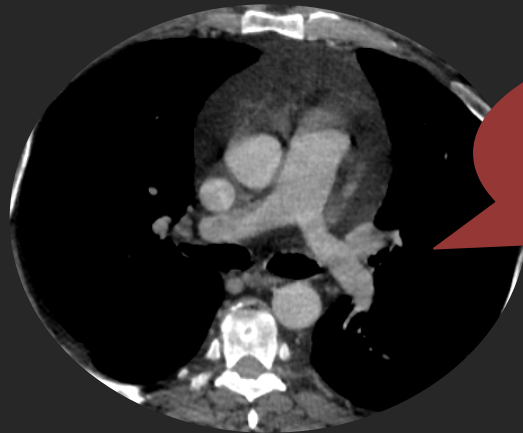


Brain parenchyma
is homogenous with
edge enhanced
tumor (e.g. pituitary
tumor)

CT CONTRAST 102



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
**More ICM → more
enhancement**

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

Acute adverse

allergic
reactions

physiologic
reactions

Delayed effects

Mild

Moderate

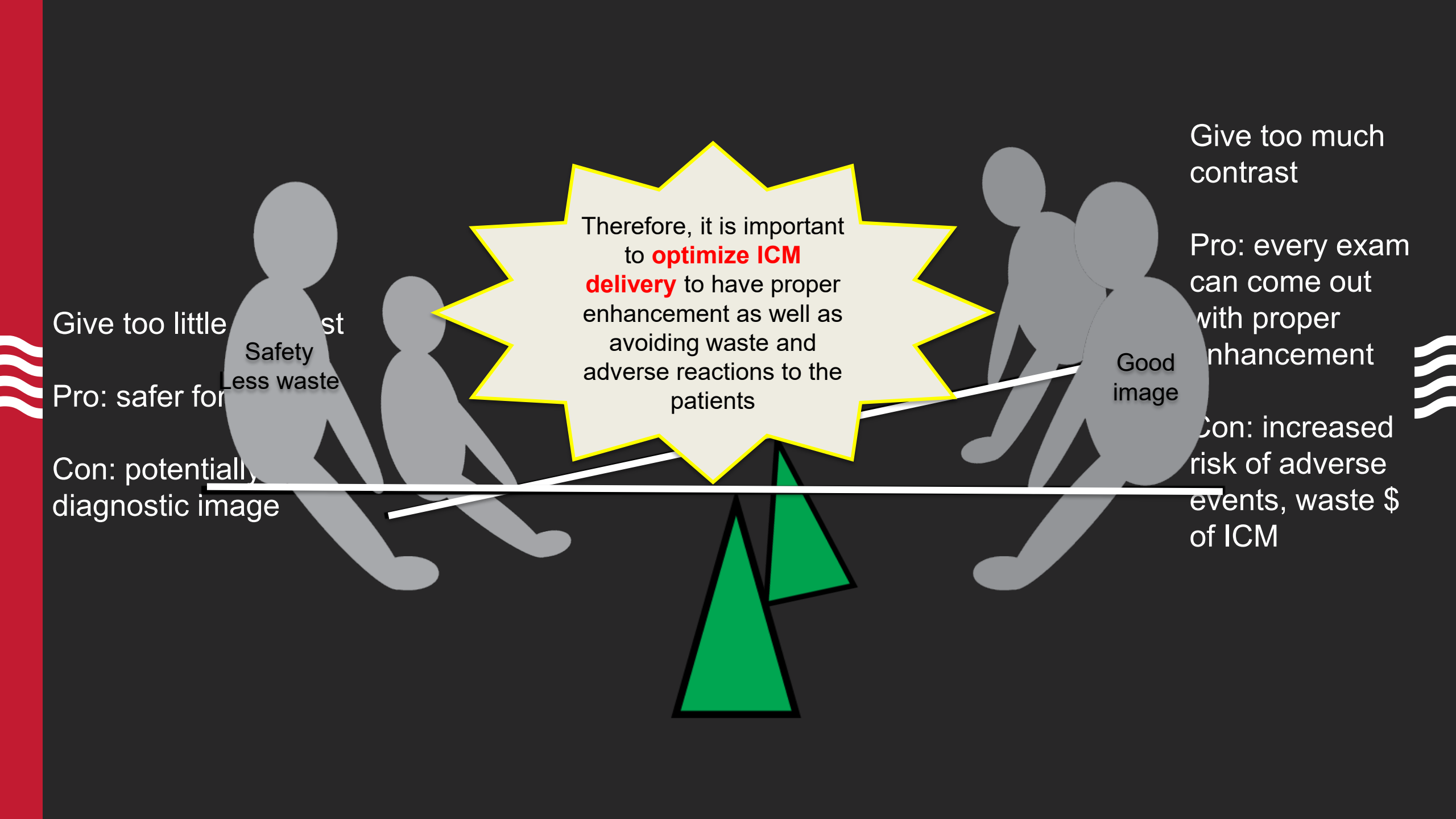
Severe

Contrast-induced acute kidney injury (CI-AKI)

- Clinical demand for ICMs with
- Environmental and Human

Therefore, it is
important to **optimize
ICM delivery** to have
proper enhancement as
well as avoiding waste
and adverse reactions
to the patients

1. ACR manual on contrast media, 2024
2. Preventing Future Global Shortages of Iodinated Contrast Media | GE HealthCare (United States) (<https://www.gehealthcare.com/insights/article/preventing-future-global-shortages-of-iodinated-contrast-media-requires-industry-action>, Accessed 21st Jun 2024)
3. Cavallo JJ, Pahade JK. Practice management strategies for imaging facilities facing an acute iodinated contrast media shortage. American Journal of Roentgenology. 2022 Oct 13;219(4):666-70.
4. England A, Rawashdeh M, Moore N, Young R, Curran G, McEntee MF. More sustainable use of iodinated contrast media—Why?. Radiography. 2024 Jun 1;30:74-80.



