Phys. 428, Lecture 5:

LECTURE	DATE	INSTRUCTOR	TOPIC
1	April 2	PK	Overview: Imaging equation, inverse problem
2	April 9	PK	2D-LSI imaging systems, X-ray physics: formation and interaction
3	April 16	WH	X-ray detection and imaging systems
4	April 23	PK	X-ray computed tomography (CT) systems
5	April 30	WH	X-ray CT part 2. Contrast Agents
6	May 7	PK	Image reconstruction and image quality
7	May 14	LM	Nuclear decay schemes and isotopes
8	May 21	RM	Gamma cameras: components and systems
9	May 28	WH	Tomography in molecular imaging: SPECT scanners
10	June 4	SB	Positron emission tomography (PET) and hybrid PET/CT scanners
11	June 11	WH/PK	Group project presentations

Each student should email at least one question on today's lecture to our TA, Jackie (jackie24@uw.edu) by Friday.

Please include "Phys 428 Lecture 5 Question" in the subject line.

Class Project

- Pick:
  - An imaging modality covered in class
  - A disease or disease and treatment
- Review:
  - what is the biology of the imaging
  - what is the physics of the imaging
  - what are the competing imaging (and non-imaging) methods
  - what is the relative cost effectiveness of your imaging modality for this disease?
- Form groups (or let me know) by Friday April 26
- **1 page outline** ~~**Friday May 3**~~ **(20%)**
  - **Outline DELAYED to May 7 (See email from Dr. Kinahan)**
- Background summary Friday May 10 (15%)

  (what background material you will use & capsule summaries)
- Rough draft Friday May 17 (15%)
- Final version Friday May 31 (30%)
- Presentation / slides Friday June 7 (10%)
- Presentation Tuesday June 11 (10%)

Mid-Term & Weekly questions

- Since we are behind in the material, there will be no midterm.

- Instead the questions that are due each Friday will now count for a larger portion of the final grade.

Discussion of Questions from Last Lecture

- How many projections are obtained for a CT?
  - 500 to 1000 is typical.
  - More projections helps to reduce streak artifacts in reconstruction.
- How is the internal structure of the body revealed form projection images?
  - We can mathematically reconstruct an attenuation map from several projections. More projections give more accurate image. Reconstruction algorithms include “Filtered Back Projection (FBP)” and a variety of “Iterative Reconstruction” methods (recent for CT).
- Why is fan-beam used rather than a cone.
  - It’s computationally easier
  - Spectral variations with oblique rays
  - Increased patient thickness at oblique angles

Discussion of Questions from Last Lecture

- What is beam hardening in more detail?
  - There is a broad spectrum of energies emitted by the X-ray tube.
  - The rate of attenuation of these X-rays depends on energy, with lower energies being absorbed more readily.
  - After passing through a thickness of material, the left over X-rays will have an spectrum that has relatively fewer low energy photons than higher energy photons (compared to what it started with).
- Are variations in X-ray fluence versus fan angle plot previously shown due to more mass attenuation in the patient or something else?
  - The intensity emitted from the X-ray tube will vary over the fan beam
  - A bow-tie filter can be used to make this intensity more uniform, however, the X-rays become more hardened (effective energy) at larger angles, where the filter is thicker.

Discussion of Questions from Last Lecture

Answering a few questions about Imaging Equation

- In this case I_d is our measured data, and we want to recover an image of $\mu(x,y)$

$$I_d = \int_0^{E_{\max}} S_0(E) E e^{-\int_0^d \mu(s,E)\,ds} \, dE$$

- Simplifying assumption to alleviate mathematical difficulty for this double integration:

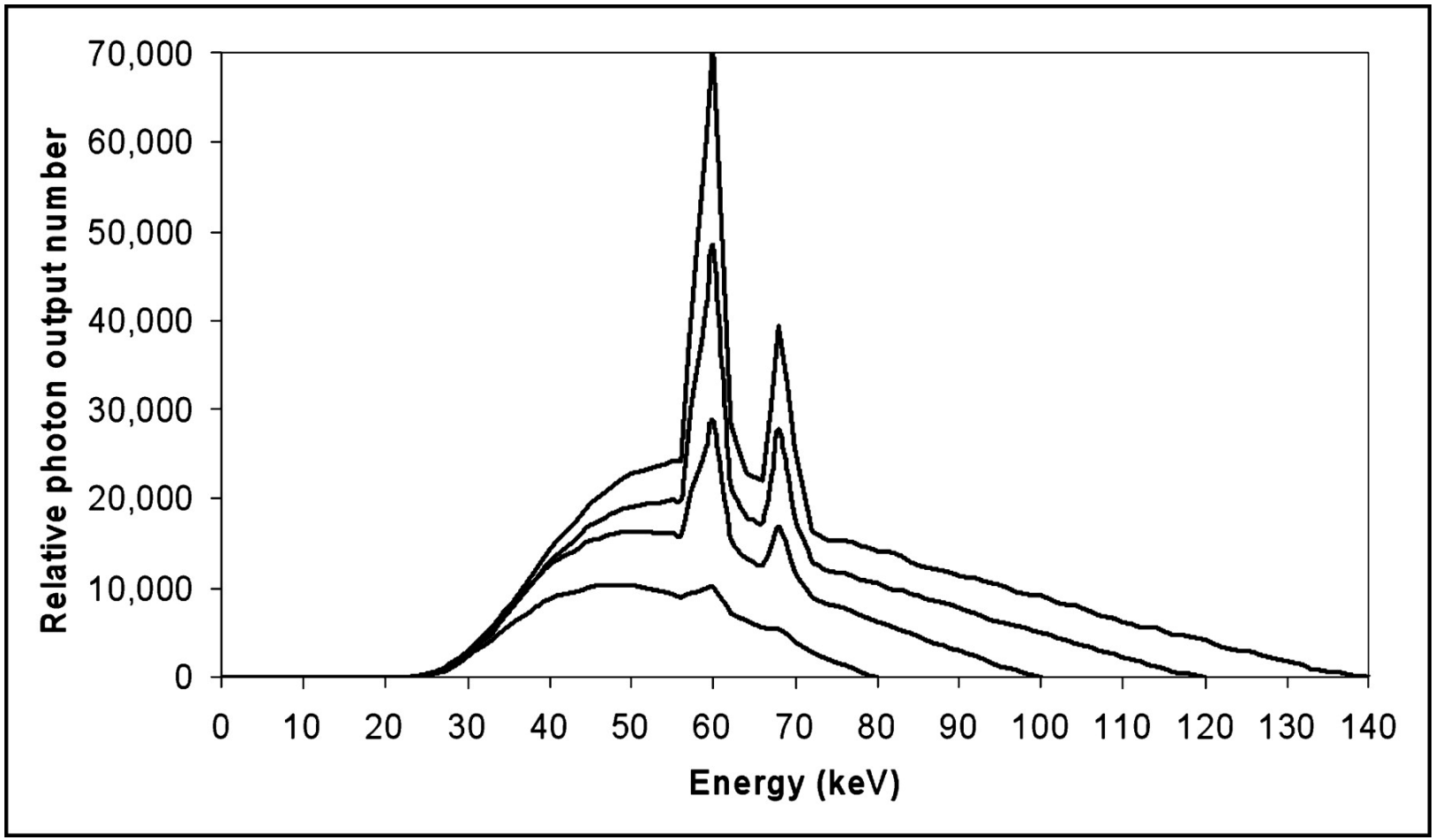
$$\bar{E} = \frac{\int_0^{E_{\max}} E S(E)\,dE}{\int_0^{E_{\max}} S(E)\,dE}$$

Note: detector quantum efficiency and characteristic X-ray contribution is included in the effective energy.

$$I_d = I_0 e^{-\int_0^d \mu(s,\bar{E})\,ds}$$

- We measure the reference intensity I_0, typically with a detector at the edge of the fan

Emission spectra for various kVp

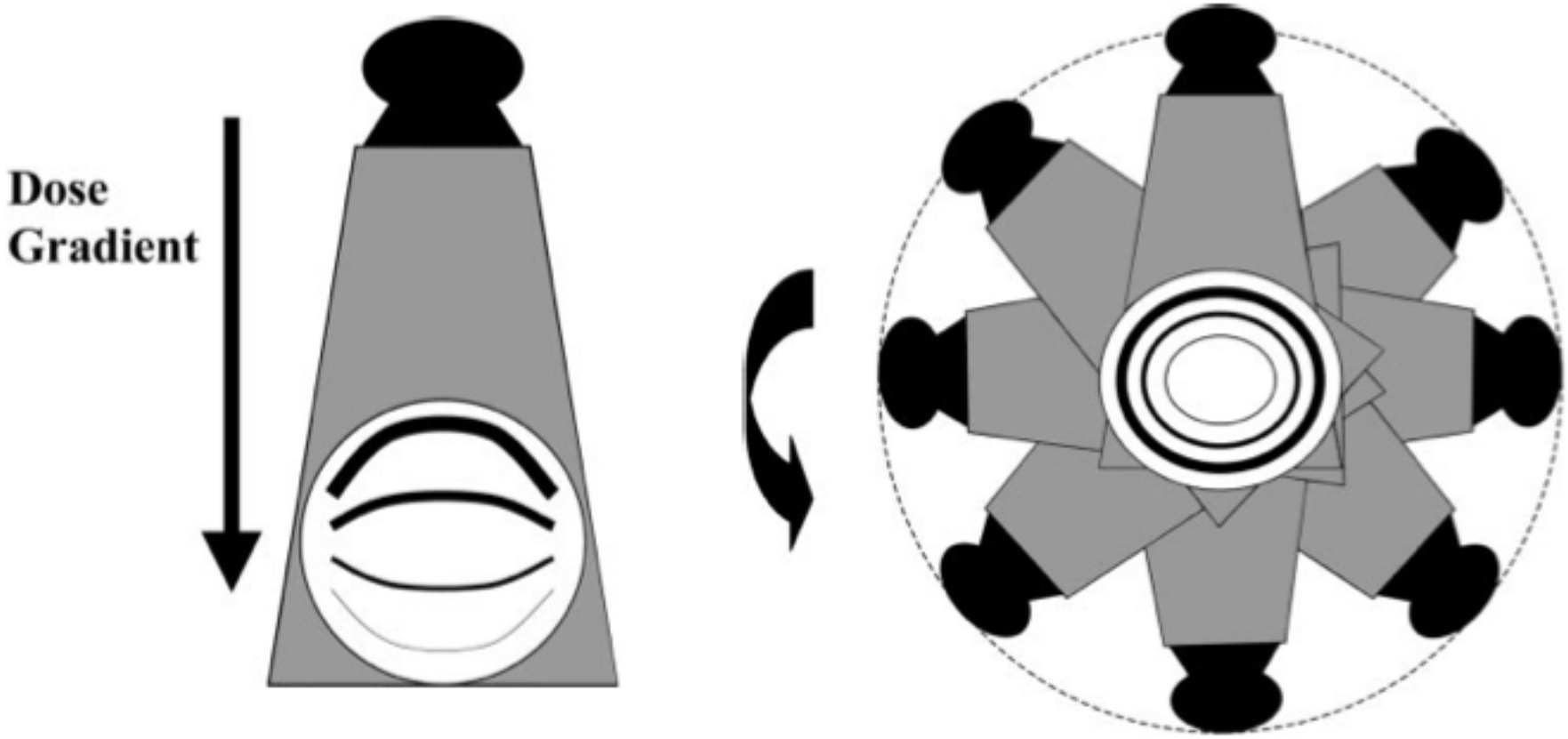


CT Radiation Dose and Technique

X-ray radiation dose

- Loss of photon energy means some is being transferred to tissue
- Basic concepts:
  - Exposure: number of ion pairs produced in a specific volume of air by radiation
    - Units are coulombs per kilogram of air (C/kg)
    - Useful in medical imaging is the roentgen (R) 2.58 × 10−4 C/kg
    - Can easily be measured with an ionization chamber
  - Absorbed dose: amount of absorbed energy per mass
    - Note this a implicity a concentration, not a total
    - Units are J/kg, with a special unit of *gray* (Gy)
    - Useful in medical imaging is the rad, which is the absorption of 100 ergs per gram of material
    - 1 roentgen of yields one 1 rad of absorbed dose in soft tissue
  - Equivalent dose: Takes into account type of radiation for tissue T
    - w_R = 1 for photons, 2 for protons, 20 for nuclear fragments $H_T = \sum_R w_R D_{T,R}$
  - Effective dose: Takes into account cumulative effect over all tissues
    - meant to compare relative risks between different procedures
    - wildly inaccurate
    - Units are also J/kg, with a special unit of *sievert* (Sv) $E = \sum_T w_T H_T$
    - 1 Gy give 1 Sv for x-rays in soft tissue

