Imaging Modalities for Granulosa Cell Tumo(u)r Imaging

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Disclosures: None

Tu ng

Everything I want to know about medical imaging--

in about an hour....

… Well, how about an introduction to some of the technologies and how they are used

Brief Introduction to Ultrasound, CT and MRI

- Enough information to be informed
- …or just enough knowledge …to be … misinformed
- Lets hope for the former

Granulosa Cell Tumors

Rare ovarian neoplasms that constitute 2% to 5% of ovarian cancer.

A GCT is derived from the granulosa cell, which is responsible for estradiol production in ovarian stroma.

Clinical symptoms and signs of GCTs are caused by exposure of the endometrium to tumor-derived increased estradiol and include postmenopausal bleeding, endometrial hyperplasia, and endometrial adenocarcinoma.

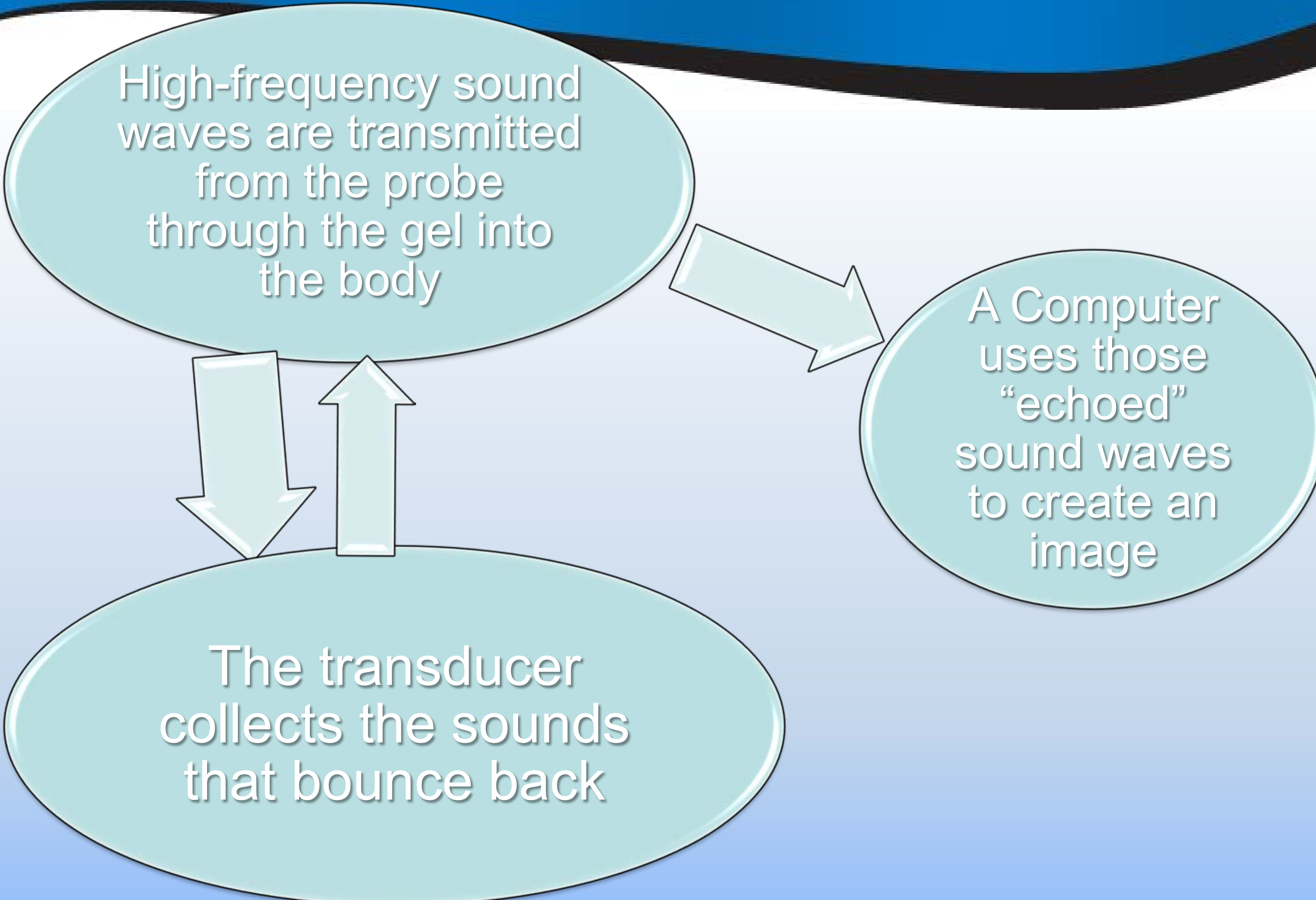
Multiple Imaging Modalities for Assessment of Pelvis and Tumors

- Ultrasound
- CT
- MRI
- PET/CT

Ultrasound (AKA Sonography)

- Safe and painless
- Produces pictures of the inside of the body using sound waves
- Involves the use of
  - a small transducer (probe)
  - Ultrasound gel placed directly on the skin

Ultrasound Imaging (AKA Sonography)



Ultrasound

Benefits of Ultrasound

- Pelvic ultrasound scanning is noninvasive (no needles, no injections, no preps)
- May be temporarily uncomfortable, almost never painful
- Less expensive than CT and MRI
- Does not use any ionizing radiation
- Provides real-time imaging
  - Can show structure and movement of the body's internal organs
  - Blood flowing through blood vessels

Doppler Ultrasound Exam

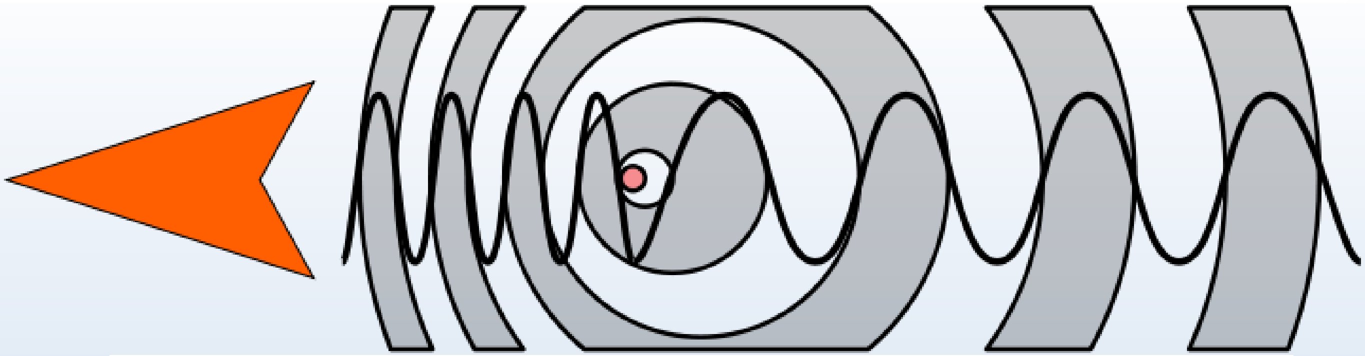
Special ultrasound technique that allows the physician to see and evaluate blood flow through arteries and veins or within various body organs

the use of Doppler technology allows determination of the speed and direction of blood flow by utilizing the Doppler effect

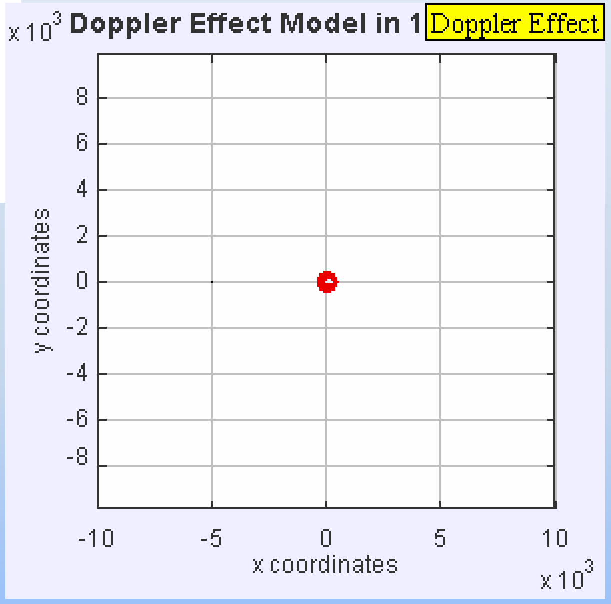
Doppler effect (or the Doppler shift)

- The change in frequency of a wave (or other periodic event) for an observer moving relative to its source
- Named after the Austrian physicist Christian Doppler, who proposed it in 1842 in Prague
- Commonly heard when a vehicle sounding a siren or horn approaches, passes, and recedes from an observer
  - Compared to the emitted frequency, the received frequency is
    - Higher during the approach
    - Identical at the instant of passing by, and
    - Lower during the recession

Doppler effect (or the Doppler shift)

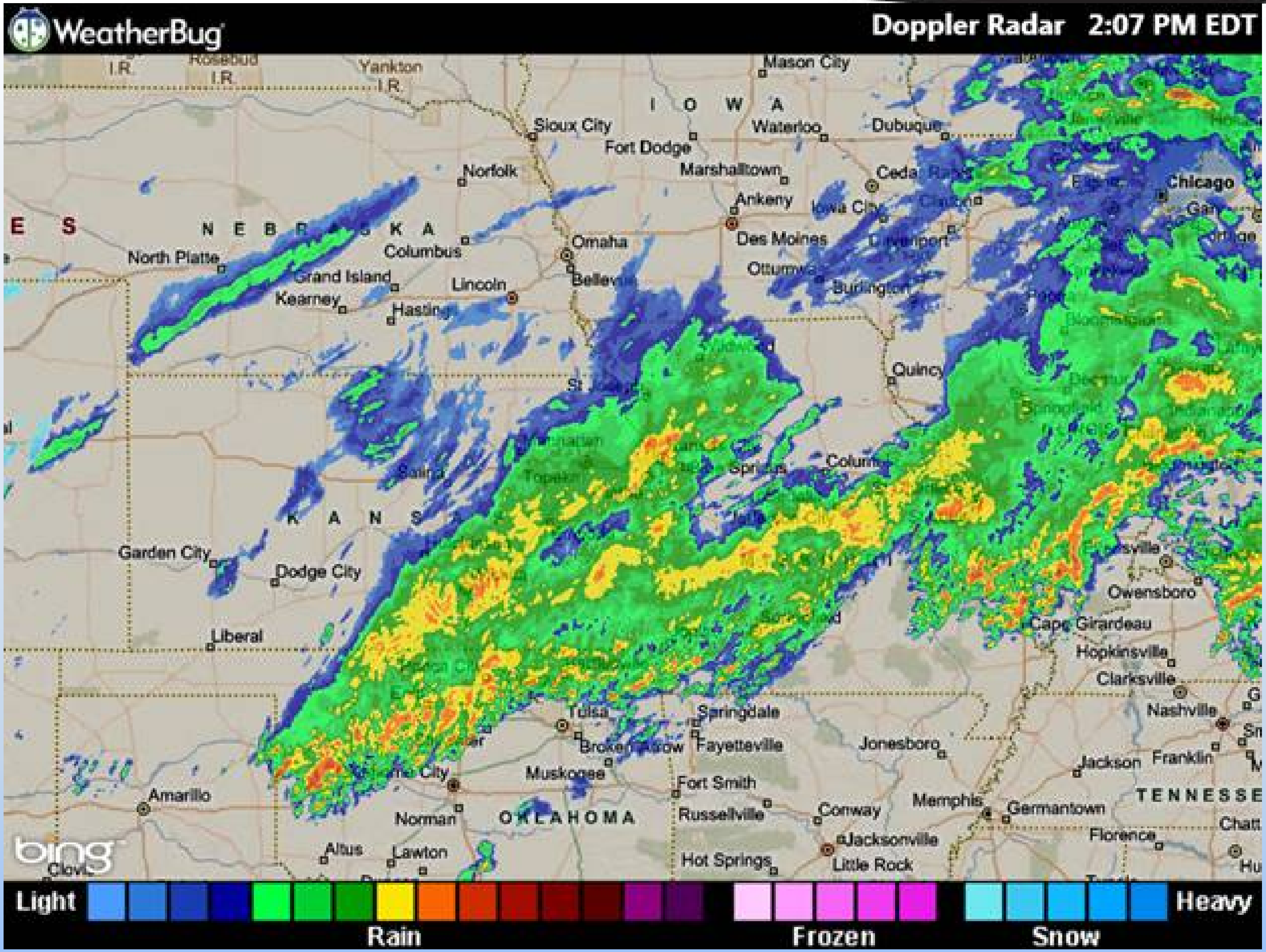


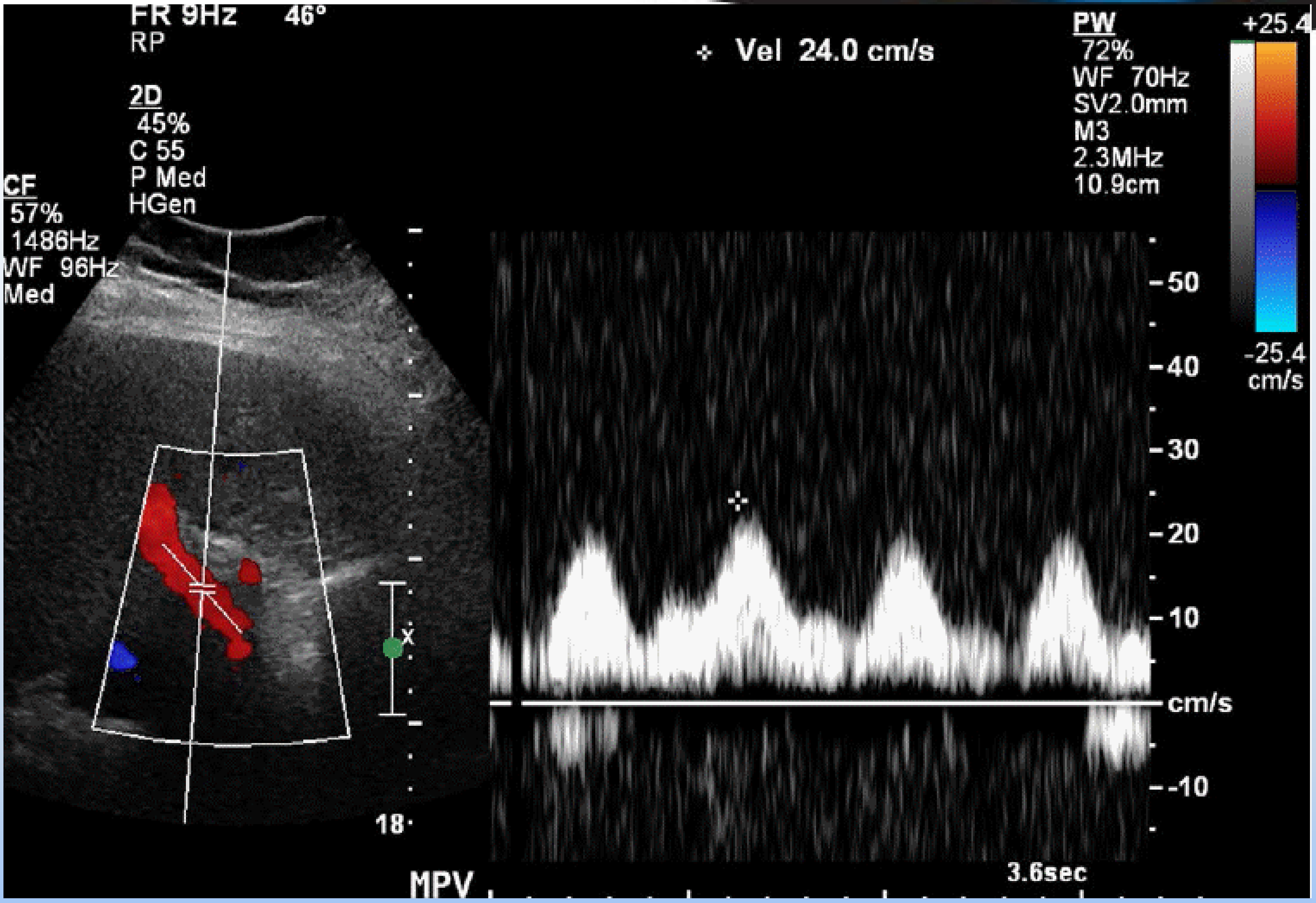
Speeding-car-horn_doppler_effect_sample.ogg



Doppler effect (or the Doppler shift)

Color Doppler Weather




FR 9Hz 46°
RP
2D
45%
C 55
P Med
HGen
CF
57%
1486Hz
WF 96Hz
Med
Vel 24.0 cm/s
PW
72%
WF 70Hz
SV2.0mm
M3
2.3MHz
10.9cm
+25.4
-25.4
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50
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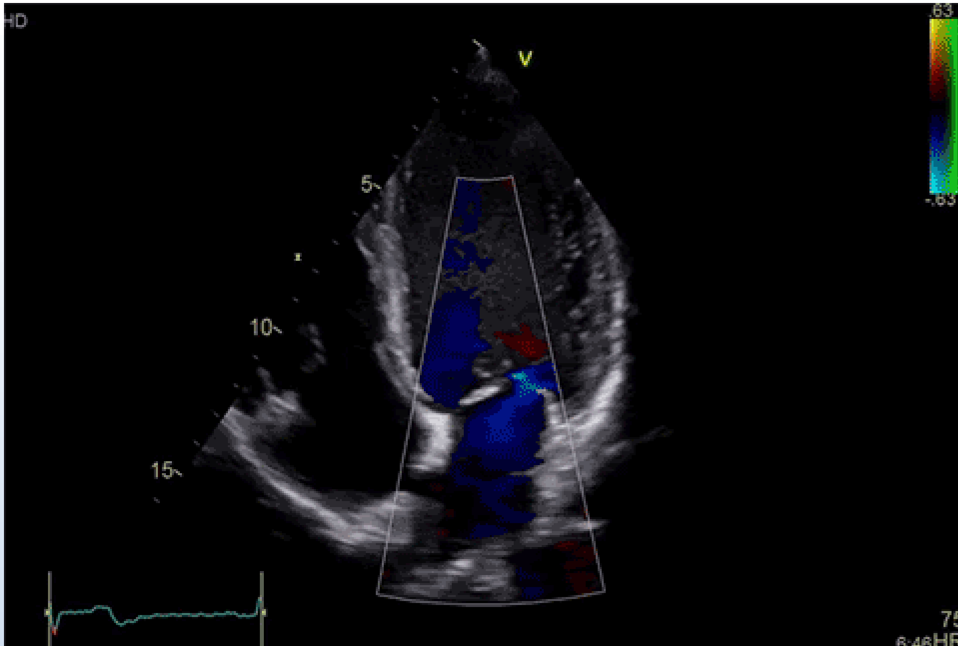
30
20
10
cm/s
-10
18
MPV
3.6sec


HD
.63
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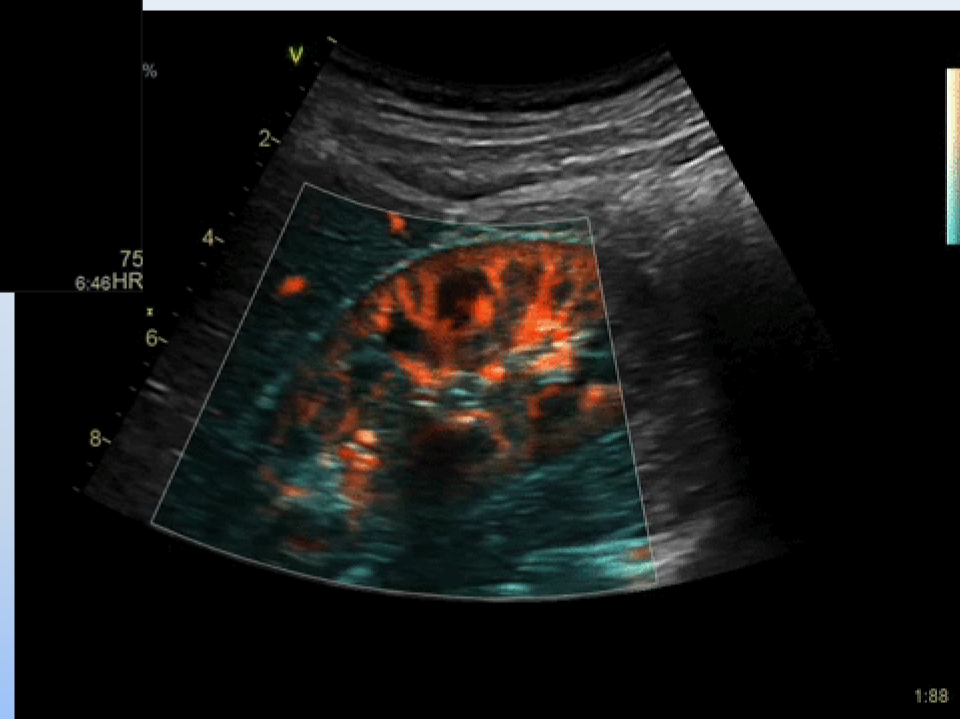
75
6:46HR