Therefore, it is important
to **optimize ICM
delivery** to have proper
enhancement as well as
avoiding waste and
adverse reactions to the
patients

Give too little contrast

Pro: safer for patient

Con: potentially
degraded
diagnostic image

Safety
Less waste

Good
image

Give too much
contrast

Pro: every exam
can come out
with proper
enhancement

Con: increased
risk of adverse
events, waste \$
of ICM

Factors Affecting Iodine Contrast Enhancement

Following is a list of factors affecting iodine contrast enhancement in CT:

Physics-based factors

- ✓ Tube potential
- ✓ Beam hardening
- ✓ Scan duration

Patient-related factors

- ✓ Blood volume
- ✓ Cardiac output

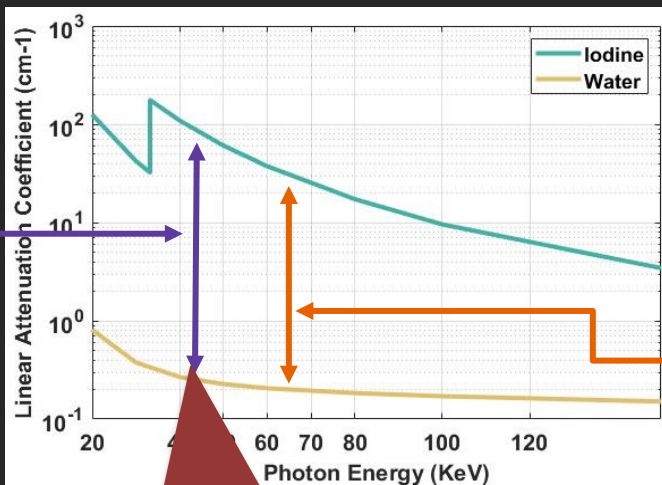
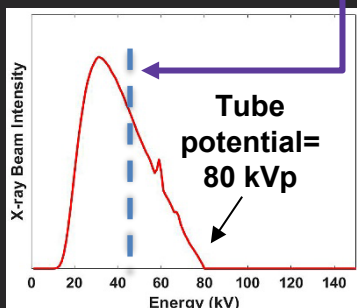
Contrast Protocol-based factors

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

Tube Potential (kV)

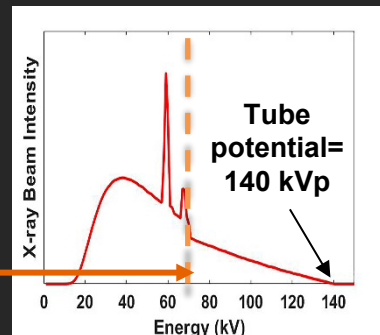
80 kV acquisition X-ray spectrum

Effective energy= 45 keV



140 kV acquisition X-ray spectrum

Effective energy= 67 keV

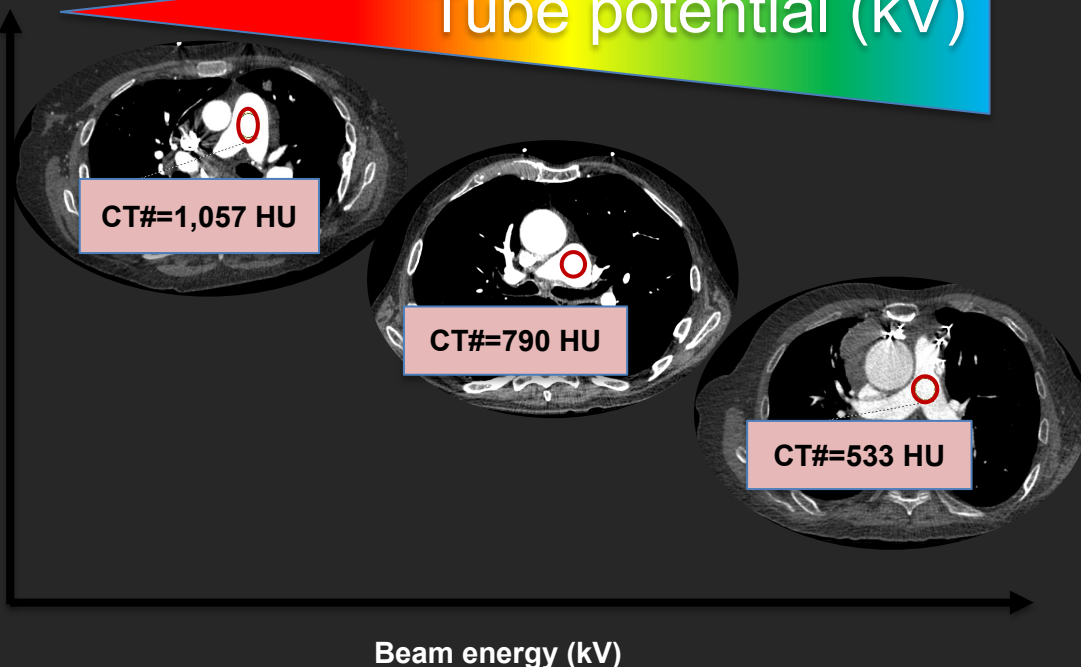


$$\mu(\vec{X}, E) = \tau_{PE}(\vec{X}, E) + \sigma_{Compton}(\vec{X}, E)$$

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

Larger difference between linear attenuation coefficient of Iodine and water at 80 kV (lower energy) → Increased contrast

CT number (HU)