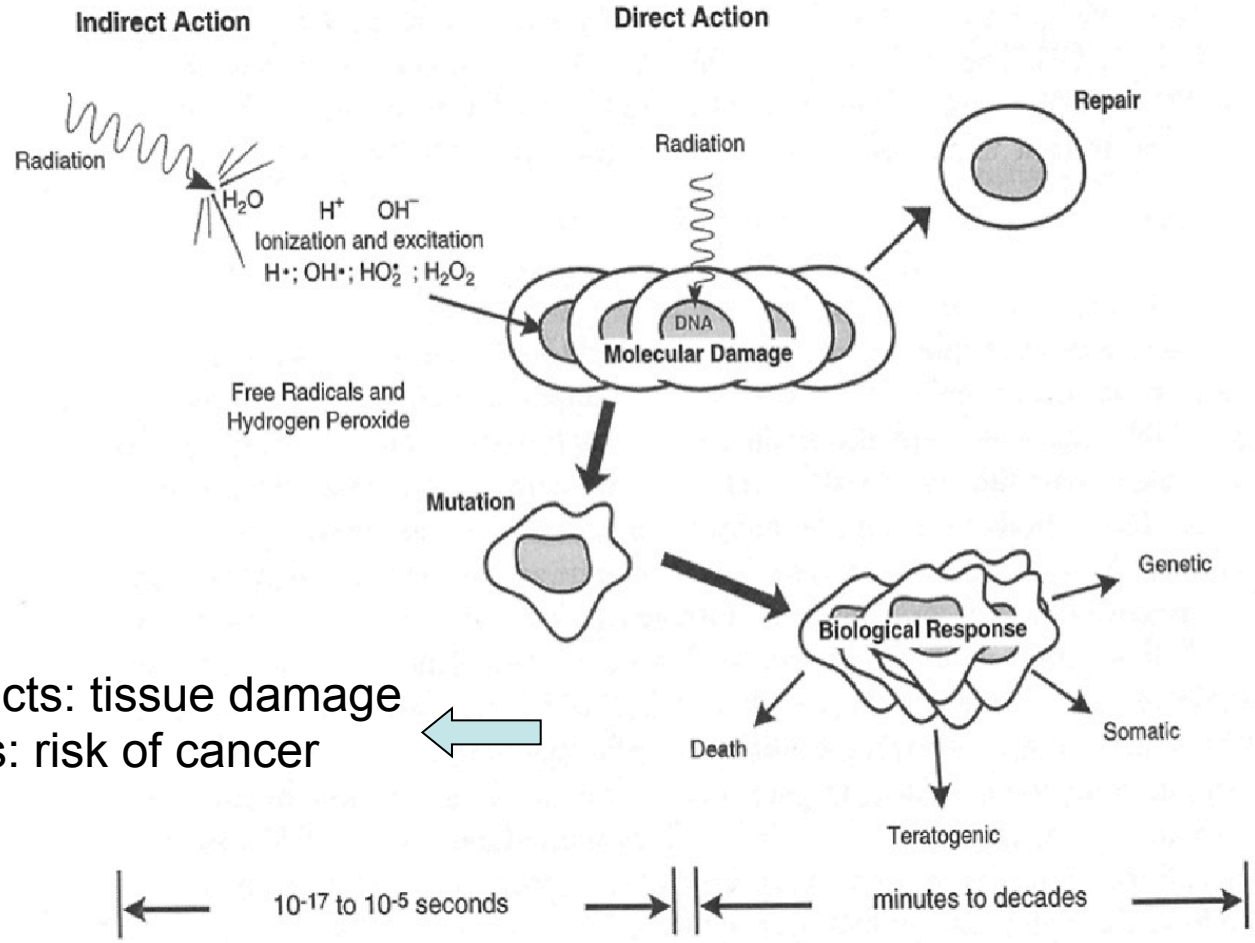
X-ray radiation dose (continued)



Projection Image Computed Tomography

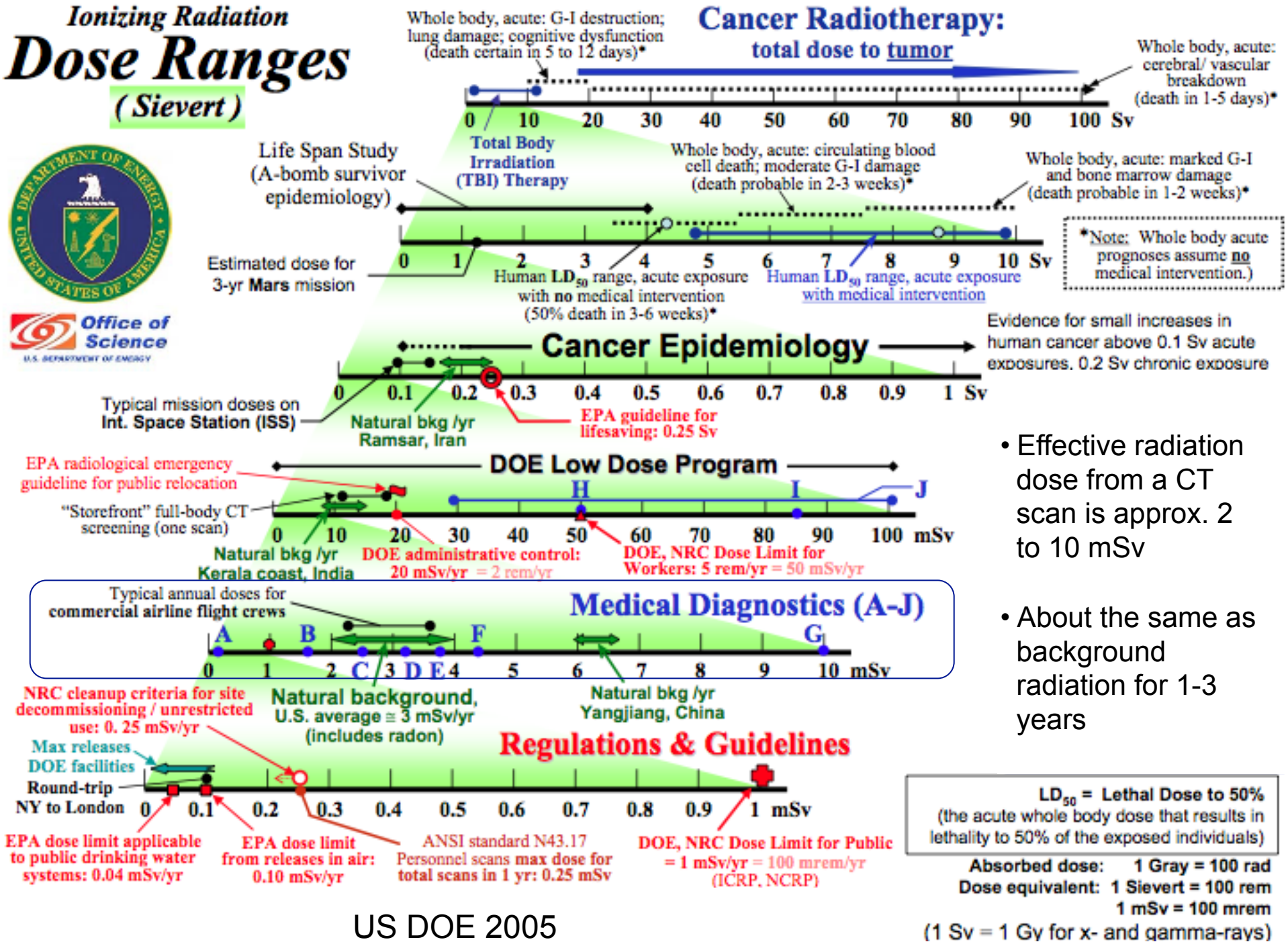
Projection: Uniform over 2D collimated region and exponentially attenuated
CT: Dose is rotationally symmetric over plane and falls off axially

Effects of ionizing radiation



Deterministic effects: tissue damage
Stochastic effects: risk of cancer

Bushberg et al. The Essential Physics of Medical Imaging. 2002



- Effective radiation dose from a CT scan is approx. 2 to 10 mSv
- About the same as background radiation for 1-3 years

US DOE 2005

NCRP Report 160 (2009) for 2006 data

TABLE 4.6—*Effective doses and collective effective doses for CT.*

Categories	Number of Scans (millions)	Scans (%)	Effective Dose per Scan (mSv)	Collective Effective Dose (person-Sv)	Collective Effective Dose (%)
Head [a]	19.0	28.4	2	38,044	8.7
Chest	10.6	15.9	7	74,326	17.0
Abdomen/pelvis	21.2	31.7	10	212,538	48.6
Extremity	3.5	5.2	0.1	515	0.1
CT angiography: heart	2.3	3.4	20	46,000	10.5
CT angiography: head	2.0	3.0	5	10,000	2.3
Spine	4.1	6.2	10	41,369	9.5
Interventional	2.3	3.4	0.1	230	0.05
Whole-body screening	0.2	0.3	10	2,000	0.5
Calcium scoring	0.5	0.8	2	1,000	0.2
Cardiac[b]	0.3	0.5	20	6,000	1.4
Virtual colonography	0.2	0.3	10	2,000	0.5
Miscellaneous	0.7	1.1	5	3,500	0.8
Total [c]	67.0			437,523	
2006 U.S. population				300 million	
E_{US} from CT				1.46 mSv	

[a]Head: Includes brain and head and neck.
[b]Cardiac: Procedures other than CT angiography of the heart.
[c]Total: The 62 million procedures for 2006 as listed in IMV (2006a) adjusted by category for procedures with two scans.

Statistical Radiation Dose Effects (>100 mSv)

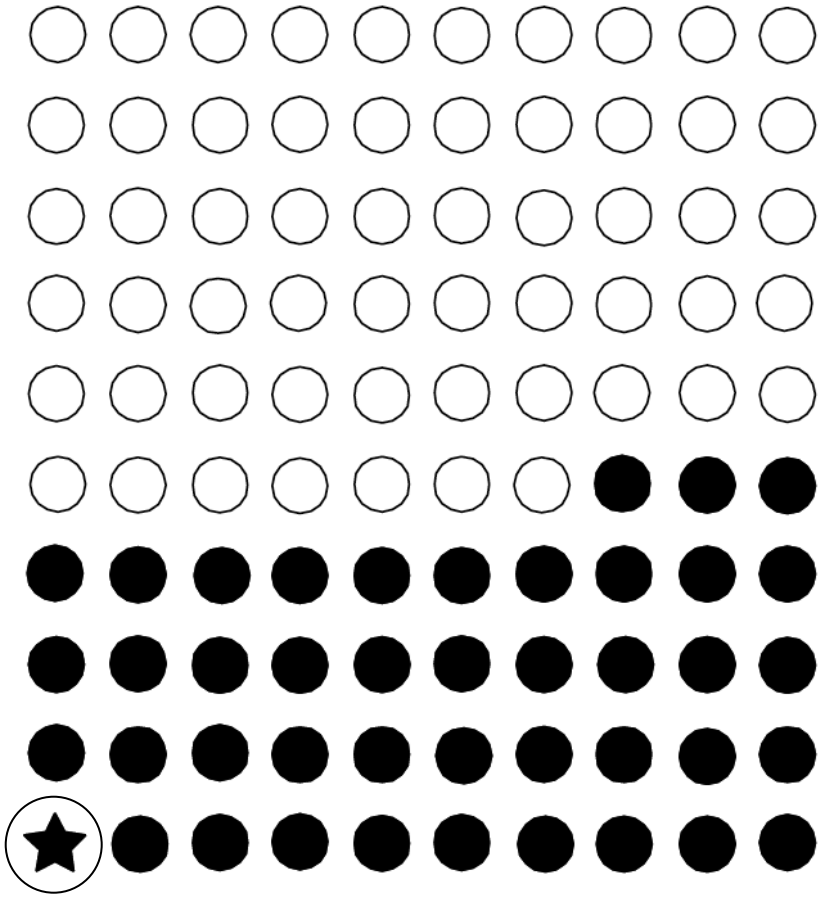
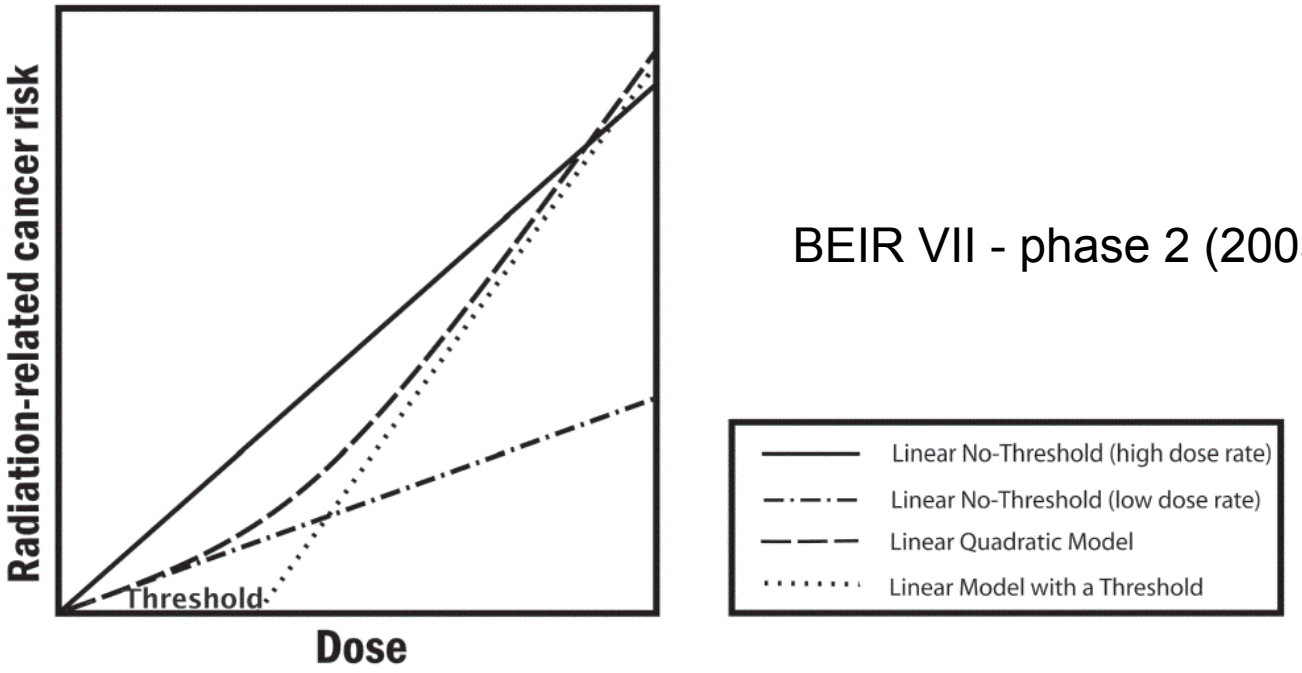


FIGURE PS-4 In a lifetime, approximately 42 (solid circles) of 100 people will be diagnosed with cancer (calculated from Table 12-4 of this report). Calculations in this report suggest that approximately one cancer (star) per 100 people could result from a single exposure to 0.1 Sv of low-LET radiation above background.

