# Phys. 428, Lecture 5:

| LECTURE | DATE | INSTRUCTOR | TOPIC |
|---|---|---|---|
| 1 | March 29 | PK | Overview: Imaging equation, inverse problem |
| 2 | April 5 | PK | 2D-LSI imaging systems, X-ray physics: formation and interaction |
| 3 | April 12 | WH | X-ray detection and imaging systems |
| 4 | April 19 | WH | X-ray computed tomography (CT) systems |
| 5 | April 26 | WH | X-ray CT part 2. Contrast Agents |
| 6 | May 3 | PK | Image reconstruction and image quality |
| 7 | May 10 | PK | Nuclear decay schemes and isotopes |
| 8 | May 17 | PK | Gamma cameras: components and systems |
| 9 | May 24 | PK | Tomography in molecular imaging: SPECT scanners |
| 10 | May 31 | PK | Positron emission tomography (PET) and hybrid PET/CT scanners |

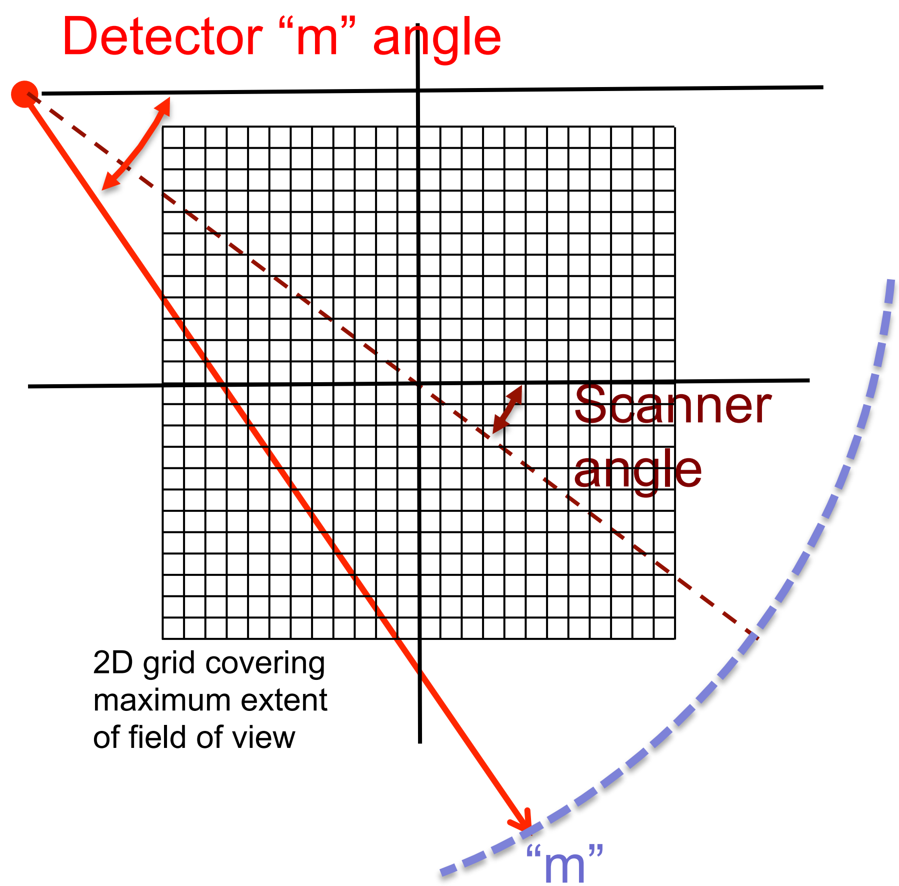
- Plans for the mid-term and final exam will be communicated later this week.
- Your assignment will be emailed this evening. It will include asking two questions about today's lecture. Please email assignments as a PDF to Dr. Kinahan (kinahan@uw.edu) by next Monday, 6:30pm.
- Please include "Phys 428 Lecture 5 Question" in the subject line.

# Clinical PET/CT Tour

- Observer approval form.
- Meet at North entrance of UW Med Cafeteria (Plaza Cafe)
- Arrive between 11:50:00 and 12:00:00. Please do not be late. I can not come and get you if you are late.
- You will be met and be brought up to the clinic by:

# Projector Algorithm assignment

- Matlab is free through UW IT to all students who use it to complete class assignments: https://itconnect.uw.edu/wares/uware/matlab/




**Example of Psueduo Code:**

For a given scanner angle, "n":

→Determine focal spot coordinate

→Determine the coordinate and projection angle of each detector element

→For each detector element, "m":

- Compute the intersection coordinate with each of the grid line (i=vertical grid-line index, and j=horizonal grid-line index) that are between the start and end coordinates (X-ray tube focal spot and detector element).