V
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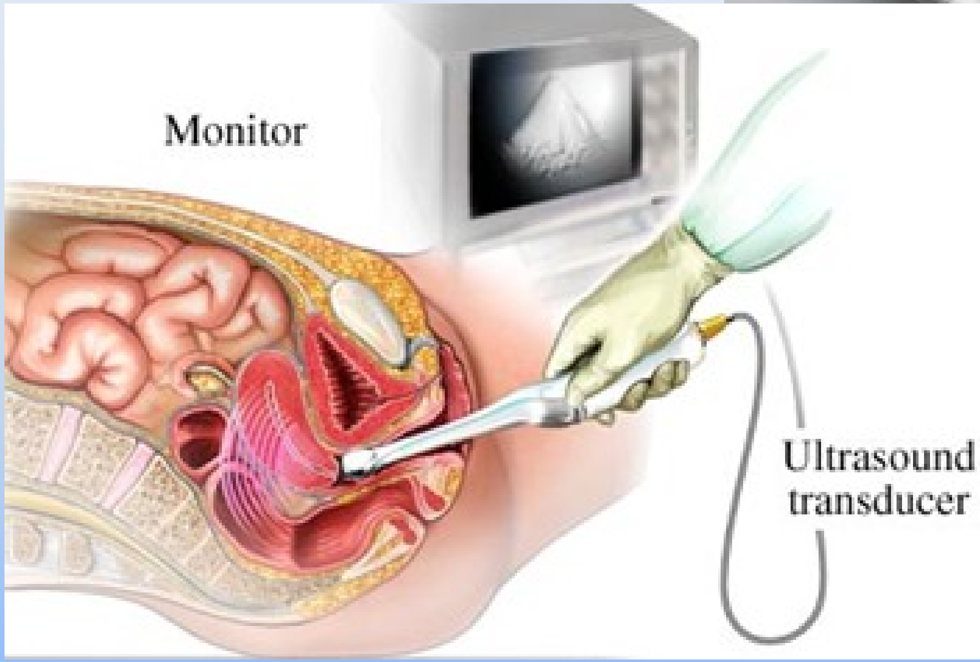
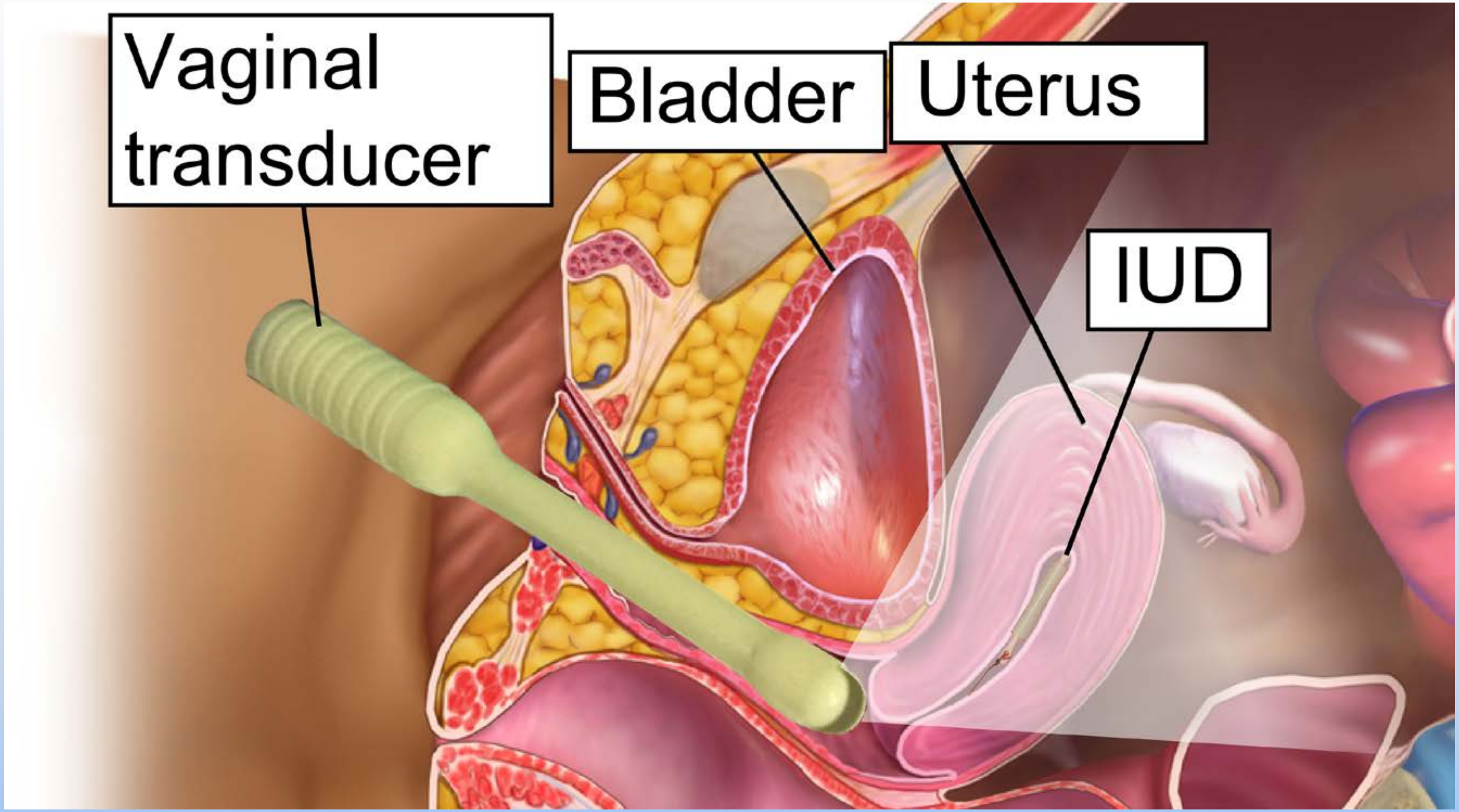
2
4
6
8
1:88

Ultrasound Probes come in Different Varieties




Vaginal transducer
Bladder
Uterus
IUD

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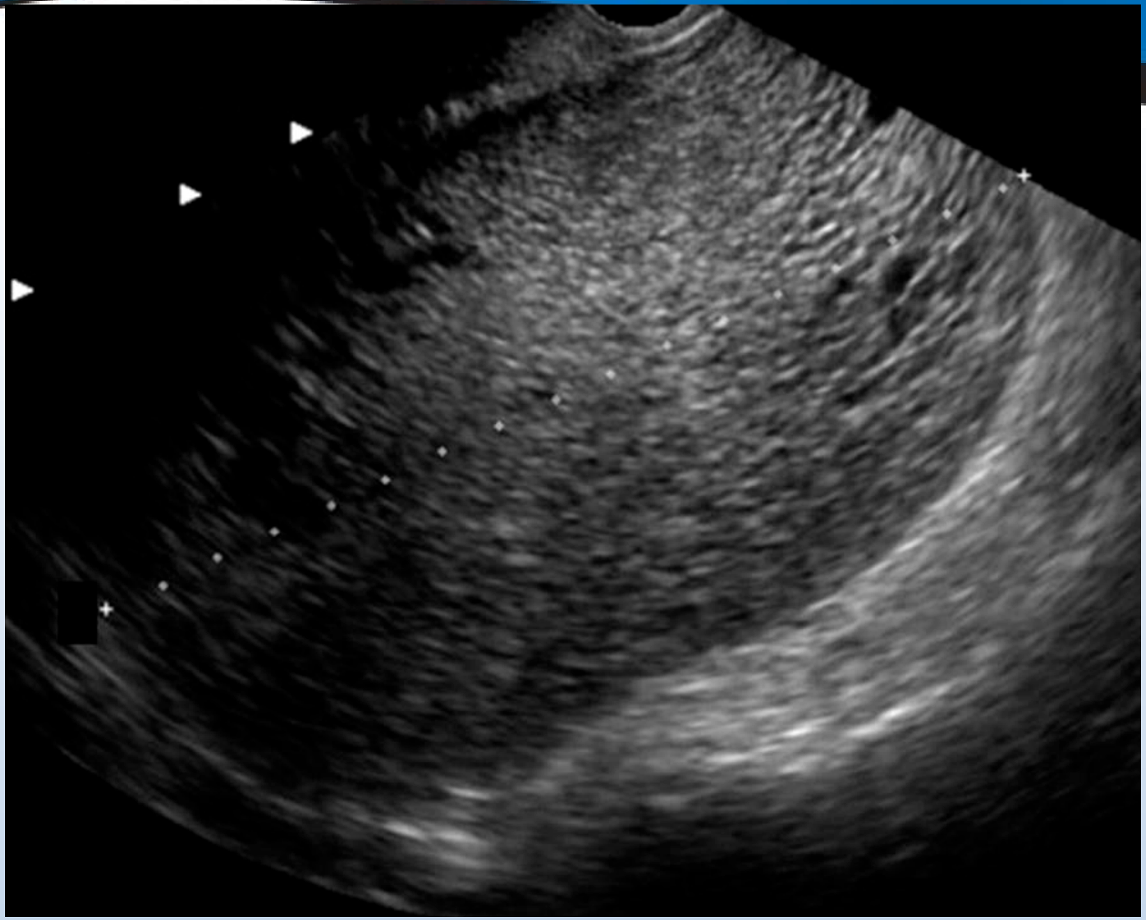
Granulosa cell tumor in a 46-year-old woman

Transvaginal ultrasonography reveals a multilocular solid mass

This tumor has mainly solid components, some with and some without a multilocular cystic appearance

Diagnosis is Combination of Clinical and Imaging Findings

1) Ultrasound Imaging of a large solid mass with heterogeneous echogenicity of the solid tissue or a multilocular – solid mass with many (small) locules, high color content on color or power Doppler examination, and hemorrhagic components in girls and women
   - *With*
2) Signs of hyperestrogenism
   - Isosexual pseudoprecocity
     - Isosexual precocious puberty refers to the appearance of phenotypically appropriate secondary sexual characteristics before age 8 years in girls
     - pseudo-isosexual precocity is due to sex steroid production which is independent of hypothalamic-pituitary regulation
   - Bleeding disorders
3) Should raise the suspicion of a GCT



Granulosa cell tumor in 44-year-old woman. Transvaginal ultrasound image reveals 13-cm predominantly solid-appearing mass. Uterus and left ovary were unremarkable (not shown). Normal right ovary was not seen.

MRI, CT, and PET/CT for Ovarian Cancer Detection and Adnexal Lesion Characterization
Veena R. Iyer[1] and Susanna I. Lee
http://www.ajronline.org/doi/full/10.2214/AJR.09.3522?src=recsys

Computed Tomography (CT) scan

Computed tomography, more commonly known as a CT or CAT scan, is a diagnostic medical test that, like traditional x-rays, produces multiple images or pictures of the inside of the body.

The cross-sectional images generated during a CT scan can be reformatted in multiple planes, and can even generate three-dimensional images. These images can be viewed on a computer monitor, printed on film or transferred to a CD or DVD.

CT images of internal organs, bones, soft tissue and blood vessels typically provide greater detail than traditional x-rays, particularly of soft tissues and blood vessels.

Patient undergoing computed tomography (CT) scan

Sir Godfrey Newbold Hounsfield

(28 August 1919 – 12 August 2004)

Godfrey Hounsfield with an early version of the CT scanner, then called the EMI Scanner

English electrical engineer

Shared the 1979 Nobel Prize for Physiology or Medicine with Allan McLeod Cormack for his part in developing the diagnostic technique of X-ray computed tomography (CT)

Concept of Radiodensity

- The CT scanner uses a set of software algorithms to determine the amount of x-radiation absorbed by every element in a plane of tissue
- Each of these elements is represented by a pixel on the video display, and the density (amount of x-radiation absorbed) is measured in **Hounsfield units**

Hounsfield's Unit

If mw, ma, and m are the linear attenuation coefficients of water, air and a substance of interest, the CT number of the substance of interest is:

$$H = 1000 (m - mw) / (mw - ma)$$

Thus, a change of one Hounsfield unit (HU) corresponds to 0.1% of the attenuation coefficient difference between water and air, or approximately 0.1% of the attenuation coefficient of water since the attenuation coefficient of air is nearly zero

Substance Densities in Hounsfield Units

Air: -1000

Fat: -50

Water: 0

Soft tissue such as muscle: +40

Calculus: +100 to +400

Bone: +1000 to +3000

From his Nobel Award Address:

Hounsfield (1980) Med Phys 7:283-90

General Clinical Guide

o Fatty Tissue	-130 to -10
o Simple Fluid:	~0 to +18 (20)
o Soft Tissue	+20 to ~+70
o Complex Fluid	+18 to +80+ (heme)

The scale extends in the positive direction to about +4000, which represents very dense metals

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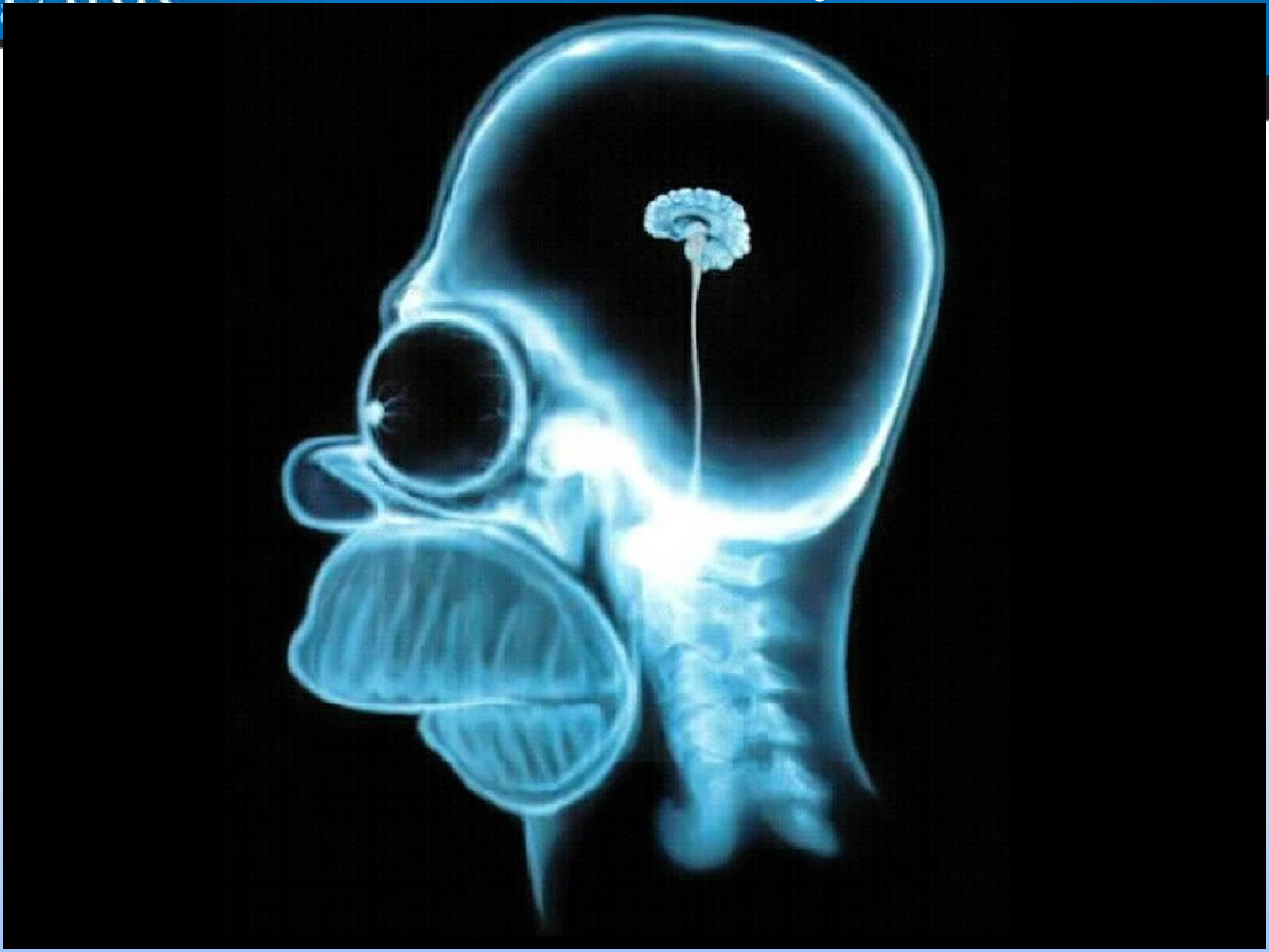
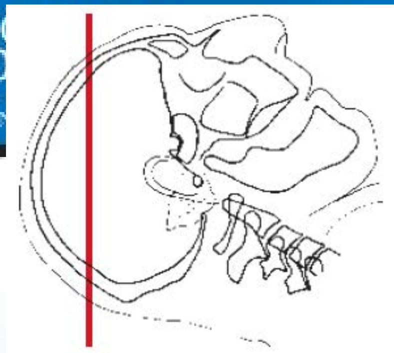
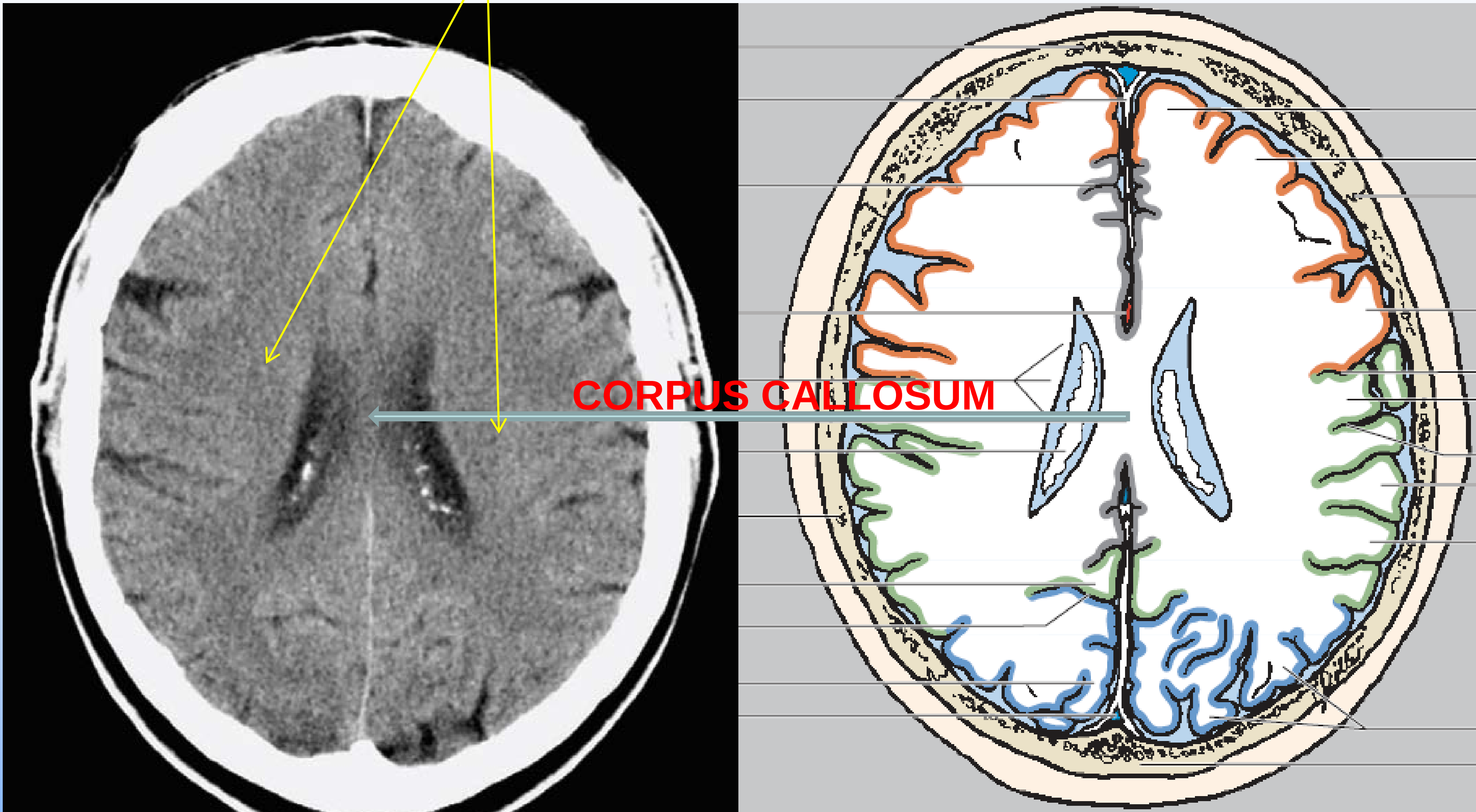
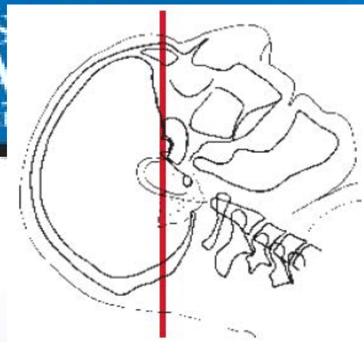
The First Scans were Brain Imaging

