University of Wisconsin Madison

CT EDUCATION AND COLLABORATION CENTER

CT Contrast Agents and Enhancement Principles

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CONFLICT OF INTEREST

No Conflict of interest to declare.

TEACHING POINTS

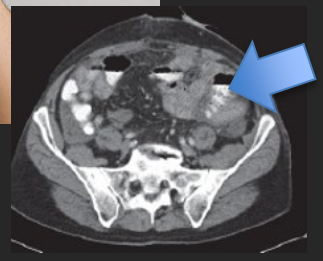
1. Learn about the major types of contrast agents used in CT: why they work and their clinical applications

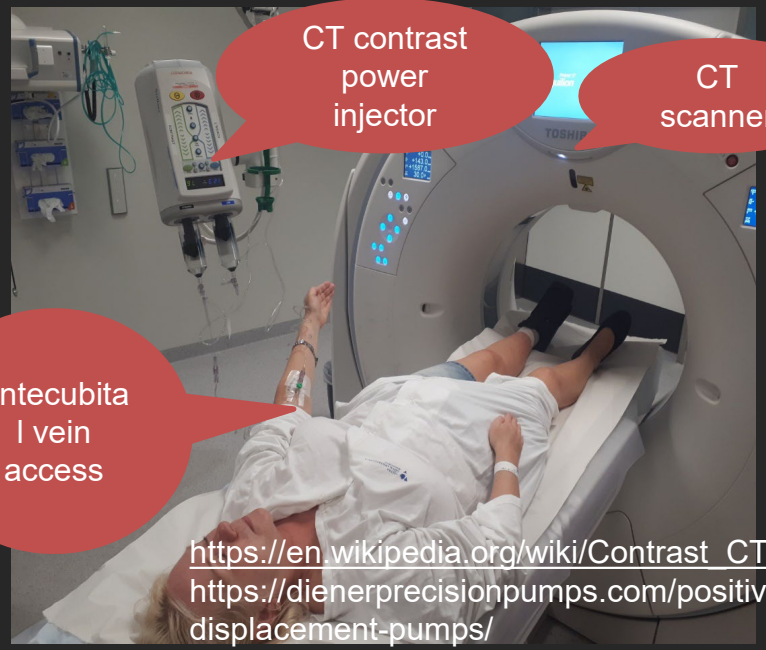
2. Understand the route IV contrast agents take through the body: speed of travel, changes in enhancement, and commonly used imaging phases

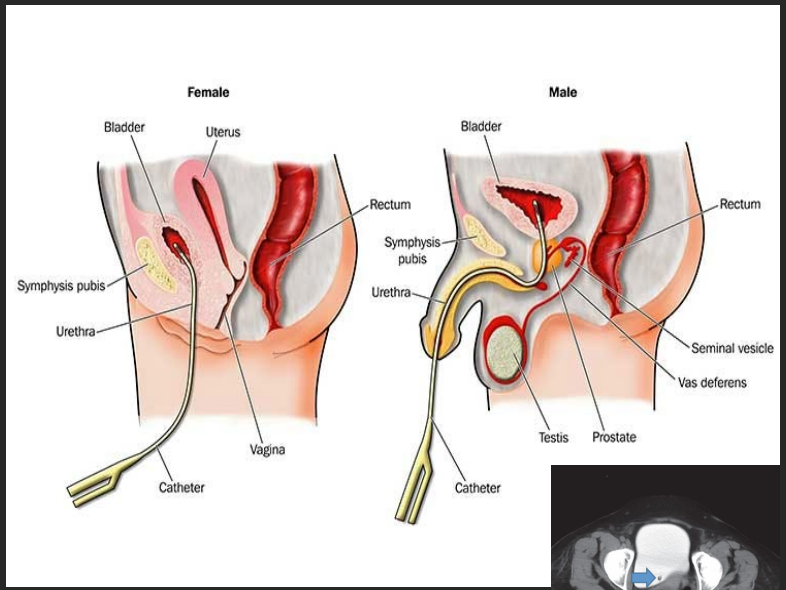
3. Review the factors that influence CT contrast agent enhancement

DIFFERENT TYPES OF CONTRAST AGENTS IN CT

CT contrast agents make soft tissue contrast in CT





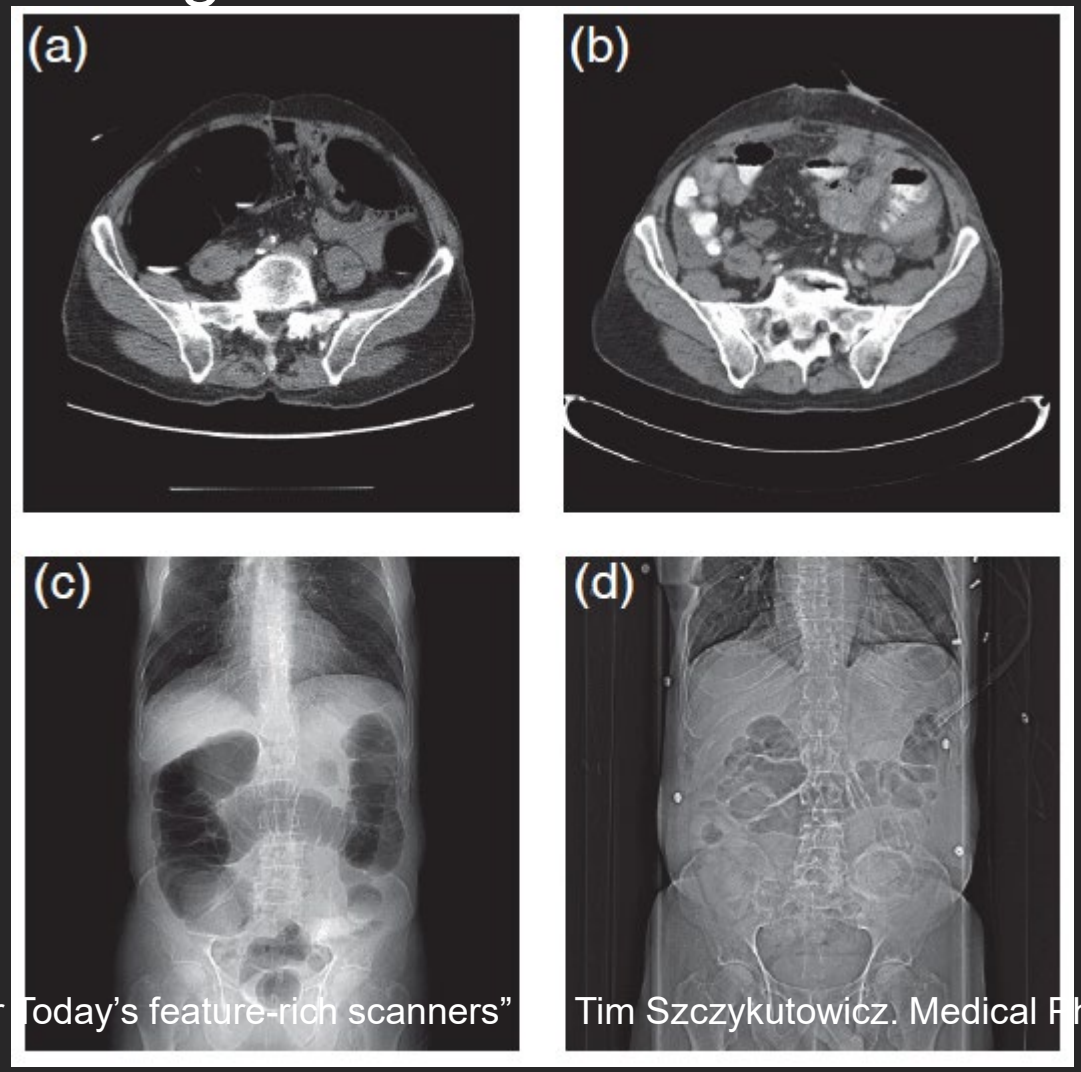


"The CT Handbook: Optimizing Protocols for Today's feature-rich scanners" By Tim Szczykutowicz. Medical Physics Publishing 2020

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

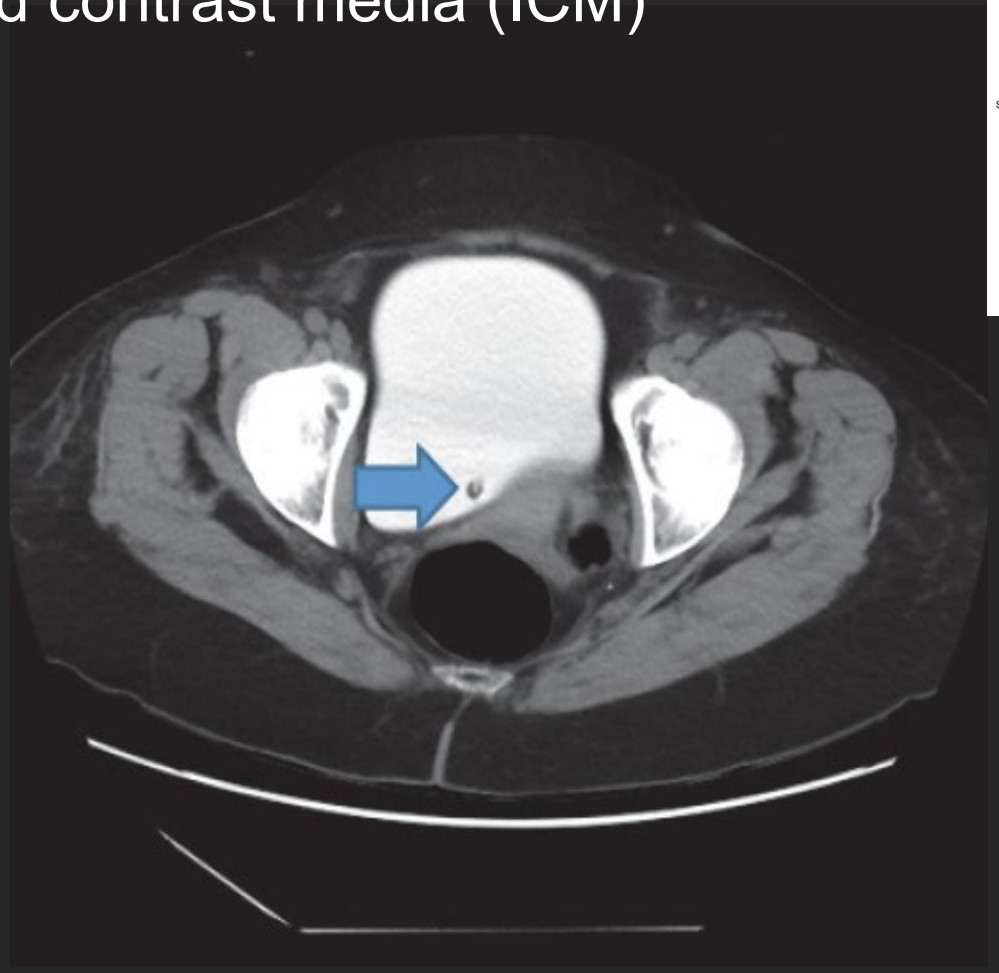
"The CT Handbook: Optimizing Protocols for Today's feature-rich scanners" Tim Szczykutowicz. Medical Physics Publishing 2020

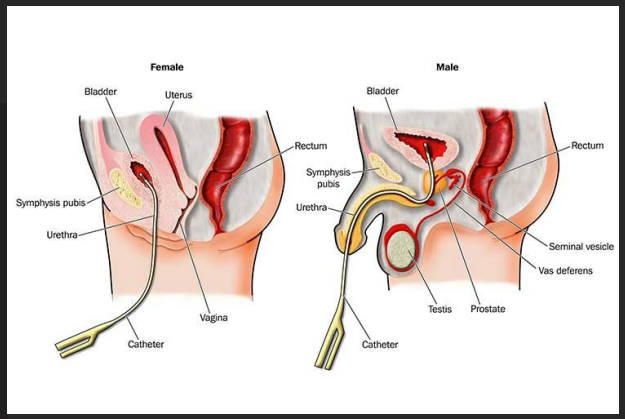
CT CONTRAST 101-POSITIVE AGENTS

Positive agents are Iodinated contrast media (ICM)