  $x_i = x_0 + (x_m-x_0)*(y_i-y_0)/(y_m-y_0)$

  $y_j = y_0 + (y_m-y_0)*(x_j-x_0)/(x_m-x_0)$

- By similar triangles, we can show

  $(y_i-y_0)/(y_m-y_0) = (x_i-x_0)/(x_m-x_0) = t$

  Where "t" is a single parameter that we can use to sort the intersection points in ordery that they occur along the line integral. Thus:

  $x=x_0 + a*t$, and $y=y_0 + b*t$

- Solve for "t" for each grid intersection point
- Order the points using "t".
- Determine cord length through each grid square intersected.
- Using your voxelized attenuation object, sum up the product of the attenuation times times the cord length through each intersected voxel. *This is our line integral of the attenuation!*

Repeat for each detector and each scanner angle

Note: this example ignores detector and focal spot width

# Discussion of Questions from Last Lecture

- What is difference between Radon transform and FBP?
  - The inverse Radon transform is in essence back projection. However, the inverser Radon transform does necessarily include filtering (but it can).
- How often are Hounsfield units used in the clinic?
  - Almost always.
- How often are Hounsfield units used in the clinic?
  - Almost always.
- Is the area where the flash of scintillator light comes from limited by the grid?
  - The grid limits scatter, not optical light. The scintillator is usually segmented.
- How is beam hardening due to metal object accounted for?
  - Beam hardening might be addressed iteratively. Get a first estimate, then model the beam hardening.
  - Artifacts (shadows and streaks) due to isolated metal objects might similarly be addressed.

# Discussion of Questions from Last Lecture

- How does CT detector material affect performance?
  - A lot of progress has been made with CT detectors. Older detectors were very inefficient at stopping photons and had lower signal to noise.
- What are beta and gamma for the helical CT acquistion?
  - They are the projection index and the detector index, respectively.
- As photons go through matter they usually lose energy by different interaction mechanisms; however, in beam hardening it is stated that ‘mean energy increases with depth’. Would you please further explain this?
  - Lower energy photons are more likely to be absorbed than higher energy ones.
- How does the computational engine ‘know’ which Hounsfield value (compact bone, water, lungs, etc) to apply to any particular voxel – doesn’t this require anatomical knowledge of the image??
  - The system response is calibrated quarterly using phantoms with know attenuation values.

# Discussion of Questions from Last Lecture

- Are all contrast agents generally toxic? Are some intrinsically ‘safer’ than others?
  - Many are toxic, but in trace amounts, they can be tolerated. Barium and Iodine are two common CT contrast agents:
    - Barium carbonate is relatively insoluble in water, it is toxic to humans because it is soluble in the gastrointestinal tract.
    - Many grams of iodine can cause acute iodine poisoning, with symptoms including burning of the mouth, throat, and stomach, fever, nausea, vomiting, diarrhea, a weak pulse, cyanosis, and coma.
  - We will talk more on contrast agents later in this lecture.

# CT Radiation Dose and Technique

# X-ray radiation dose

*From Lecture 3*

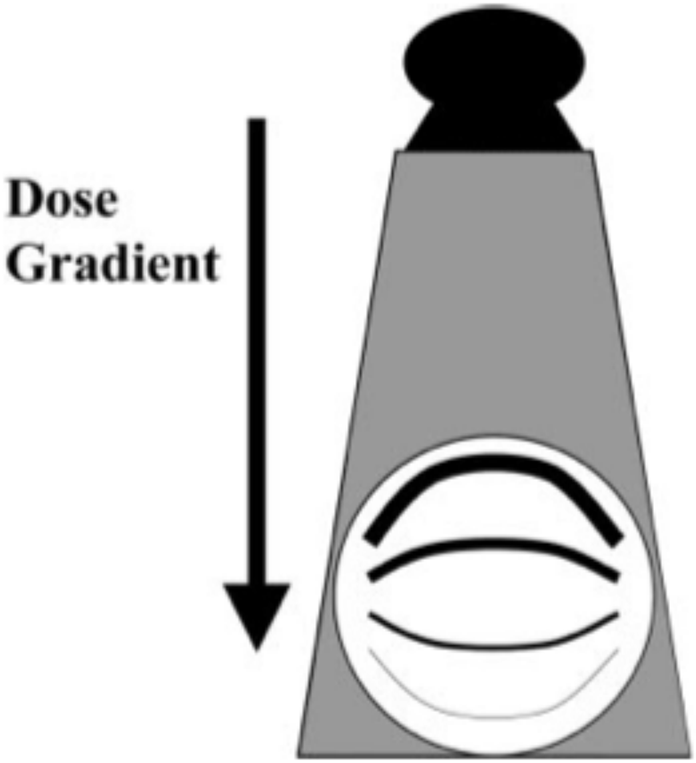
- Loss of photon energy means some is being transferred to tissue
- Basic concepts:
  - Exposure: number of ion pairs produced in a specific volume of air by radiation
    - Units are coulombs per kilogram of air (C/kg)
    - Useful in medical imaging is the roentgen (R) 2.58 × 10−4 C/kg
    - Can easily 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