BEIR VII - Phase 2 (2005)

Controversy over very low-dose effects (<10 mSv)



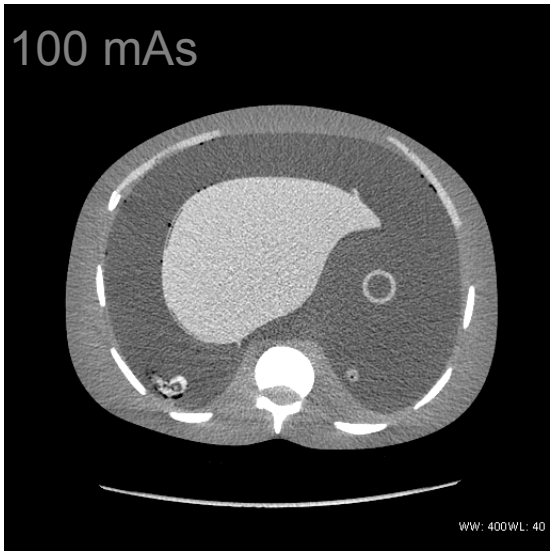
BEIR VII - phase 2 (2005)

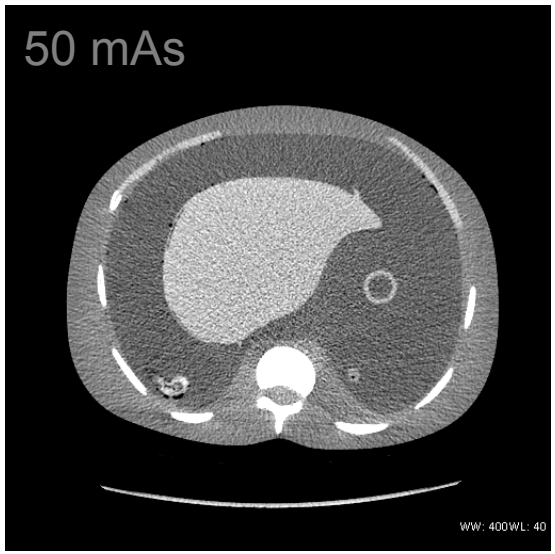
FIGURE PS-3 The committee finds the linear no-threshold (LNT) model to be a computationally convenient starting point.

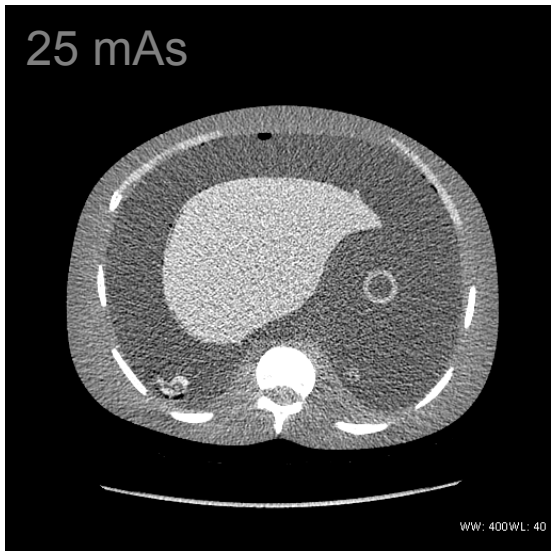
•*The American Association of Physicists in Medicine (AAPM) 2011:*

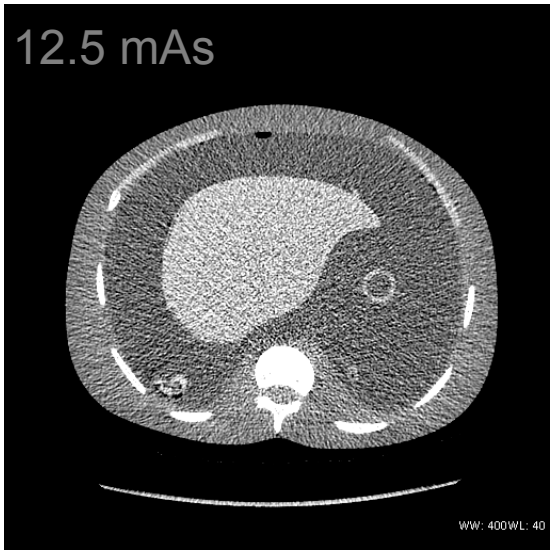
"... Risks of medical imaging at effective doses below 50 mSv for single procedures or 100 mSv for multiple procedures over short time periods are too low to be detectable and may be nonexistent. Predictions of hypothetical cancer incidence and deaths in patient populations exposed to such low doses are highly speculative and should be discouraged. ..."

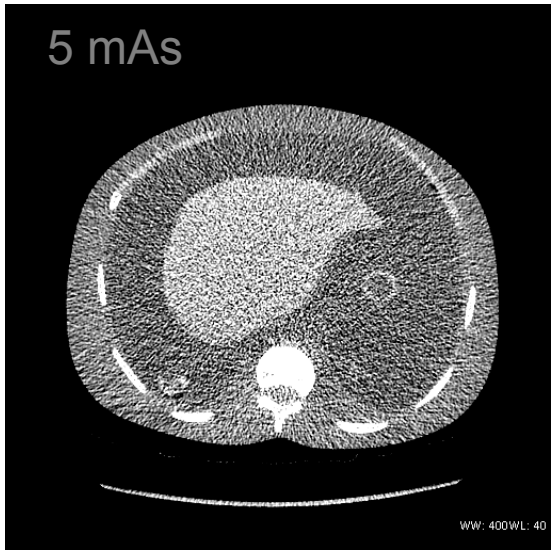
Decreased radiation dose = Higher noise

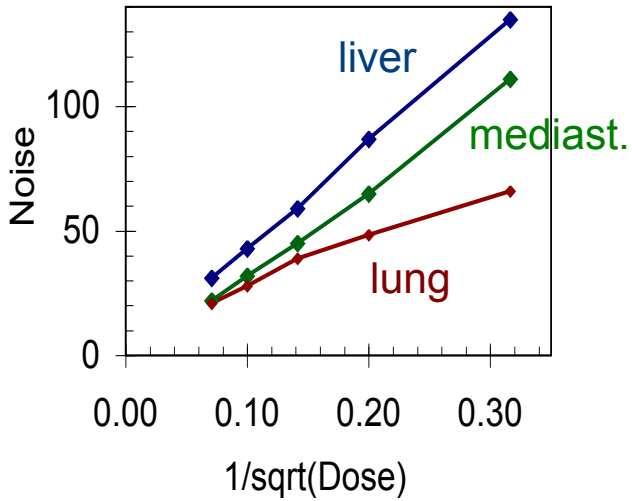












Technique

- Technique refers to the factors that control image quality and patient radiation dose
- kVp (kV potential) - energy distribution of X-ray photons (recall lower energy photons are absorbed more readily
- mA - number of X-ray photons per second (controlled with tube current)
- s - gantry rotation time in seconds
- mAs - total number of photons (photons per second X seconds)
- pitch
- slice collimation
- filtration - filters placed between tube and patient to adjust energy and/or attenuation (not discussed here)

Radiation dose versus kVp

- kVp not only controls the dose but also controls other factors such as image contrast, noise and x-ray beam penetration through patient

Parameter	80 kVp	120 kVp	140 kVp
Image Contrast	***Best***	Intermediate	Poor
Noise	Most	Average	***Least***
Penetration	Least	Average	***Most***

Effective Dose Comparison with Chest PA Exam

Procedures	Eff. Dose [mSv]	Equivalent no. of chest x-rays	Approx. period of background radiation
Chest PA	0.02	1	3 days
Pelvis	0.7	35	4 months
Abdomen	1	50	6 months
CT Chest	8	400	3.6 years
CT Abdomen or Pelvis	10-20	500	4.5 years

Typical Background Radiation - 3 mSv per year

Benefits of CT

- A diagnosis determined by CT scanning may eliminate the need for exploratory surgery and surgical biopsy
- CT scanning is painless, noninvasive, reliable, and accurate
- Images bone, soft tissue and blood vessels at the same time
- More accurate than conventional x-rays
- In emergency cases, can reveal internal injuries and bleeding quickly enough to help save lives

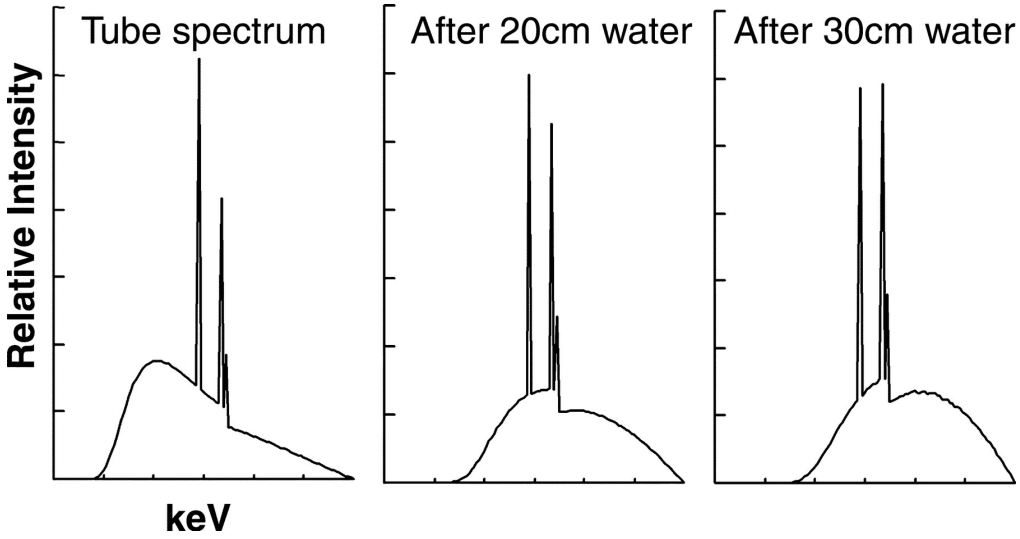
CT Artifacts

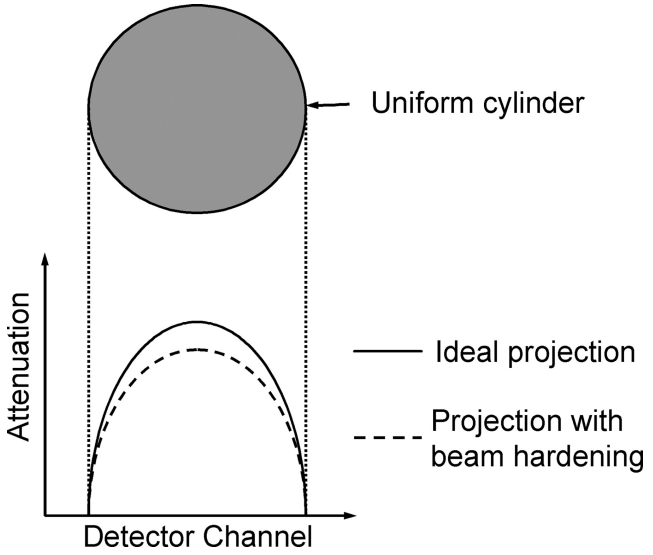
Types of CT Artifacts

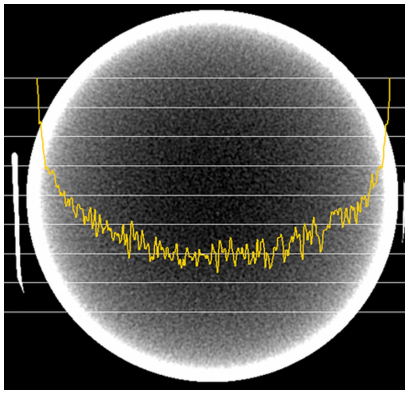
- Physics based
  - beam-hardening
  - partial volume effects
  - photon starvation
  - scatter
  - undersampling
- Scanner based
  - center-of-rotation
  - tube spitting
  - helical interpolation
  - cone-beam reconstruction
- Patient based
  - metallic or dense implants
  - motion
  - truncation

Beam Hardening

- Energy spectrum of an x-ray beam as it passes through water (rescaled)
- Mean energy increases with depth
- More photons get through, so measured attenuation is less than we would expect



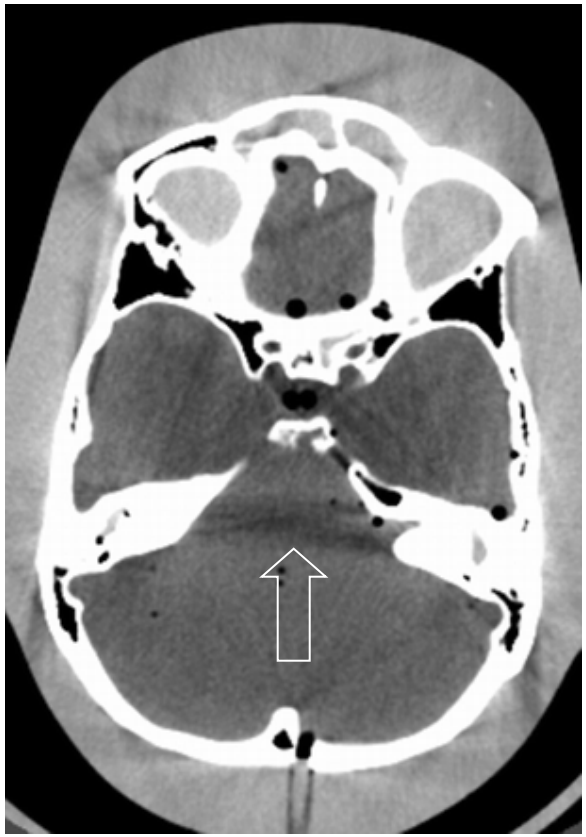




CT *image* profiles across the centre of a uniform water phantom without beam hardening correction