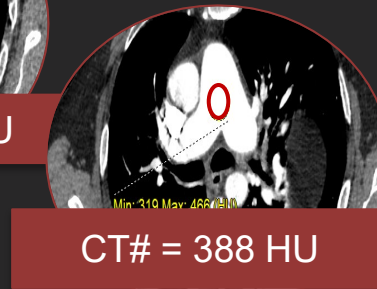
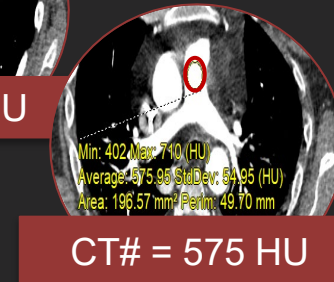
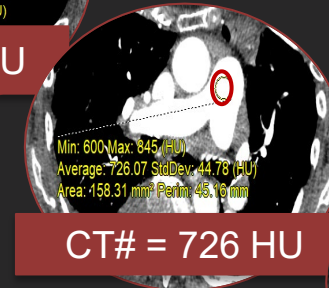
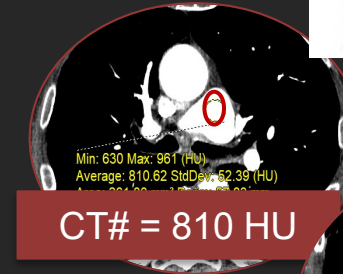
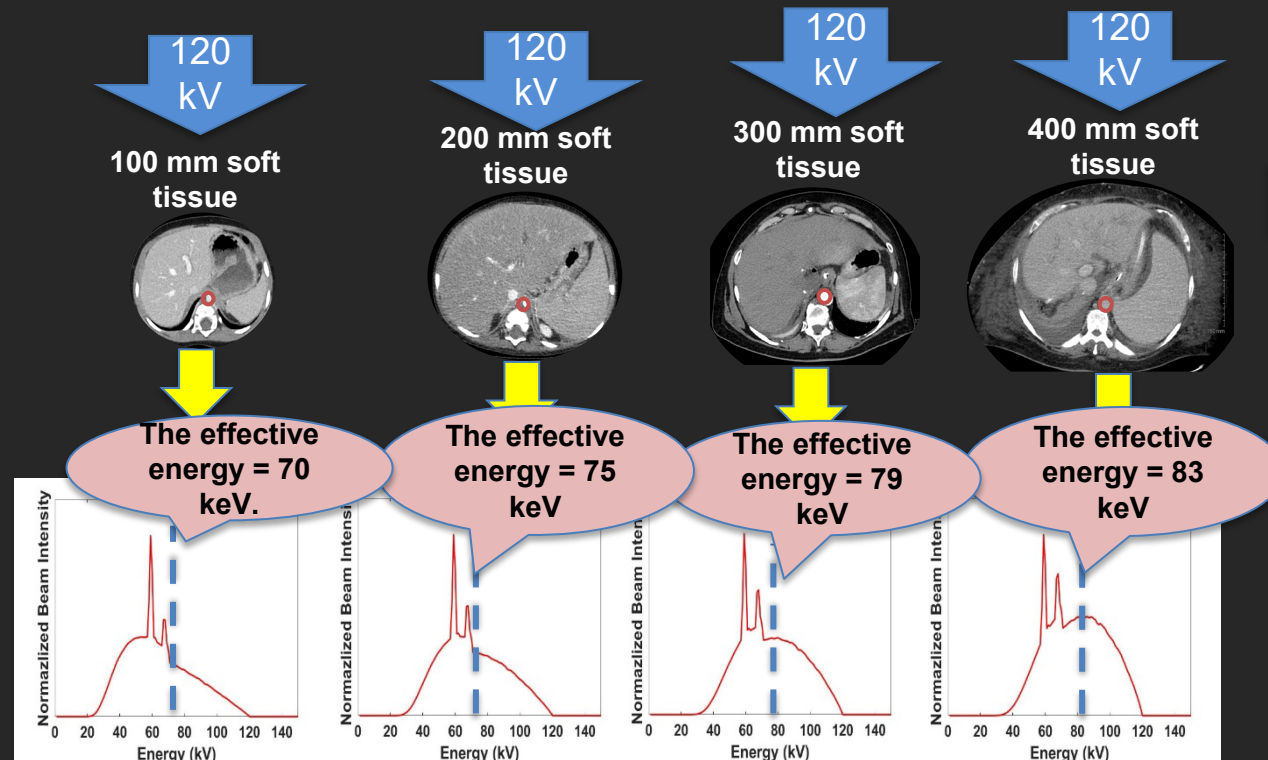
1. Jiang, Hsieh. "Computed tomography: principles, design, artifacts, and recent advances." Bellingham, Washington USA (Published by SPIE and John Wiley & Sons, Inc.): SPIE 2009: 39-44.
2. Szczykutowicz T. The CT handbook: optimizing protocols for today's feature-rich scanners. Medical Physics Publishing,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

Material	80 kV	100 kV	120 kV	140 kV	N/A
Water	0	0	0	0	[-4 4]**
Air	-1,000	-1,000	-1,000	-1,000	[-1005 -995]**
Fat	-152*	-111*	-89*	-69*	[-100 -80]**
Brain	47*	43*	39*	37*	
Soft Tissue	62*	58*	54*	52*	
Solid Cortical Bone	3,760*	2,590*	1,940*	1,330*	[≈200 > 1000]**
Pure Calcium	9,570*	5,960*	3,950*	2,090*	
Pure Iodine	405,000*	267,000*	180,000*	93,200*	
Iodine Contrast	See footnote a	See footnote a	See footnote a	See footnote a	
Relative Iodine Enhancement ^b	1.68	1.27	1	0.826	
Relative Iodine Enhancement ^c	1.70	1.28	1	0.81	
Kidney					[20 40]**
Pancreas					[30 50]**
Blood					[50 60]**
Liver					[50 70]**
PMP					-200***
Low-Density Polyethylene					-100***
Polystyrene					-35***
Acrylic					120***
Delrin®					340***
Teflon®					990***

“The CT Handbook: Optimizing Protocols for Today’s feature-rich scanners” By Tim Szczykutowicz. Medical Physics Publishing 2020

Beam Hardening (BH) Related to Patient Size

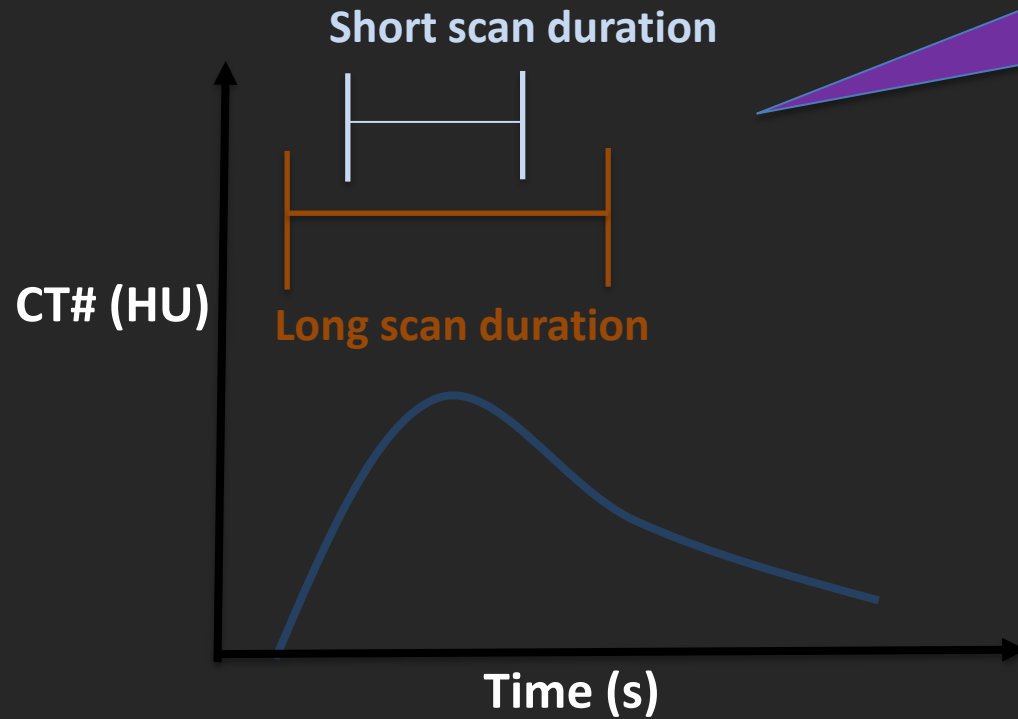
Beam hardening: the gradual increase of average x-ray beam energy as it passes through more patient tissue.