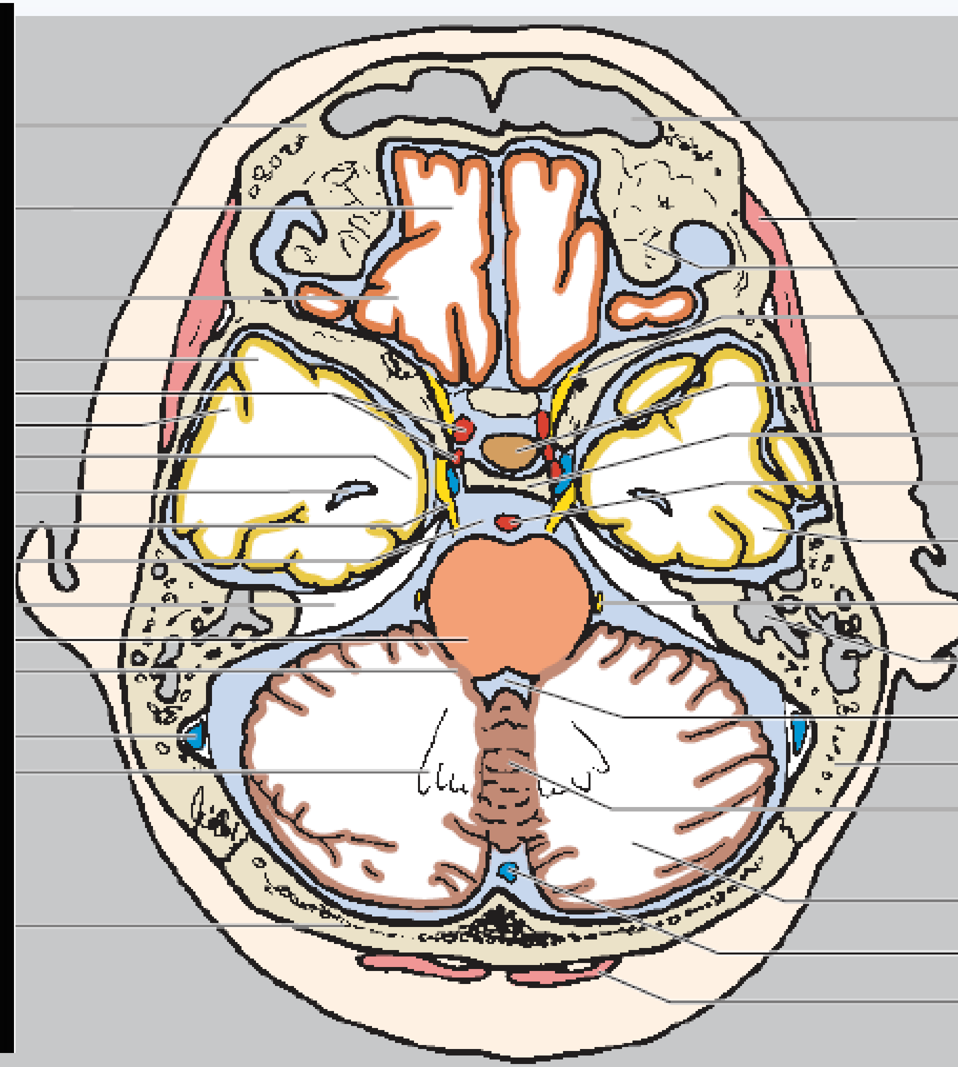
Early CT Scans



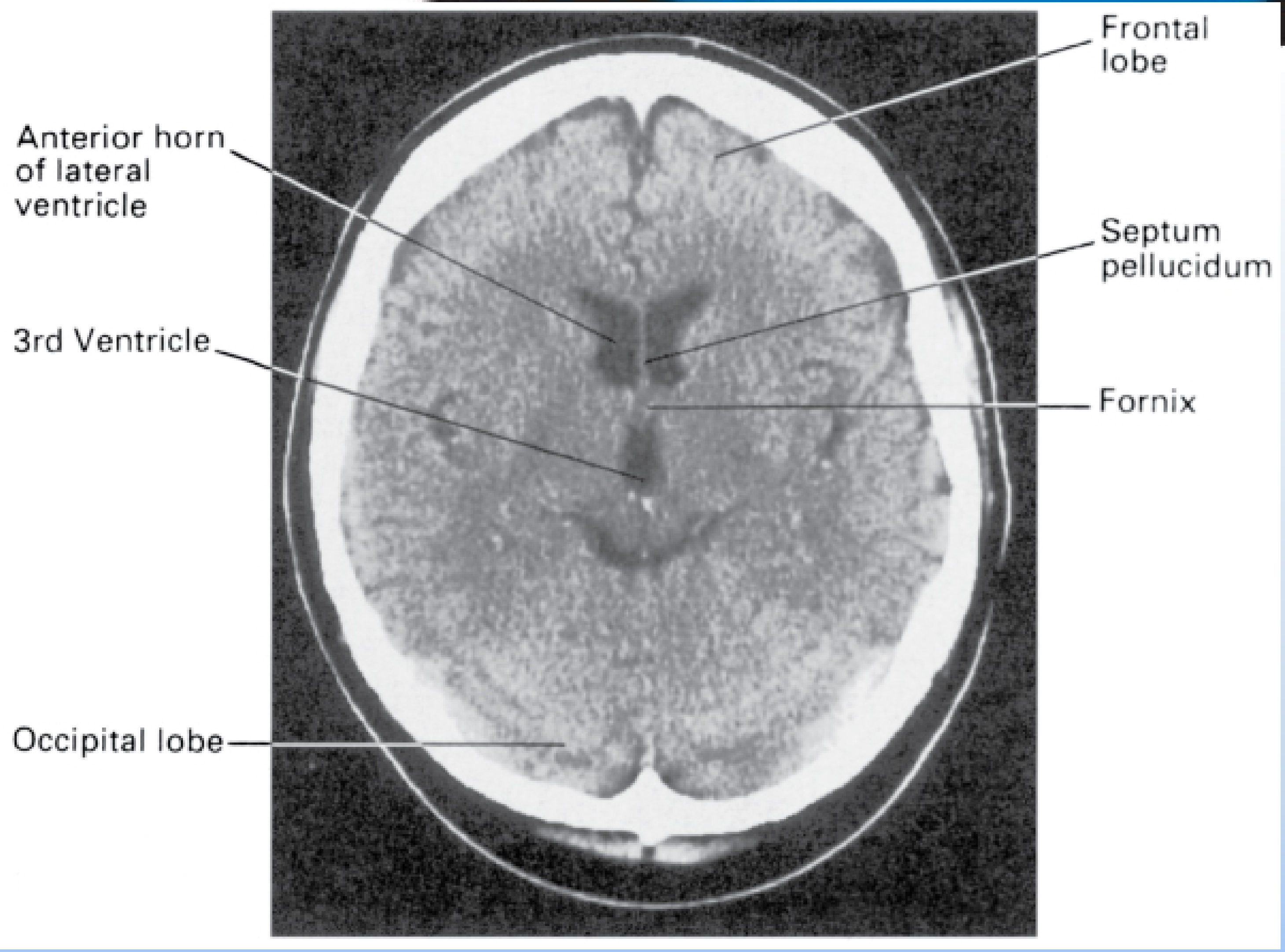



CORONA RADIATA
CORPUS CALLOSUM
Frontal lobe
Parietal lobe
Occipital lobe

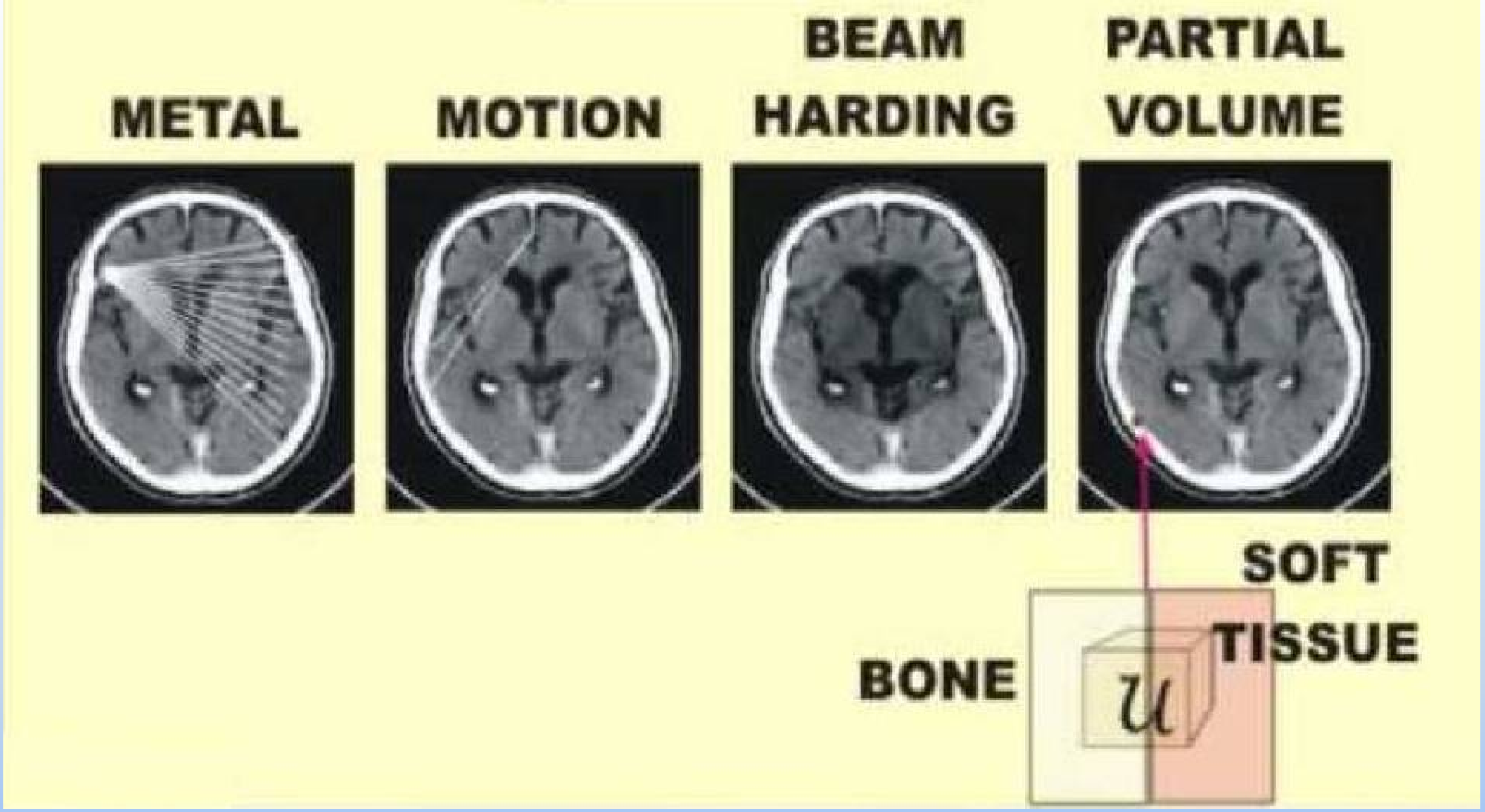



Frontal lobe
Temporal lobe
Cerebellum
Pons

Basic Structures in Head CT



CT Artifacts



Artifacts

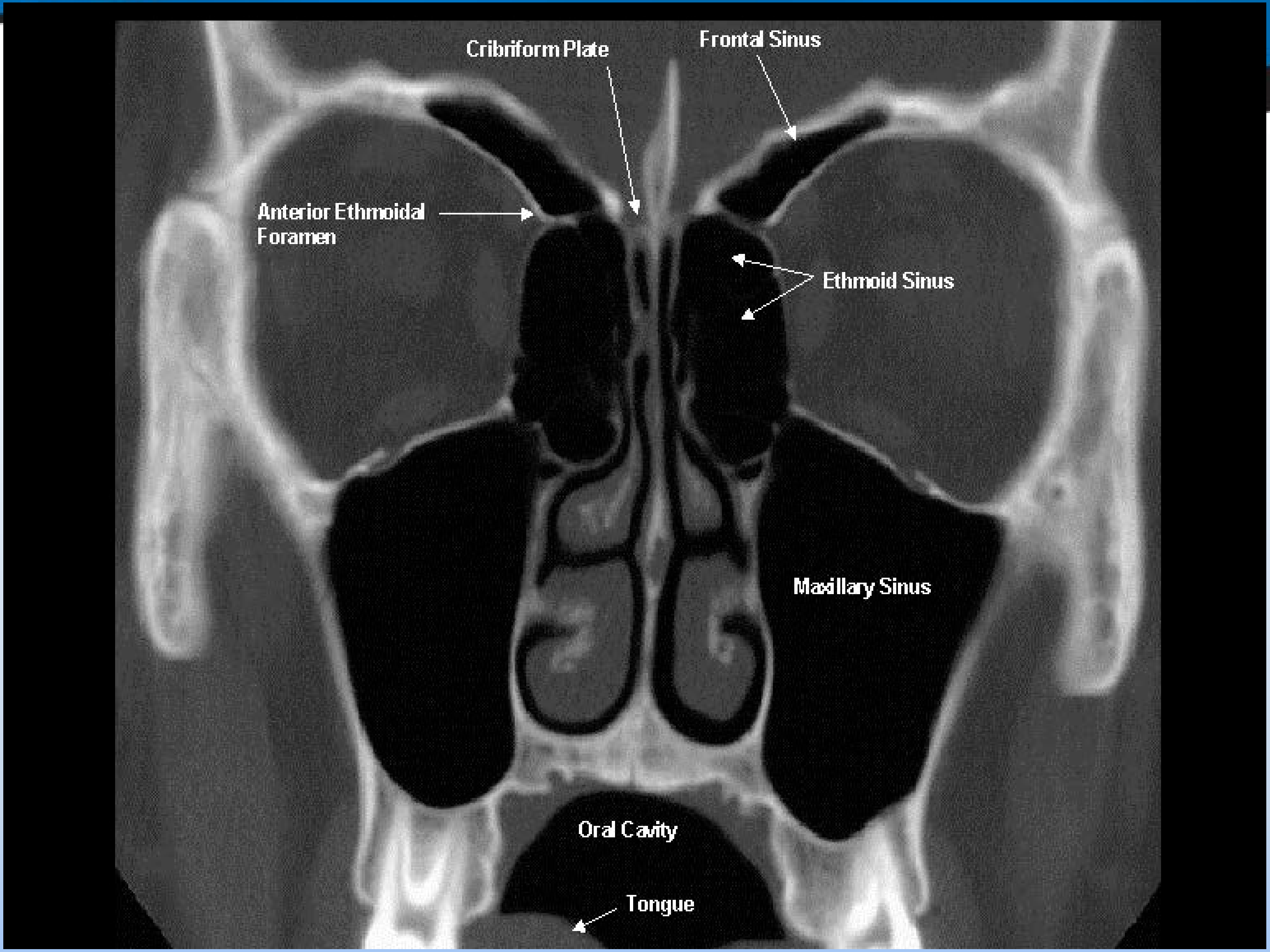
Beam hardening artifact:

- Corrected by processing during the reconstruction process.

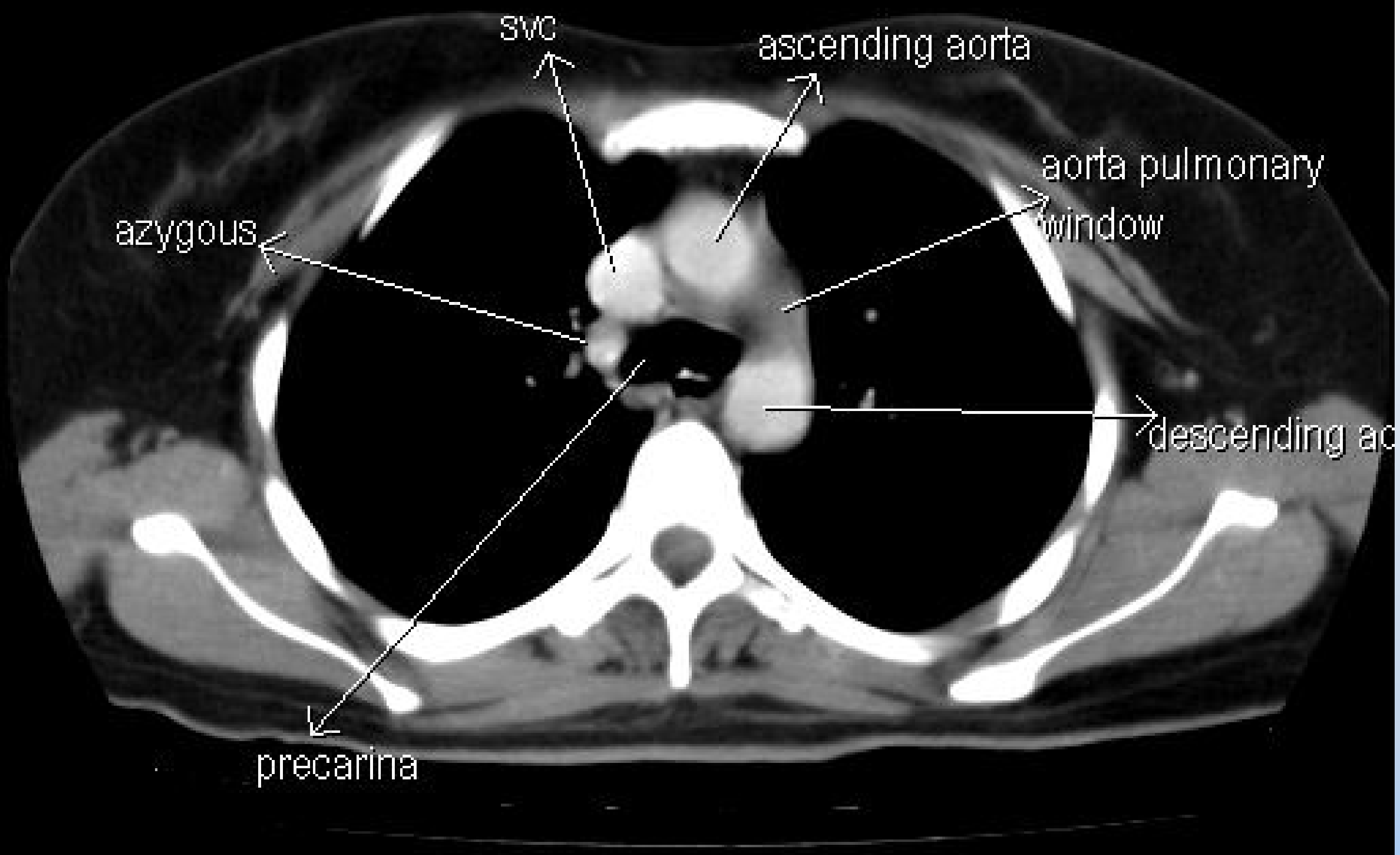
Partial volume artifact:

- Occurs when a voxel contains two very different materials, like bone and soft tissue.
- The resulting CT number will be somewhere between the correct values for the different materials.
- Depending on the window setting, a structure such as bone, can appear thinner or thicker than it's actual dimension.