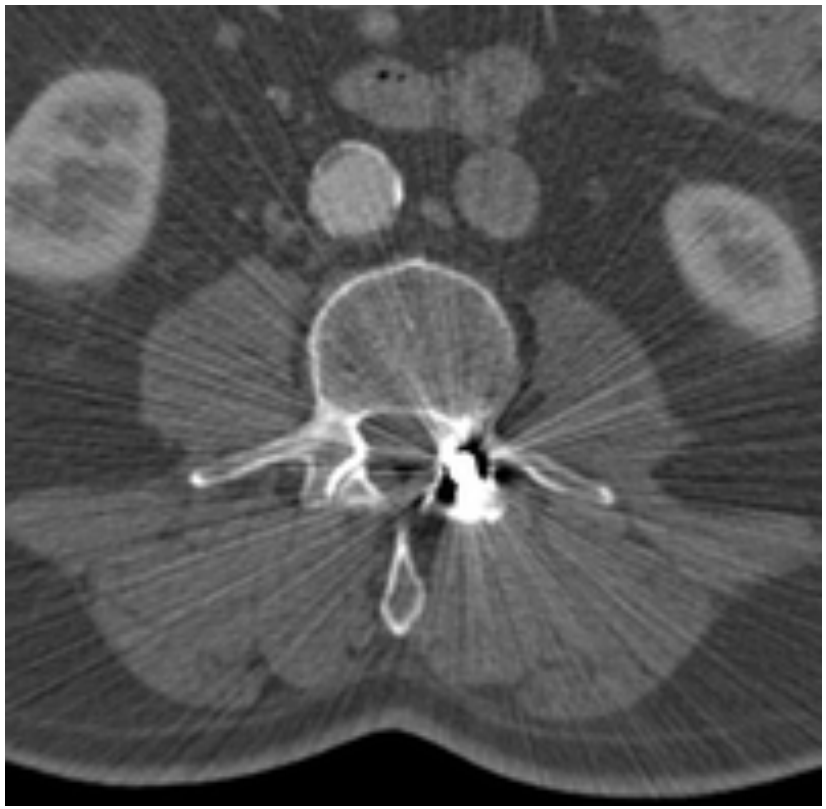
Beam Hardening

- If there are significant contrast changes, beam-hardening can be difficult to correct



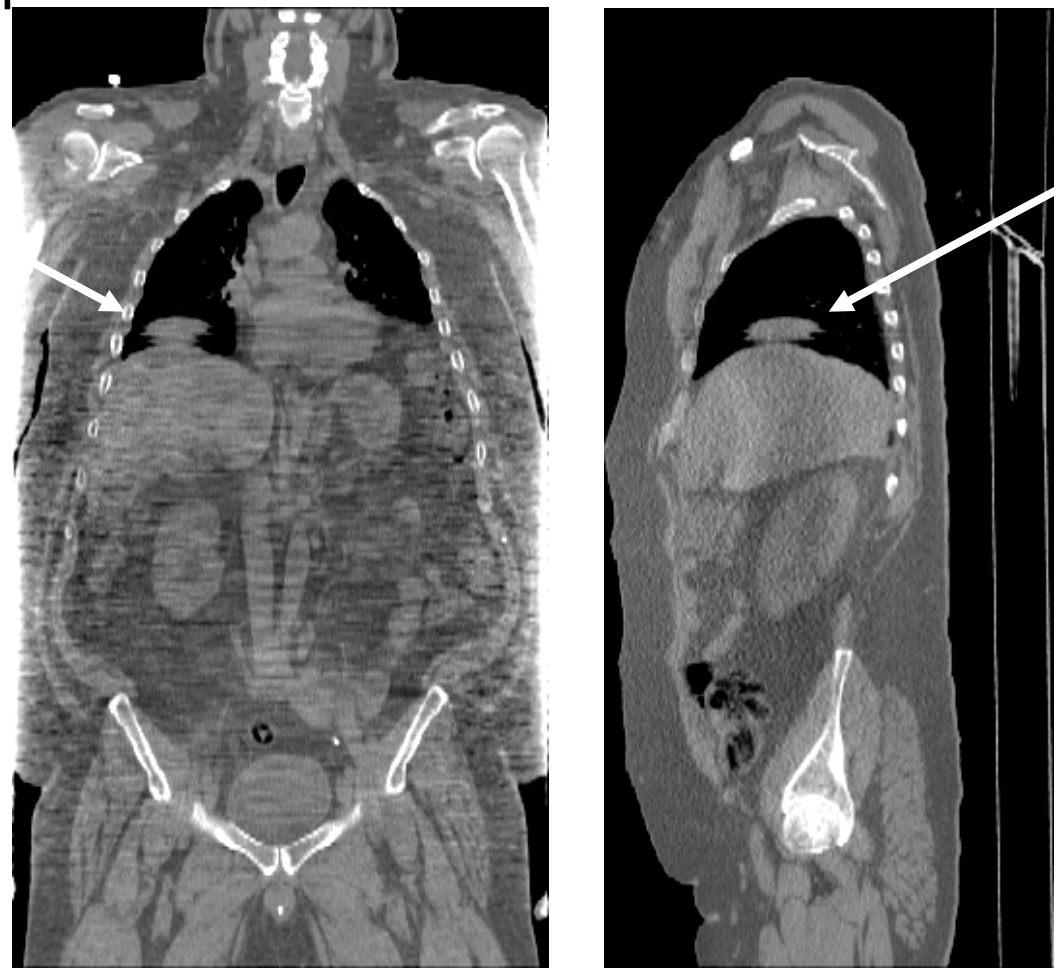
Metallic Objects

- Occur because the density of the metal is beyond the normal range that can be handled
- Additional artifacts from beam hardening, partial volume, and aliasing are likely to compound the problem



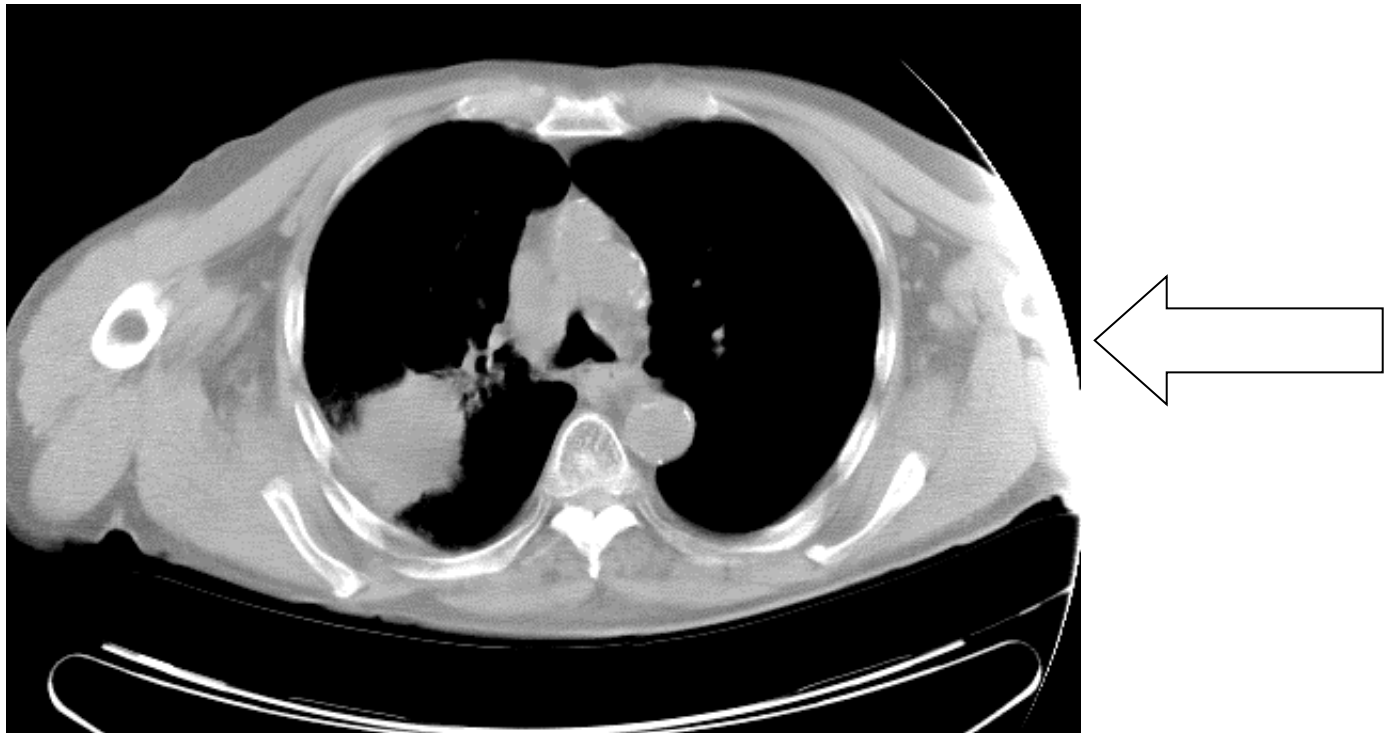
Patient Motion

- Respiratory motion effects during helical CT scans lead to well known artifacts at the dome of the diaphragm

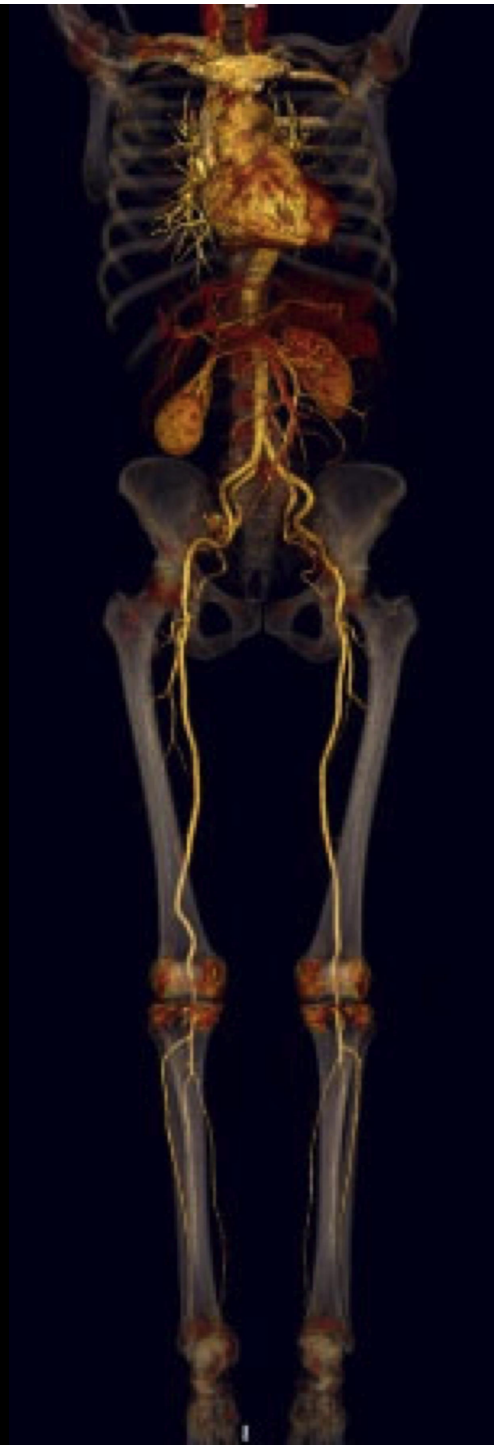


Truncation

- Standard CT field of view is 50 cm, but many patients exceed this
- Not often a problem for CT, but can be a problem when a truncated CT is used for PET attenuation correction



Contrast agents



Contrast / Contrast Agents / Tracers

- To image inside the body we need something to provide a signal (i.e. a difference or contrast) that we can measure
- Contrast can be *intrinsic* or *extrinsic*
  - Intrinsic: Already present, e.g. tissue density differences seen with x-ray imaging
  - Extrinsic: A contrast agent put into a patient (ingested, injected, etc.) to provide a signal. Acts as a signal amplification.
- Targeted contrast agents use different mechanisms (e.g. antibodies) to attach to specific objects or processes
- Needed amount of contrast agent is a critical parameter
  - Ideally, a contrast agent does not alter anything (i.e. a *tracer*)
  - Safety and toxicity are critical parameters