$$H_T = \sum_R w_R D_{T,R}$$

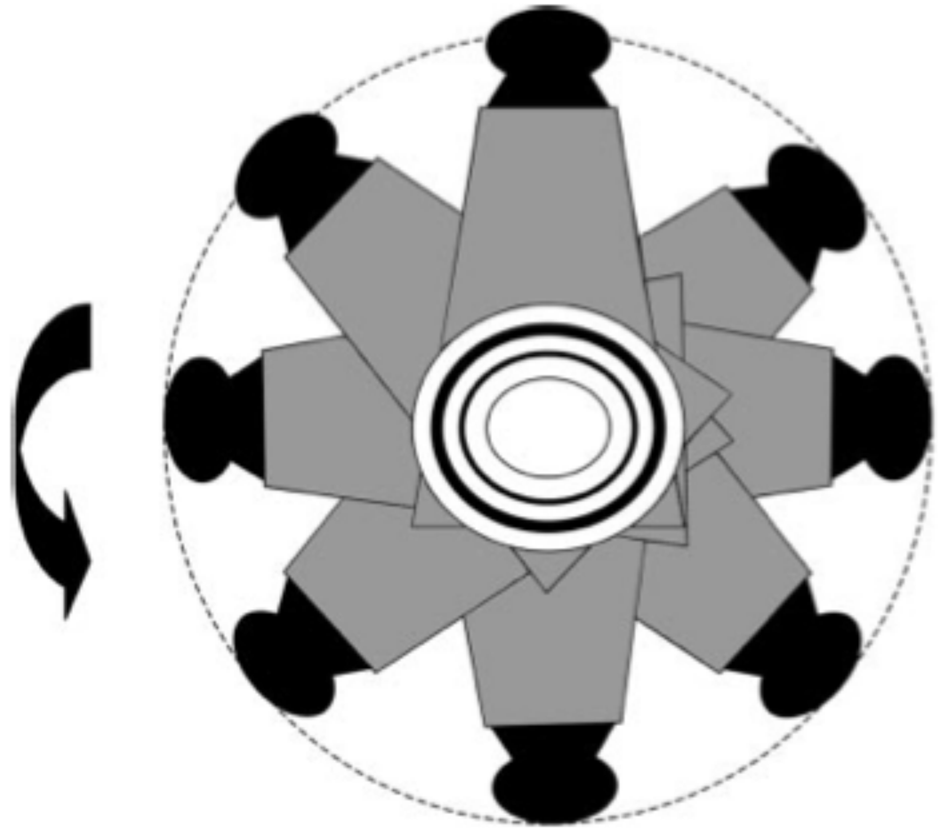
  - Effective dose: Takes into account cumulative effect over all tissues
    - meant to compare relative risks between different procedures
    - wildly inaccurate
    - Units are also J/kg, with a special unit of *sievert* (Sv)
    - 1 Gy give 1 Sv for x-rays in soft tissue