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

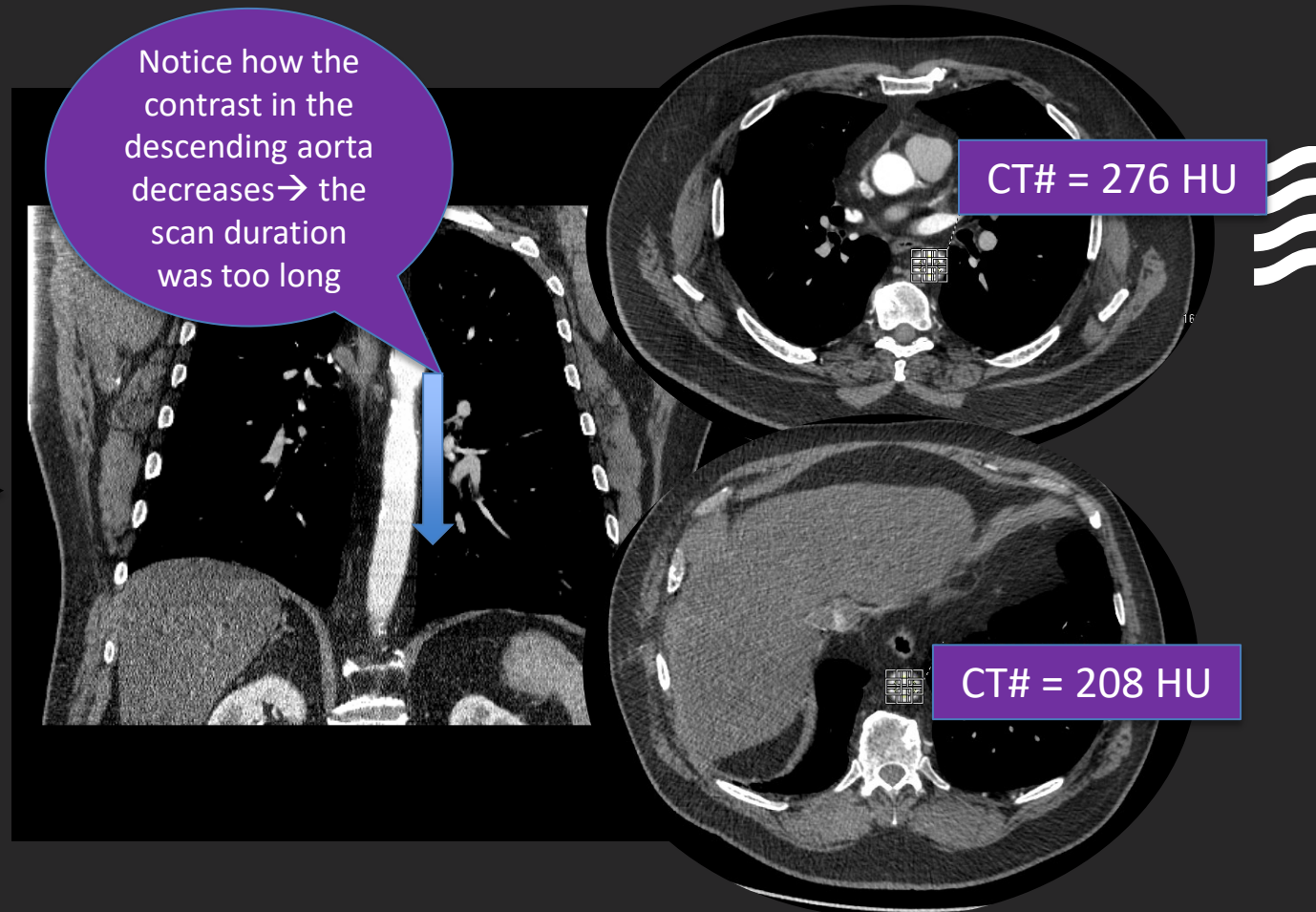
- Iodine concentrations in the ROIs (central circles) are identical
- Low energy X-rays are more attenuated by a larger patient

SCAN DURATION



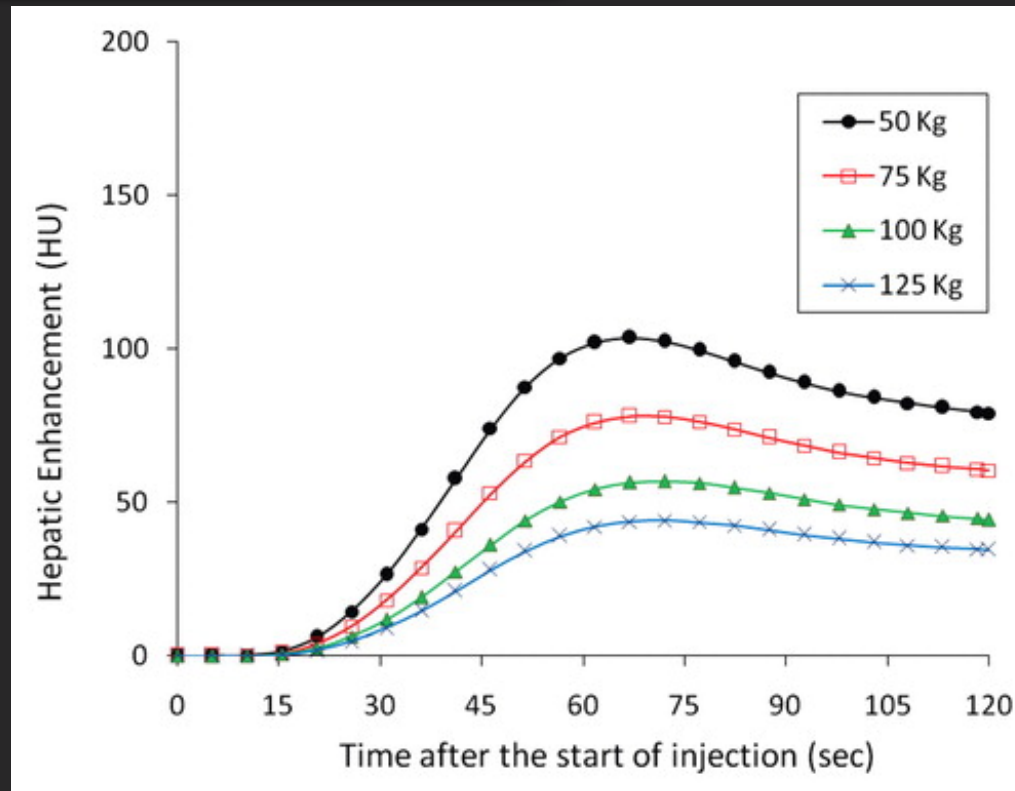
Shorter scan duration should have slightly longer scan delays, so to coincide with maximum contrast enhancement