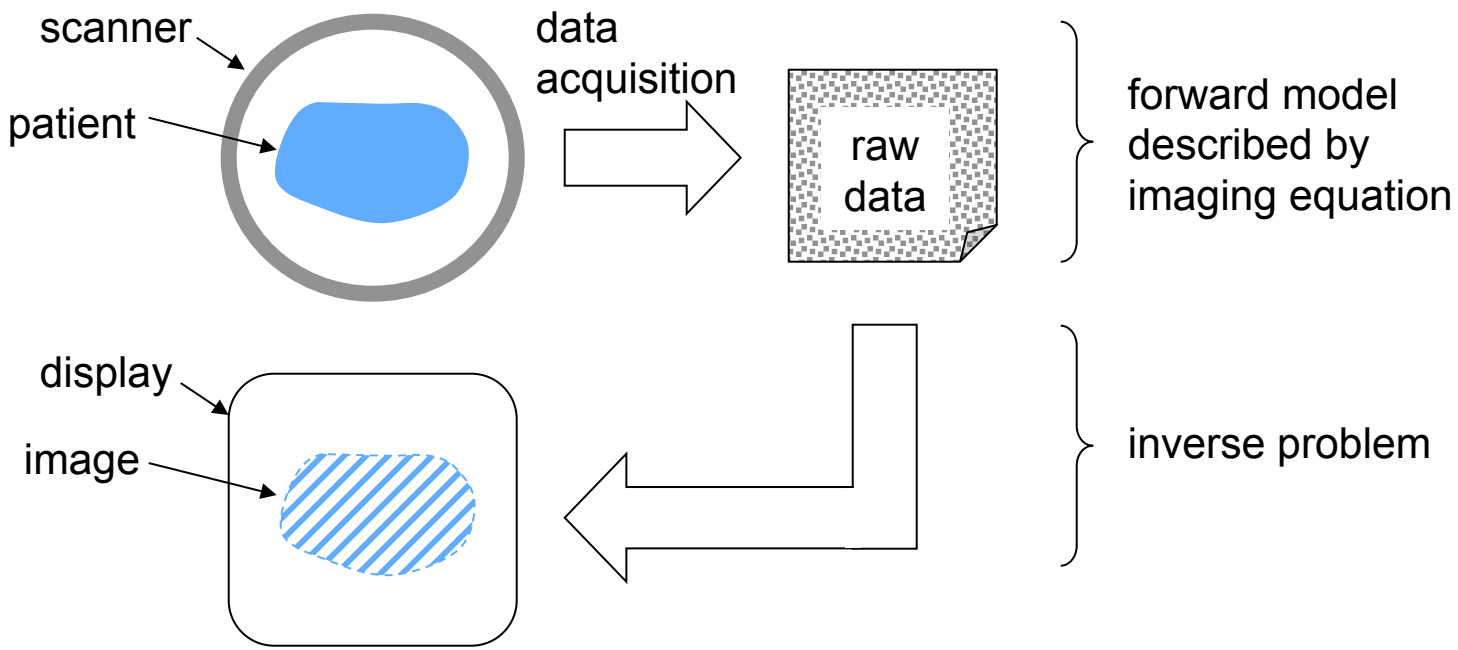
Contrast / Contrast Agents / Tracers

Modality	Intrinsic (already present)	Extrinsic (added)
Nuclear, SPECT, PET	None	Radioisotope-labeled tracers (radiotracers)
x-ray, CT	Photon absorption by Compton scattering (density) and photoelectric absorption	Iodine, barium to enhance photon absorption
Ultrasound	Vibrational wave reflectance due to tissues differences	Micro-bubbles to enhance reflectance
MRI	Radiofrequency (RF) signals generated by stimulated oscillating nuclear magnetic moments. RF signal depends on density and magnetic relaxation time differences in local microenviroment	chelated gadolinium and superparamagnetic iron oxide (SPIO) particles to alter magnetic relaxation times
Optical tomography	Changes in scattering, absorption, polarization. Also time- or frequency-dependent modulation of amplitude, phase, or frequency	microspheres, absorbing dyes, plasmon-resonant or magnetomotive nanoparticles

Intrinsic versus extrinsic contrast

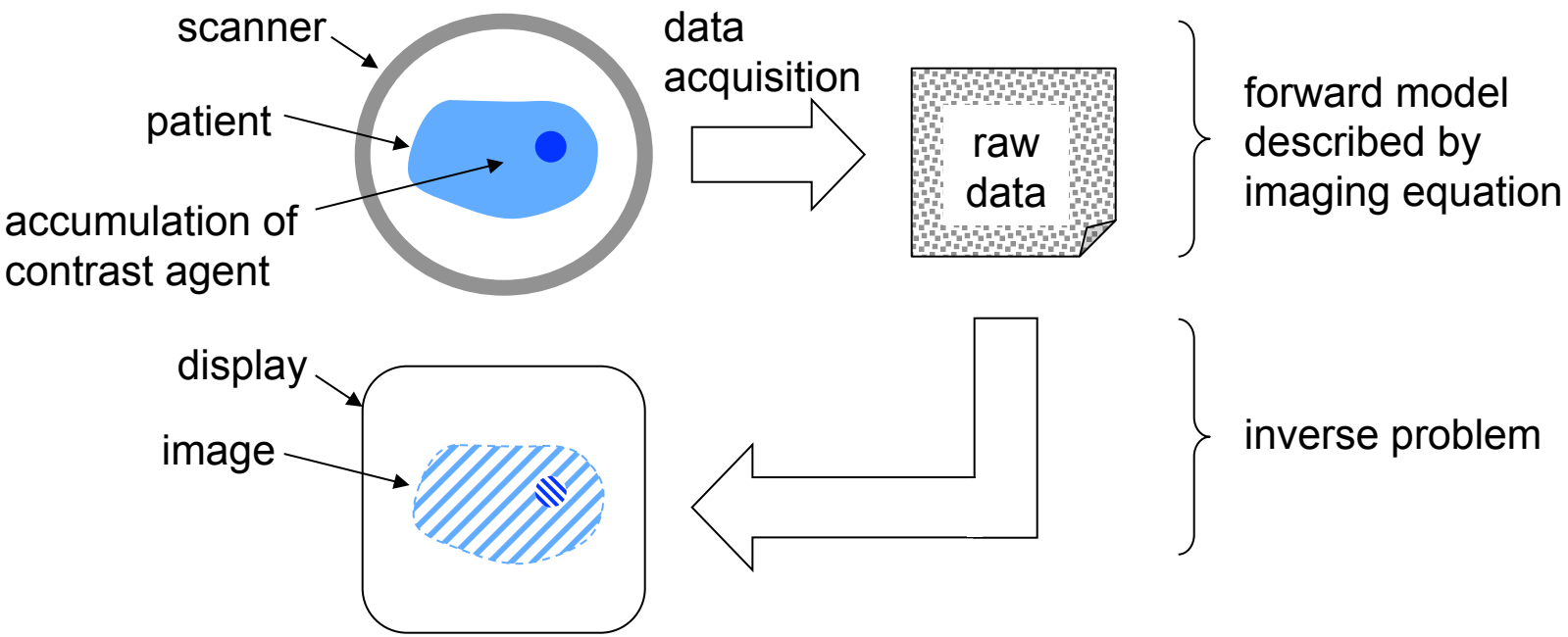
- The differential attenuation of various tissues provides an intrinsic contrast, i.e. we don't need to inject anything into the patient
- Many medical questions, however, can be answered more readily if we could 'amplify' the potential difference we are looking for
- These differences could be structural, physiological, or biochemical properties
- With x-ray imaging we can amplify some properties by enhancing attenuation by using 'contrast agents', typically iodine (injected) or barium (ingested)
- These are a form of extrinsic contrast, i.e. something that needs to be added

Biomedical Imaging Systems



- To estimate an image of property of interest, e.g. $\mu(x,y)$, from the raw data, we have to solve the inverse problem

Imaging Systems + Contrast Agents

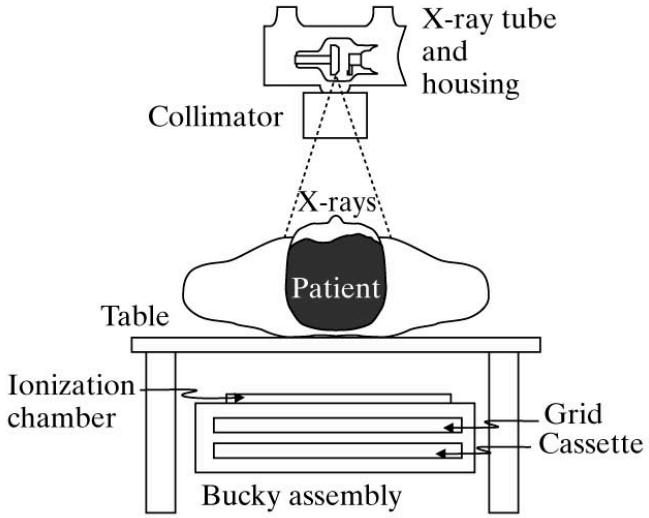


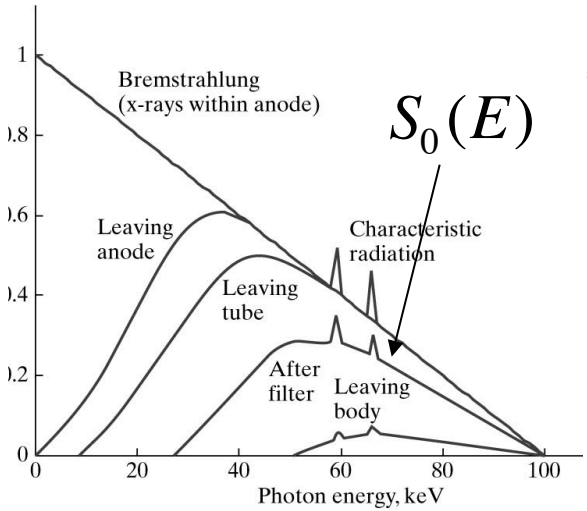
- The use of a contrast agent can amplify the signal of interest, e.g. $\mu$for iodine is much higher than μ for tissue.

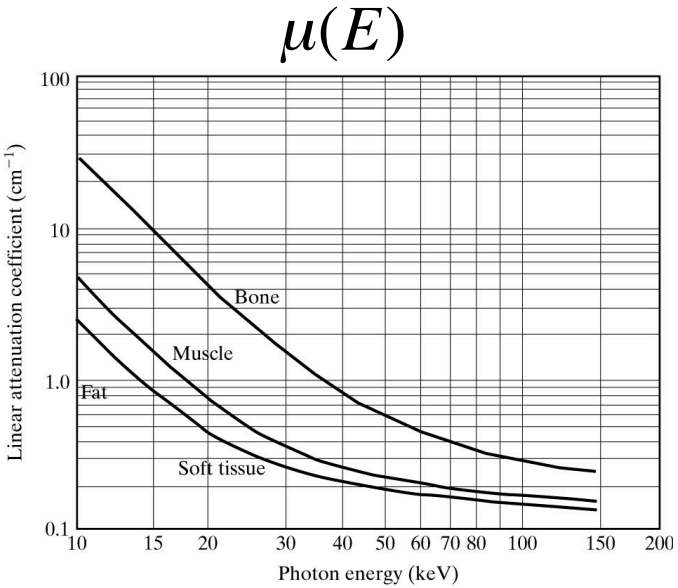
X-ray contrast agents

Interaction of X-rays in the Body

- At this point we have a beam of x-rays at different energies entering the body







- The attenuation of x-rays in the body depends on material and energy

CT Numbers or Hounsfield Units

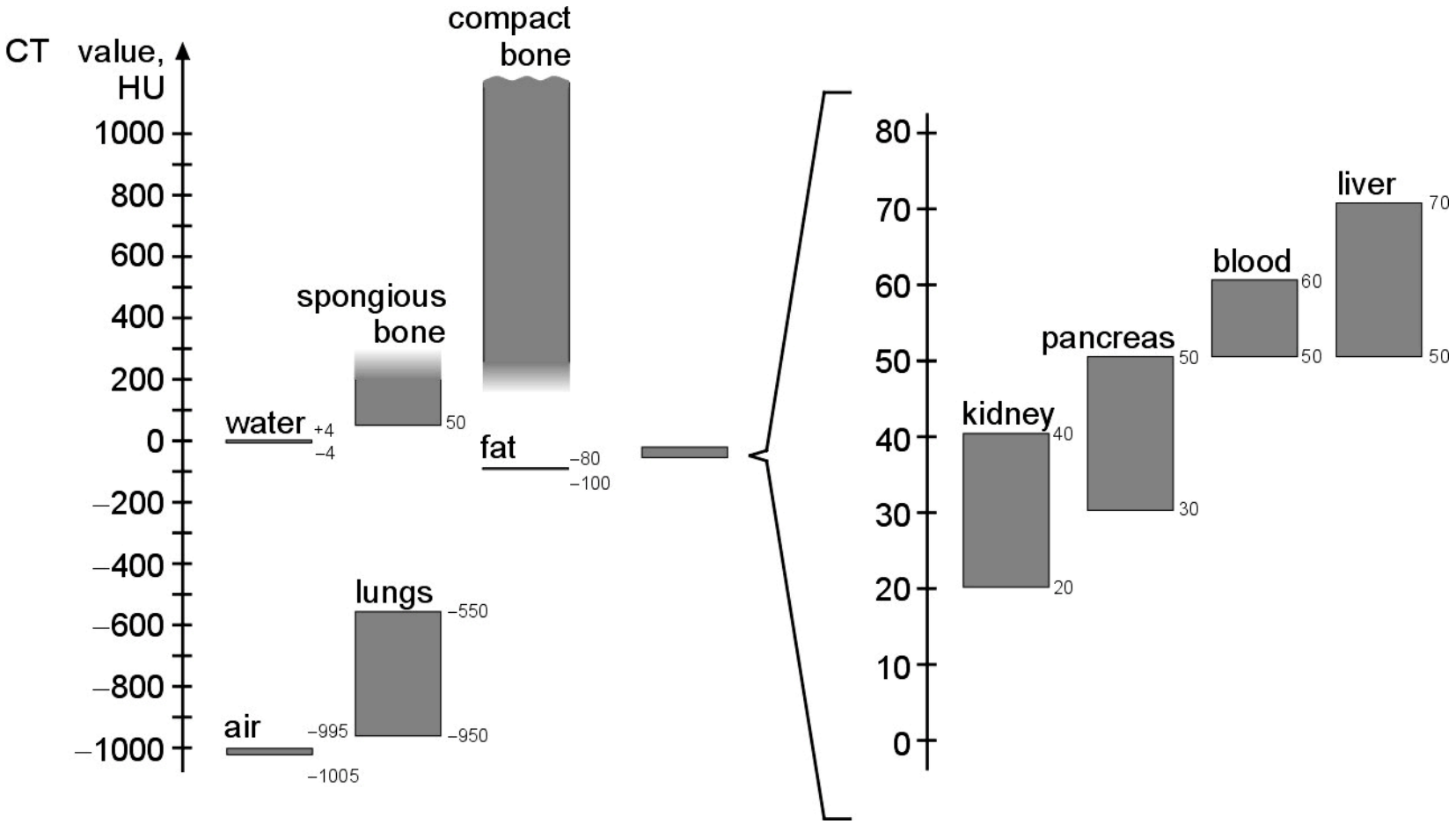
- We can't solve the real inverse problem since we have a mix of densities of materials, each with different Compton and photoelectric attenuation factors at different energies, and a weighted energy spectrum
- The best we can do is to use an *ad hoc* image scaling
- The CT number for each pixel, (x,y) of the image is scaled to give us a fixed value for water (0) and air (-1000) according to:

$$\mathrm{CT}(x,y) = 1000\left[\frac{\mu(x,y) - \mu_{water}}{\mu_{water}}\right]$$