Positive oral contrast introduced via Foley catheter

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



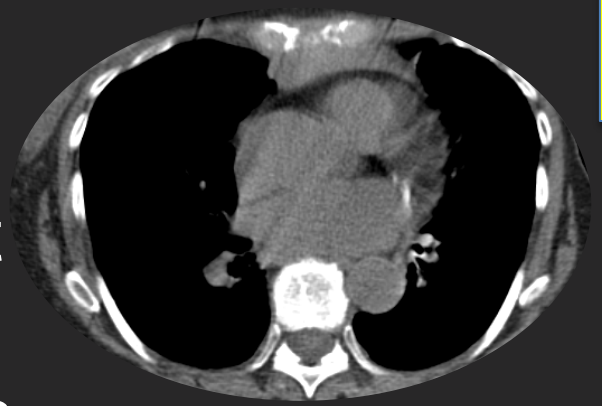


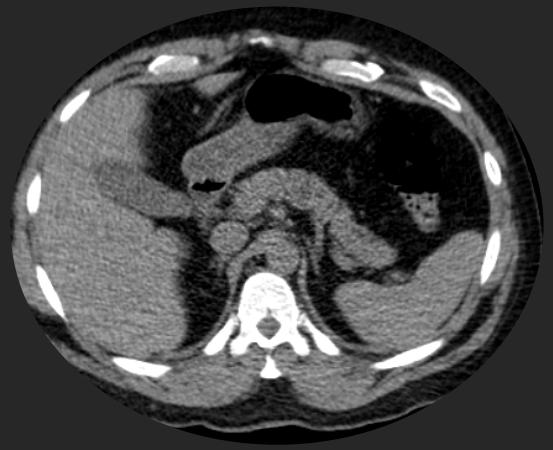
https://www.ausmed.com/cpd/articles/urinary-catheter

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

CT CONTRAST 101

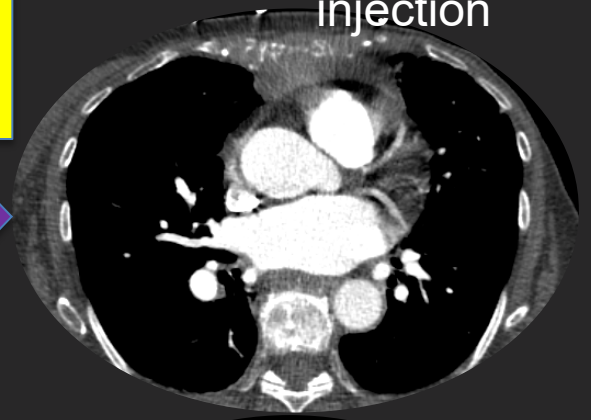
Positive IV contrast (ICM) introduced through intravenous injection

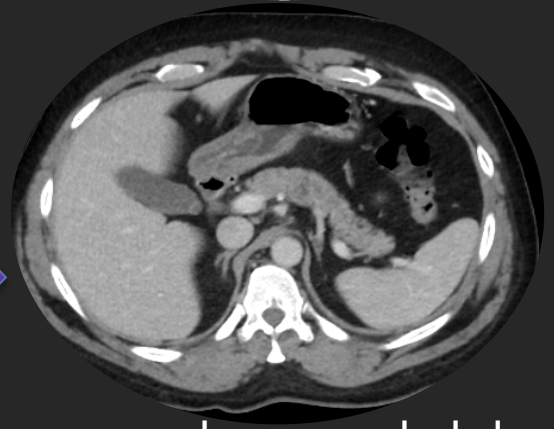




Put your ICM glasses on

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





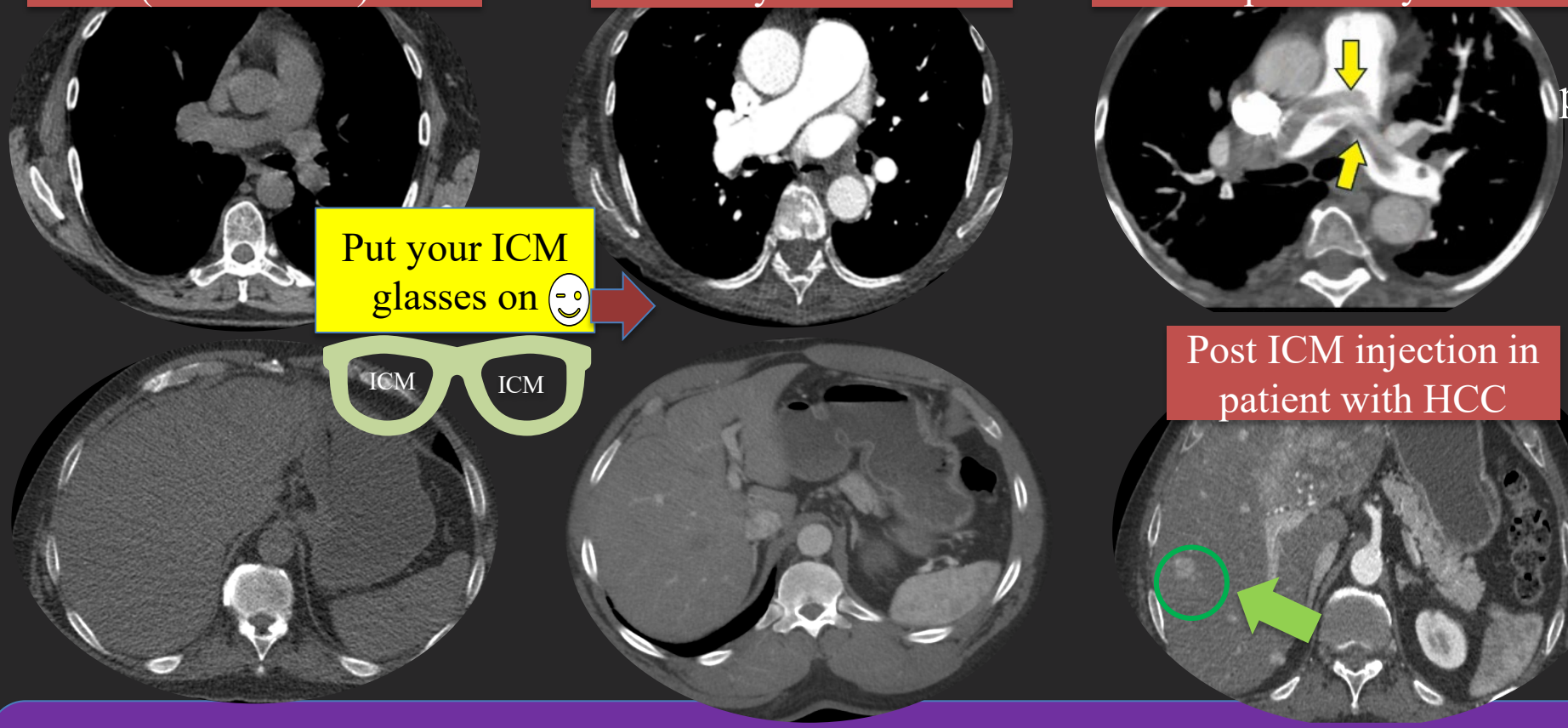
Liver parenchyma and abdominal vessels are better visualized after ICM injection

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



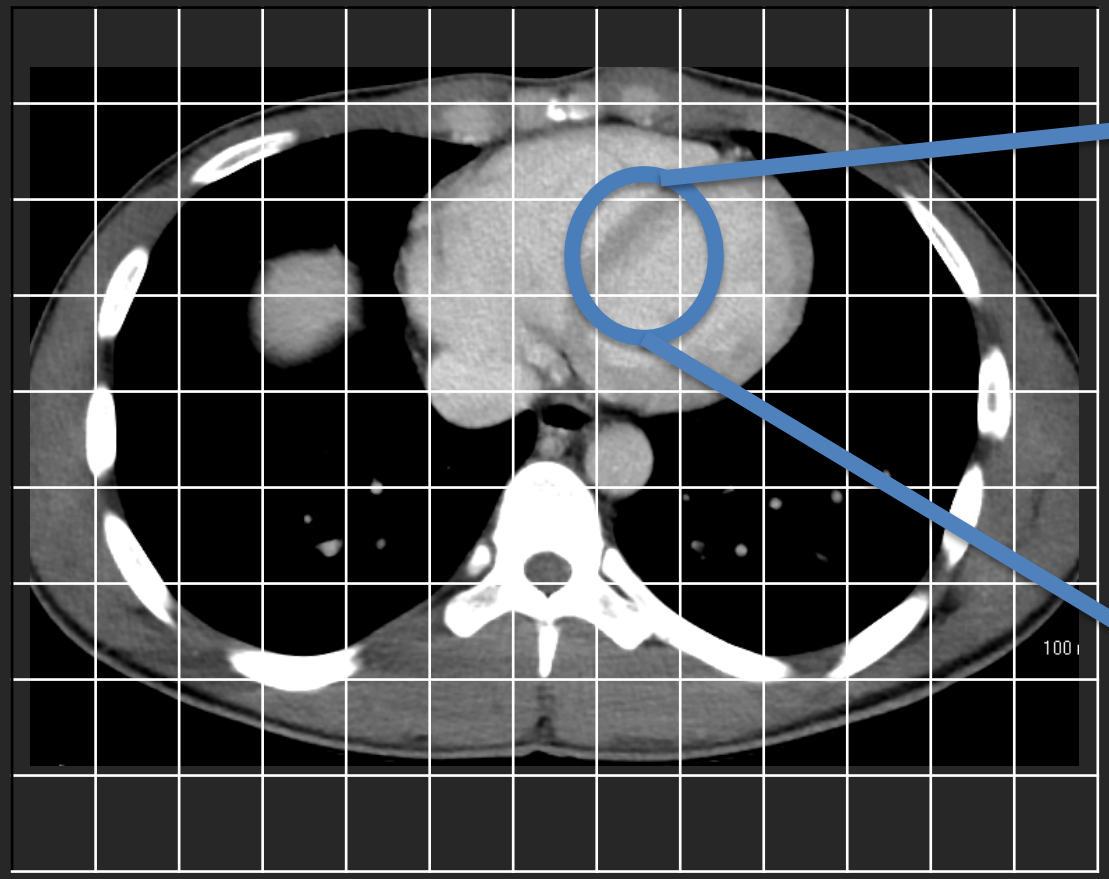
A segment of the pulmonary artery remains unopacified due to pulmonary embolism, clearly visible following ICM injection.

Post ICM injection in patient with HCC

Hepatocellular carcinoma is detectable only after ICM injection

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

WHY CONTRAST AGENTS WORK?



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

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.

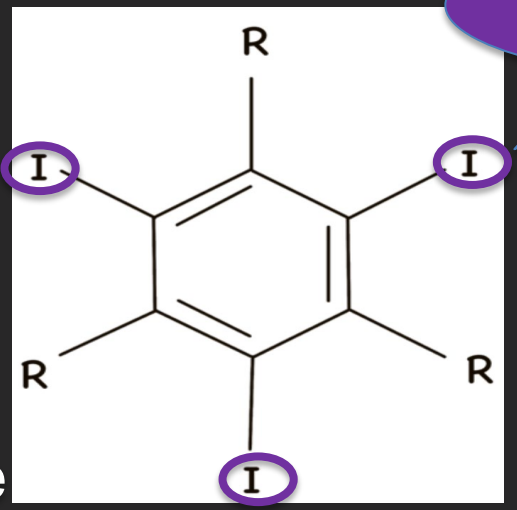
Positive ICM agent:

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

$Z_I=53$

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

Increased CT number when voxel contains iodine



3 Iodine atoms per contrast molecule

Iohexol is a common CT ICM and in different concentrations

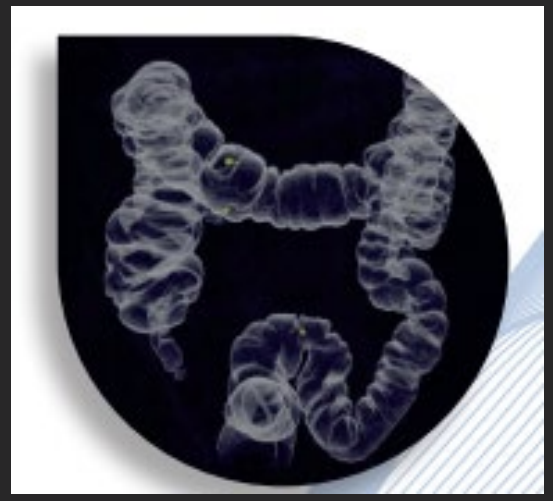
Common concentrations of ICM used for diagnostic CT in the USA is 300-370 mgI/ml.