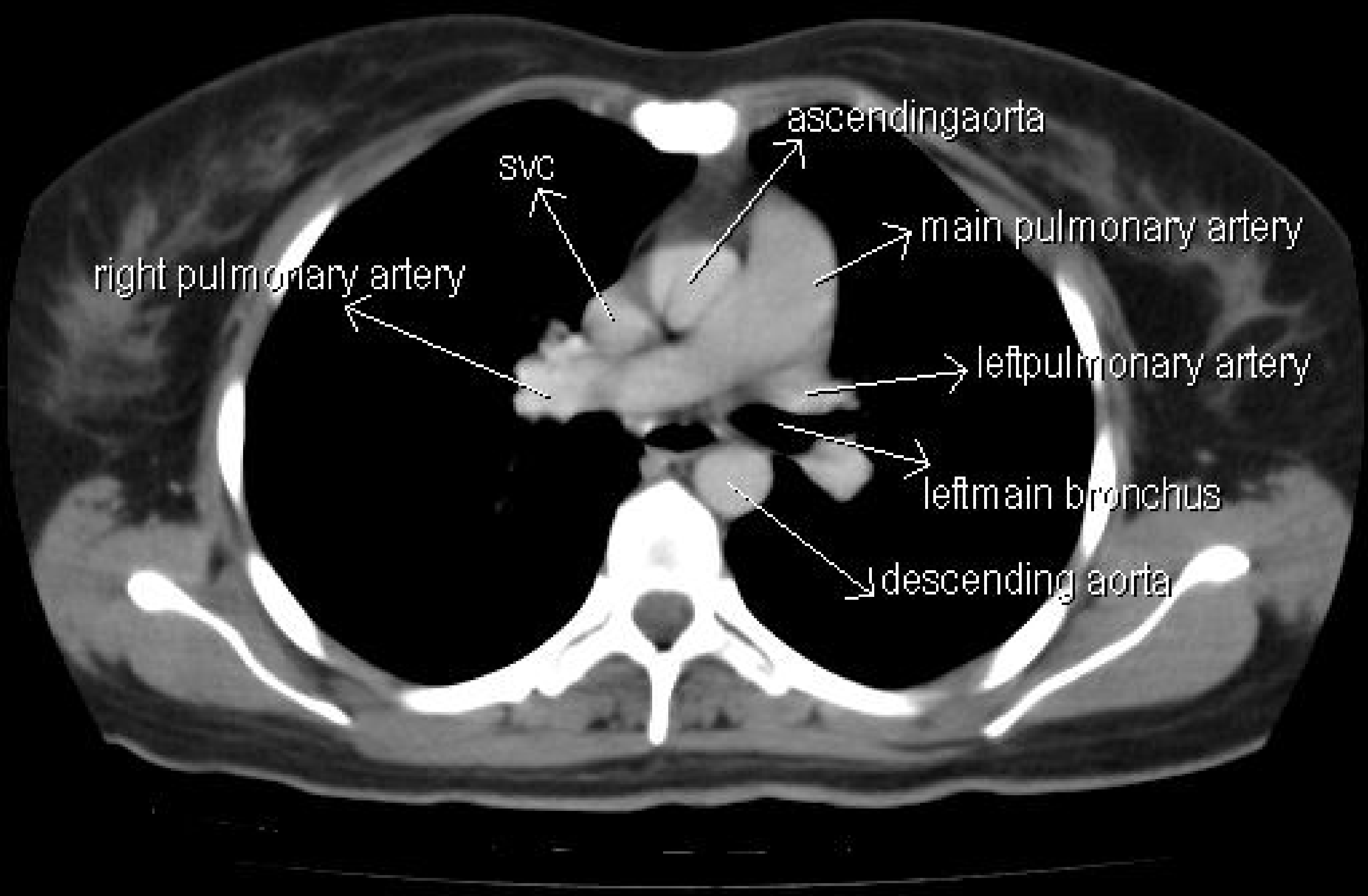
Coronal CT Through Paranasal Sinuses



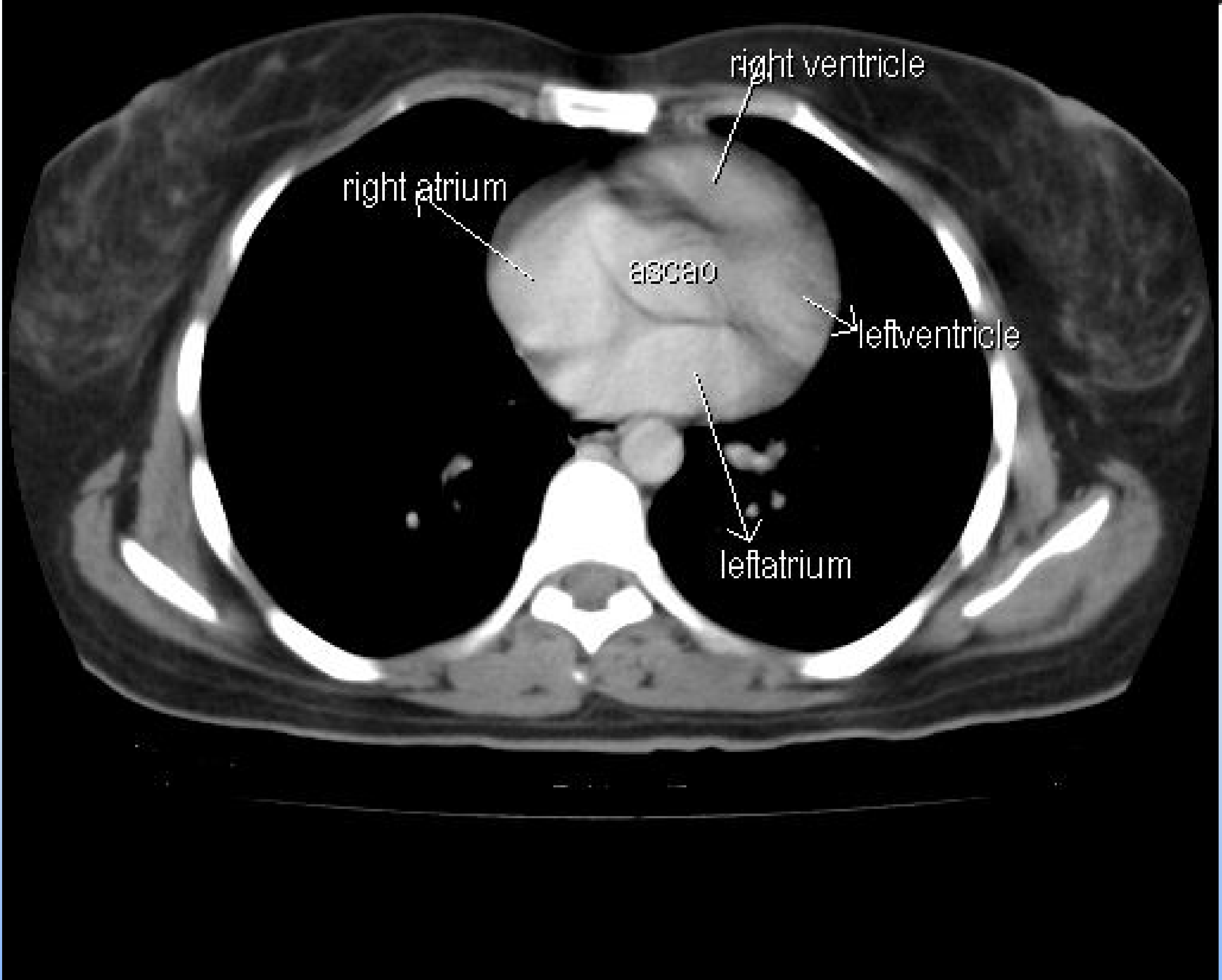
Major Anatomical Stuctures Within the Thorax



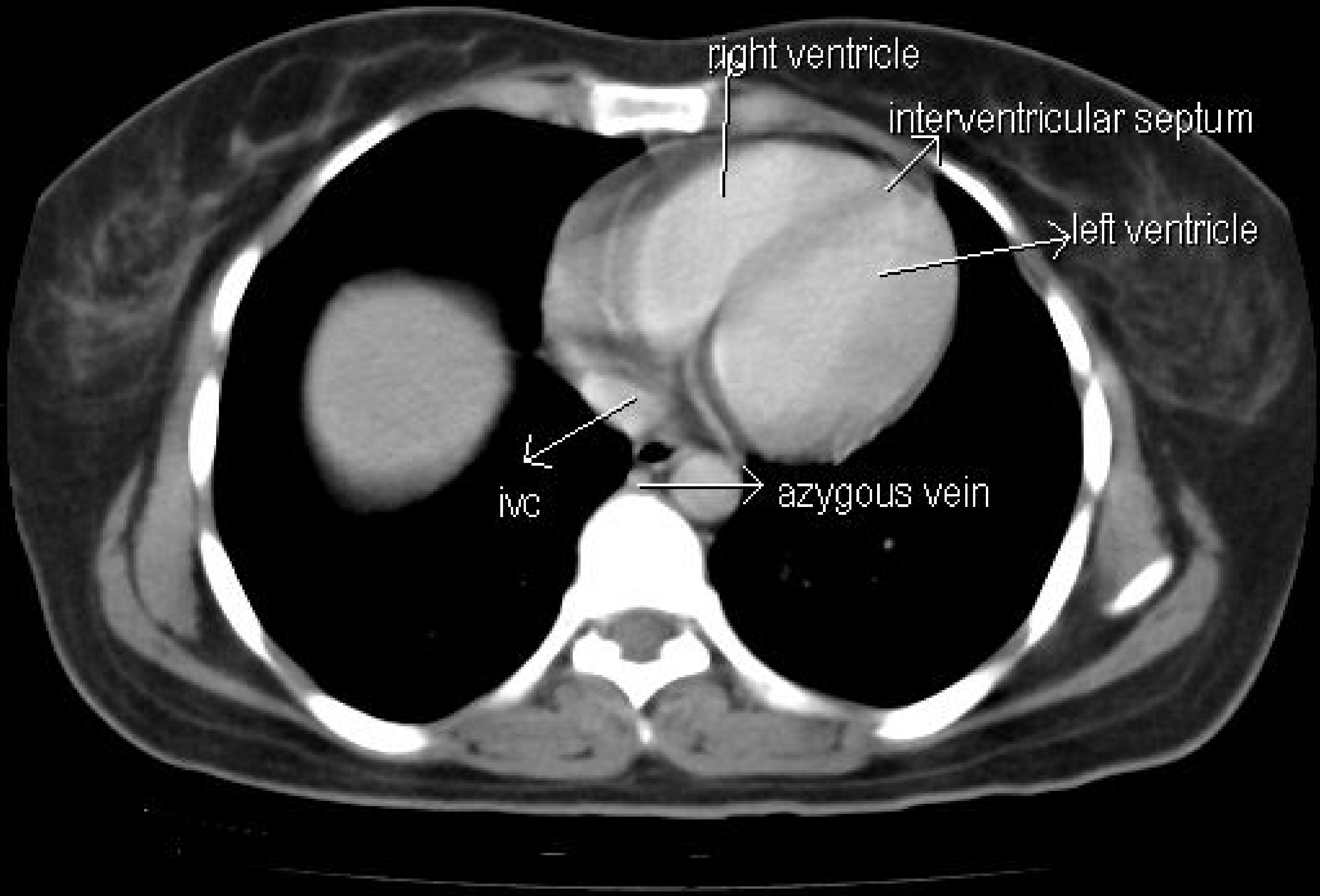
Major Anatomical Stuctures Within the Thorax



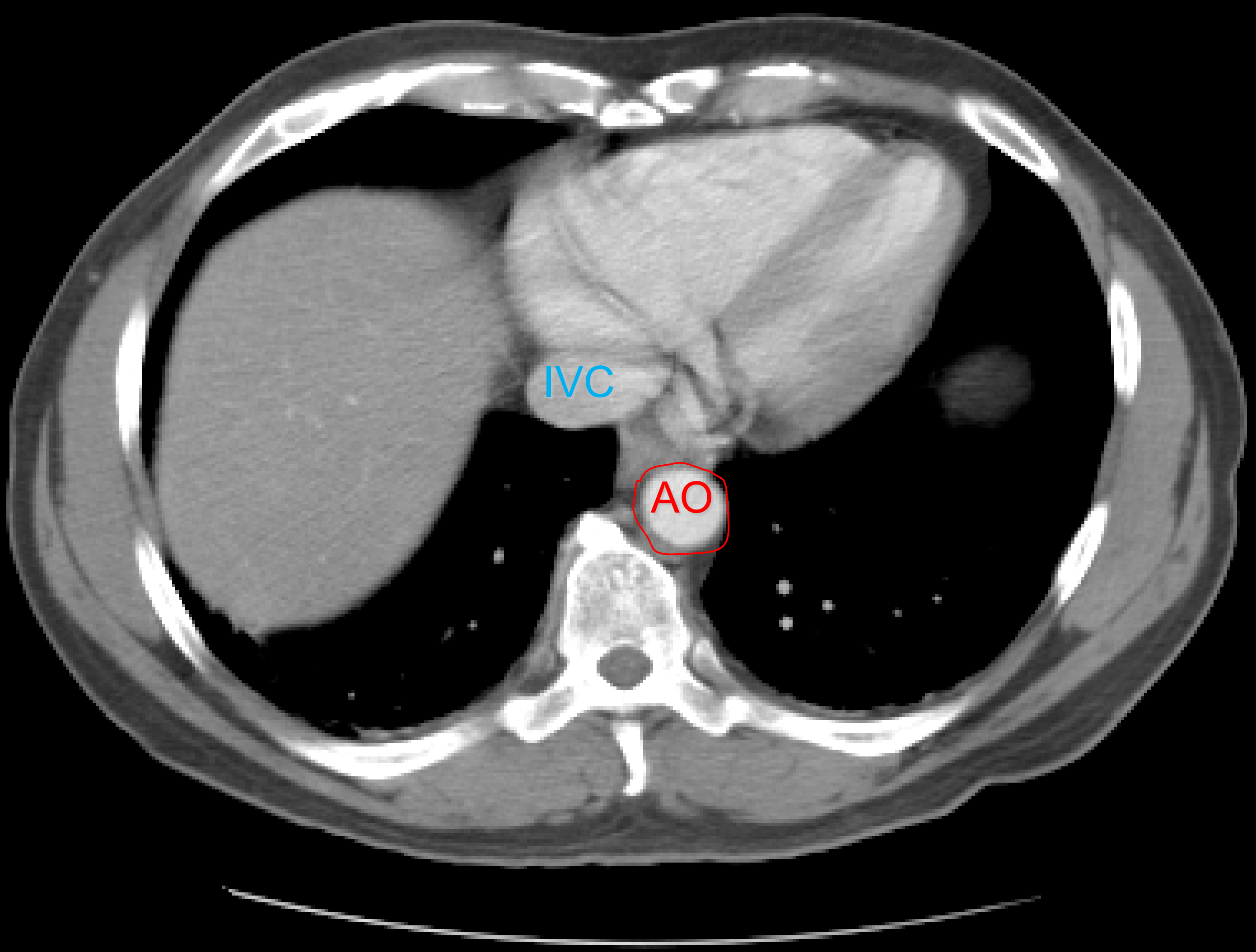
Major Anatomical Stuctures Within the Thorax



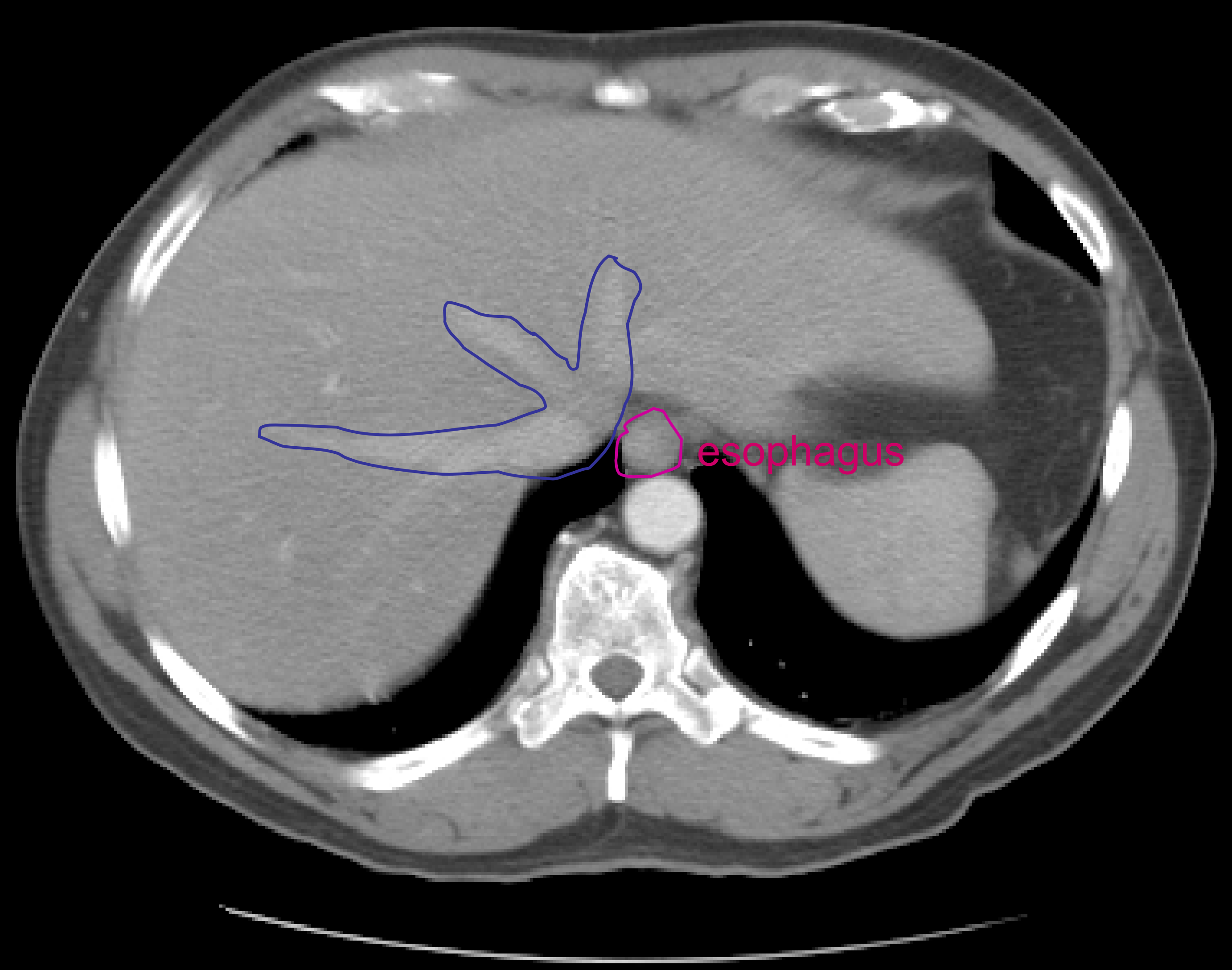
Major Anatomical Stuctures Within the Thorax