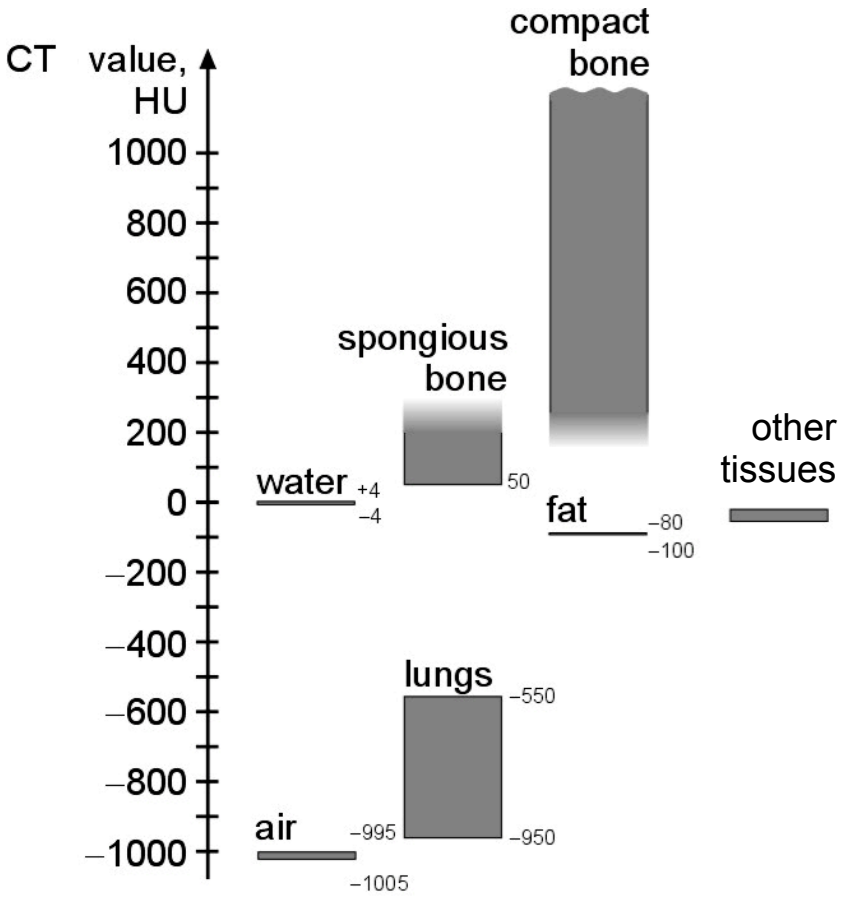
- $\mu(x, y)$ is the reconstructed attenuation coefficient for the voxel, μ_{water} is the attenuation coefficient of water and CT(x,y) is the CT number (using *Hounsfield units*) of the voxel values in the CT image

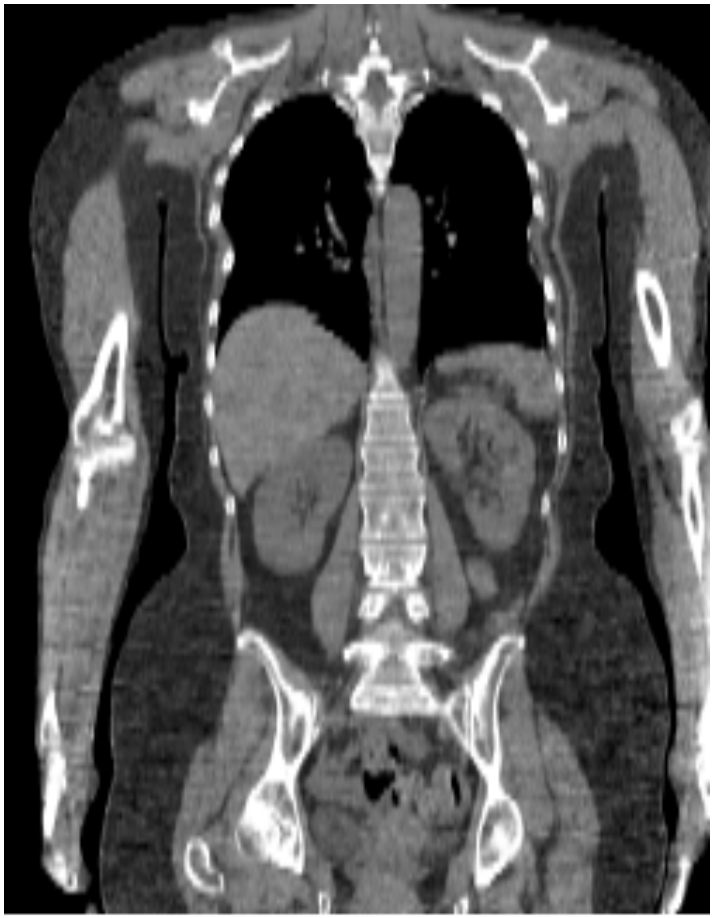
CT Numbers

- Typical values in Hounsfield Units



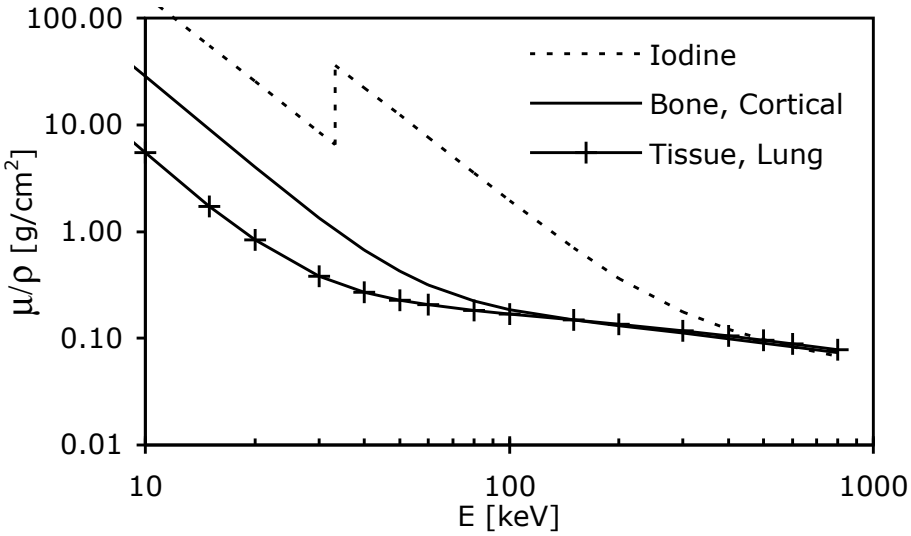
CT scan showing 'apparent' density



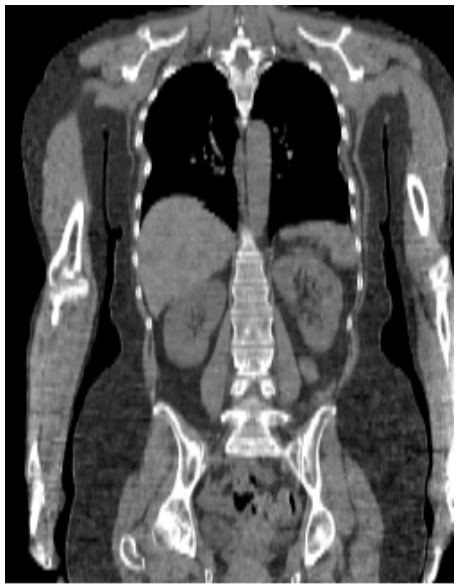


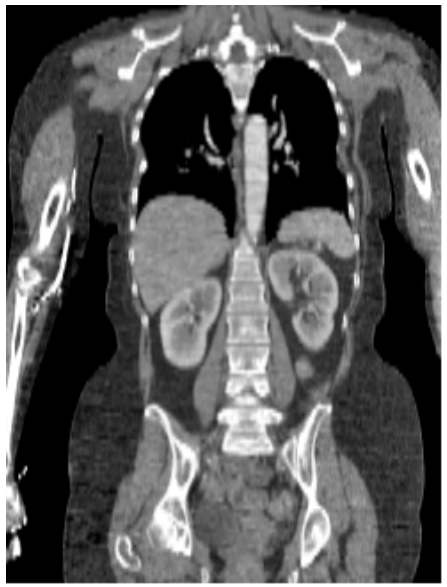
Contrast Agents

- Iodine- and barium-based contrast agents (very high Z) can be used to enhance small blood vessels and to show breakdowns in the vasculature
- Enhances contrast mechanisms in CT
- Typically iodine is injected for blood flow and barium swallowed for GI, air and water are sometimes used as well



CT scan without contrast showing 'apparent' density

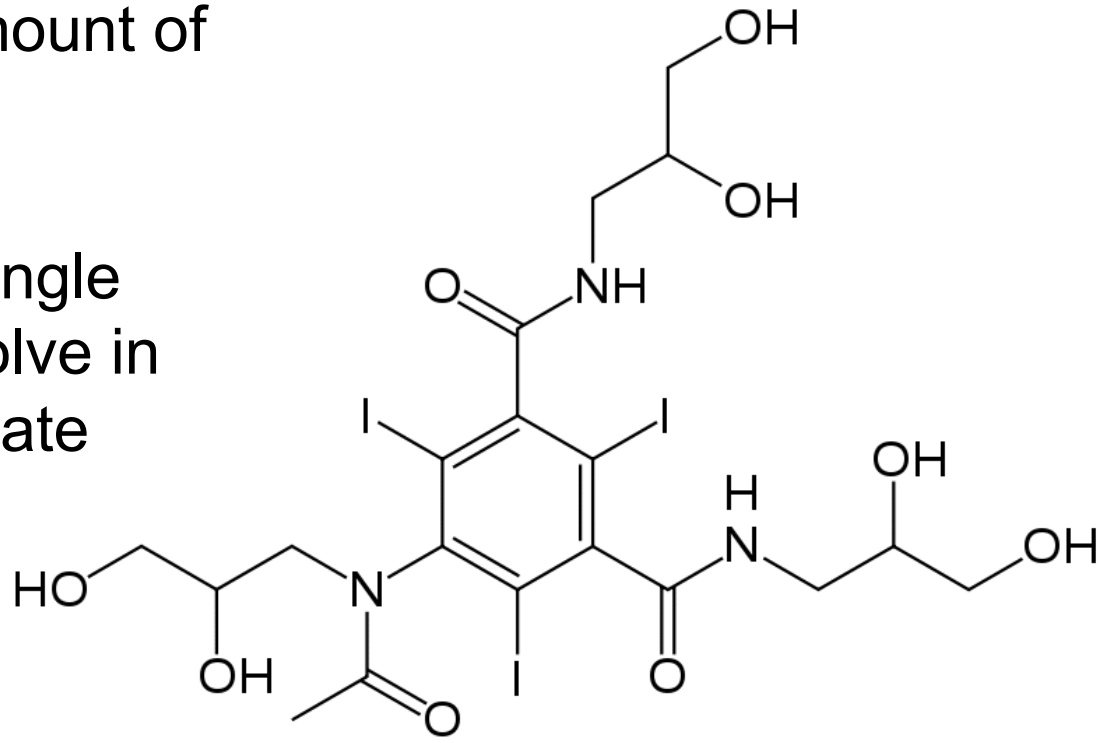




CT scan with i.v. injection iodine-based contrast agent

iohexol (Omnipaque)

- Nonionic compounds with low osmolarity and large amount of tightly bound iodine are preferred
- Many are monomers (single benzene ring) that dissolve in water but do not dissociate