$$E = \sum_T w_T H_T$$

# X-ray radiation dose (continued)



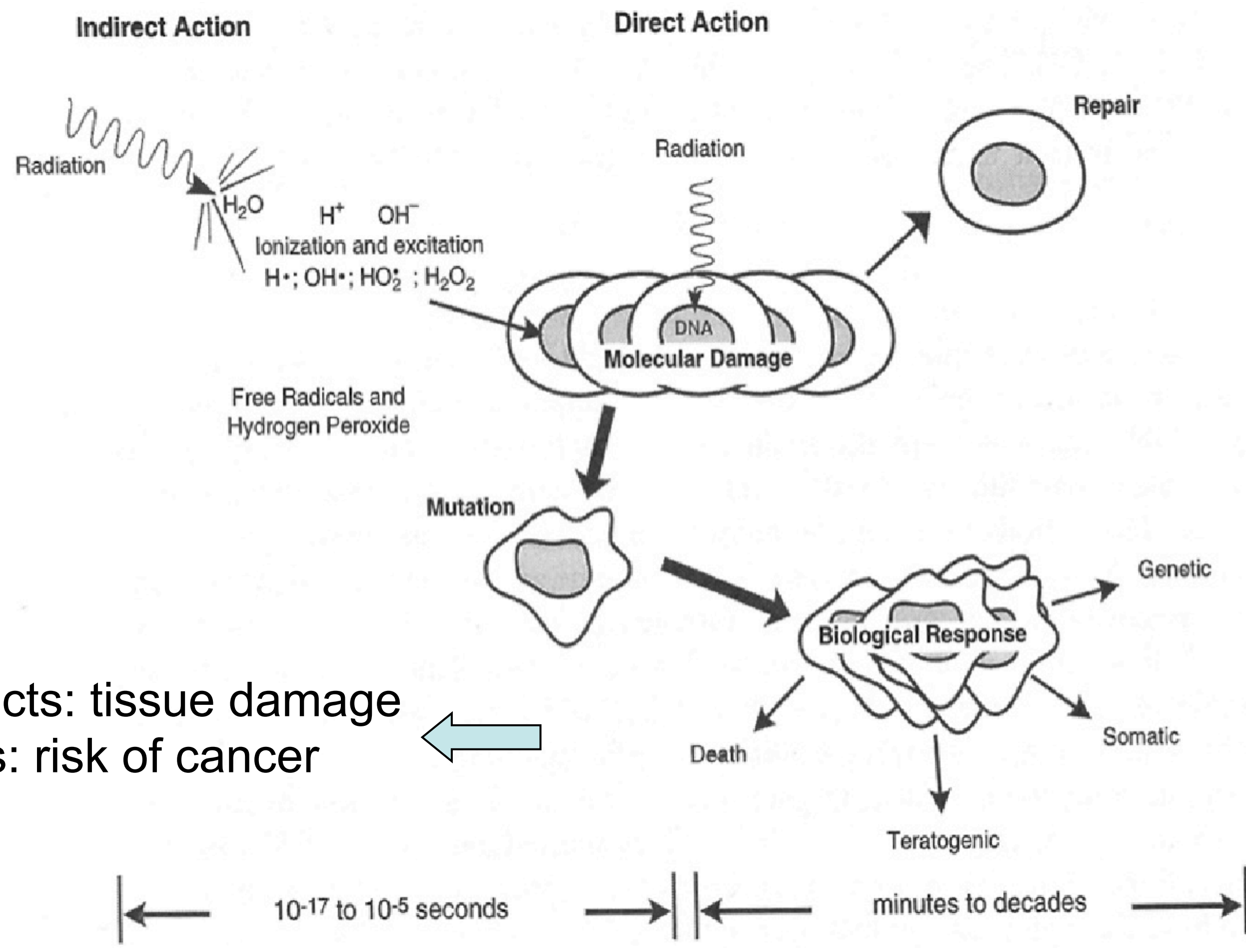

Projection Image



Computed Tomography