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

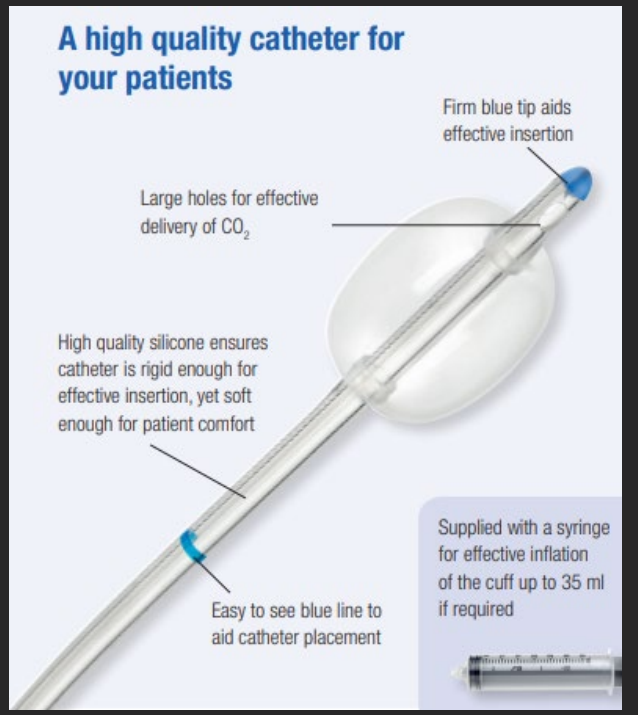
Most common application of CO2 in CT is patients with allergy to ICM and poor renal function used in both arteriography and venography



Air/CO2

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

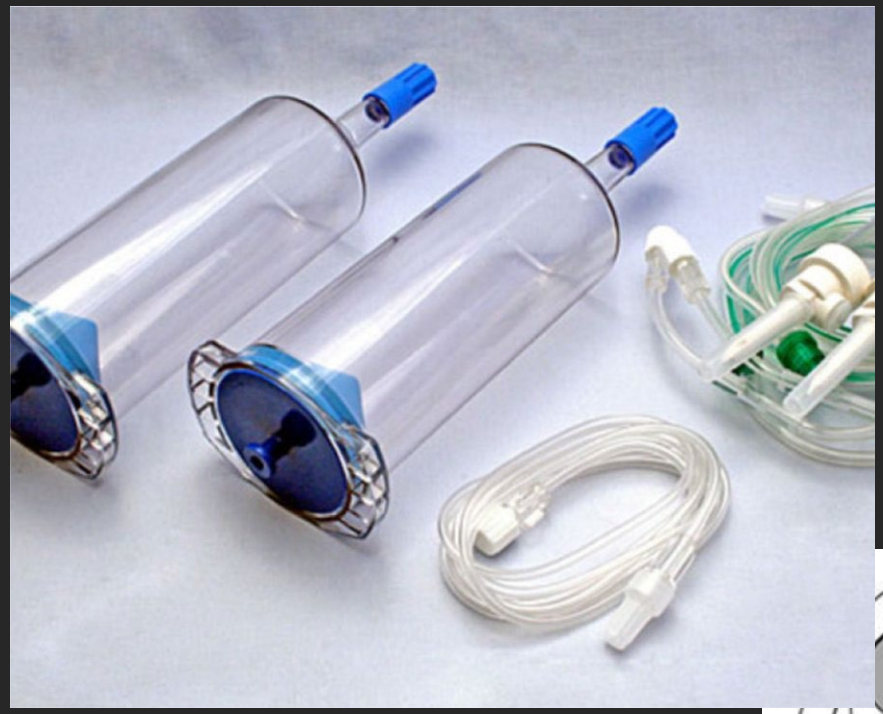
Used for CTC



Images from “Automated Carbon Dioxide Insufflation System for Virtual Colonoscopy” by Bracco sales brochure

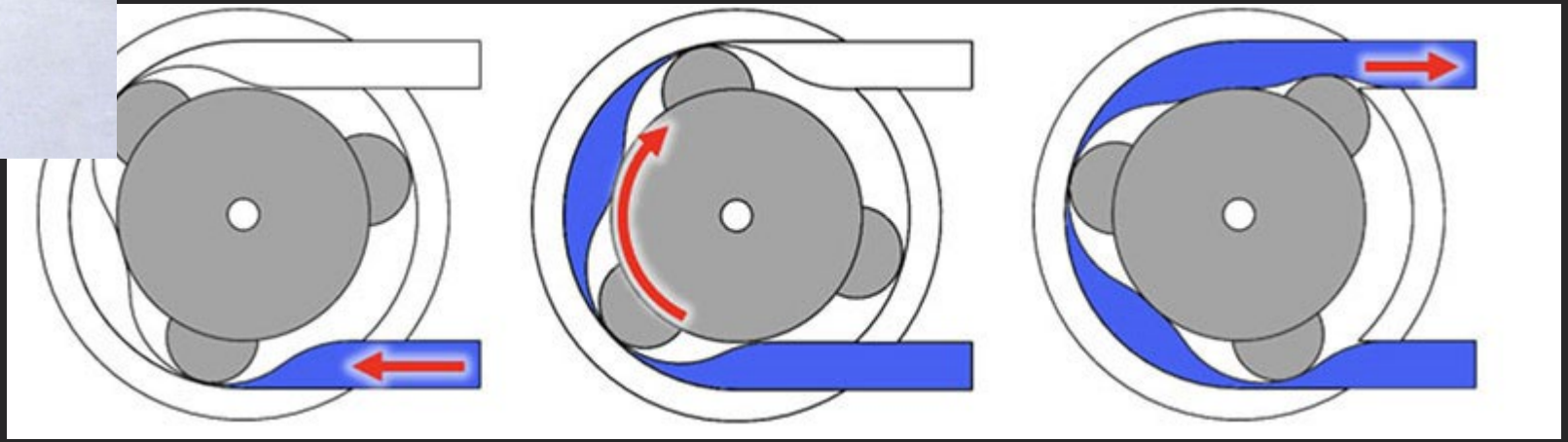
IV INJECTION OF ICM

CT CONTRAST 101



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

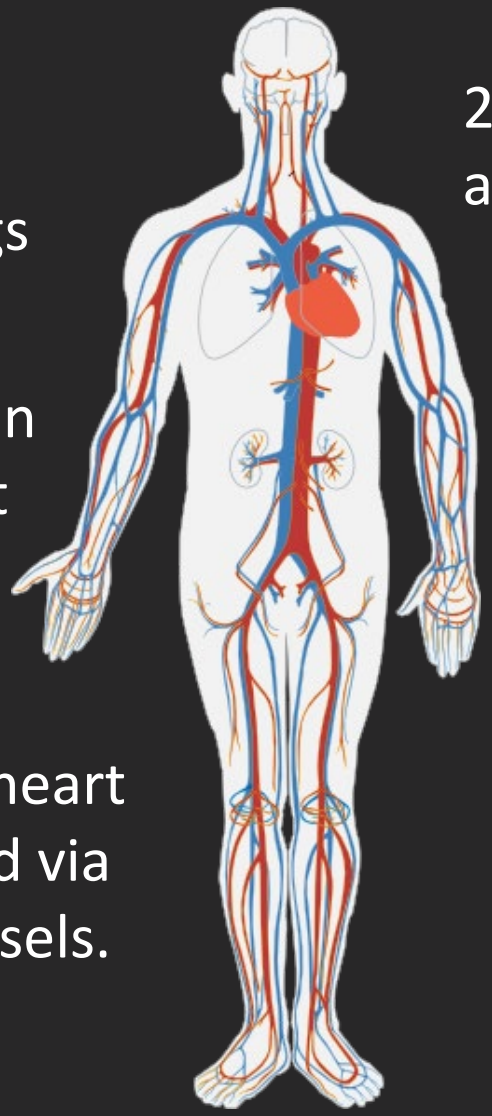
Peristaltic pump, the rotating action pushes agent along a flexible tube



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

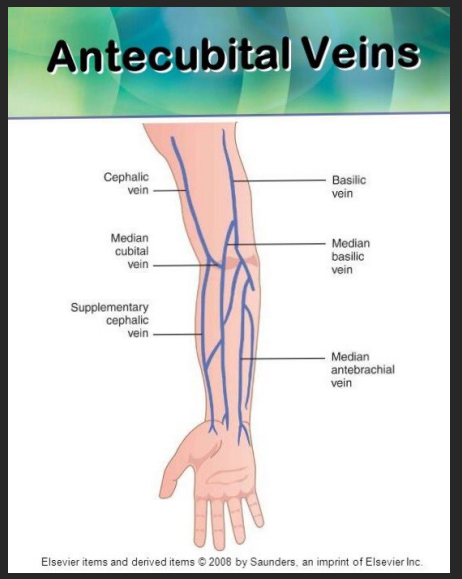
THE ROUTE OF IV CONTRAST AGENTS

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



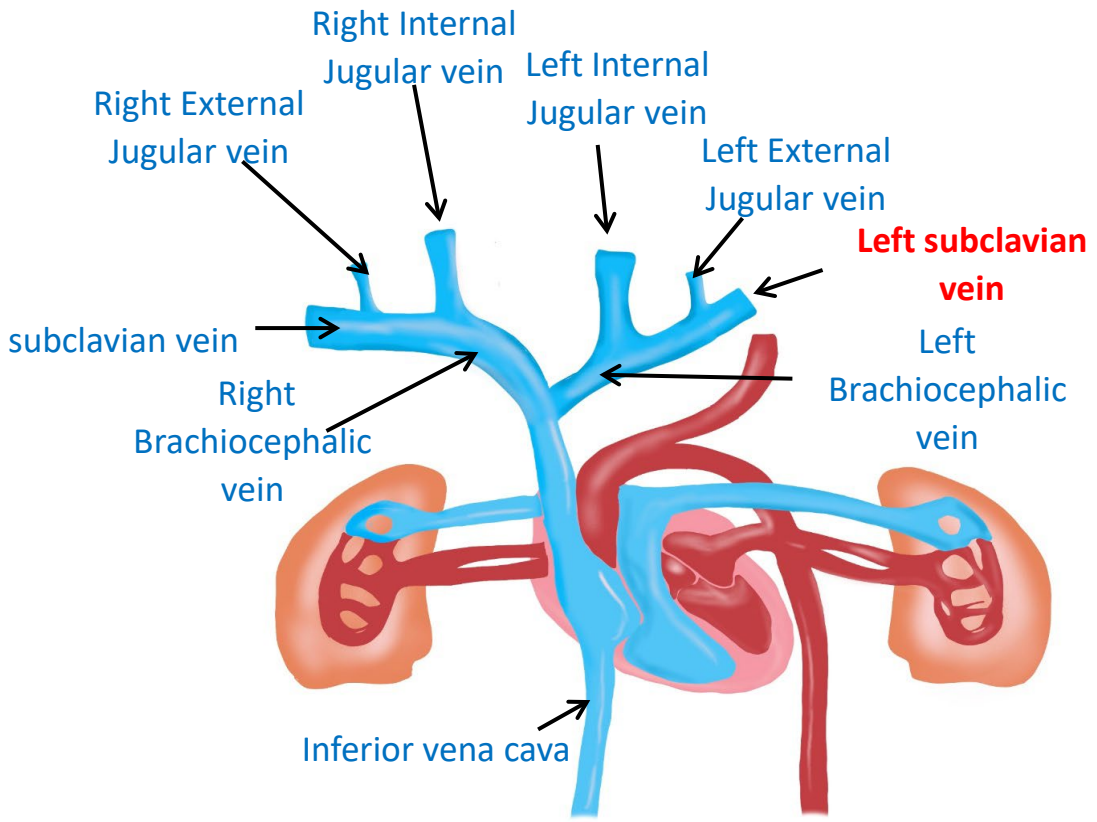
2. Blood goes into SVC and then into right atrium