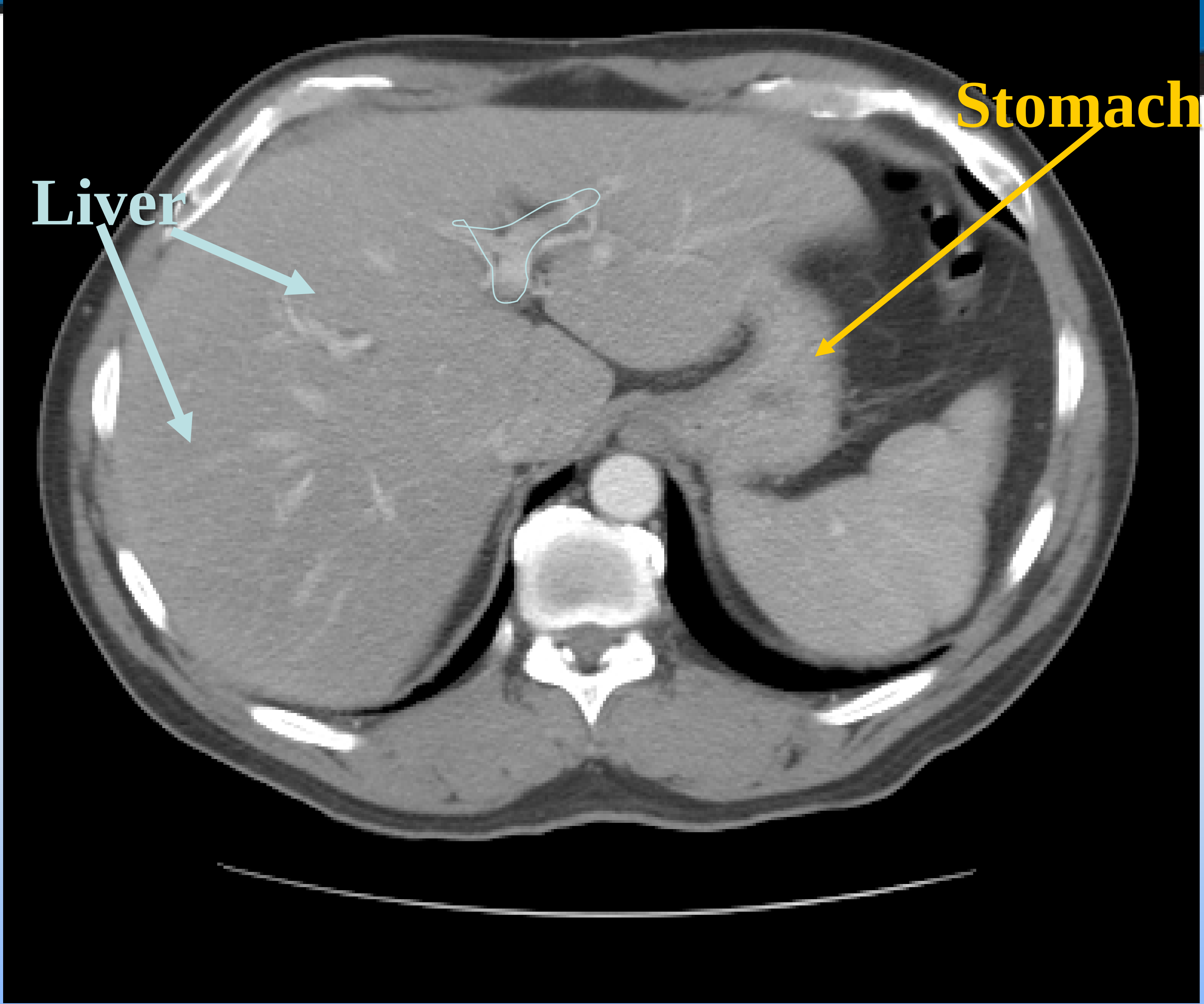
Descending Aorta filled with intravenous contrast



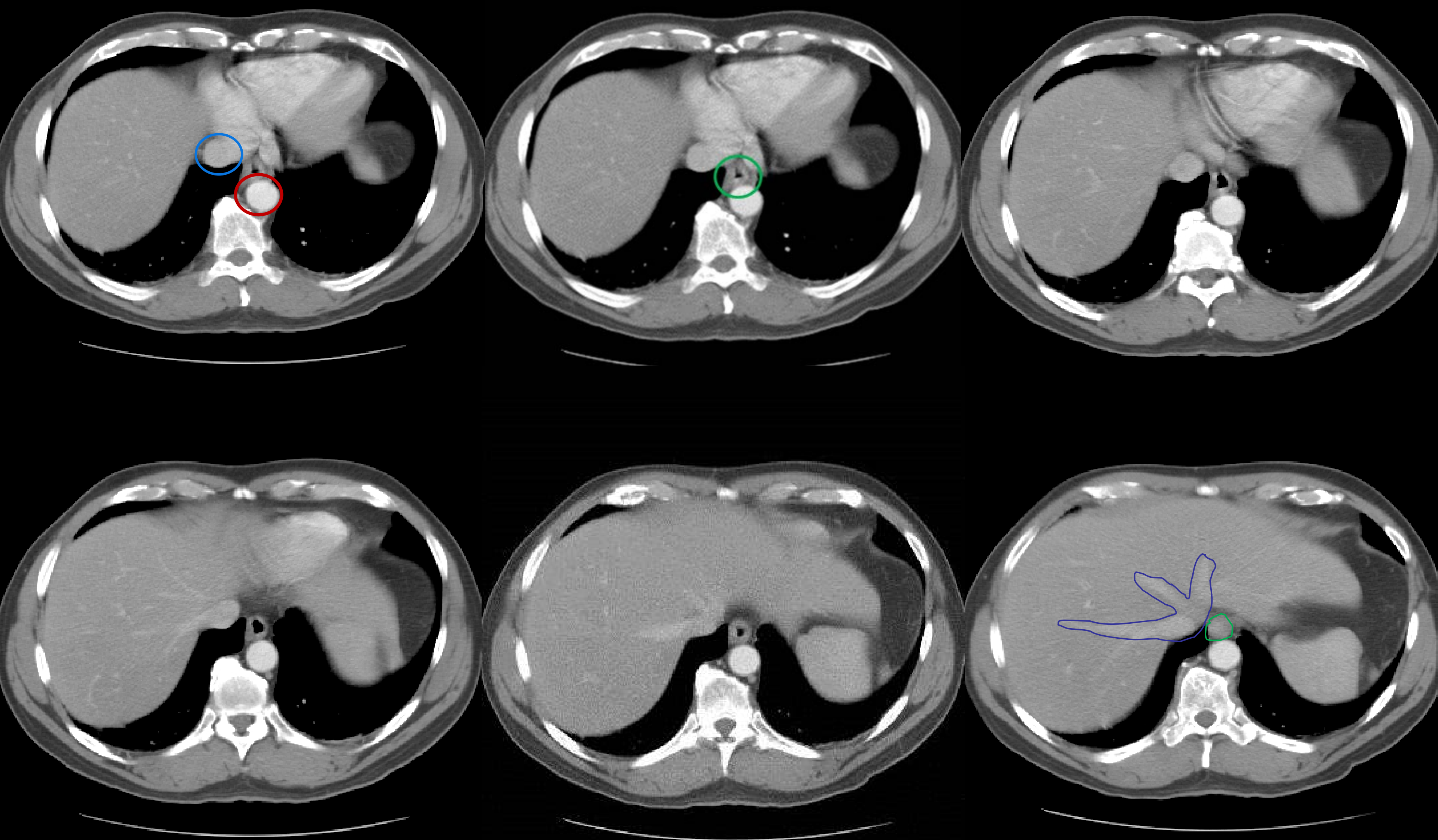
Right, Middle and Left Hepatic Veins draining into the Inferior Vena Cava



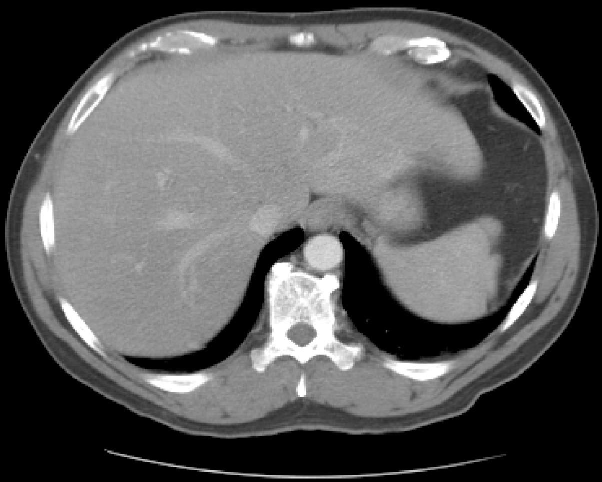
Portal Vein Branching into the Liver

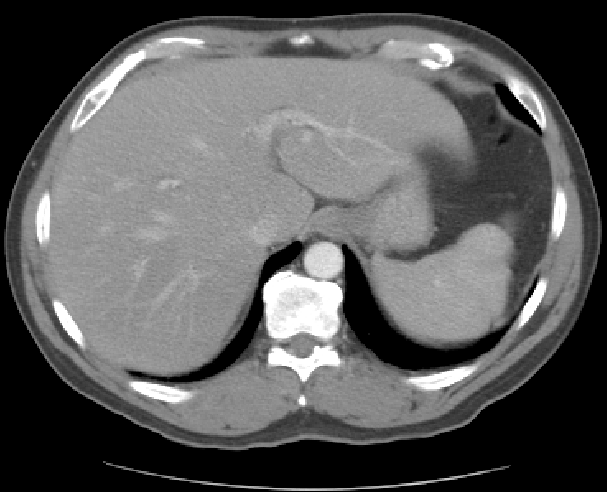


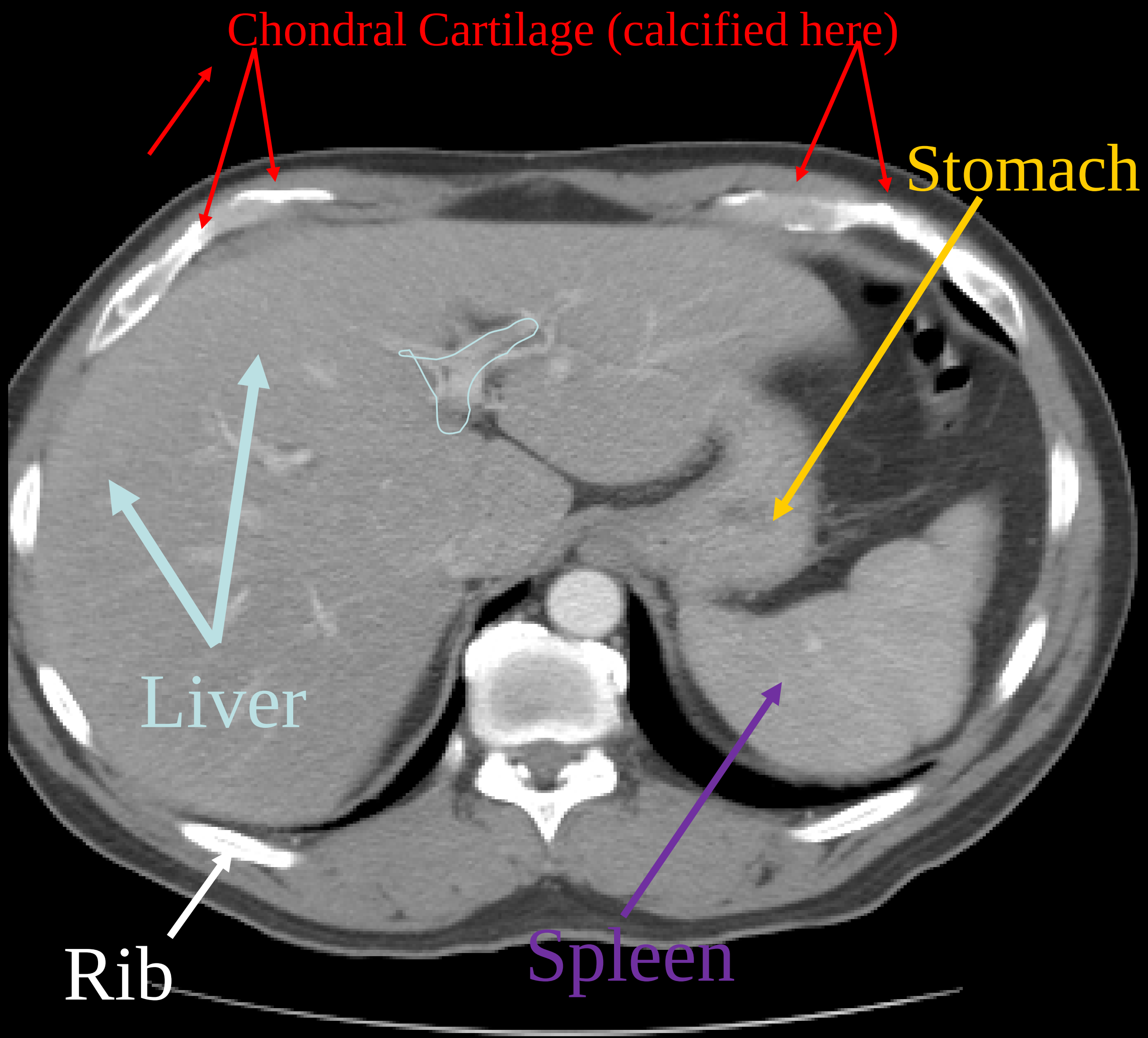
IVC, Aorta, Esophagus, Portal Veins



Upper Abdomen

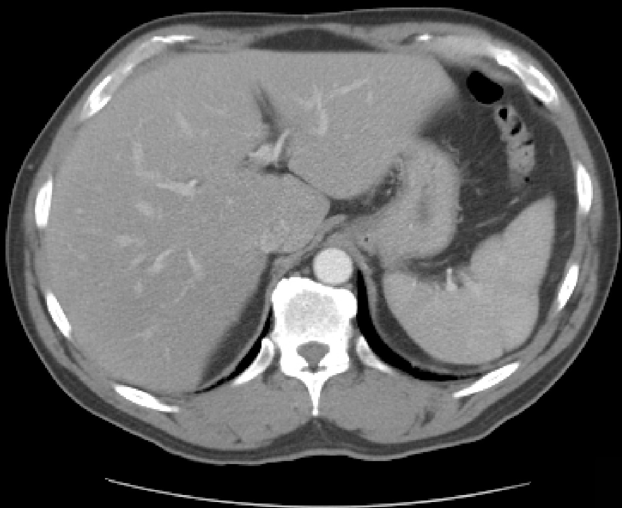


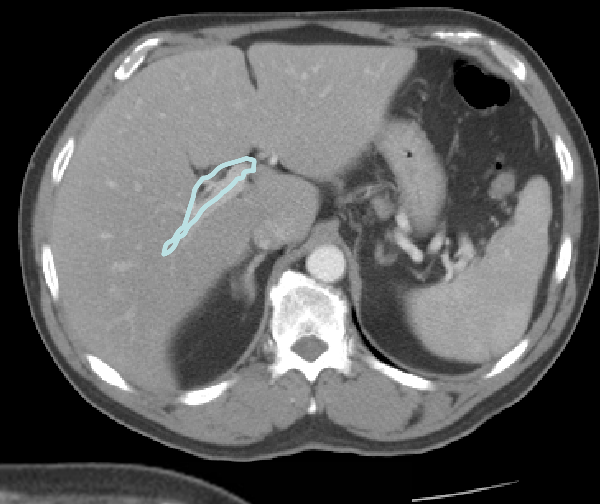


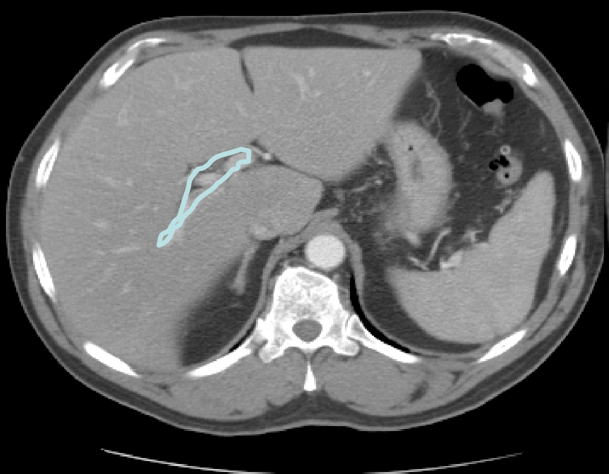


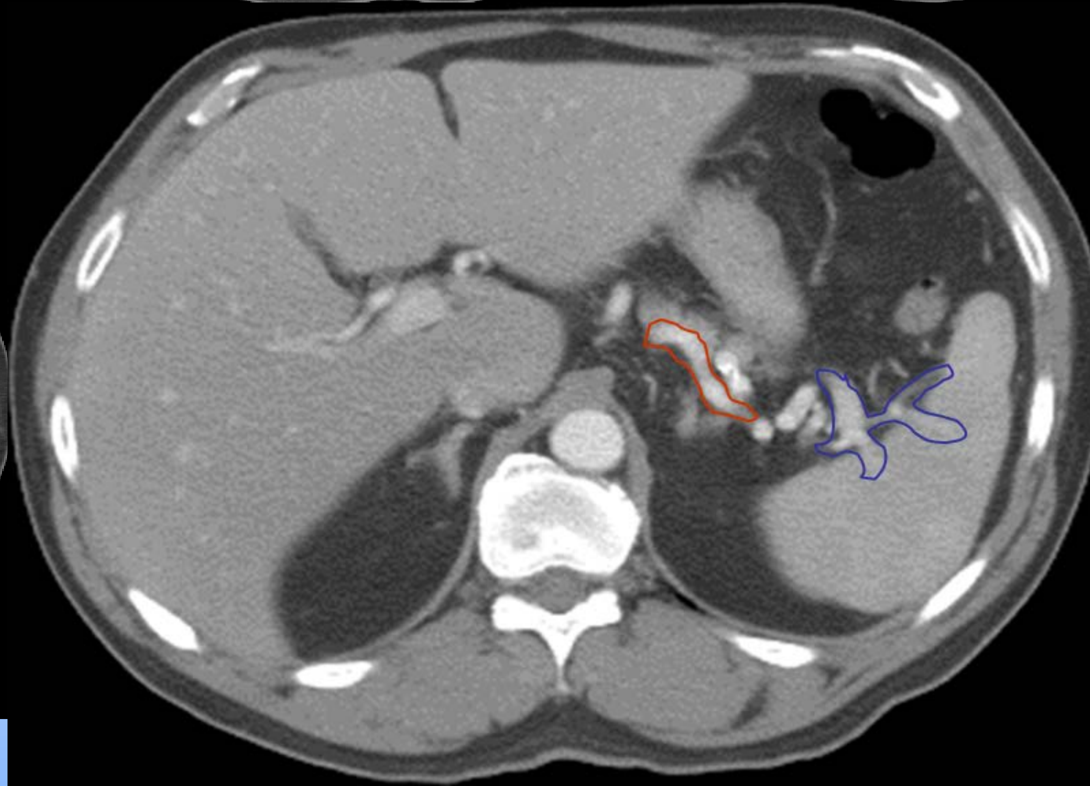
Splenic Artery Splenic Vein Portal Veins

Scroll up and down to confirm.