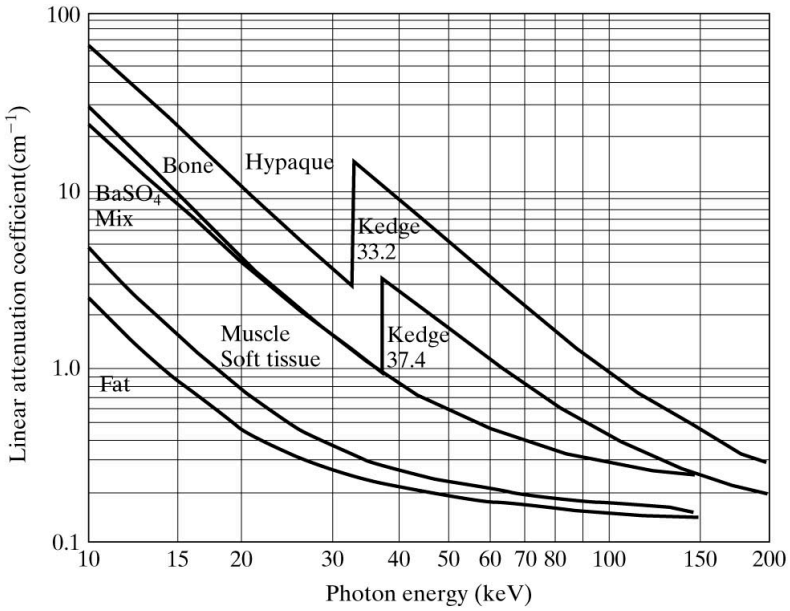


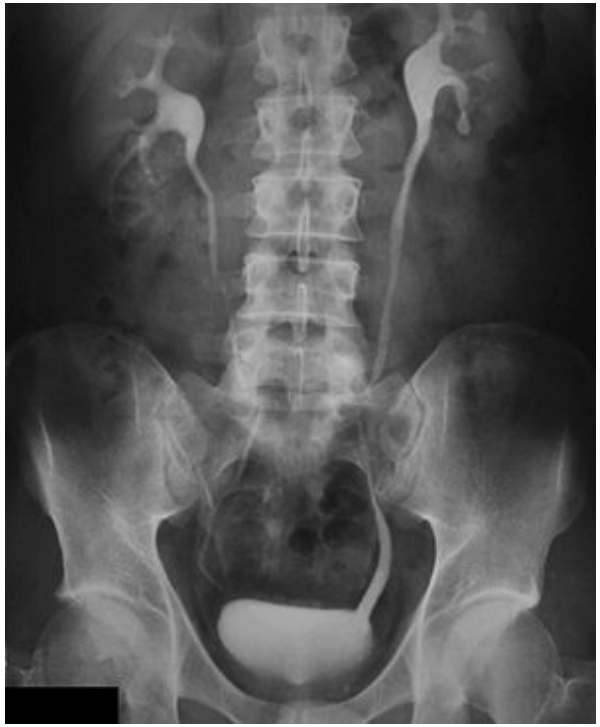
iohexol

- Being nonionic there are fewer particles in solution, thus have low osmolarity (which is good)

Contrast Agents - Iodine

- For intravenous use, iodine is always used
- There is a very small risk of serious medical complications in the kidney
- Example of an *intravenous pyelogram* used to look for damage to the urinary system, including the kidneys, ureters, and bladder





Different Iodinated contrast agents

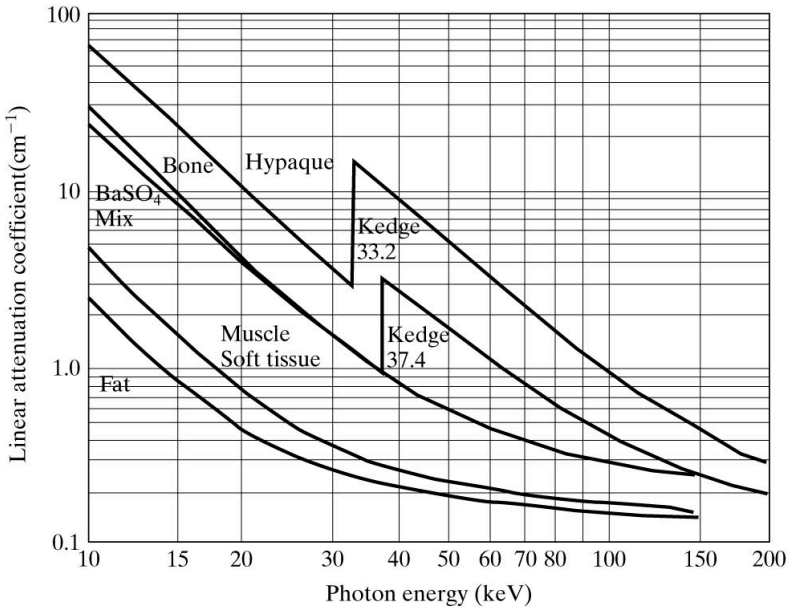
Appendix A–Contrast Media Specifications

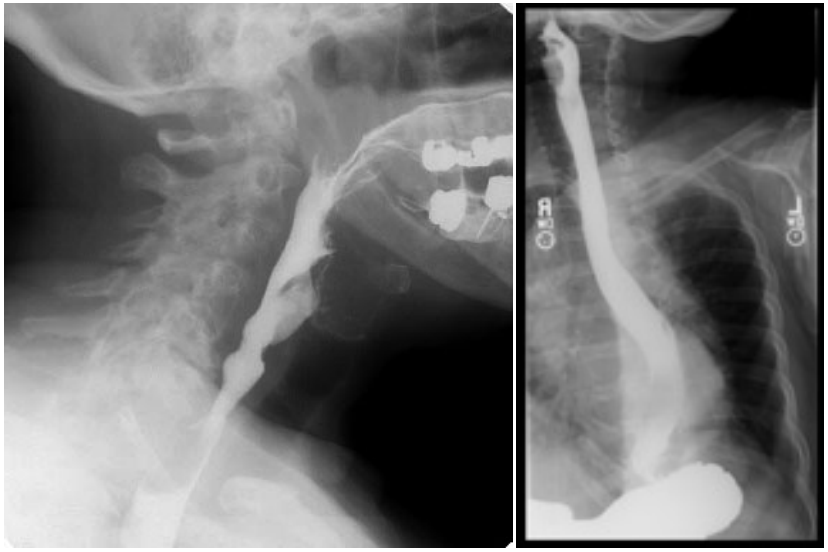
Product	Chemical Structure	Anion	Cation	% Salt Concentration	% Iodine Concentration	Iodine+ (mgI/ml)	Viscosity+ 25° C (cps)	Viscosity+ 37° C (cps)	Osmolality (mOsm/kg H_2O)
INTRAVASCULAR									
Omnipaque® 140 (GE Healthcare)	Iohexol	Nonionic	Nonionic	None	14	140	2.3*	1.5	322
Conray™ 30 (Covidien)	Ionic	Iothalamate	Meglumine	30	14.1	141	2	1.5	600
Ultravist® 150 (Bayer HealthCare)	Iopromide	Nonionic	Nonionic	<0.1	15	150	2.3*	1.5	328
Optiray™ 160 (Covidien)	Ioversol 34%	Nonionic	Nonionic	None	16	160	2.7	1.9	355
Isovue®-200 (Bracco)	Iopamidol 40.8%	Nonionic	Nonionic	None	20	200	3.3*	2.0	413
Conray™ 43 (Covidien)	Ionic	Iothalamate	Meglumine	43	20.2	202	3	2	1000

6 of about 35 currently available

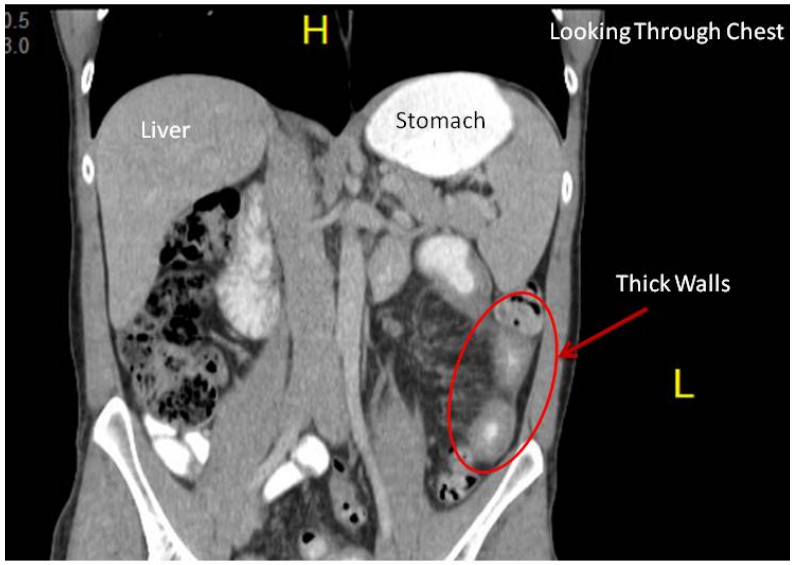
Contrast Agents - Barium

- Barium has a high Z = 56, strongly attenuating
- Pure barium is highly toxic
- As barium sulfate $BaSO_4$ it is a white crystalline solid that is odorless and insoluble in water (i.e. safe)





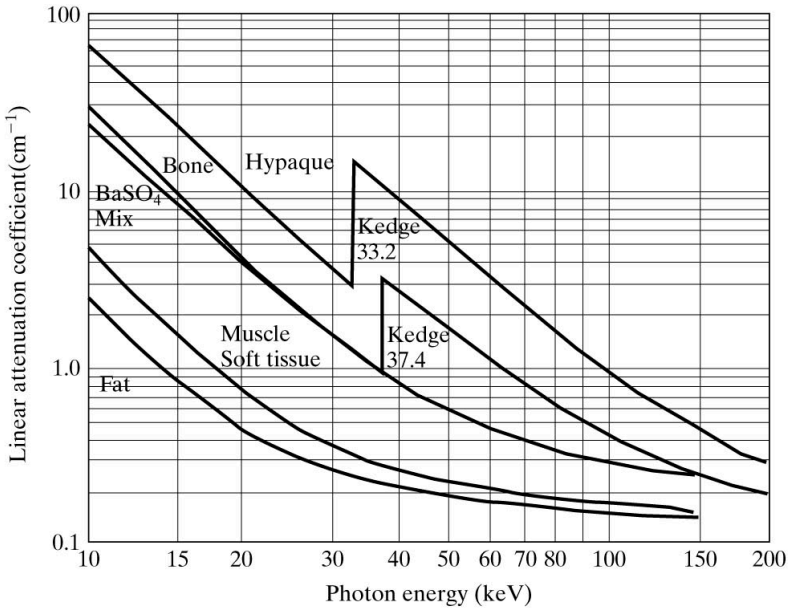
Projection images

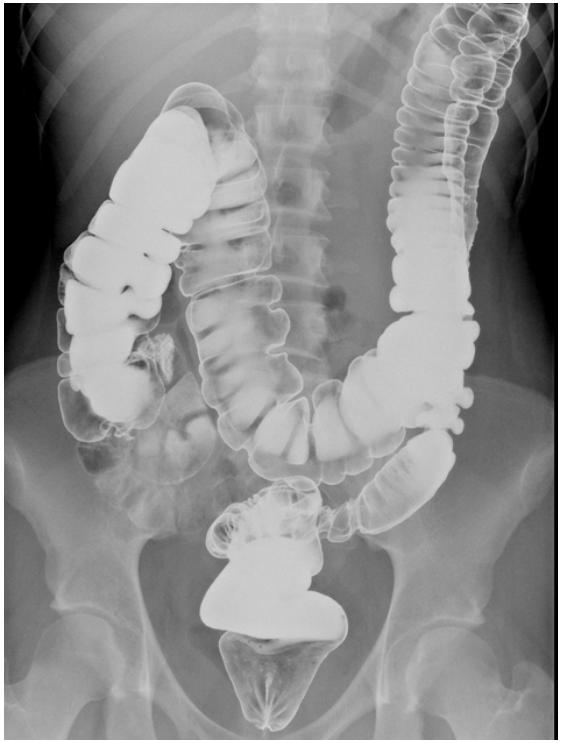


section through a 3D CT image

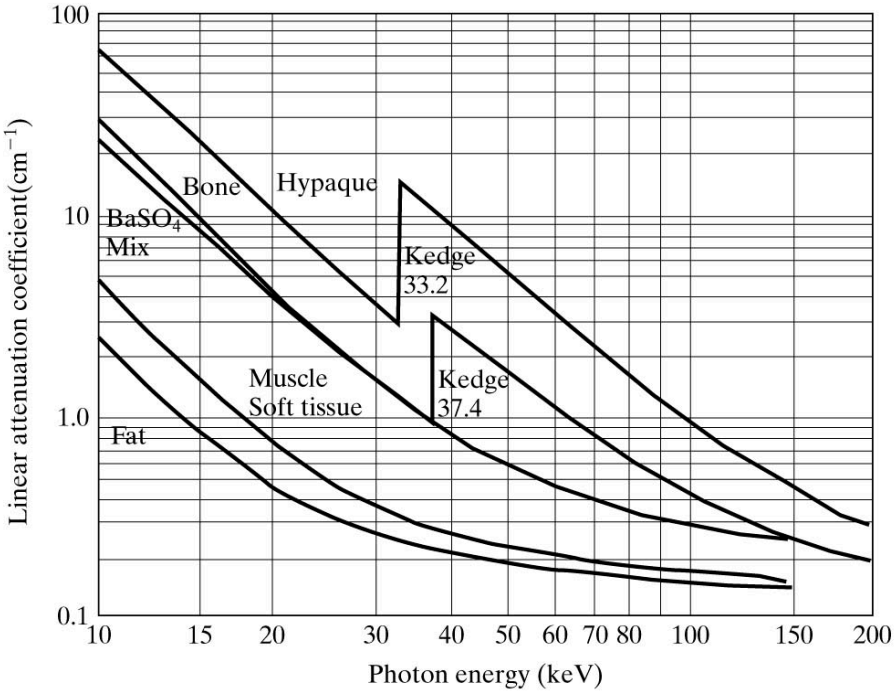
Contrast Agents - Barium

- Example of an combined use of barium and air
- The colon is clearly seen
- The white areas are barium (contrast) and the black regions are air