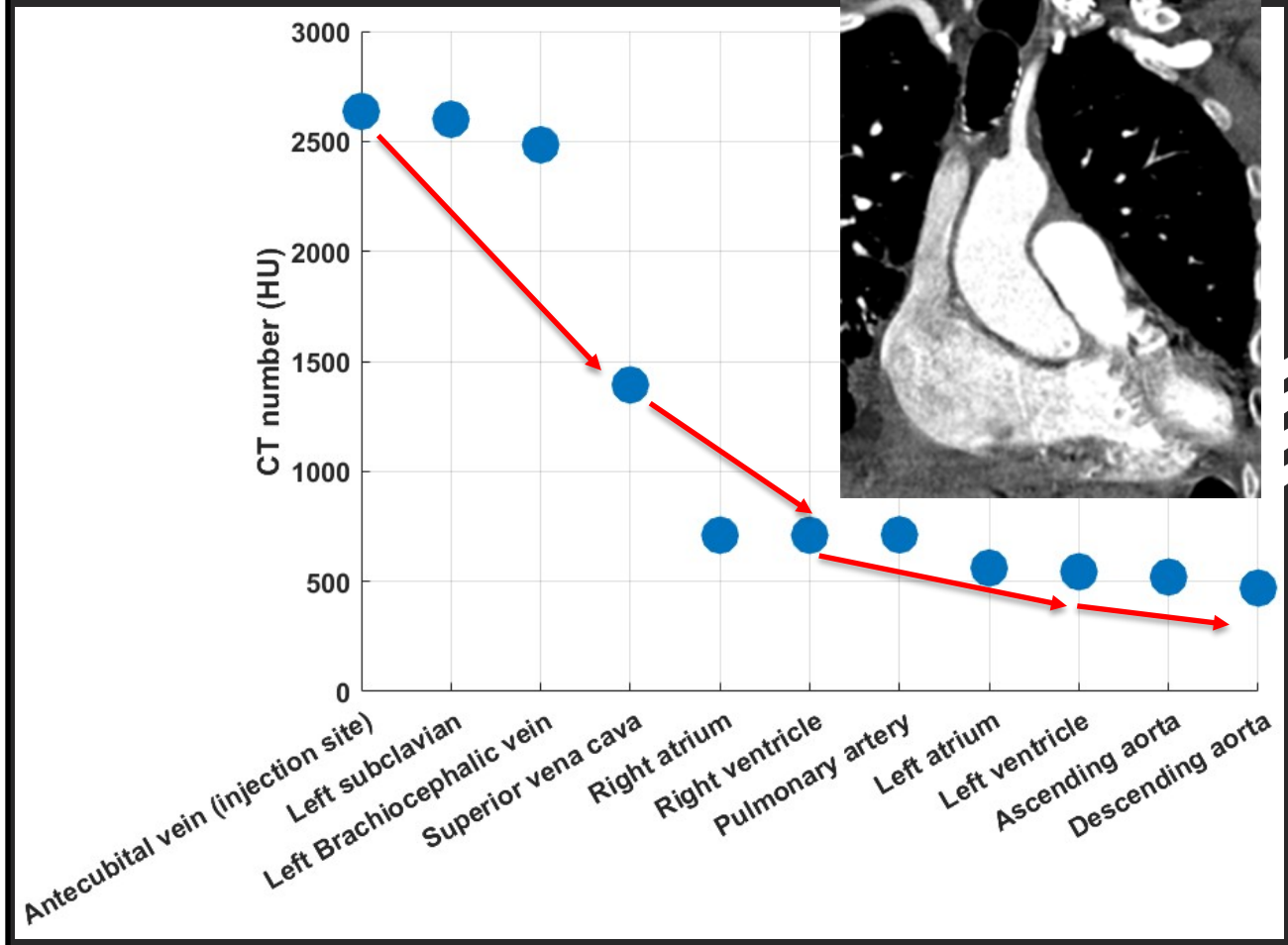
1. Inject via antecubital vein



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.


Right Internal
Jugular vein
Left Internal
Jugular vein
Right External
Jugular vein
Left External
Jugular vein
Left subclavian
vein
subclavian vein
Left
Brachiocephalic
vein
Right
Brachiocephalic
vein
Inferior vena cava


3000
2500
2000
1500
1000
500
0
CT number (HU)
Antecubital vein (injection site)
Left subclavian
Left Brachiocephalic vein
Superior vena cava
Right atrium
Right ventricle
Pulmonary artery
Left atrium
Left ventricle
Ascending aorta
Descending aorta

SPEED OF ICM TRAVEL

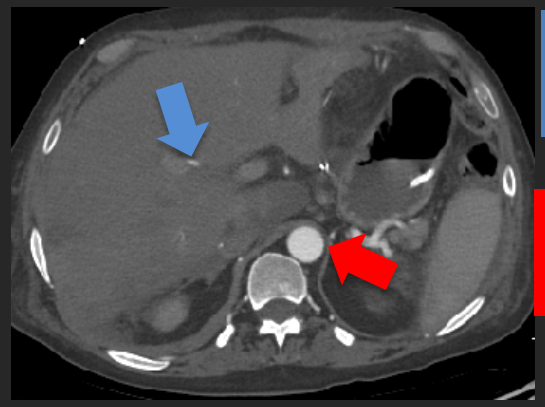
Contrast time of arrival will vary from person to person, but assuming an antecubital injection, values will generally be in the range of
7 to 10 seconds for the pulmonary artery,
12 to 15 seconds for the ascending aorta,
15 to 18 seconds for the abdominal aorta,
and 30 to 40 seconds for hepatic parenchyma.

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.

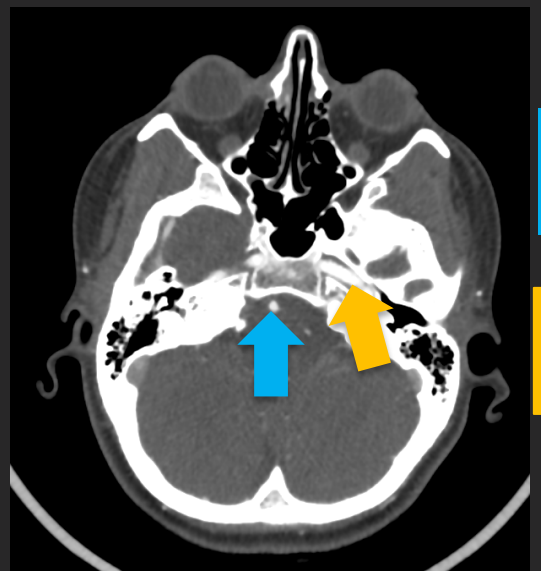
COMMONLY USED IMAGING PHASES

Arterial phase



Intrahepatic artery

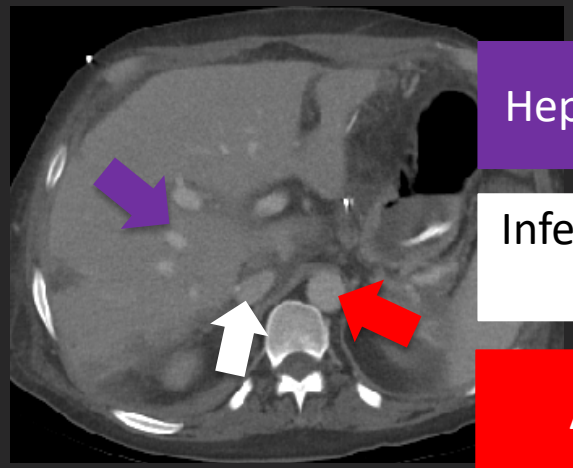
Aorta



Basilar artery

Carotid artery

Venous phase

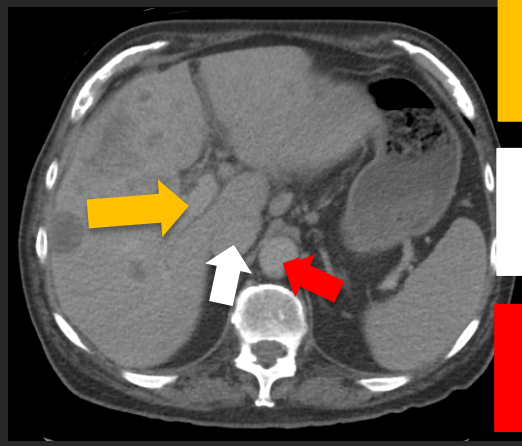


Hepatic vein

Inferior vena cava

Aorta

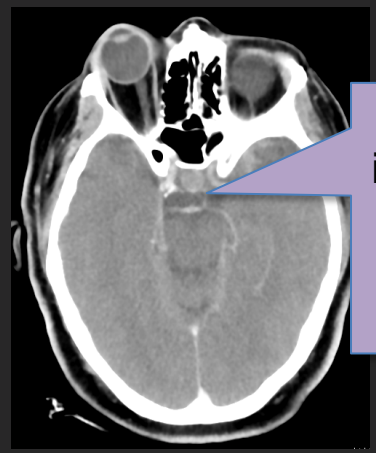
Delayed phase



Portal vein

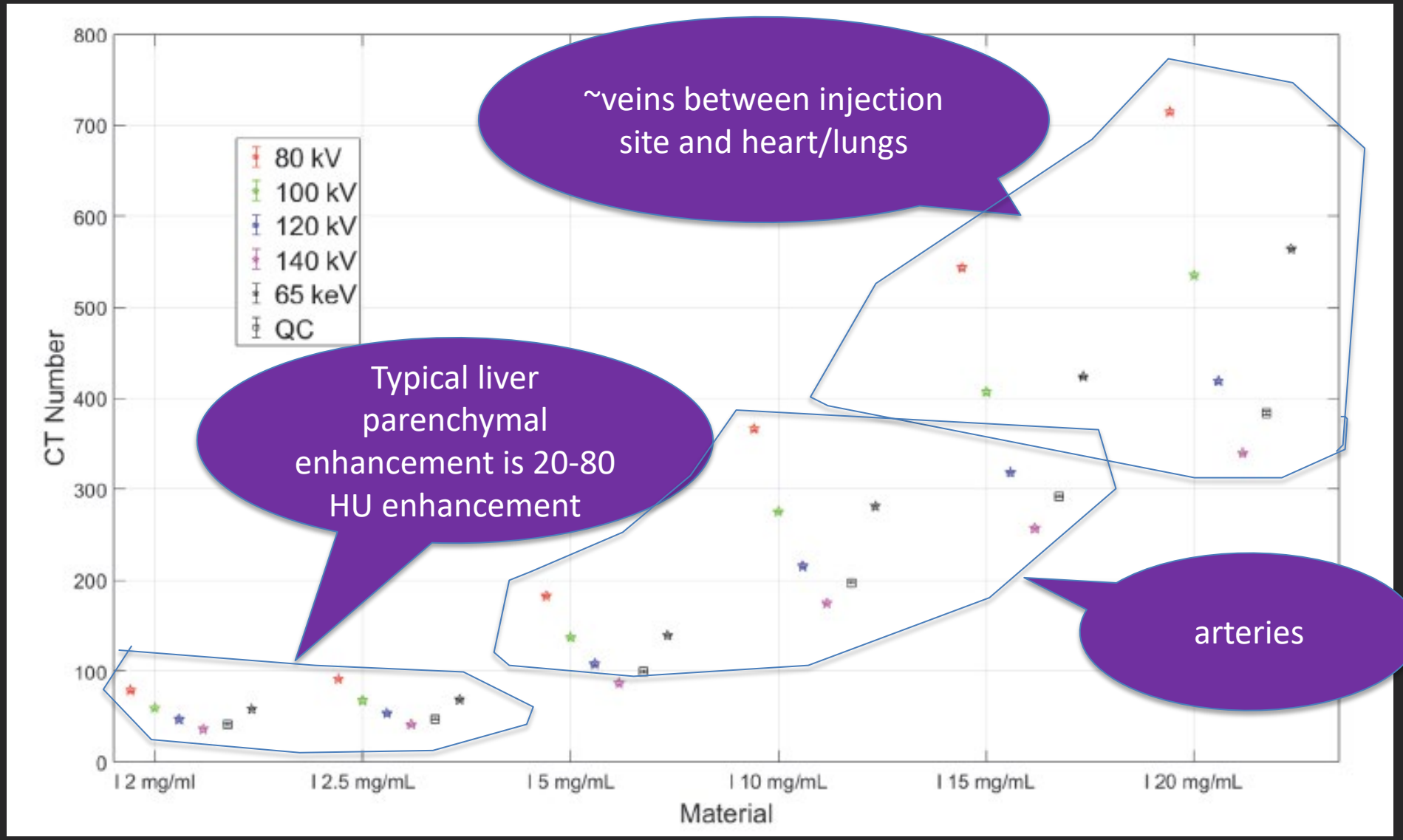
Inferior vena cava

Aorta



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

CT CONTRAST 102



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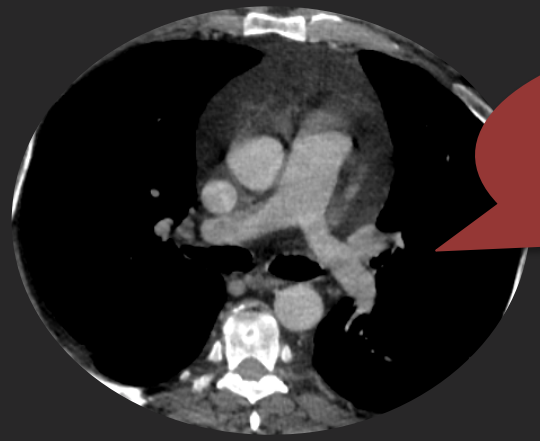
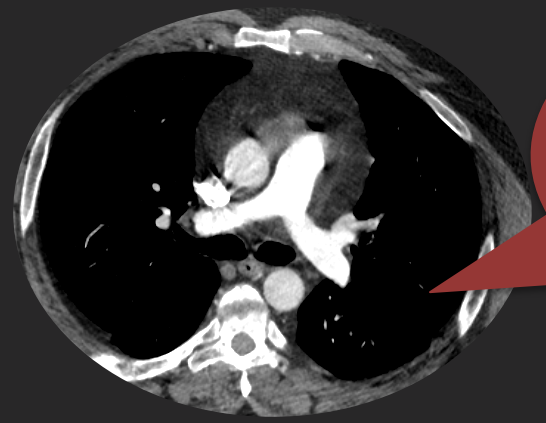
Examples of Good and Poor Contrast Enhancement