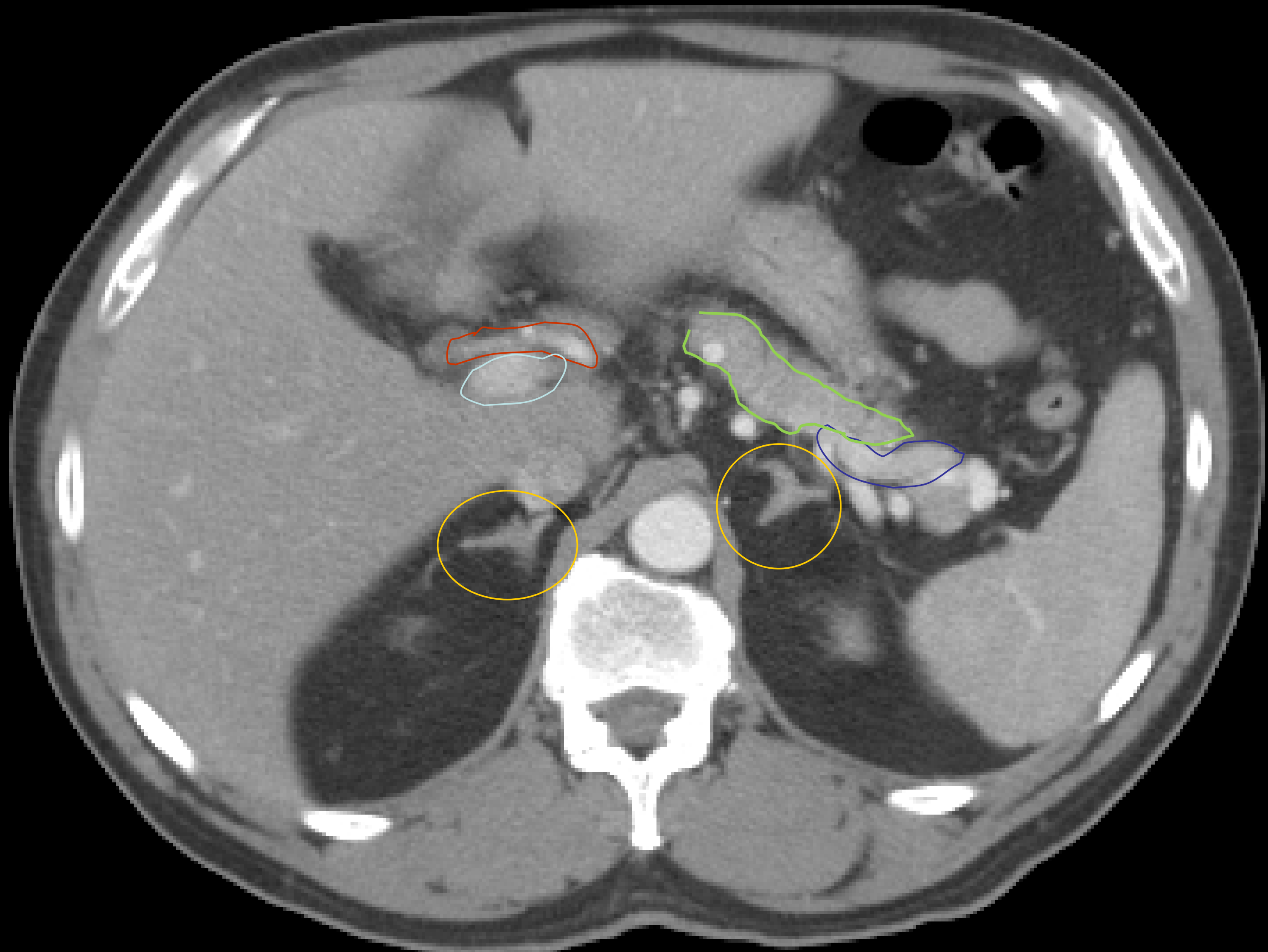




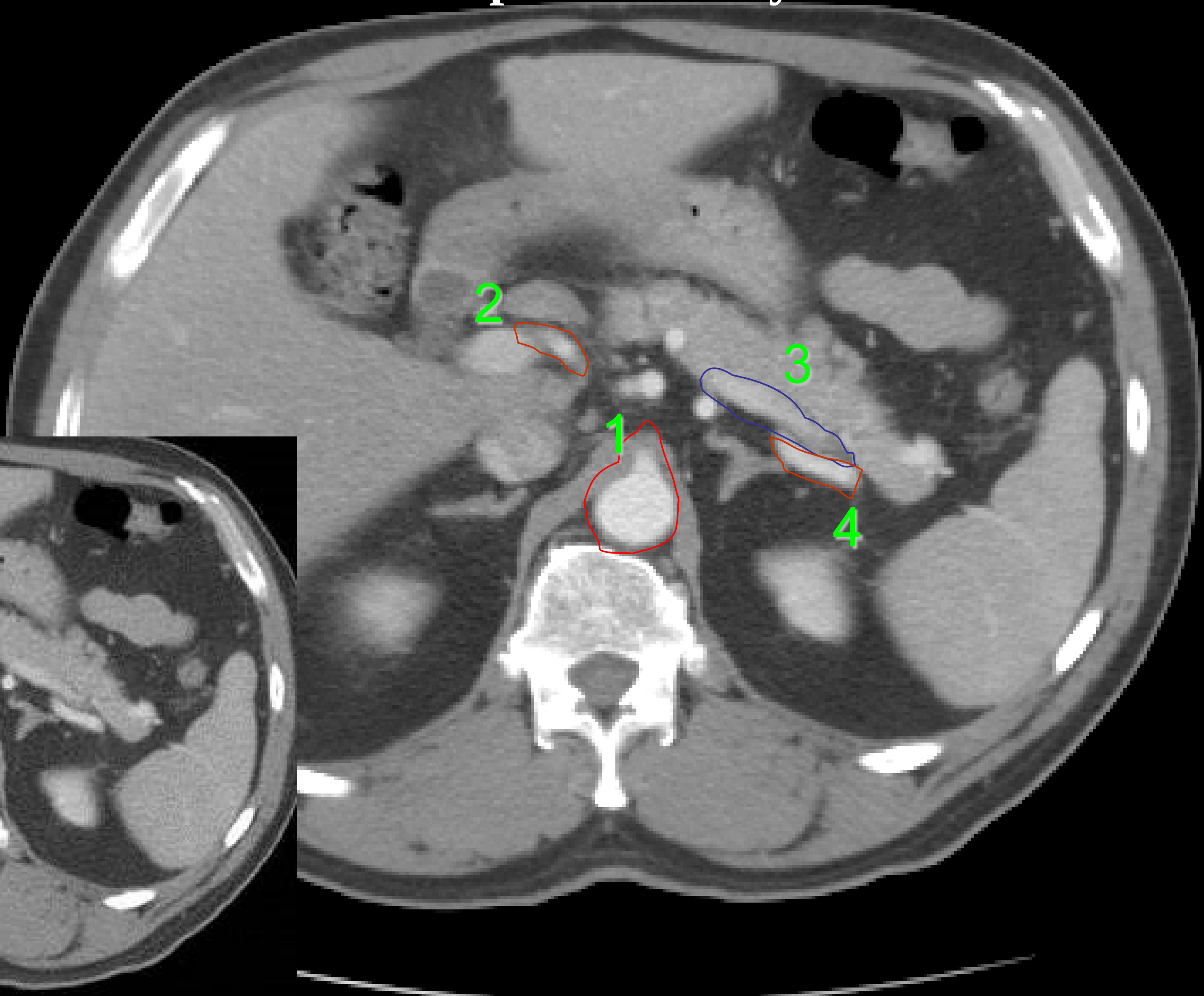




Proper Hepatic Artery, Splenic Vein, Portal vein, Adrenal Glands, Pancreas

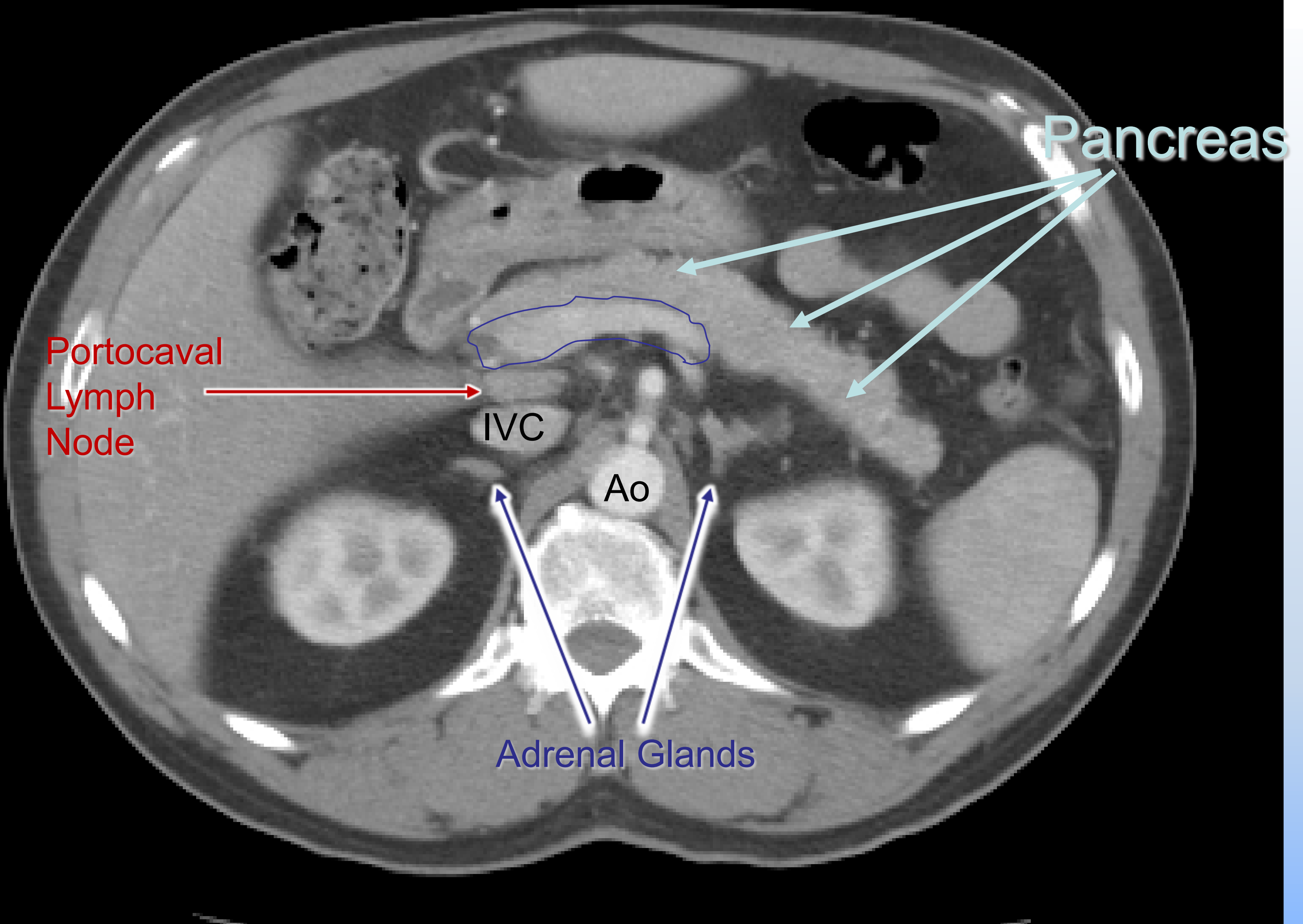


1. Celiac Artery originates from the Aorta
2. Proper Hepatic Artery
3. Splenic Vein
4. Splenic Artery

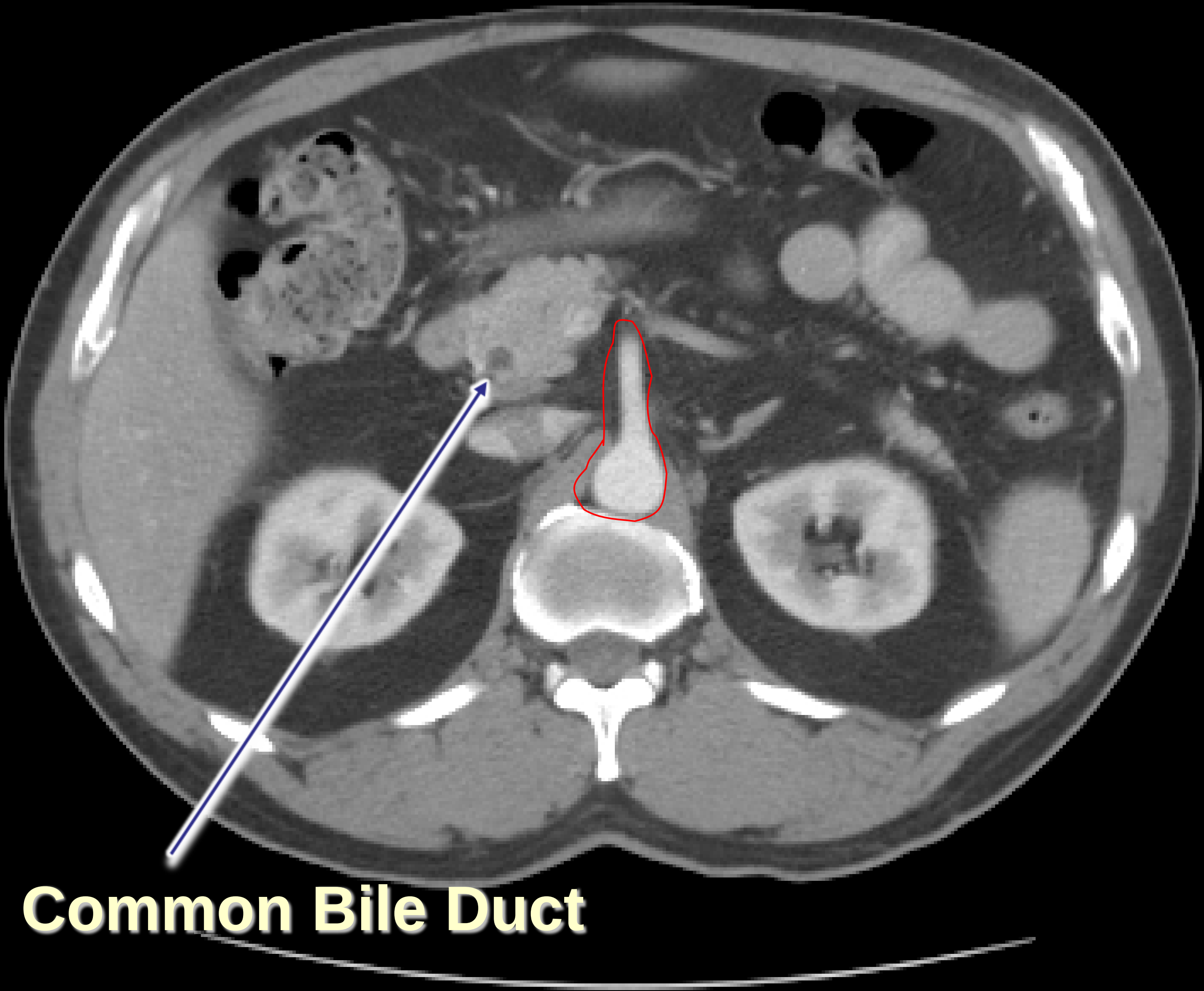


Proper Hepatic Artery & Splenic Artery
(Splenic Artery is the circle)
Splenic Vein

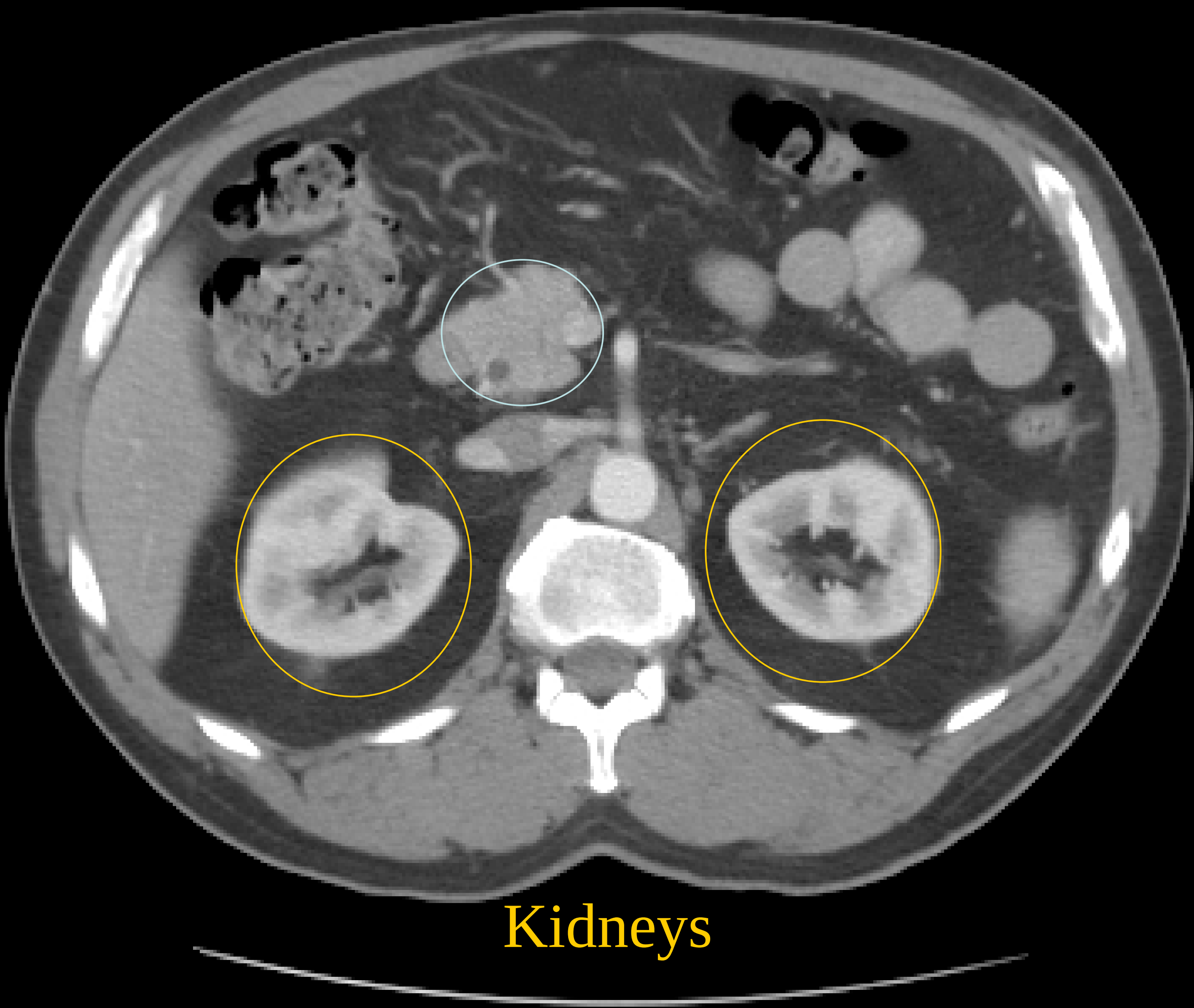
Here the Splenic Vein joins the Superior Mesenteric Vein (below slice level) to form origin of the Portal Vein