Notice how the contrast in the descending aorta decreases → the scan duration was too long



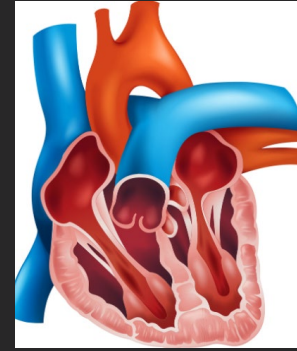
BLOOD VOLUME

Blood volume effect: Bigger people have more blood... which dilutes contrast agent



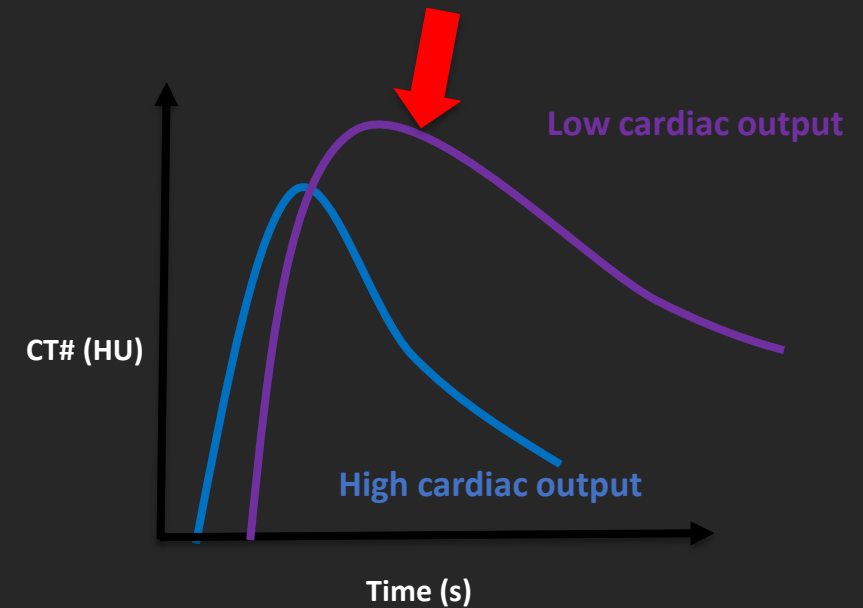
CARDIAC OUTPUT

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



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

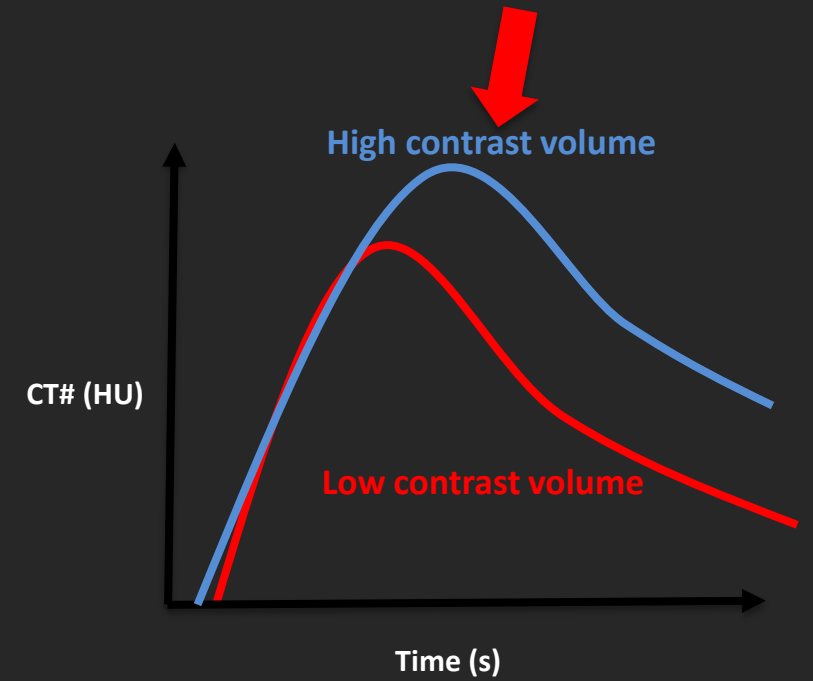
Low cardiac output → Contrast enhancement increases because less un-opacified blood mixes with ICM when the cardiac output is low