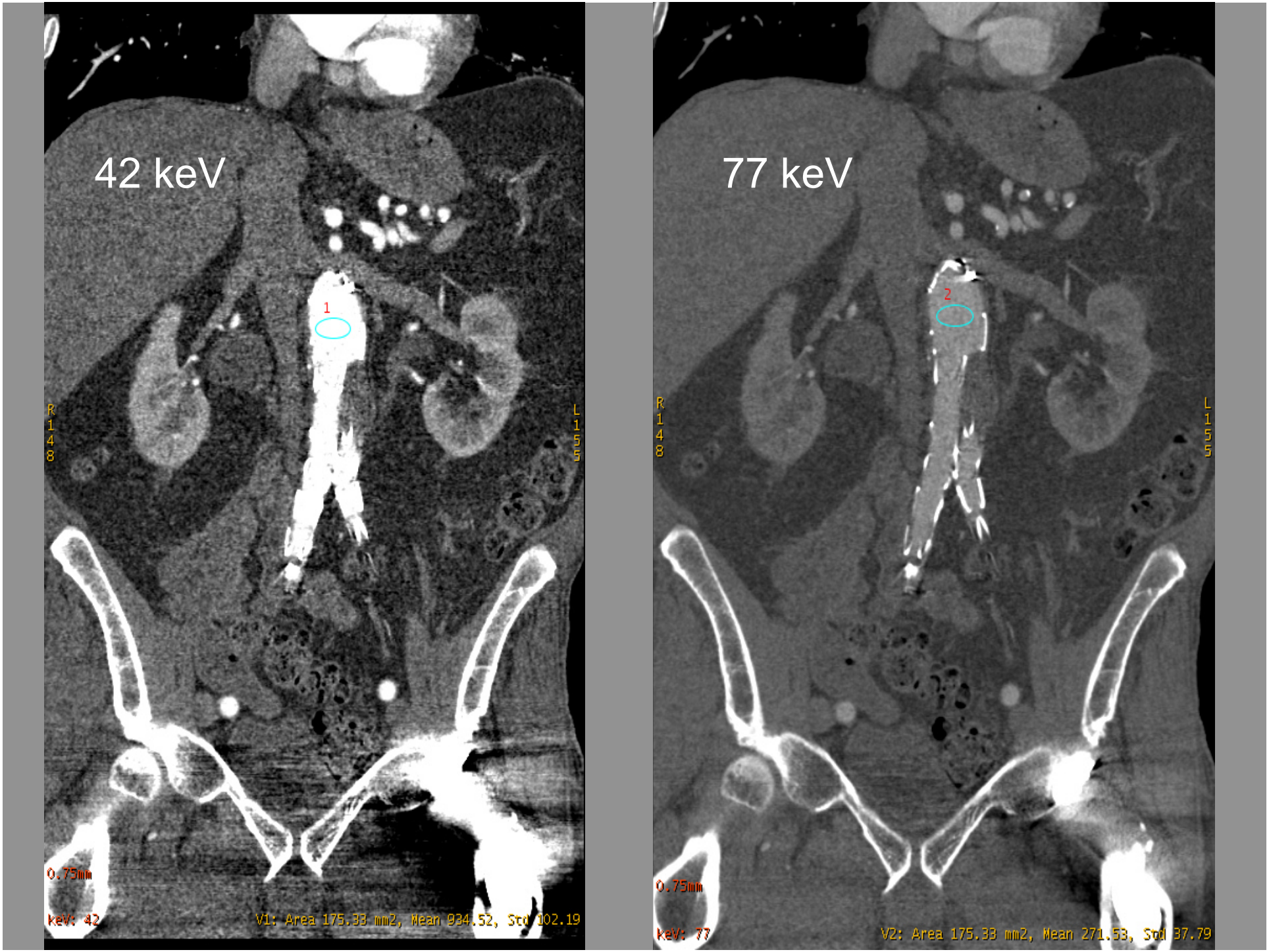




Contrast Agents - Energy dependence

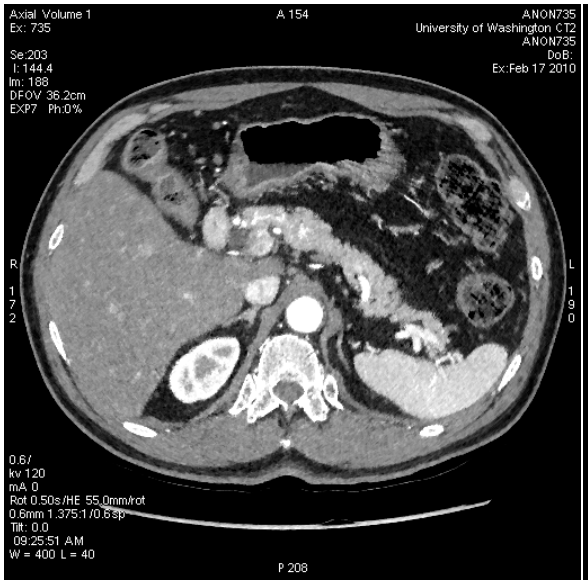


- Reducing energy of photons increases difference in attenuation between contrast agent and tissues
  - and increases difference in attenuation between different tissues
- Reducing energy of photons also increases noise, since fewer photons are transmitted through tissue

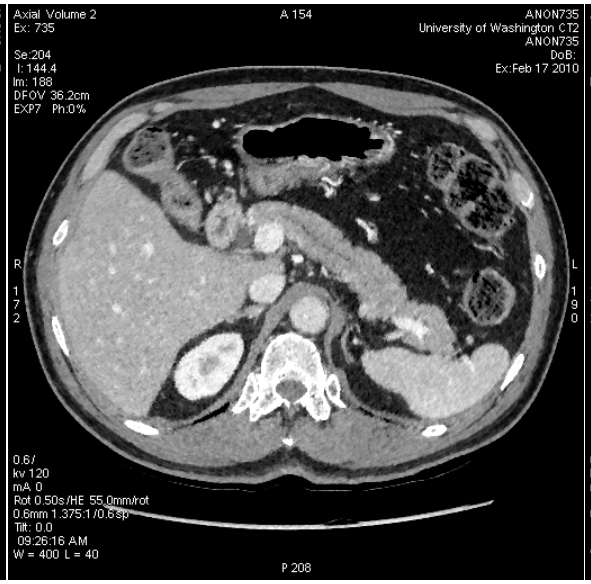

42 keV
77 keV
1
2
R 148
L 155
0.75mm
keV: 42
V1: Area 175.33 mm2, Mean 934.52, Std 102.19
keV: 77
V2: Area 175.33 mm2, Mean 271.53, Std 37.79

Dynamic contrast enhanced CT

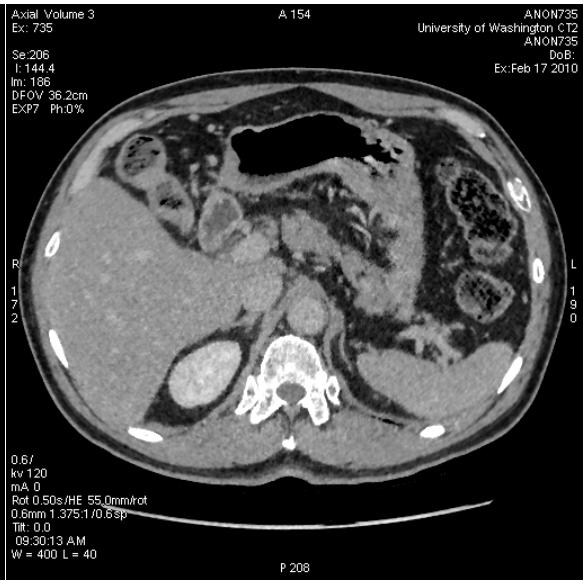
A: 'Arterial'

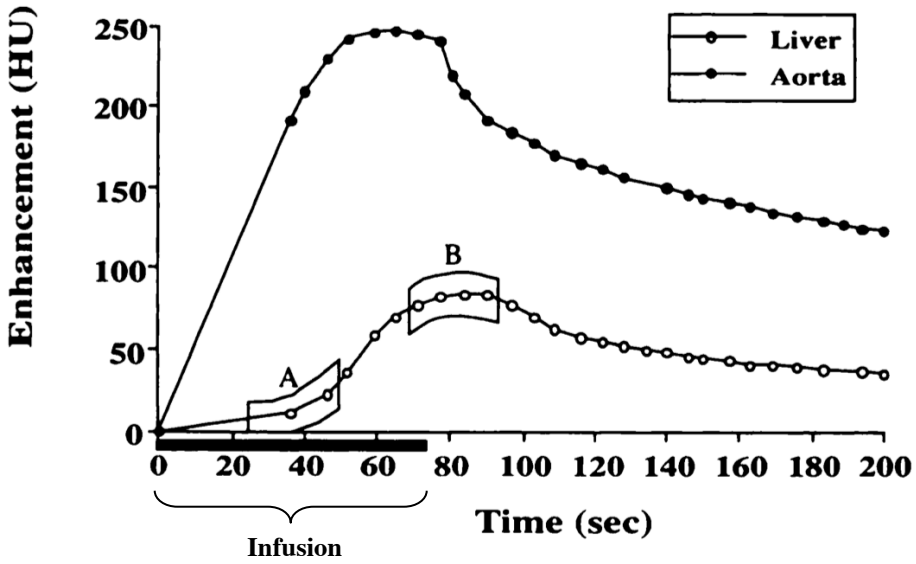


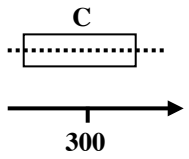
B: 'Venous'



C: 5 min delay



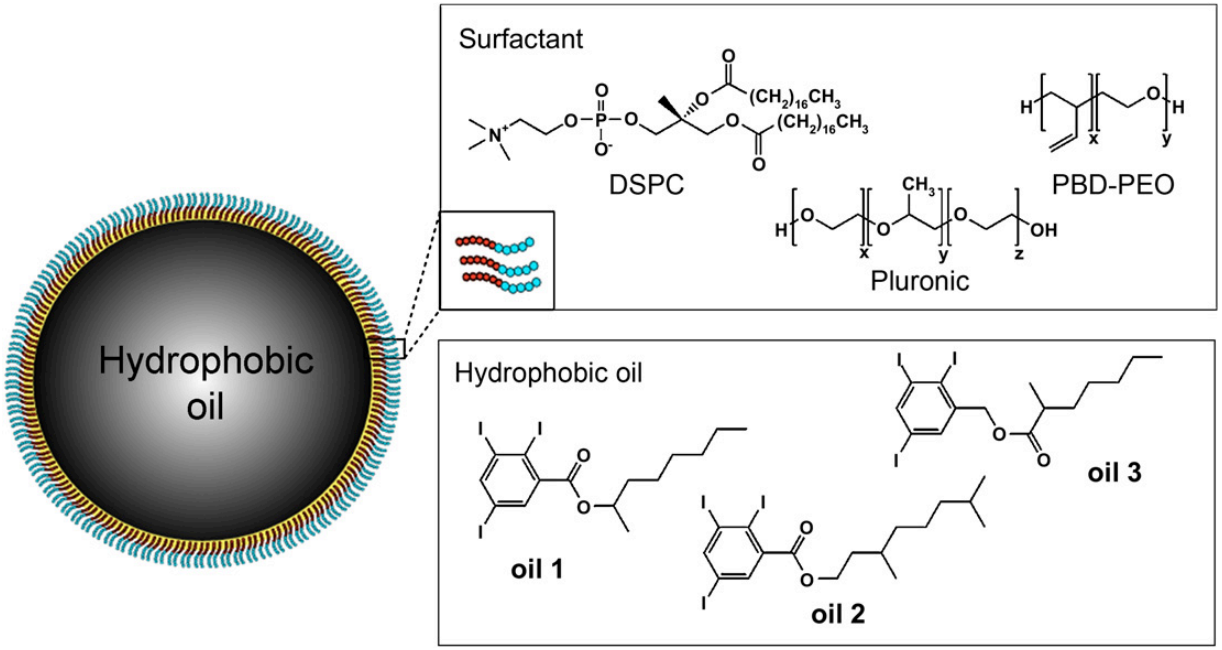


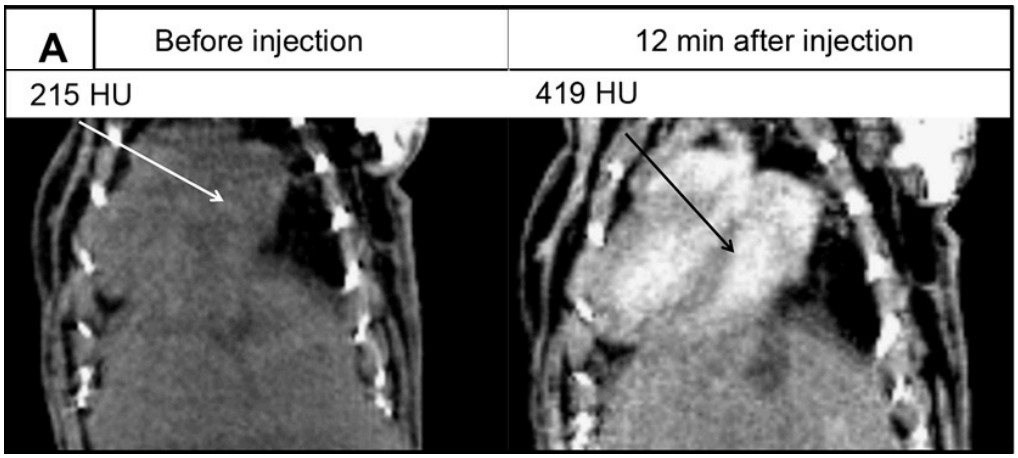


- Distribution and amount of contrast agent enhancement varies with time

Nanoparticle-based iodine contrast agent

- CT contrast agents with a high iodine 'payload' avoid injection of a large volume
- Research-only compounds so far





- Nanoparticles having sizes larger than c.a. 5.5 nm (hydrodynamic size) could prohibit rapid renal excretion