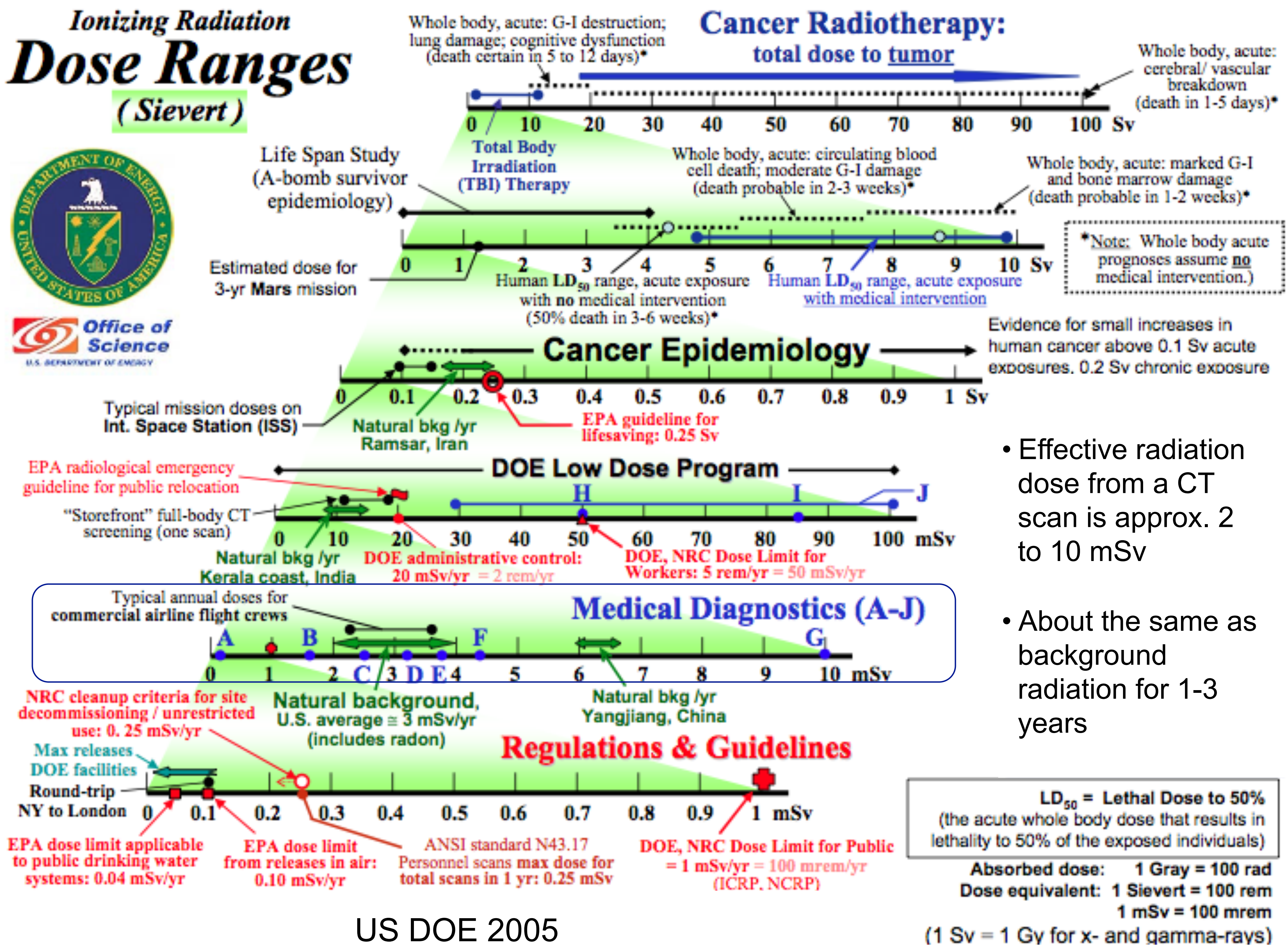
Projection: Uniform over 2D collimated region and exponentially attenuated
CT: Dose is rotationally symmetric over plane and falls off axially