CONTRAST VOLUME

High contrast volume → high peak arterial enhancement

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



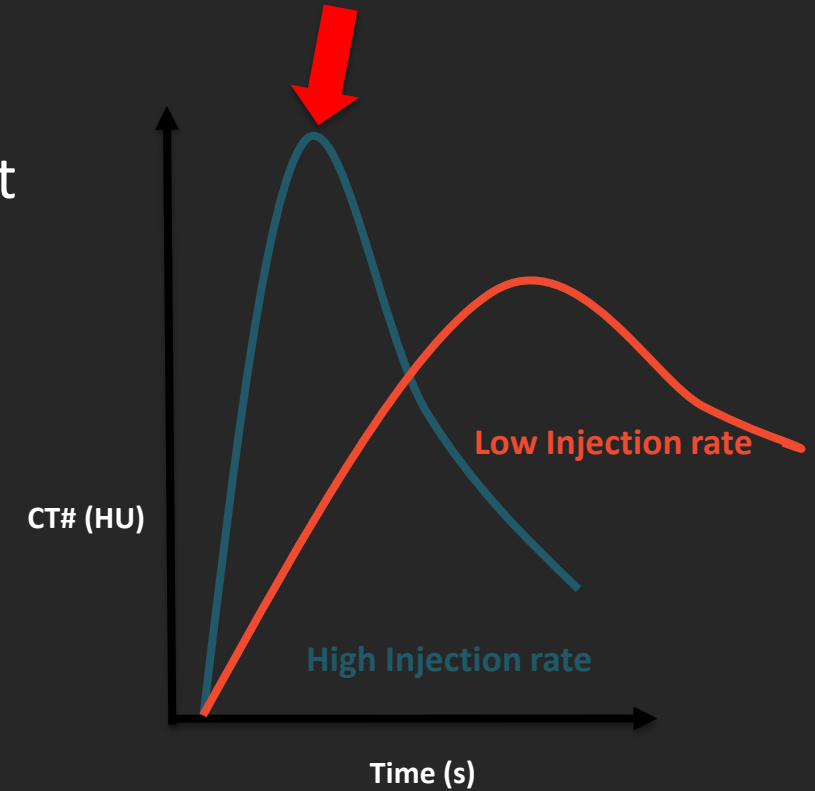
INJECTION RATE

High injection rate → Increased peak arterial enhancement

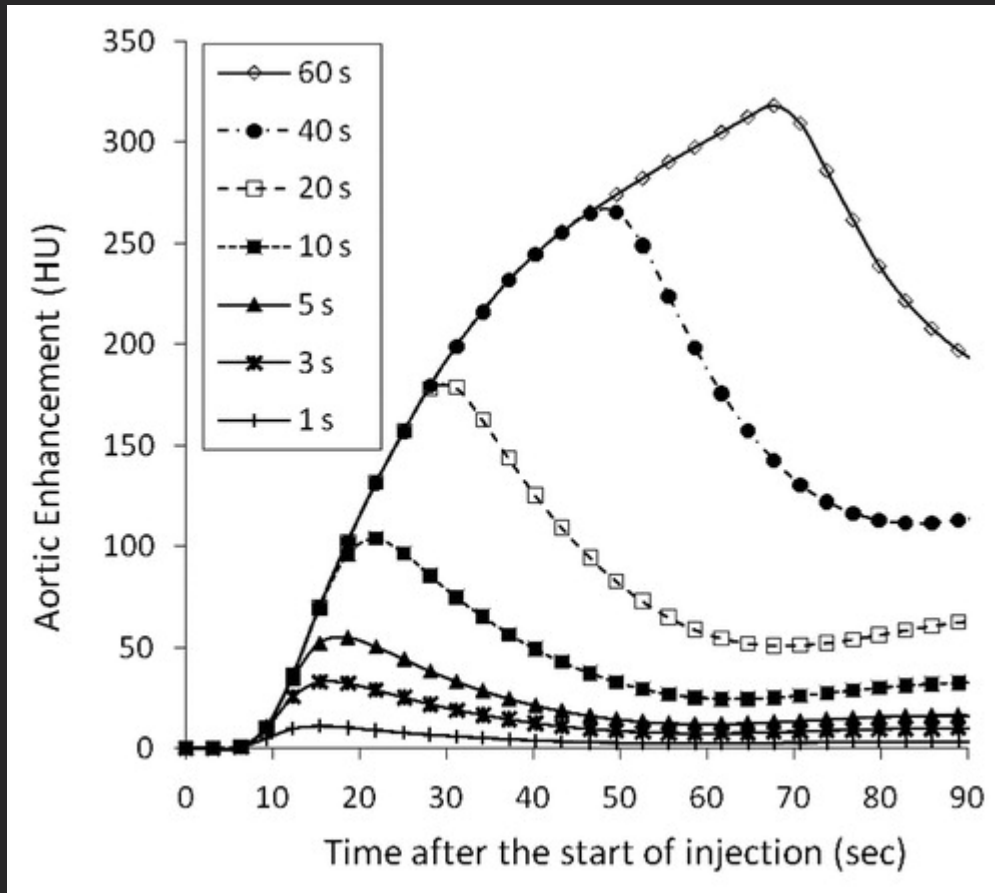
High injection rate → Decreased time to peak arterial enhancement.

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



INJECTION DURATION



Injection duration effect: Longer and longer injections push CT enhancement up and delay peak enhancement

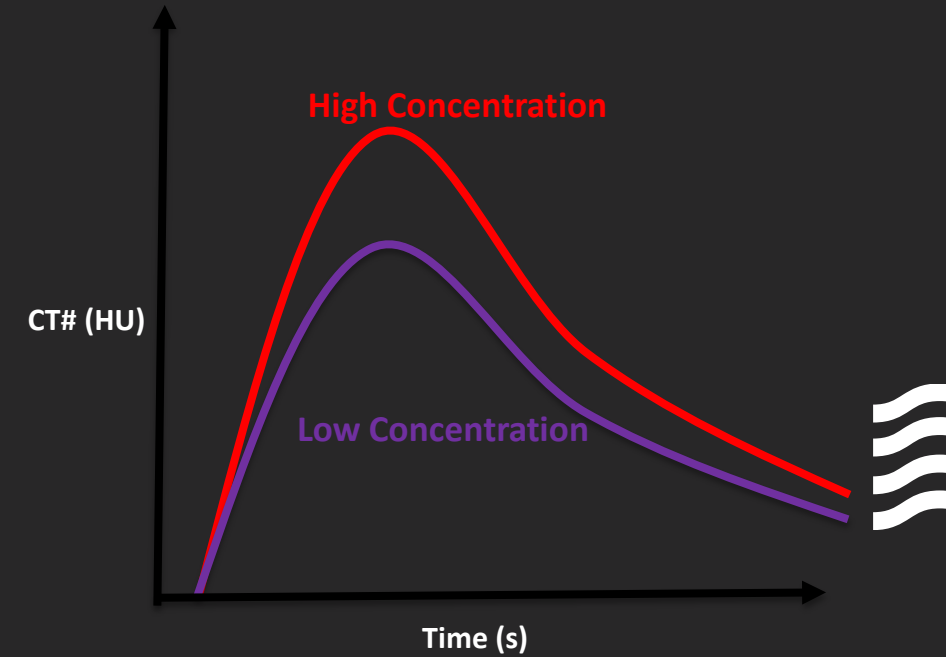
Arterial enhancement is “in and out” faster relative to parenchymal

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.

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.