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 wi
- Environmental and Hu

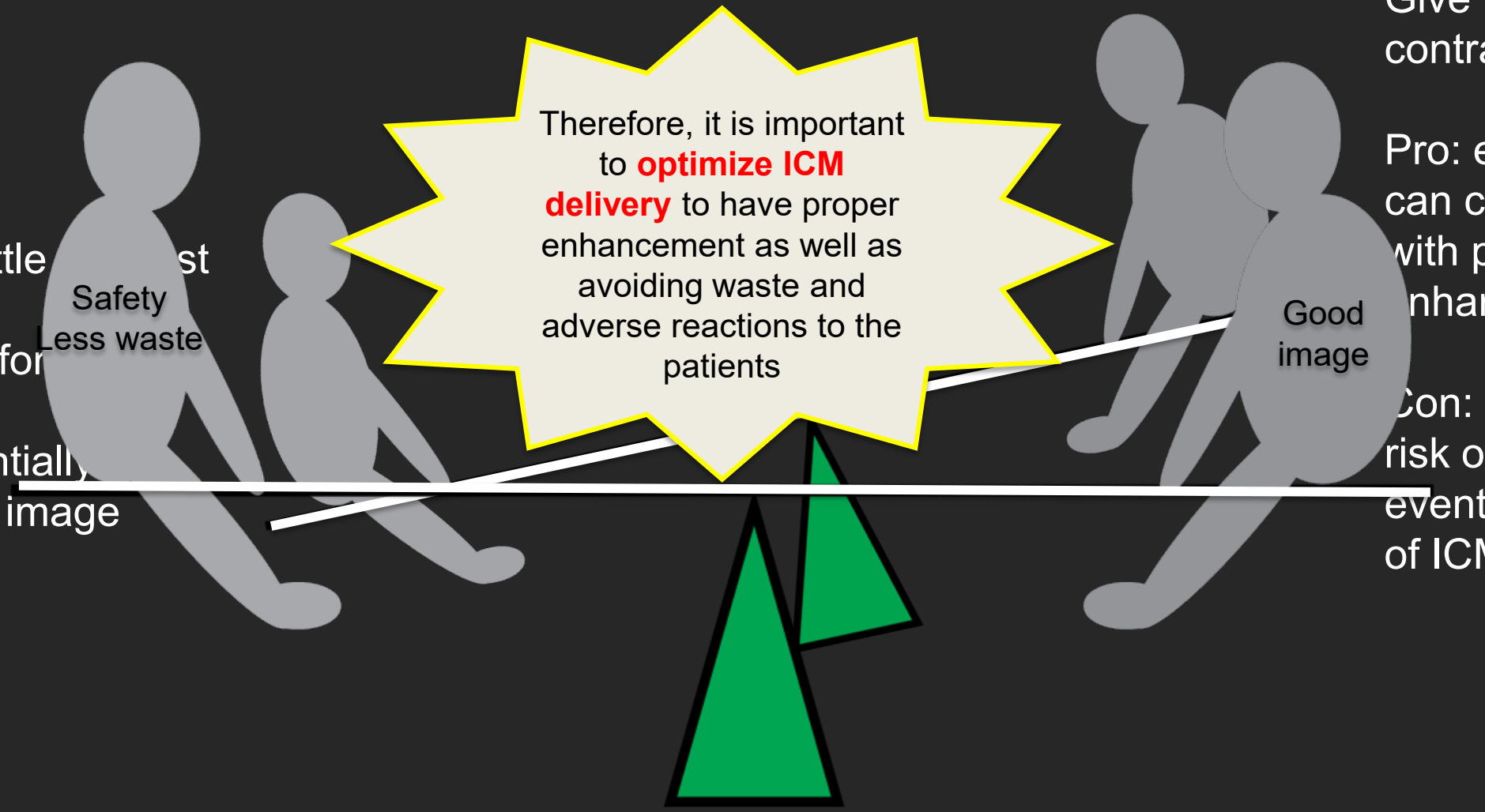
Therefore, it is important to **optimize ICM delivery** to have proper enhancement as well as avoiding waste and adverse reactions to the patients

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.

Give too little contrast

Pro: safer for

Con: potentially diagnostic 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	Patient-related factors	Contrast Protocol-based factors
✓Tube potential ✓Beam hardening ✓Scan duration	✓Blood volume ✓Cardiac output	✓Contrast volume ✓Injection rate ✓Iodine concentration ✓Scan timing (scan delay) ✓Saline flush

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

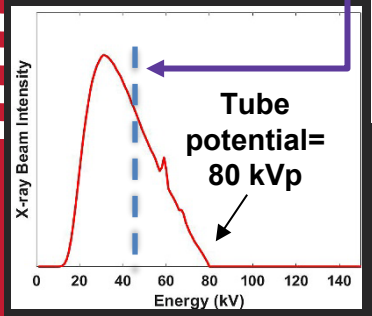
Tube Potential (kV)

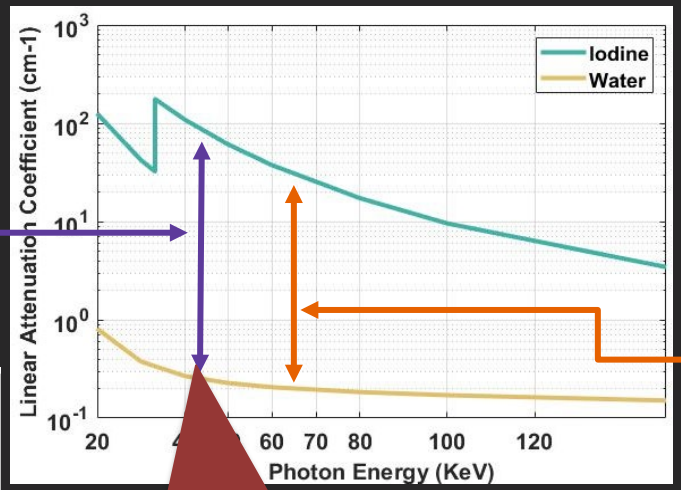
$$\mu(\vec{X},E)=\tau_{PE}(\vec{X},E)+\sigma_{Compton}(\vec{X},E)$$