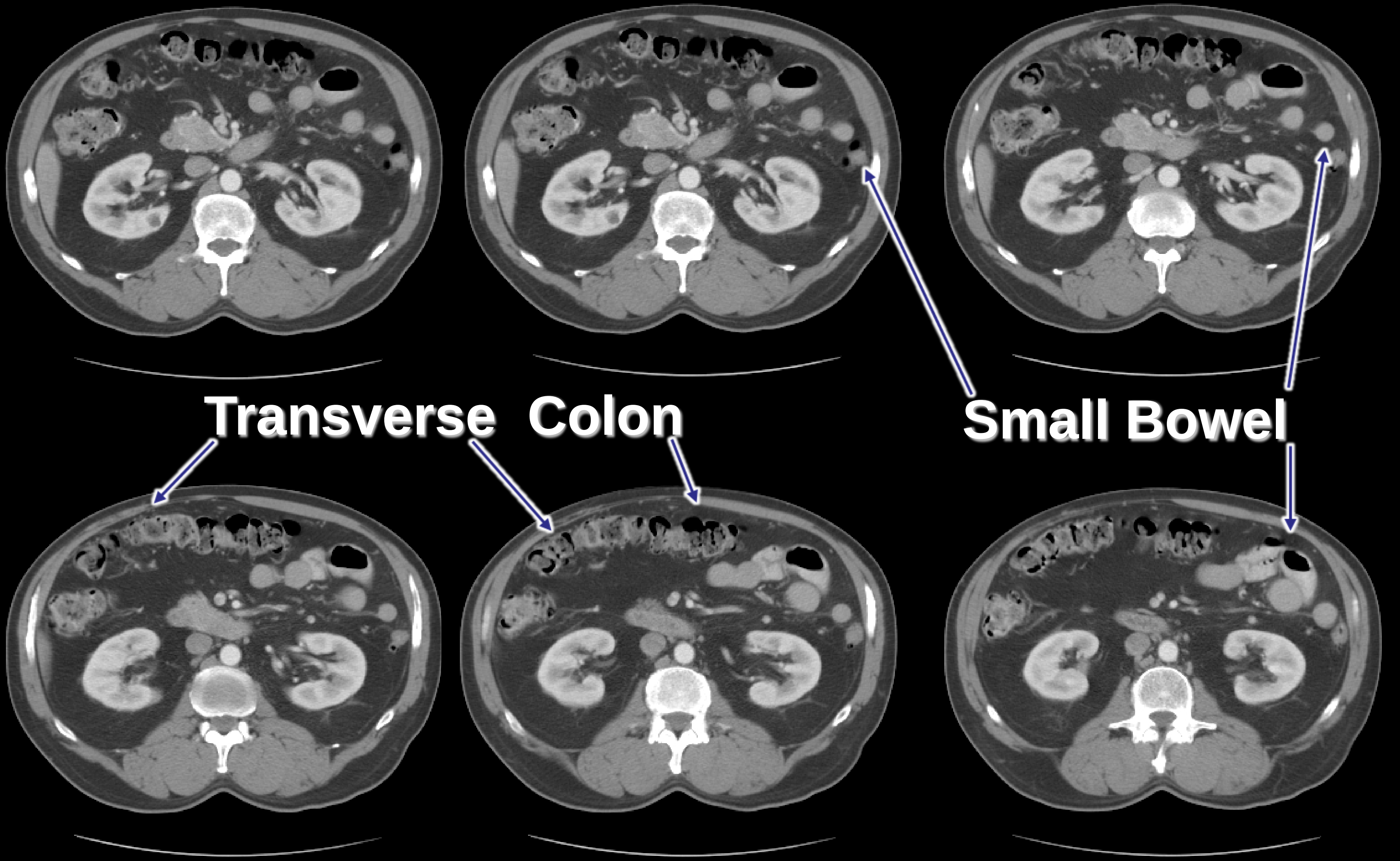


Superior Mesenteric Artery originating from the Aorta

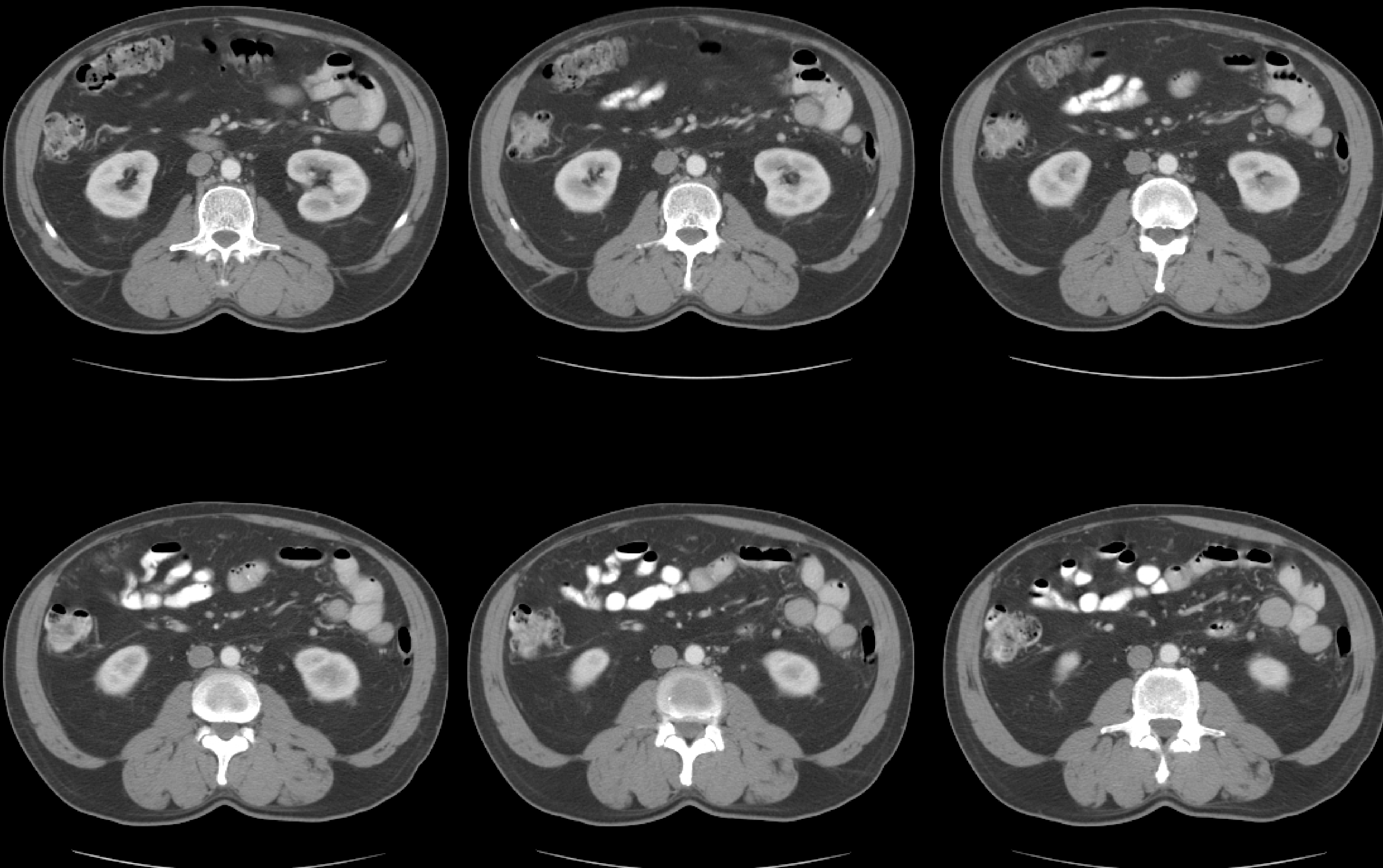


Head of Pancreas

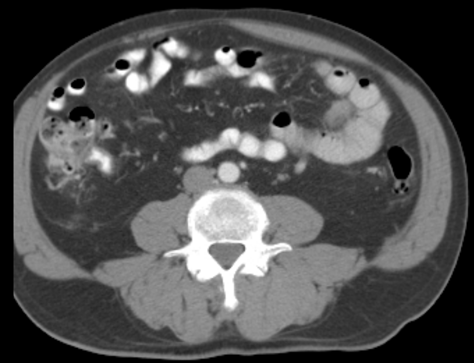




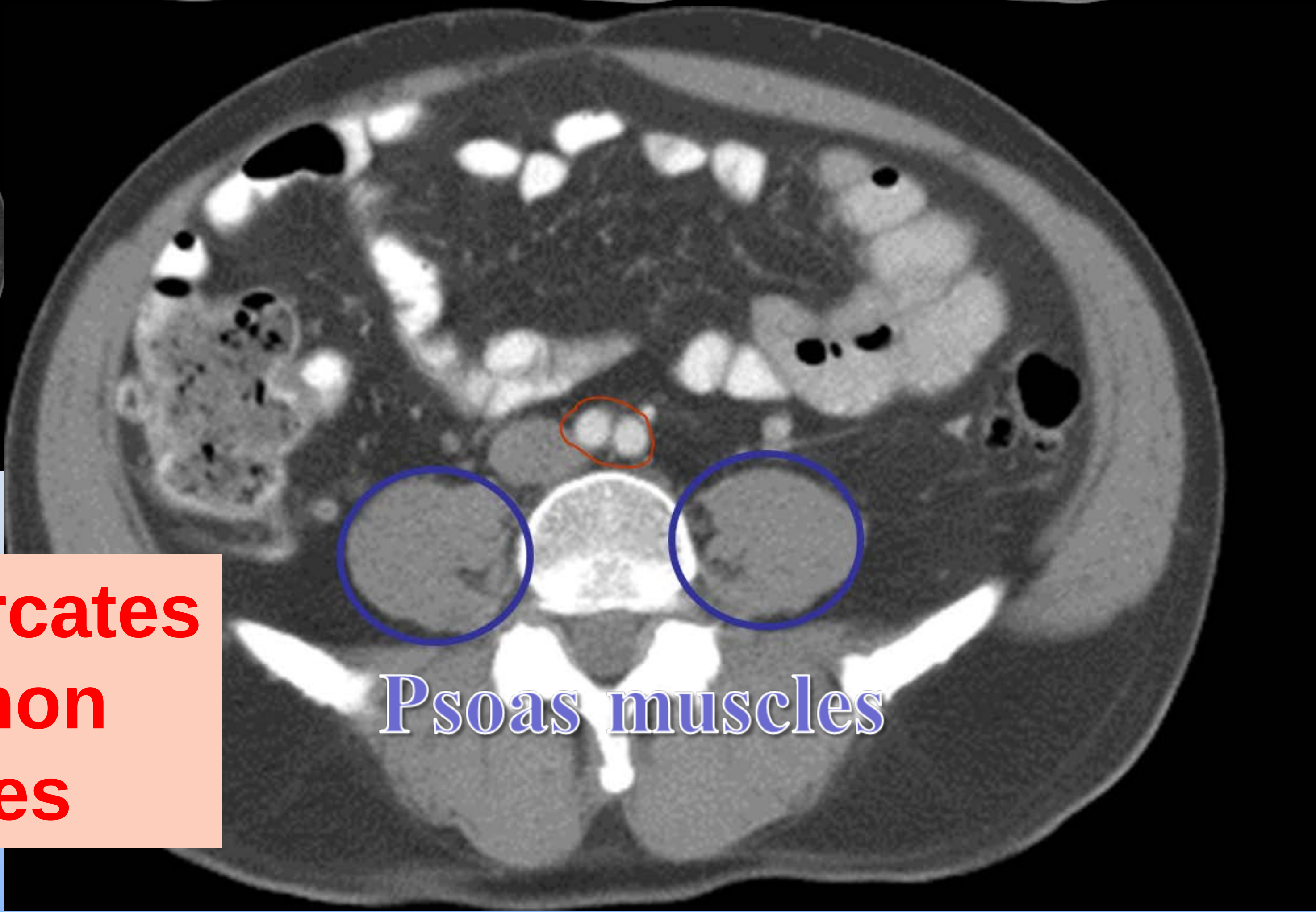
Transverse Colon
Small Bowel







Aorta bifurcates into Common Iliac Arteries



Radiation Risks

- There is always a slight chance of cancer from excessive exposure to radiation. However, the benefit of an accurate diagnosis far outweighs the risk.
- The effective radiation dose for this procedure varies.
- Women should always inform their physician and x-ray or CT technologist if there is any possibility that they are pregnant.

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Radiation Dose to Patients From Common Imaging Examinations

Procedure		**Approximate effective radiation dose	Comparable to natural background radiation for	* Estimated lifetime risk of fatal cancer from examination
WOMEN'S IMAGING	Bone Densitometry (DEXA)	0.001 mSv	3 hours	Negligible
	Mammography	0.4 mSv	7 weeks	Very Low
CHEST	Computed Tomography (CT) — Chest	7 mSv	2 years	Low
	Computed Tomography (CT) — Lung Cancer Screening	1.5 mSv	6 months	Very Low
	Radiography — Chest	0.1 mSv	10 days	Minimal

*Risk Level	Negligible	Minimal	Very Low	Low	Moderate
Estimated additional risk of fatal cancer for an adult from examination	Less than 1 in 1,000,000	1 in 1,000,000 to 1 in 100,000	1 in 100,000 to 1 in 10,000	1 in 10,000 to 1 in 1,000	1 in 1,000 to 1 in 500

Note: These risk levels represent very small additions to the 1 in 5 chance we all have of dying from cancer.

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Radiation Dose to Patients From Common Imaging Examinations

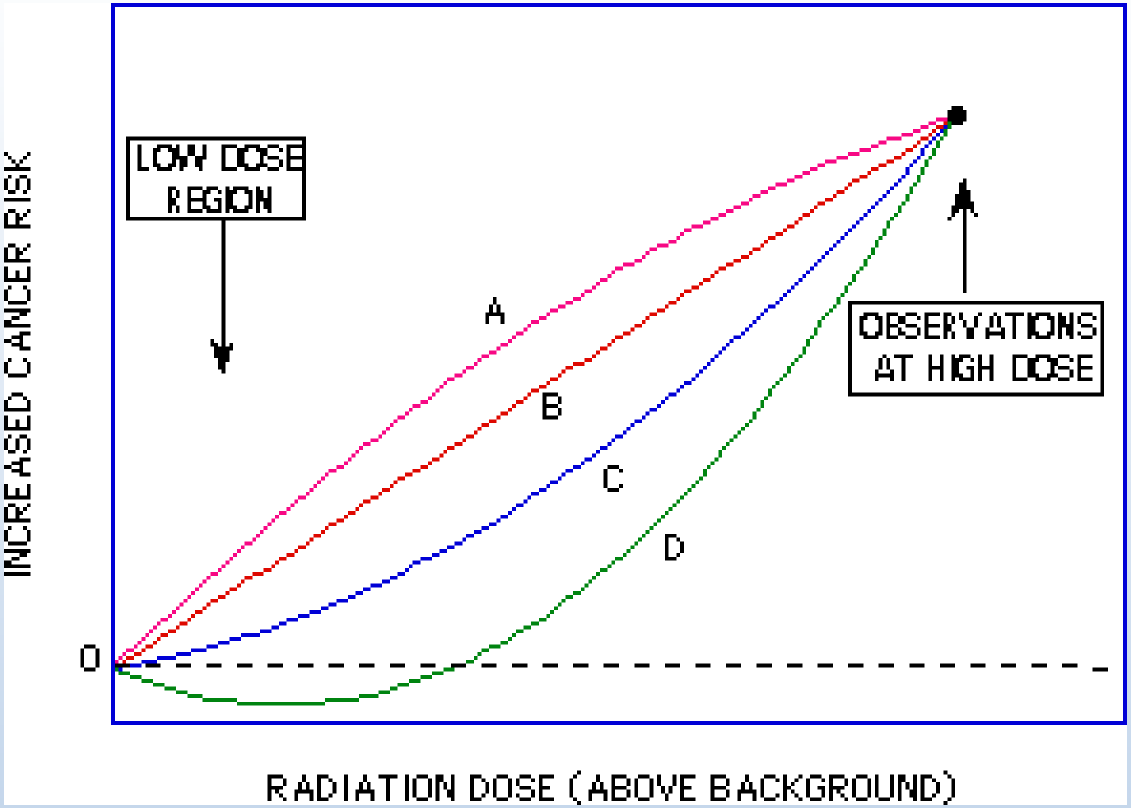
	Procedure	**Approximate effective radiation dose	Comparable to natural background radiation for	* Estimated lifetime risk of fatal cancer from examination
ABDOMINAL REGION	Computed Tomography (CT) — Abdomen and Pelvis	10 mSv	3 years	Low
	Computed Tomography (CT) — Abdomen and Pelvis, repeated with and without contrast material	20 mSv	7 years	Moderate
	Computed Tomography (CT) — Colonography	10 mSv	3 years	Low
	Intravenous Pyelogram (IVP)	3 mSv	1 year	Low
	Radiography (X-ray) — Lower GI Tract	8 mSv	3 years	Low
	Radiography (X-ray) — Upper GI Tract	6 mSv	2 years	Low
NUCLEAR MEDICINE	Positron Emission Tomography — Computed Tomography (PET/CT)	25 mSv	8 years	Moderate

*Risk Level	Negligible	Minimal	Very Low	Low	Moderate
Estimated additional risk of fatal cancer for an adult from examination	Less than 1 in 1,000,000	1 in 1,000,000 to 1 in 100,000	1 in 100,000 to 1 in 10,000	1 in 10,000 to 1 in 1,000	1 in 1,000 to 1 in 500

Note: These risk levels represent very small additions to the 1 in 5 chance we all have of dying from cancer.

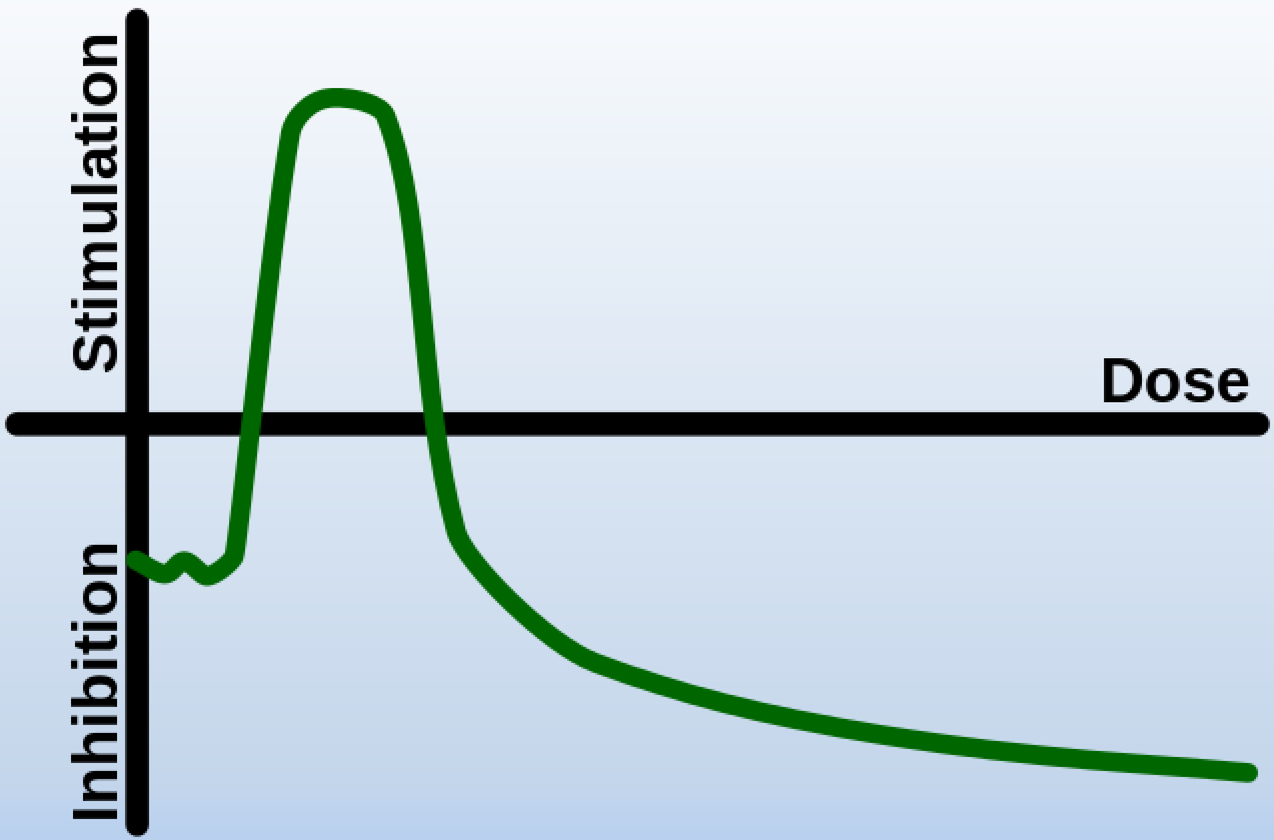
Non-Threshold and Non-Linear Radiation Exposure Theories

Linear no-threshold model -B



Alternative assumptions for the extrapolation of the cancer risk vs. radiation dose to low-dose levels, given a known risk at a high dose: **(A)** supra-linearity, **(B)** linear **(C)** linear-quadratic, **(D)** hormesis

Hormesis Theory



Radiation Hormesis Theory
(AKA radiation homeostasis)

- Hypothesis that low doses of ionizing radiation (within the region of and just above natural background levels) are beneficial
- Stimulate the activation of repair mechanisms that protect against disease, that are not activated in absence of ionizing radiation.
- Reserve repair mechanisms are hypothesized to be sufficiently effective when stimulated as to *not only* cancel the detrimental effects of ionizing radiation but to also inhibit disease not related to radiation exposure

Effects of Radiation

- Effects of high and acute doses of ionizing radiation are easily observed and understood in humans (e.g. Japanese Atomic Bomb survivors)

- Effects of low-level radiation are very difficult to observe and highly controversial

- This is because the baseline cancer rate is already very high and the risk of developing cancer fluctuates 40% because of individual life style and environmental effects obscuring the subtle effects of low-level radiation

CONSISTENCY

It's Only a Virtue if You're Not a Screwup.