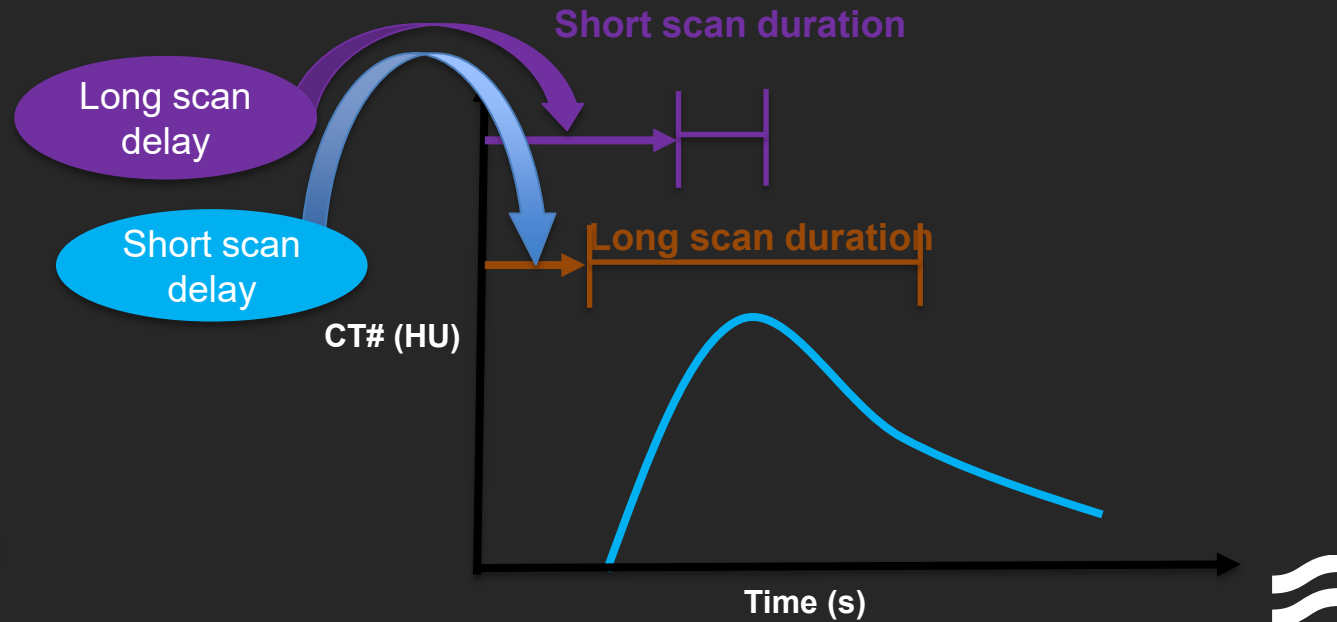
Scan Delay

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

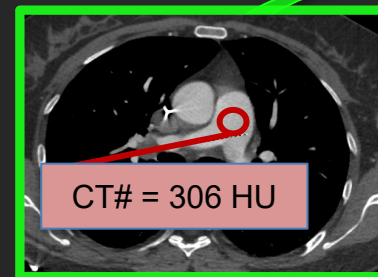
Anatomy and indication specific (i.e., for abdominal CTA this may be from an ROI in the aorta, for parenchymal liver it would be an ROI in liver)

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

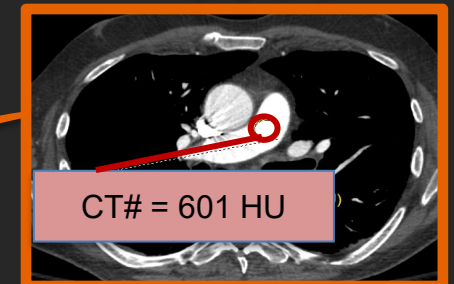
If scan delay is not set properly, peak enhancement can be missed.



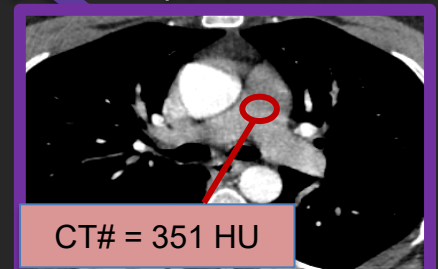
CT pulmonary angiography was performed **too early**



Well-timed CT pulmonary angiography



CT pulmonary angiography was performed **too late**



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

SALINE FLUSH

Saline flush is a saline injection immediately following a contrast injection.

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.

Usually used on CTA exams to make sure iodine is not wasted and left in venous system.

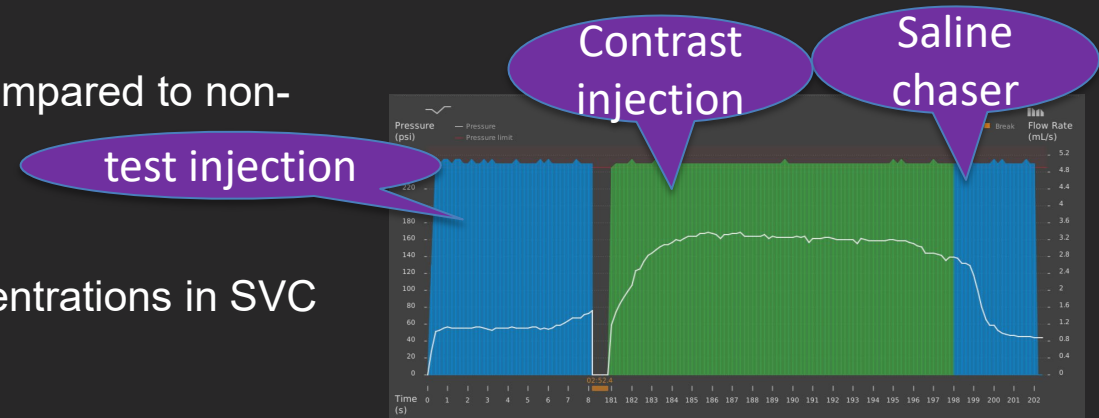
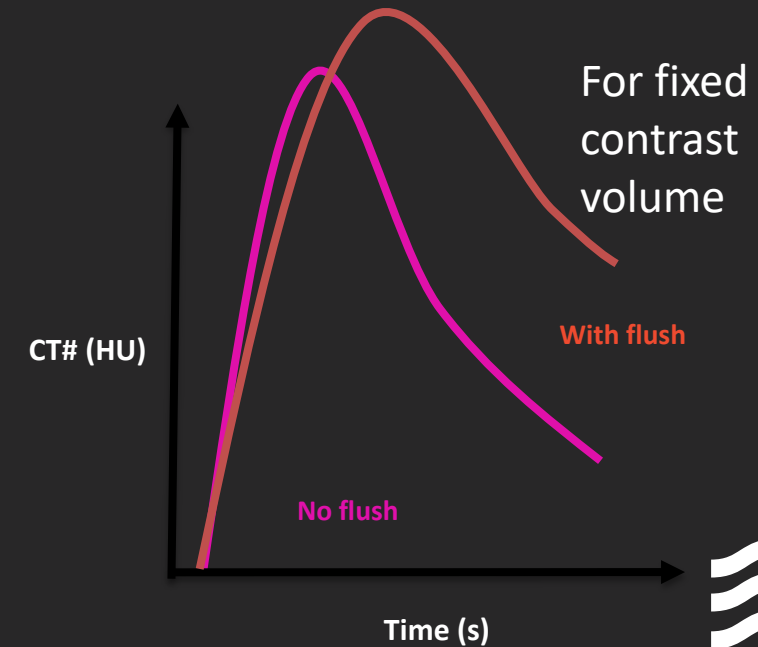
This is why we see a benefit for CTA exams and little benefit for parenchymal phase exams.