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

80 kV acquisition X-ray spectrum

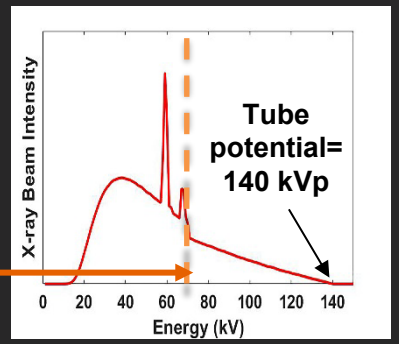
Effective energy= 45 keV



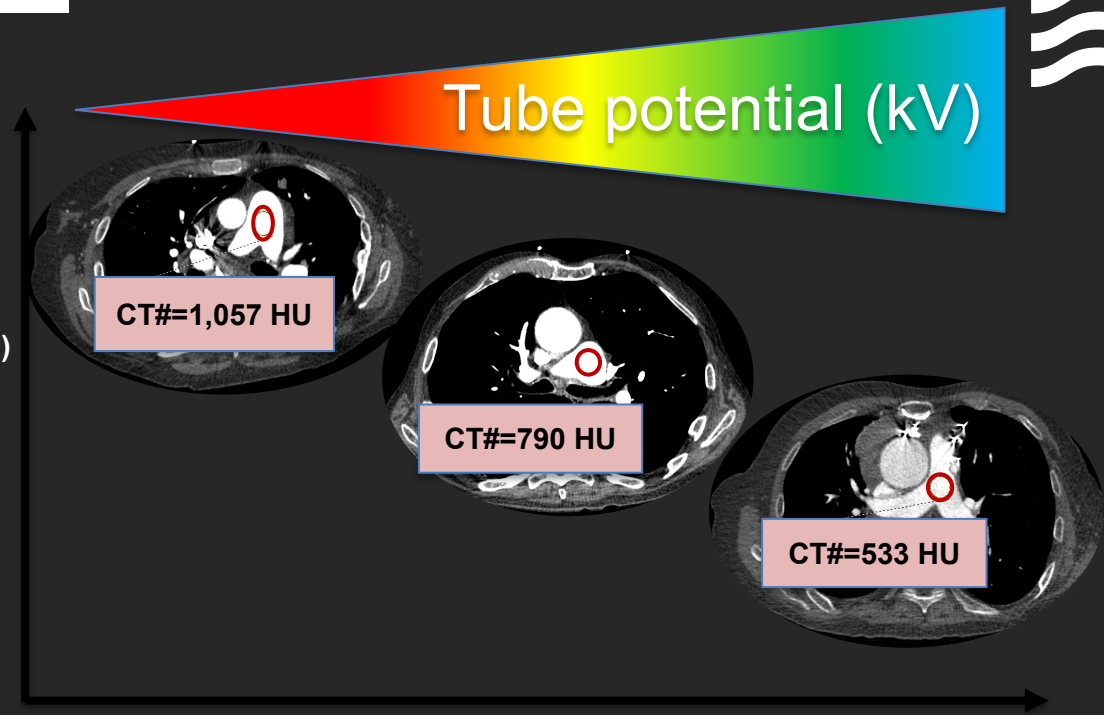


140 kV acquisition X-ray spectrum

Effective energy= 67 keV



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



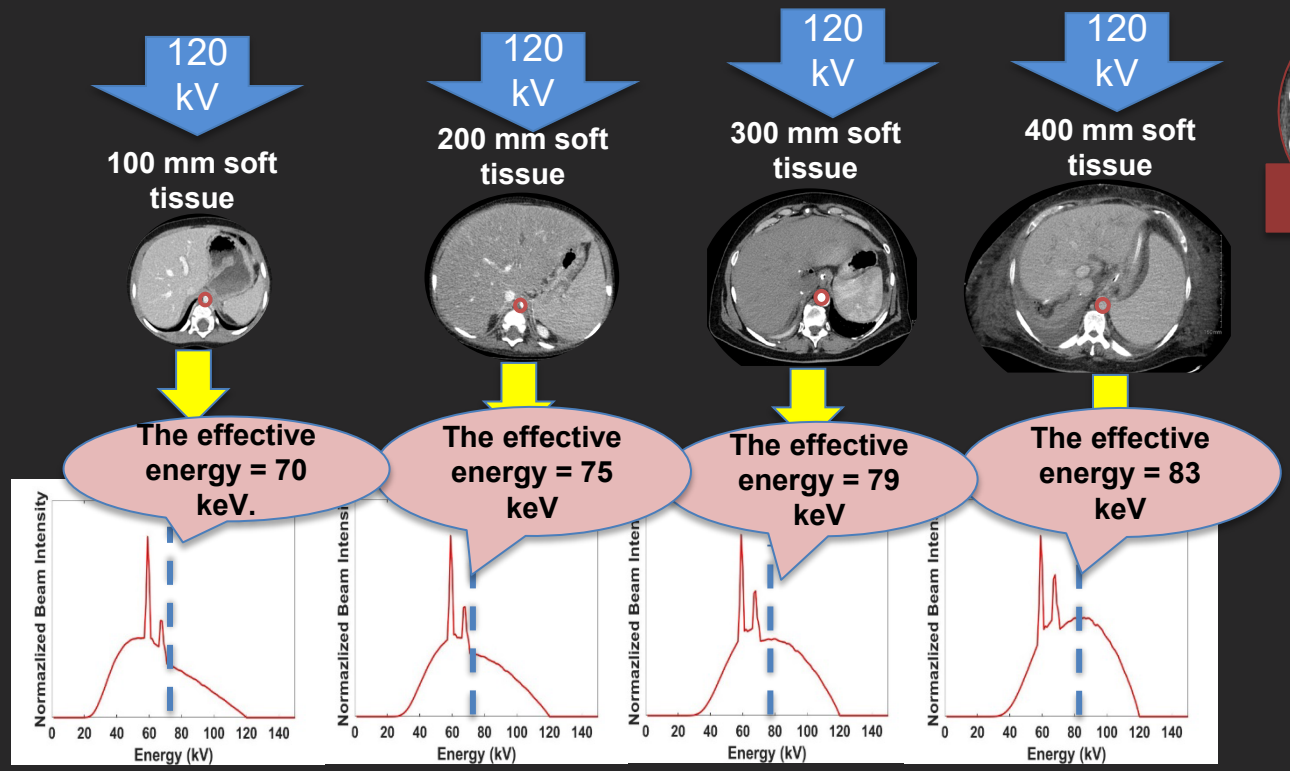
1. Jiang, Hsieh. "Computed tomography: principles, design, artifacts, and recent advances." Bellingham, Washington USA (Published by SPIE and John Wiley & Sons, Inc.): SPIE 2009: 39-44.
2. Szczykutowicz T. The CT handbook: optimizing protocols for today's feature-rich scanners. Medical Physics Publishing,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

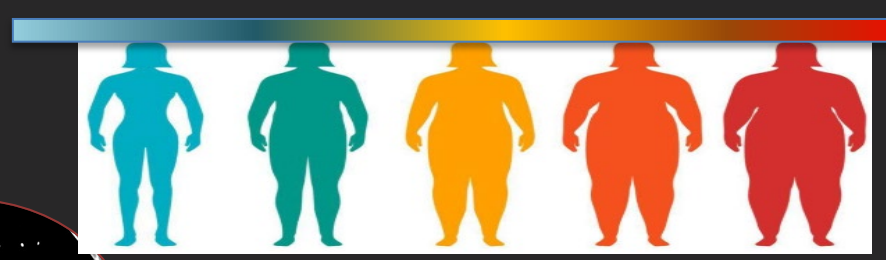
Material	80 kV	100 kV	120 kV	140 kV	N/A
Water	0	0	0	0	[–4 4]**
Air	–1,000	–1,000	–1,000	–1,000	[–1005 –995]**
Fat	–152*	–111*	–89*	–69*	[–100 –80]**
Brain	47*	43*	39*	37*	
Soft Tissue	62*	58*	54*	52*	
Solid Cortical Bone	3,760*	2,590*	1,940*	1,330*	[≈200 > 1000]**
Pure Calcium	9,570*	5,960*	3,950*	2,090*	
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***

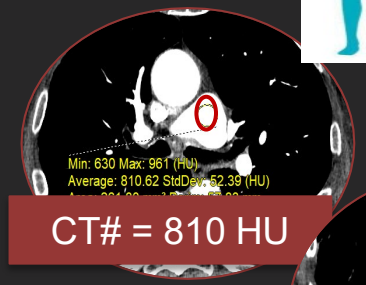
“The CT Handbook: Optimizing Protocols for Today’s feature-rich scanners” By Tim Szczykutowicz. Medical Physics Publishing 2020

Beam Hardening (BH) Related to Patient Size

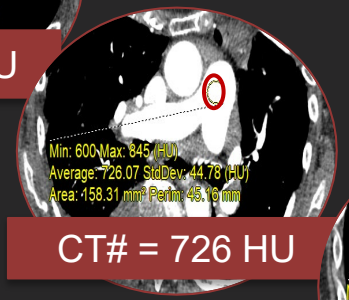
Beam hardening: the gradual increase of average x-ray beam energy as it passes through more patient tissue.



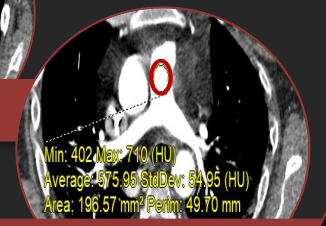




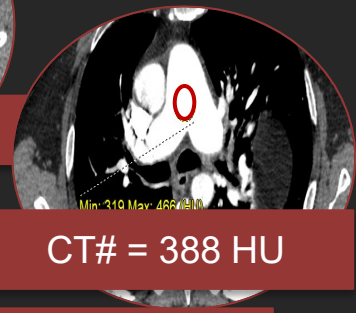
CT# = 810 HU



CT# = 726 HU



CT# = 575 HU



CT# = 388 HU

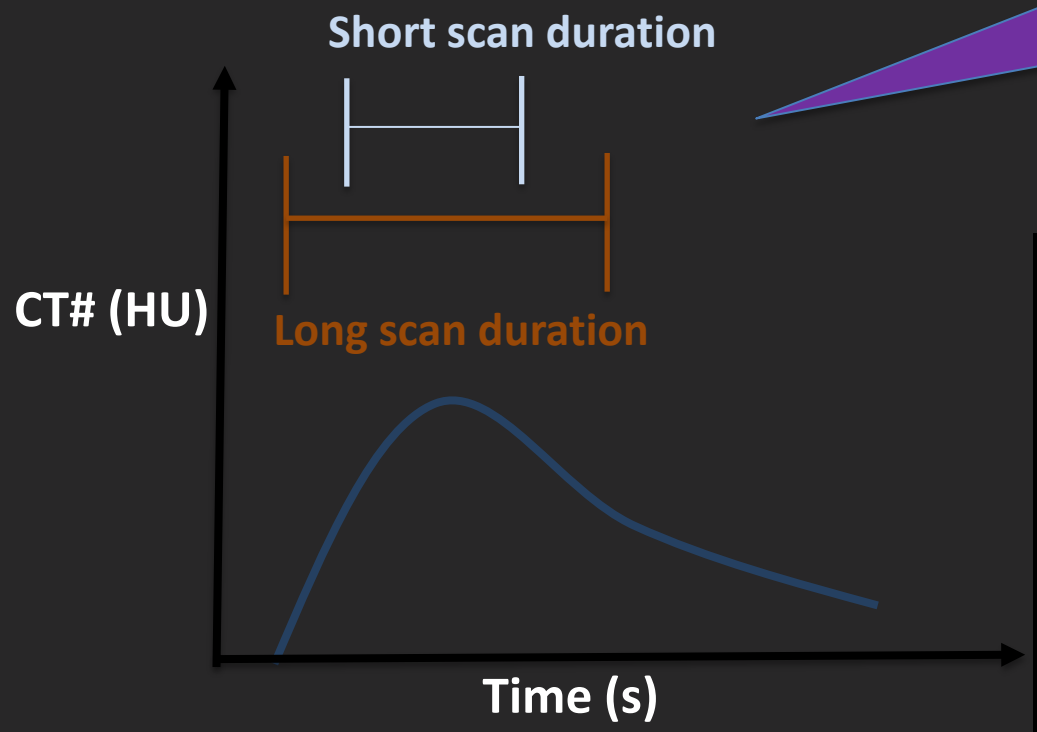
- Iodine concentrations in the ROIs (central circles) are identical
- Low energy X-rays are more attenuated by a larger patient

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

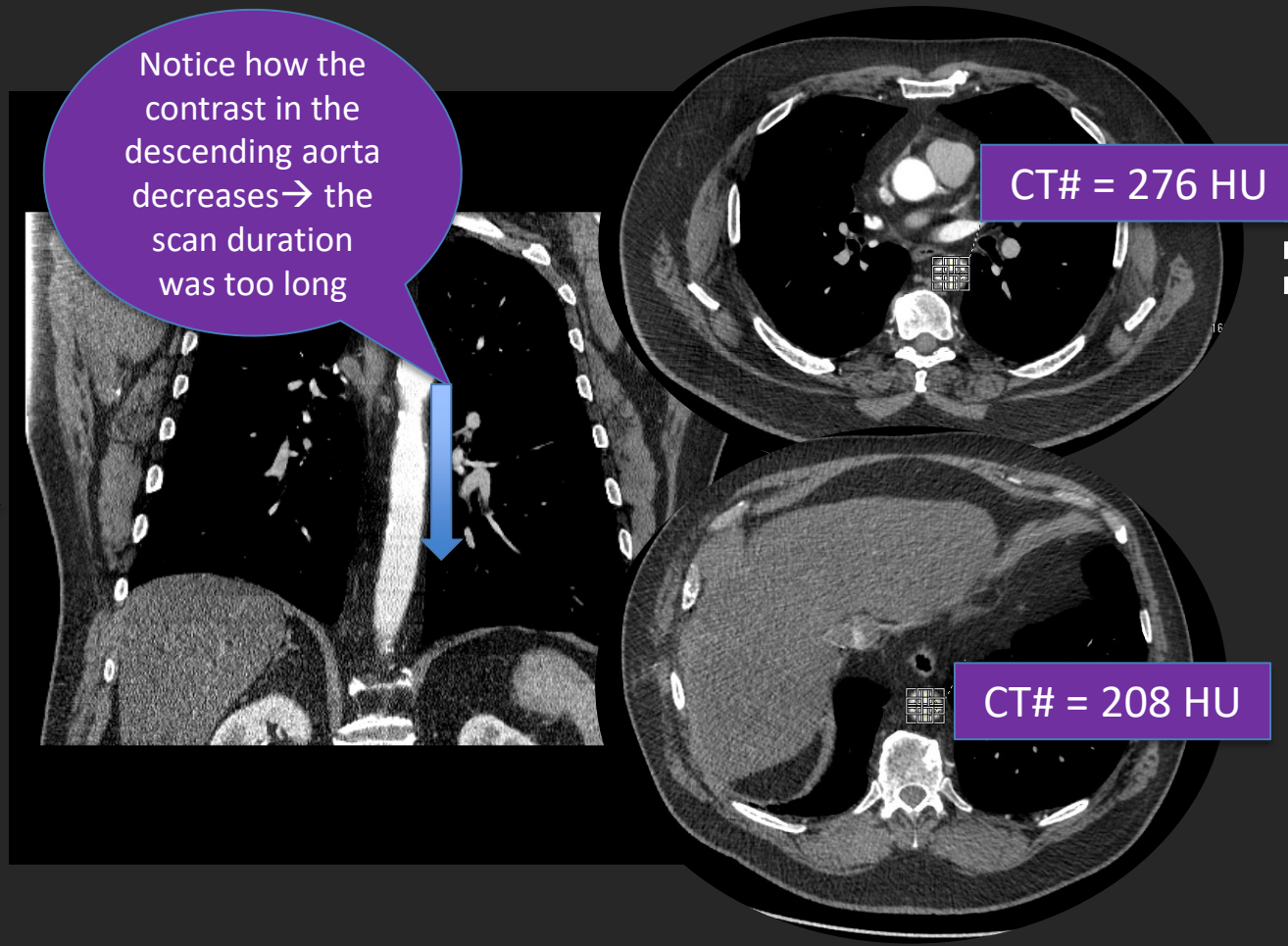
1. Schindera ST, Tock I, Marin D, et al. Effect of beam hardening on arterial enhancement in thoracoabdominal CT angiography with increasing patient size: an in vitro and in vivo study. Radiology 2010; 256(2):528-35