Magnetic Resonance Imaging (MRI)

- Magnetic resonance imaging (MRI) uses
  - Powerful magnetic field
  - Radio waves
  - Computer
- Produces detailed pictures of the body's internal structures that can be clearer or more detailed than those obtained by other imaging methods
- MRI is noninvasive
- Does not use ionizing radiation (x-rays)

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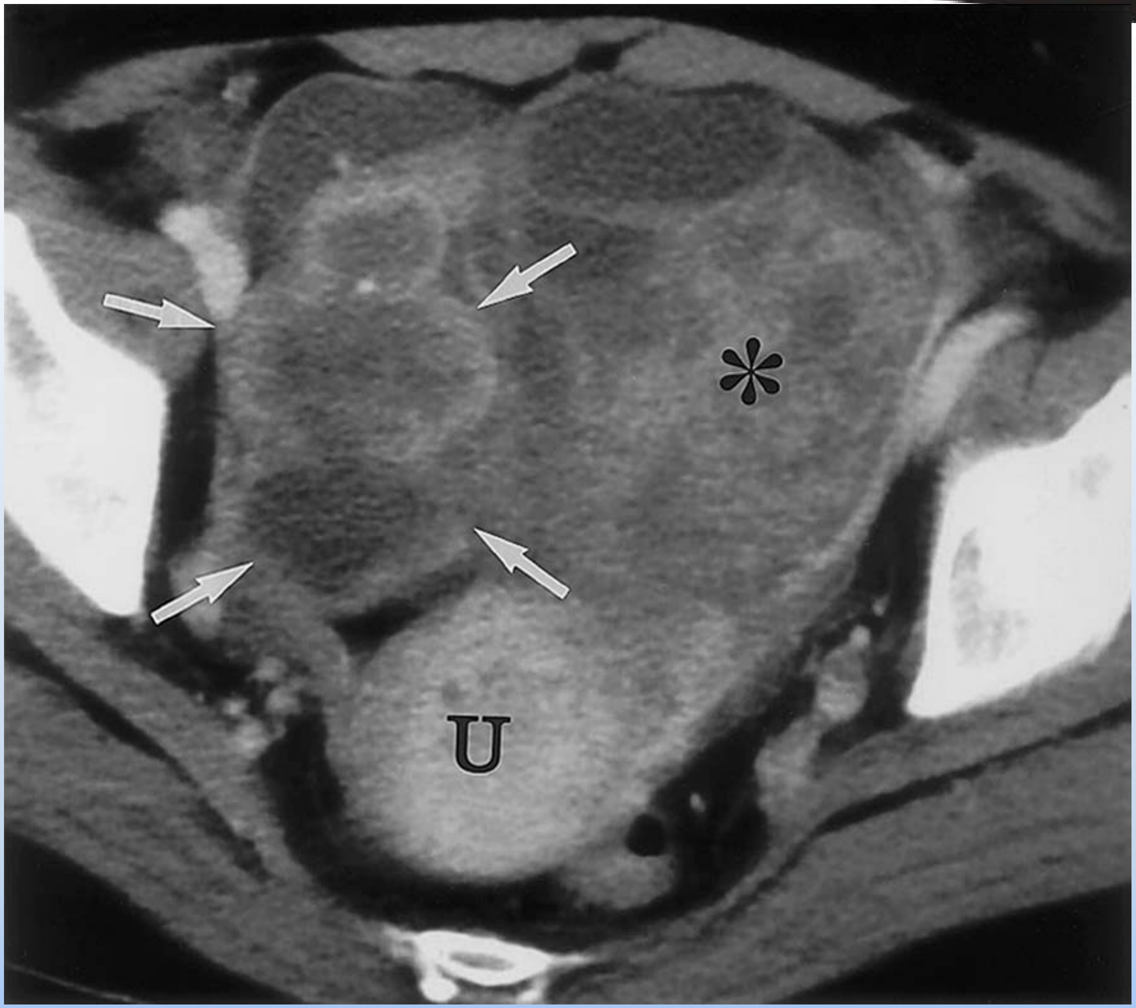


Granulosa cell tumor in a 55-year-old woman. Contrast-enhanced CT scan shows a large, complex mass with a lobular contour, multiple cysts with a “bunch of grapes” appearance on the right (arrows), and an irregularly enhancing solid portion on the left (∗). *U* = uterus.

Figure 21a. Granulosa cell tumor in a 71-year-old woman. **(a)** Sagittal turbo spin-echo T2-weighted MR image (4,275/138) shows a lobulated multilocular cystic mass that resembles a cystadenocarcinoma. However, no evidence of a papillary projection is noted. The endometrial cavity (arrows) is unusually prominent for a patient this age, a finding that is consistent with endometrial hyperplasia. **(b)** Gadolinium-enhanced fat-suppressed FLASH T1-weighted MR image (148/4.8) demonstrates multiple well-enhanced septa, with numerous large cystic spaces lined by granulosa cells. These findings represent an extreme example of the macrofollicular pattern.

18F-FDG PET/CT

- Useful tool for evaluating the recurrence of ovarian cancer after first-line therapy in patients with a high risk of relapse, equivocal radiologic findings, increased or normal levels of serum CA-125

- It can more accurately diagnose and localize recurrence, hence decreasing the rate of second look surgery and changing treatment plan

PET

- PET scanning with the tracer fluorine-18 (F-18) fluorodeoxyglucose (FDG), called FDG-PET, is widely used in clinical oncology.
- This tracer is a glucose analog that is taken up by glucose-using cells and phosphorylated by hexokinase – and gets trapped in the cells (ideal for identification of these cells)
- Uses the natural effect of Positrons for imaging

What is a Positron?

- The positron or antielectron is the antiparticle or the antimatter counterpart of the electron.
- The positron has an electric charge of +1 e, a spin of ½, and has the same mass as an electron.
- When a low-energy positron collides with a low-energy electron, annihilation occurs, resulting in the production of two or more gamma ray photons
- Positrons may be generated by positron emission radioactive decay

Electron–positron Annihilation

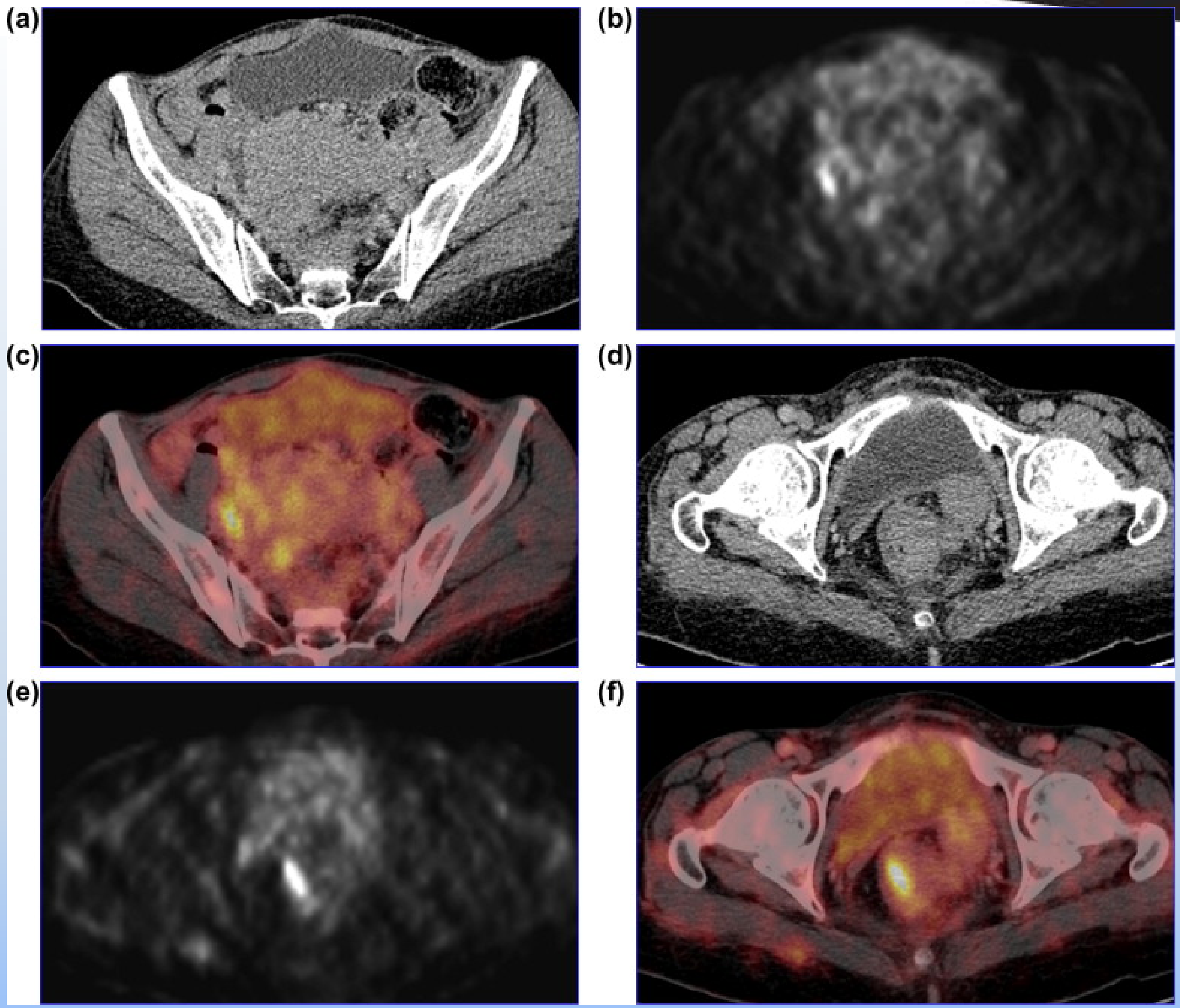
- Electron–positron annihilation occurs when an electron (e^-) and a positron (e^+, the electron's antiparticle) collide
- The result of the collision at low energies is the annihilation of the electron and positron, and the creation of gamma ray photons
- All Matter is Destroyed!
- … and changed into energy
- As per Einstein's Theory of Relativity – $E=MC^2$

Uses emissions from small amounts of injected radioactive material

- PET imaging uses the process of Electron–positron annihilation to produce high quality nuclear medicine images of injected materials labeled with radioactive isotopes which degrade by positron emission
- Florine-18 (F18) is a useful positron emitting isotope which a half-life of 110 minutes
- Needs to be made with a cyclotron
- F18FDG looks like normal sugar glucose to your cells (at the cell surface) and are taken up by energy hungry cells


THE STEAKS HAVE BEEN RAISED

Recurrent ovarian cancer in 49 y/o female with bilateral ovarian granulosa cell carcinoma underwent TAH&BSO, received chemotherapy



(a and d) Axial contrast-enhanced CT,

(b and e) FDG PET, and

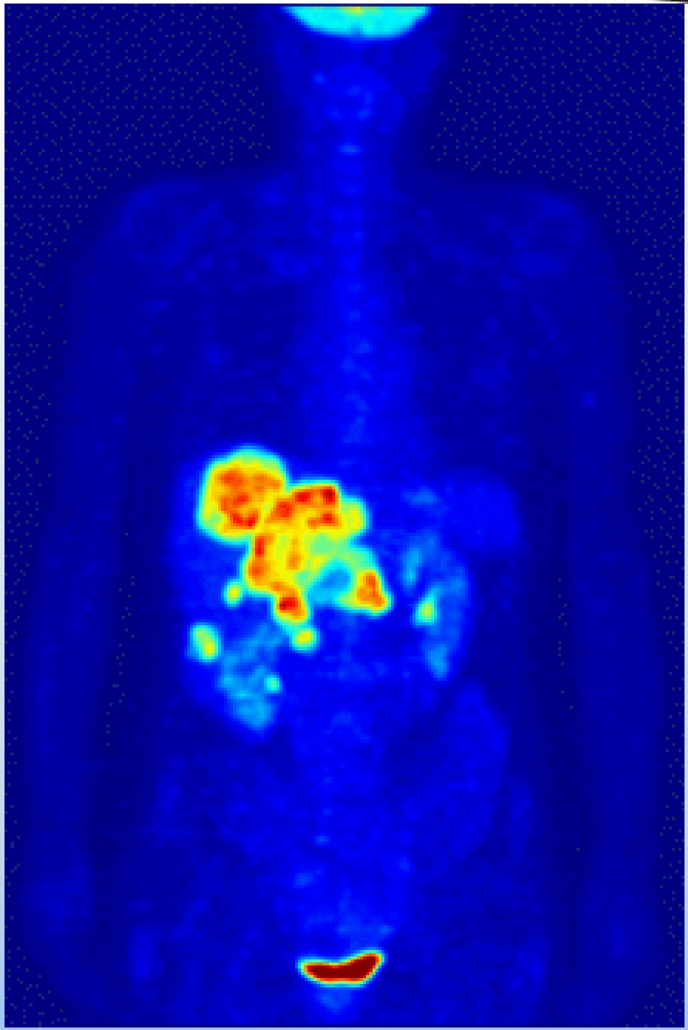
(c and f) fused PET/CT fused images

Show multiple confluent soft tissue masses (a–c) posterior and superior to the urinary bladder with low grade FDG uptake

Left lateral rectal (d–f) wall thickening

Findings suggestive of local pelvic recurrence

Volume PET (only) Image



Ovarian Cancer Tumor Staging

- Two classification organizations
  - The tumor-node-metastasis (TNM)
  - International Federation of Gynecology and Obstetrics (FIGO)
- Distinctions nearly identical – with different designations

Tumor Staging –TNM / FIGO

Primary tumor (T)

TNM	*FIGO*	
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor limited to the ovaries (one or both)
T1a	IA	Tumor limited to one ovary; capsule intact, no tumor on ovarian surface; no malignant cells in ascites or peritoneal washings
T1b	IB	Tumor limited to both ovaries; capsules intact, no tumor on ovarian surface; no malignant cells in ascites or peritoneal washings
T1c	IC*	Tumor limited to one or both ovaries with any of the following: capsule ruptured, tumor on ovarian surface, malignant cells in ascites or peritoneal washings
T2	II	Tumor involves one or both ovaries with pelvic extension
T2a	IIA	Extension and/or implants on the uterus and/or tube(s); no malignant cells in ascites or peritoneal washings
T2b	IIB	Extension to and/or implants in other pelvic tissues; no malignant cells in ascites or peritoneal washings
T2c	IIC*	Pelvic extension and/or implants (T2a or T2b) with malignant cells in ascites or peritoneal washings
T3	III*	Tumor involves one or both ovaries with microscopically confirmed peritoneal metastasis outside the pelvis
T3a	IIIA*	Microscopic peritoneal metastasis beyond the pelvis (no macroscopic tumor)
T3b	IIIB*	Macroscopic peritoneal metastasis beyond the pelvis 2 cm or less in greatest dimension
T3c	IIIC*	Macroscopic peritoneal metastasis beyond the pelvis >2 cm in greatest dimension and/or regional lymph node metastasis

Tumor Staging –TNM / FIGO

Regional lymph nodes (N)

TNM	*FIGO*	
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1	IIIC	Regional lymph node metastasis

Distant metastasis (M)

TNM	*FIGO*	
M0		No distant metastasis
M1	IV*	Distant metastasis (excludes peritoneal metastasis)

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American College of Radiology (ACR) Appropriateness Criteria

Clinical Condition: **Staging and Follow-up of Ovarian Cancer**

Variant 1: **Pretreatment staging of ovarian cancer**

Radiologic Procedure	Rating	Comments	RRL*
CT abdomen and pelvis with contrast	9		☢☢☢☢
MRI abdomen and pelvis without and with contrast	7	If CT with contrast cannot be performed (due to renal insufficiency or severe allergy) or if CT findings are indeterminate. See statement regarding contrast in text under "Anticipated Exceptions."	O
CT chest abdomen pelvis with contrast	7	Indicated with abnormal chest radiograph.	☢☢☢☢
CT abdomen and pelvis without contrast	6		☢☢☢☢
MRI abdomen and pelvis without contrast	5		O
CT chest abdomen pelvis without contrast	4		☢☢☢☢
FDG-PET/CT skull base to mid-thigh	4		☢☢☢☢
US pelvis transvaginal	3		O
US abdomen and pelvis transabdominal and US pelvis transvaginal	3		O
CT chest abdomen pelvis without and with contrast	3		☢☢☢☢
CT abdomen and pelvis without and with contrast	3		☢☢☢☢
X-ray contrast enema	2		☢☢☢
X-ray intravenous urography	2		☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

American College of Radiology (ACR) Appropriateness Criteria

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Date of origin: 1996
Last review date: 2012

Variant 2: **Rule out recurrent ovarian cancer.**

Radiologic Procedure	Rating	Comments	RRL*
CT abdomen and pelvis with contrast	9		☢☢☢☢
FDG-PET/CT skull base to mid-thigh	8		☢☢☢☢
CT chest abdomen pelvis with contrast	7	Indicated with abnormal chest radiograph.	☢☢☢☢
MRI abdomen and pelvis without and with contrast	7	If CT with contrast cannot be performed (due to renal insufficiency or severe allergy) or if CT findings are indeterminate. See statement regarding contrast in text under "Anticipated Exceptions."	O
CT abdomen and pelvis without contrast	6		☢☢☢☢
MRI abdomen and pelvis without contrast	4		O
CT chest abdomen pelvis without contrast	4		☢☢☢☢
US pelvis transvaginal	3		O
US abdomen and pelvis transabdominal and US pelvis transvaginal	3		O
CT abdomen and pelvis without and with contrast	3		☢☢☢☢
CT chest abdomen pelvis without and with contrast	3		☢☢☢☢
X-ray contrast enema	2		☢☢☢
X-ray intravenous urography	2		☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

TRADITION

Just Because You've Always Done It That Way Doesn't Mean it's Not Incredibly Stupid.

Imaging Primary Tumor

- **Ultrasound and MRI are the best imaging modalities for imaging the PRIMARY TUMOR**

- The overall best Imaging Modality for preoperative grading of the Primary Tumor is Magnetic Resonance (MR or MRI)
  - Best Tissue Differentiation
  - Can detect fat content of soft tissue structures– a feature which can help with differential diagnosis (narrowing the diagnostic possibilities of a given imaging finding)
  - Can tailor the exam for the body region of interest

Accuracy measures of PET/CT in lesion localization (Lesion-based)

Localization	Number of lesions	Sensitivity (%)	Specificity (%)	Accuracy (%)
Pelvic recurrence	24	100	100	100
Pelvic lymph node	5	80	99	97
Para-aortic lymph node	10	78	96	94
Peritoneal metastasis	22	77	96	90
Distant lymph node	8	89	100	99
Distant organ metastasis	4	100	100	100

Ghada K. Gouhar, Soha Siam, Somayya M. Sadek, Reda A. Ahmed. Prospective assessment of 18F-FDG PET/CT in detection of recurrent ovarian cancer. The Egyptian Journal of Radiology and Nuclear Medicine Volume 44, Issue 4, December 2013, Pages 913–922

Assessment of Nodal Stage and Metastatic Disease

- This can be done with CT, PET/CT and MRI
- MRI is not useful for complete staging, but is relatively sensitive for the immediate pelvic region
- **Complete Staging is best accomplished with PET/CT**
- Diagnostic CT with oral and IV Contrast is nearly equal. In recent years, PET/CT shown to be superior

Thank you for Listening

Buffalo Waterfront

This Lecture was brought to you with the cooperation of Roswell Park Cancer Institute Division of Diagnostic Imaging

~

Zachary D. Grossman, MD, FACR, Professor and Chairman