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.

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

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

Equations Governing the Major Facets of Contrast Delivery

$$Volume_{arbitrary\ strength}(ml) = \frac{Strength_{reference}(mg\ I / ml)}{Strength_{arbitrary}(mg\ I / ml)} Volume_{reference\ strength}(ml) \quad [See\ Table\ 8.2]$$

$$Volume(ml) = Duration(s) \times Injection\ flow\ rate(ml / s) \quad [See\ Table\ 8.3]$$

$$Total\ iodine\ load\ (mg\ I) = Contrast\ concentration\ (mg\ I\ per\ ml) \times Contrast\ volume\ (ml)$$

$$Scan\ delay = Time\ to\ optimal\ enhancement - \frac{1}{2} Scan\ duration$$

$$Scan\ speed\ (mm/s) = \frac{Collimation(mm) \times Pitch}{Rotation\ time(s)}$$

$$\begin{aligned} Scan\ duration\ (s) &= \frac{Scan\ range(mm)}{Scan\ speed(mm / s)} \\ &= \frac{Scan\ range(mm) \times Rotation\ time(s)}{Collimation(mm) \times Pitch} \end{aligned}$$

Contrast volume as a function of patient weight and contrast strength is shown in Table 8.3 for routine abdominal parenchymal enhancement.

Equations Governing the Major Facets of Contrast Delivery

$$Volume_{arbitrary\ strength}(ml) = \frac{Strength_{reference}(mg\ I / ml)}{Strength_{arbitrary}(mg\ I / ml)} Volume_{reference\ strength}(ml) \quad [See\ Table\ 8.2]$$

$$Volume(ml) = Duration(s) \times Injection\ flow\ rate(ml / s) \quad [See\ Table\ 8.3]$$

$$Total\ iodine\ load\ (mg\ I) = Contrast\ concentration\ (mg\ I\ per\ ml) \times Contrast\ volume\ (ml)$$

Iodine load versus contrast volume

All volumes are not created equal... a lower volume of high concentration agent can deliver the same total Iodine as a larger volume of less concentrated agent

Want more enhancement?

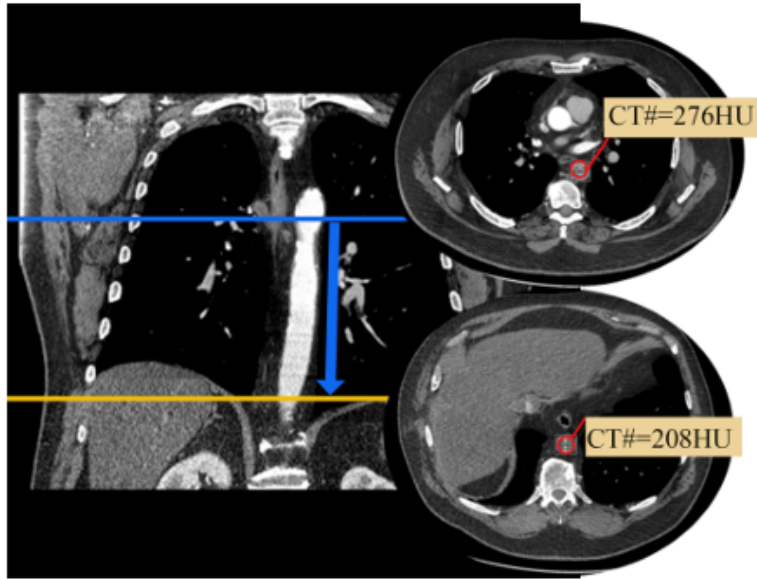
Increasing volume can give more enhancement, but change contrast timing

Increasing concentration will increase enhancement and usually won't change timing

Factors Affecting Contrast Enhancement on CT Images

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CT scans use iodinated contrast media (ICM) to increase enhancement of soft-tissue structures. Some techniques, such as CT angiography, accentuate specific anatomy. The chemical structure of ICM is rich in iodine. Because of iodine's high atomic number, use of ICM causes an increase in CT number and image contrast. Improper contrast enhancement is a leading motivator for both repeated CT examinations and those with limited or suboptimal diagnostic utility. Optimization of contrast agent administration is essential to avoid poor enhancement. Many interacting factors affect contrast enhancement and can be divided into three main categories: physics-based, patient-related, and contrast protocol-based factors. Physics-based factors include tube potential, beam hardening, and scan duration. Patient-related factors include blood volume and cardiac output. Contrast protocol-based factors include contrast agent volume, injection rate, iodine concentration, scan delay, and saline flush. These factors can be further stratified into scalar, temporal, and sampling factors. Scalar factors change the magnitude of enhancement by a fixed percentage independent of time (eg, changing tube potential or iodine concentration). Temporal factors modify the temporal dynamics of contrast enhancement (eg, changes in cardiac output or injection rate). Sampling factors affect how an ICM enhancement curve is sampled (eg, scan duration, scan delay). Understanding the available parameters and their impact on ICM enhancement equips the reader with tools to optimize contrast agent delivery and scanning protocols in CT.

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PHYSICS

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For a detailed review of factors affecting iodine contrast enhancement in CT, see our Radiographics publication

“The CT Handbook: Optimizing Protocols for Today’s feature-rich scanners” By Tim Szczykutowicz. Medical Physics Publishing 2020



Thanks!

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CT