SCAN DURATION

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

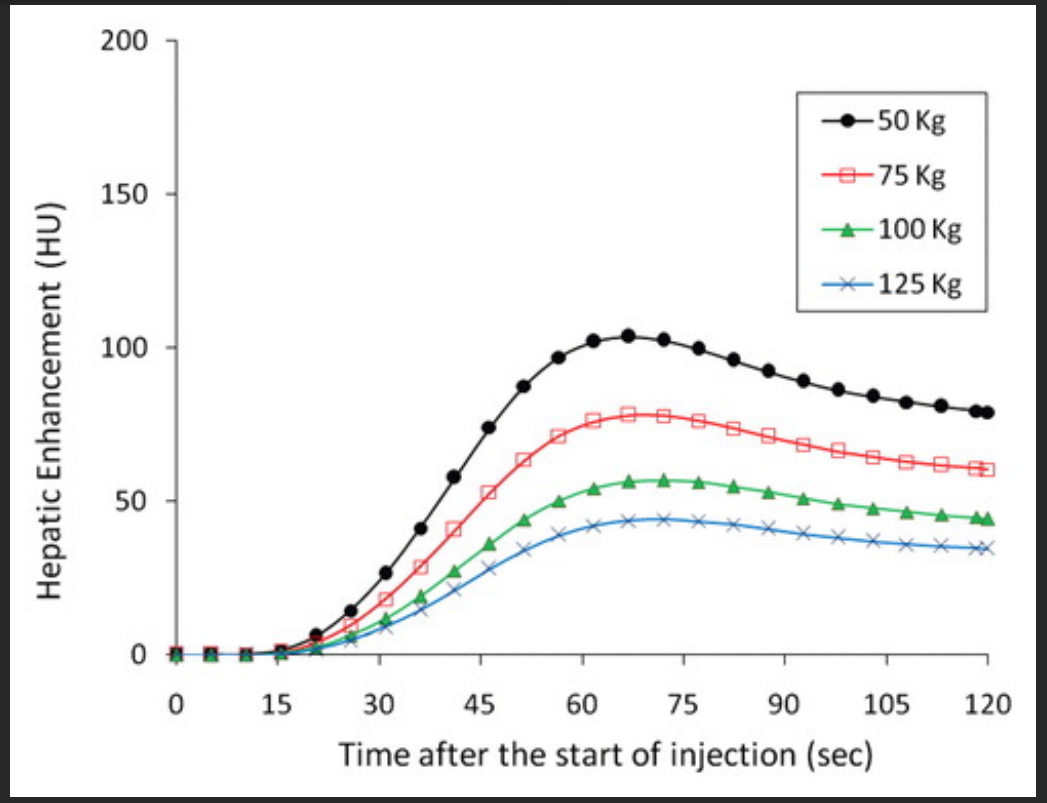


Notice how the contrast in the descending aorta decreases→ the scan duration was too long

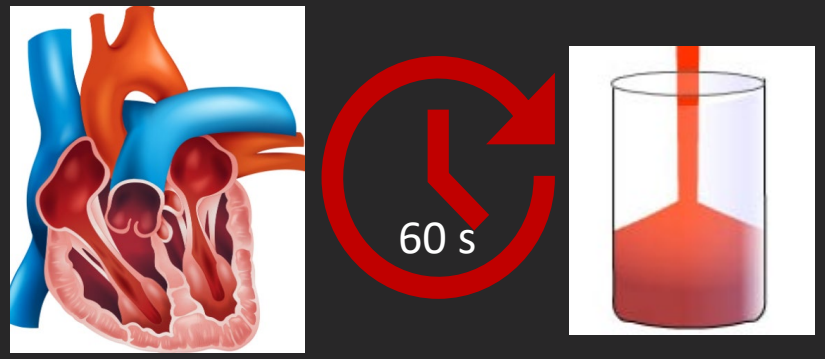


BLOOD VOLUME

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

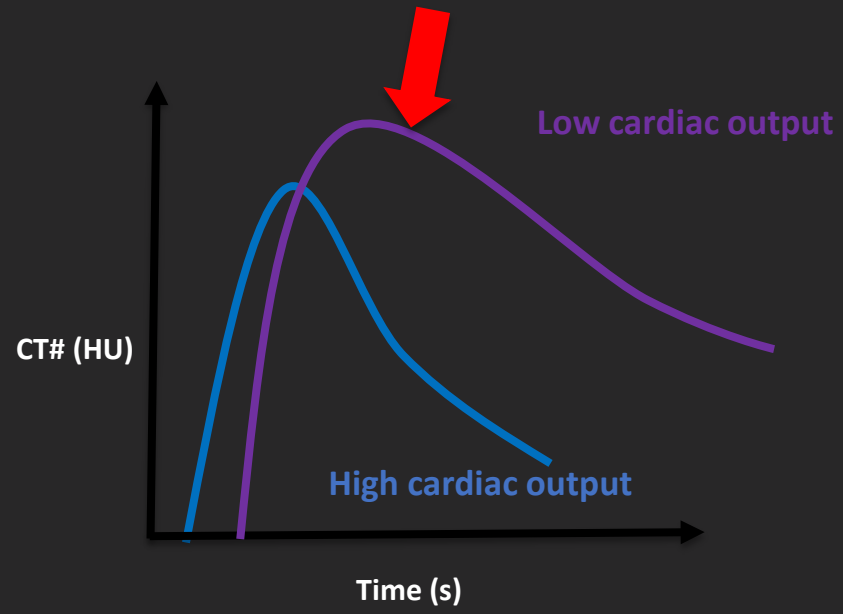


CARDIAC OUTPUT



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



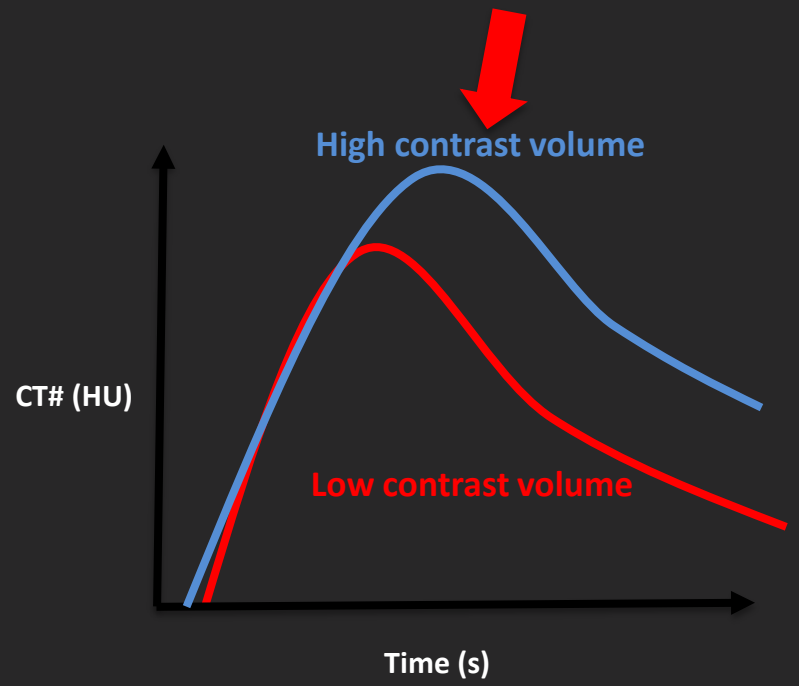
Low cardiac output → Contrast enhancement increases because less un-opacified blood mixes with ICM when the cardiac output is low

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

CONTRAST VOLUME

High contrast volume→ high peak arterial enhancement

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



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

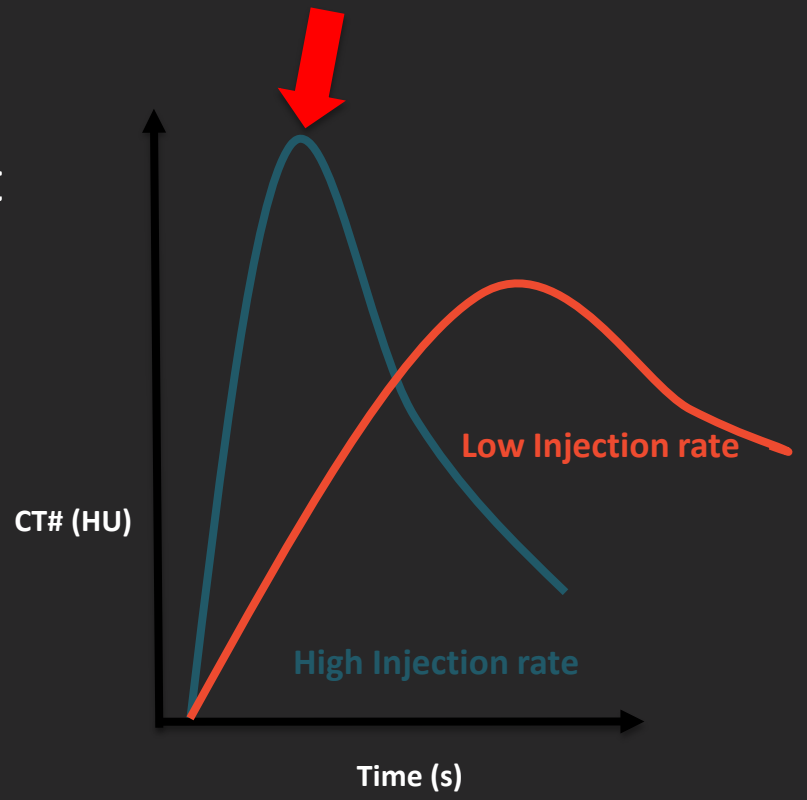
INJECTION RATE

High injection rate → Increased peak arterial enhancement

High injection rate → Decreased time to peak arterial enhancement.

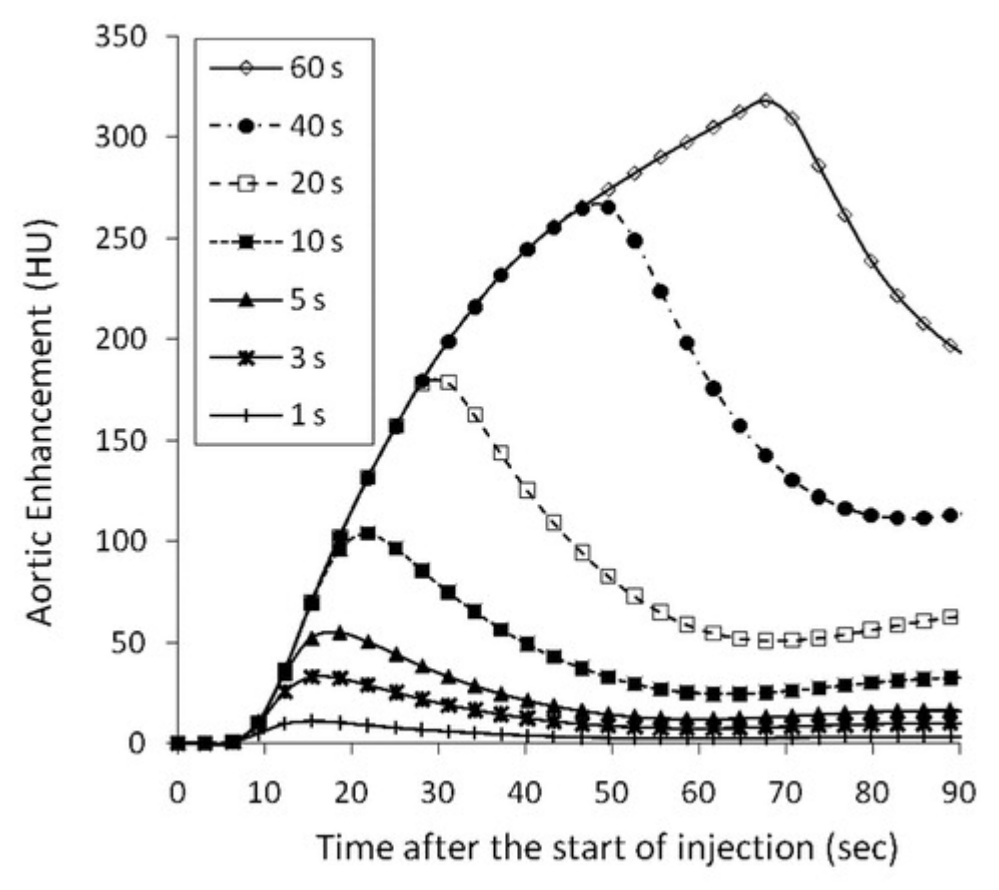
Higher injection rate → Reduces potential temporal window for CT scanning (i.e., peak of contrast plateau is shorter)

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



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

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

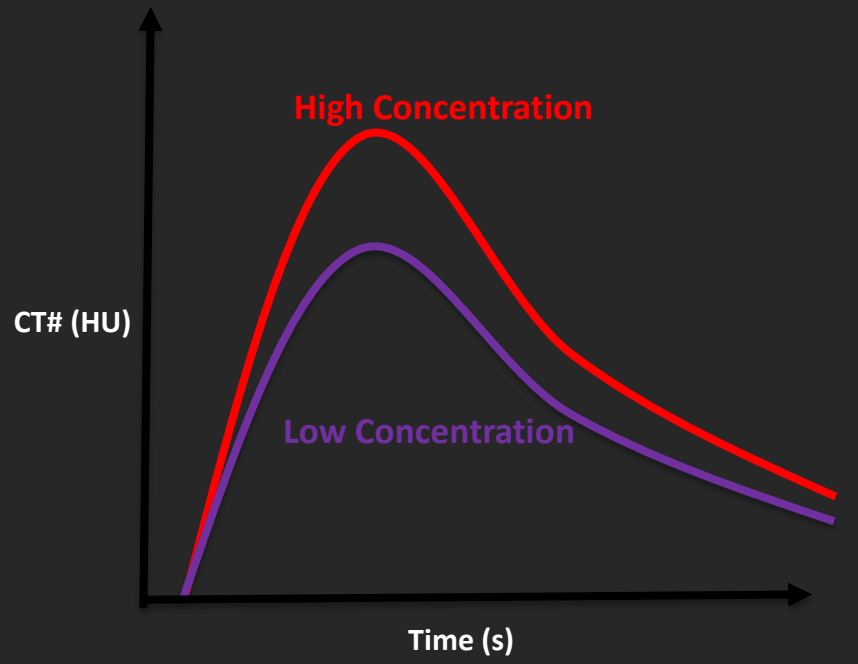
1. Bae KT. Intravenous contrast medium administration and scan timing at CT: considerations and approaches. Radiology. 2010 Jul;256(1):32-61.

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.



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

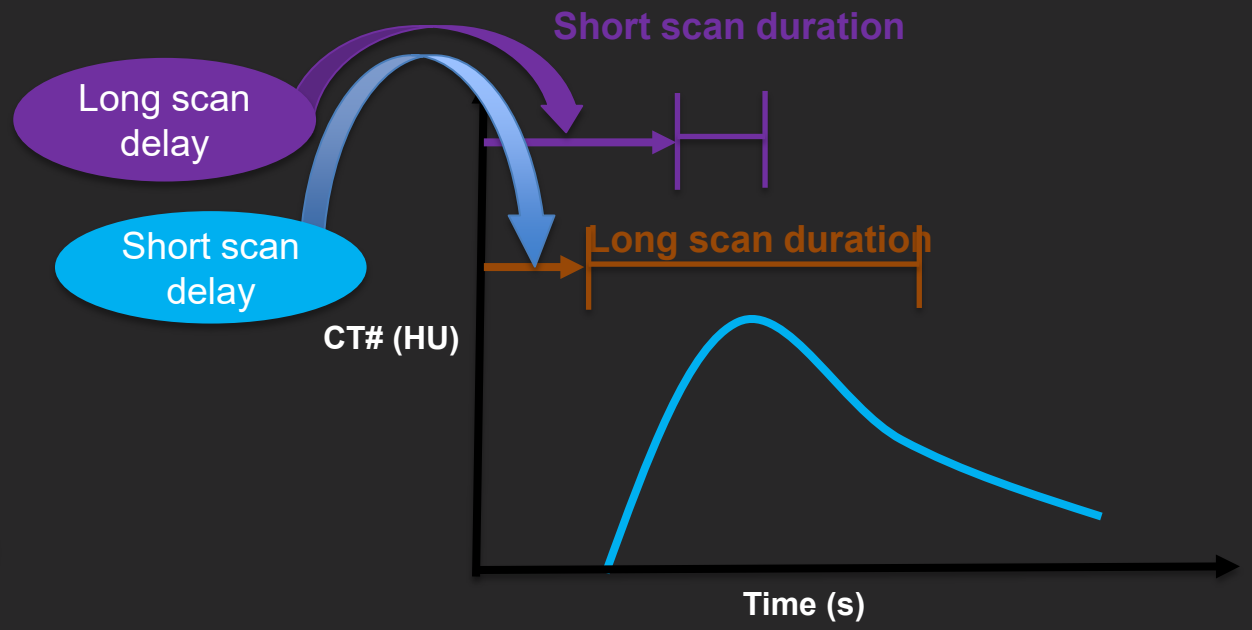
Scan Delay

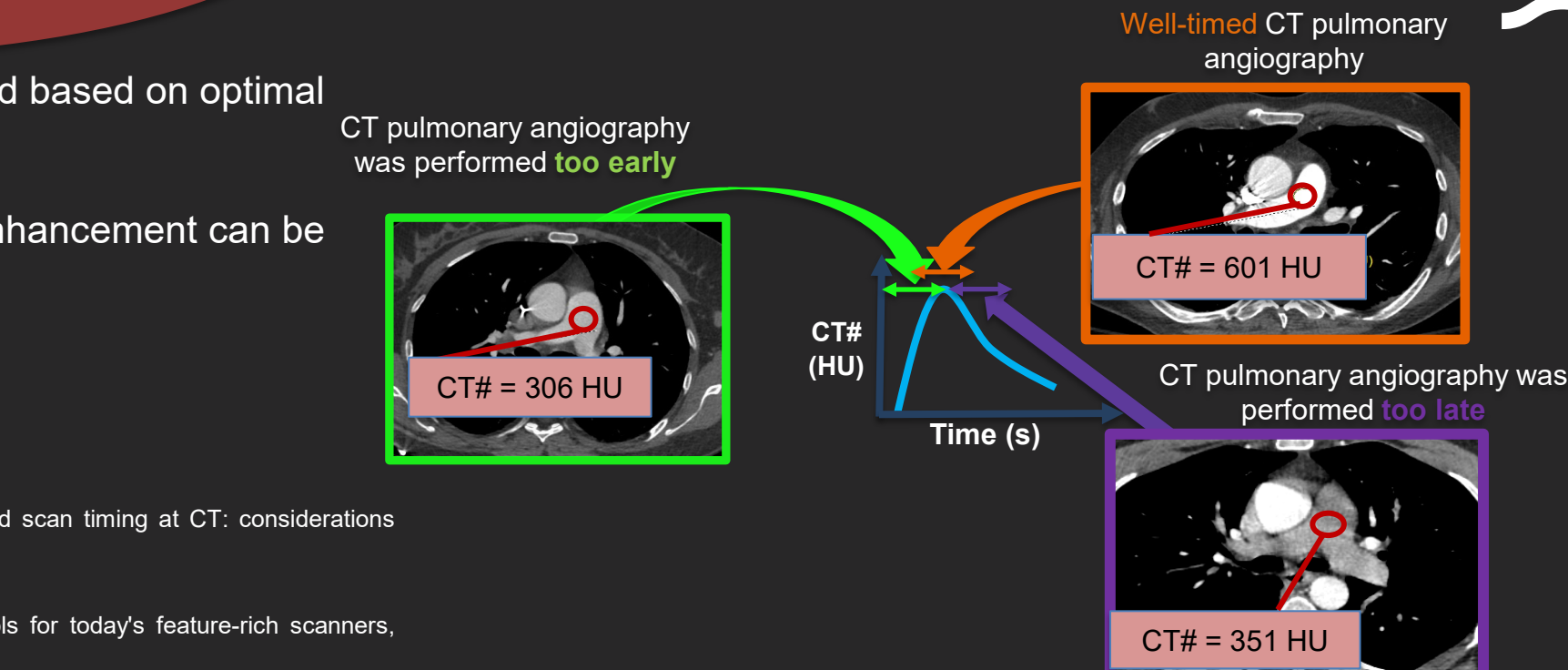
$$\text{Optimal Scan Delay} = T_{Peak} - \frac{1}{2}T_{scan\ duration}$$

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

SALINE FLUSH

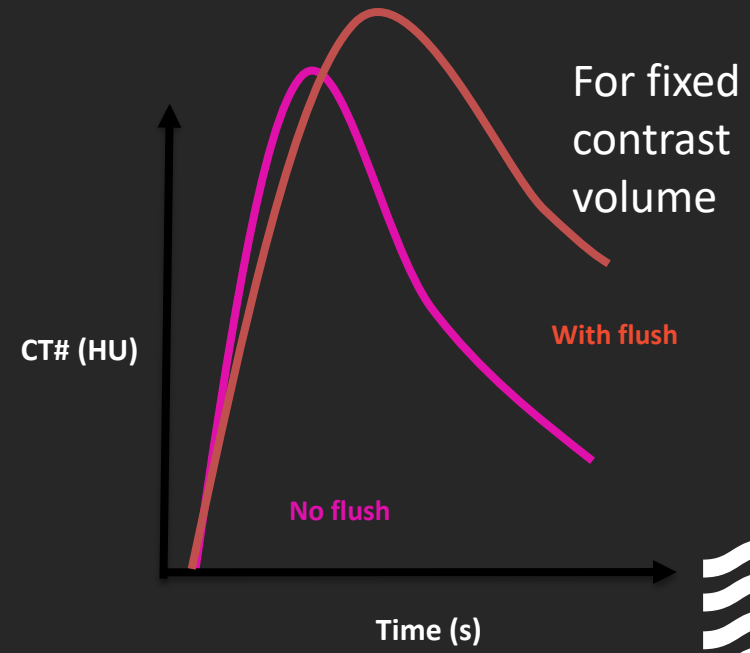
Saline flush is a saline injection immediately following a contrast injection.

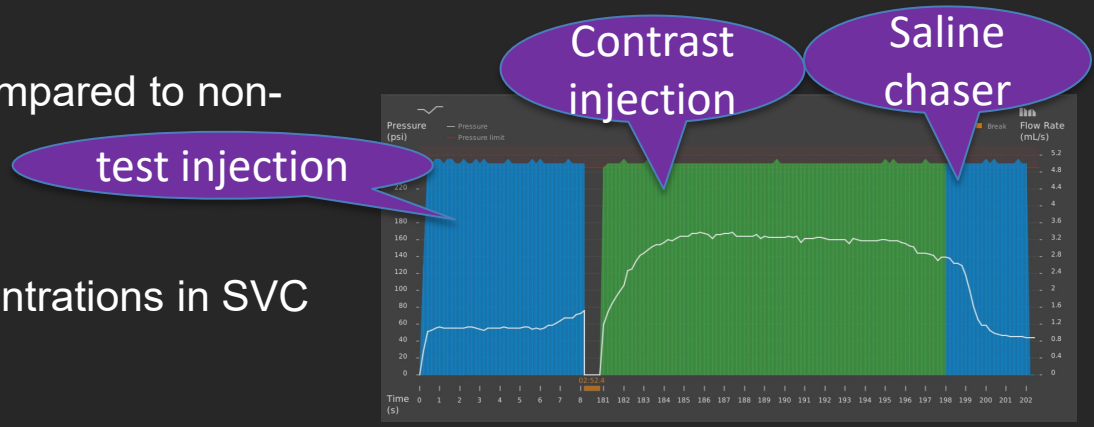
We can think of the flush as “saline pushing the contrast” as opposed to using “contrast to push the contrast” from injector to the heart.
Usually used on CTA exams to make sure iodine is not wasted and left in veinous system.
This is why we see a benefit for CTA exams and little benefit for parenchymal 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

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

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

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

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

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

$$Scan\ duration\,(s) = \frac{Scan\ range\,(mm)}{Scan\ speed\,(mm\,/\,s)}$$

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

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

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

Equations Governing the Major Facets of Contrast Delivery

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

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

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 wont change timing

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

$$\textit{Scan delay} = \textit{Time to optimal enhancement} - \tfrac{1}{2}\,\textit{Scan duration}$$

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

$$\textit{Scan duration}\,(s) = \frac{\textit{Scan range}\,(mm)}{\textit{Scan speed}\,(mm\,/\,s)}$$

$$= \frac{\textit{Scan range}\,(mm) \times \textit{Rotation time}\,(s)}{\textit{Collimation}\,(mm) \times \textit{Pitch}}$$

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Thanks!

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CT POW!