# 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)

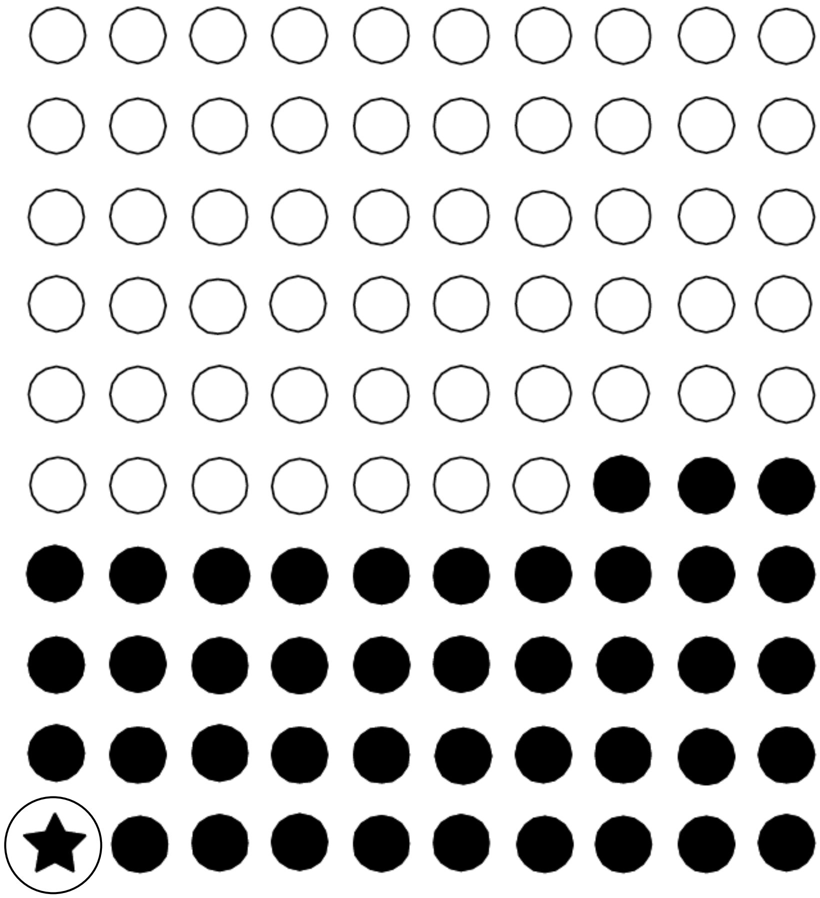
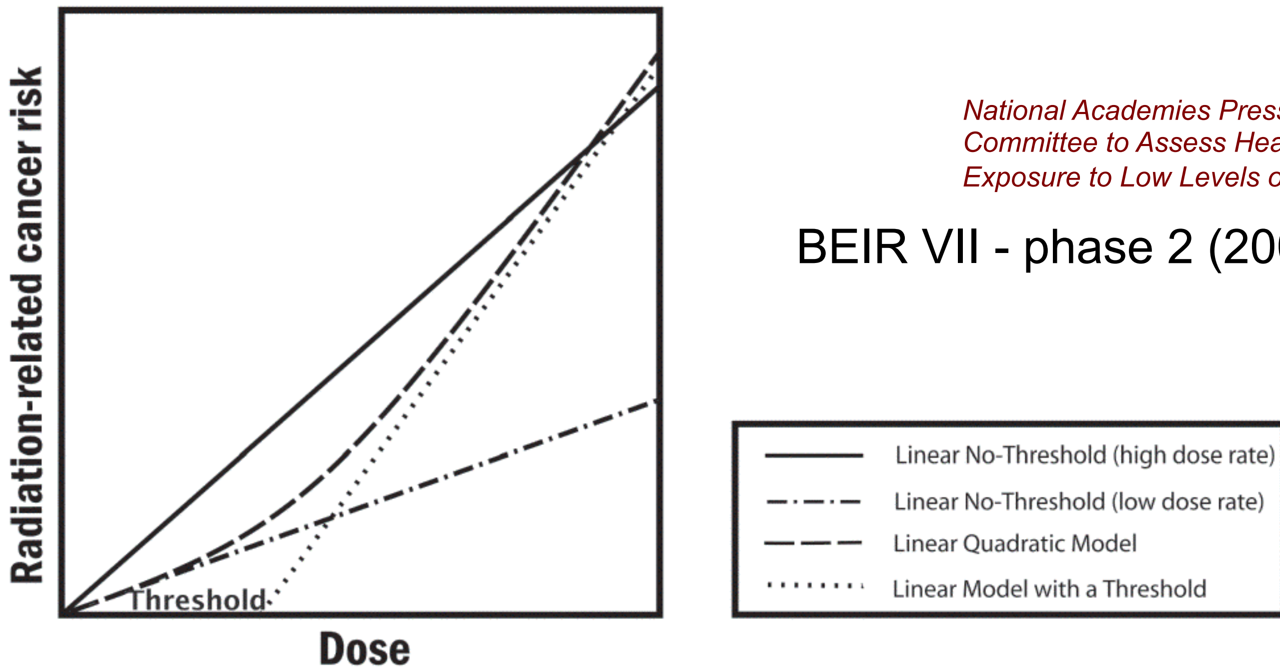


FIGURE PS-4 In a lifetime, approximately 42 (solid circles) of 100 people will be diagnosed with cancer (calculated from Table 12-4 of this report). Calculations in this report suggest that approximately one cancer (star) per 100 people could result from a single exposure to 0.1 Sv of low-LET radiation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

BEIR VII - Phase 2 (2005)

*LET = Linear Energy Transfer*
*low-LET ~ non-heavy ion*

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




*National Academies Press*
*Committee to Assess Health Risks from*
*Exposure to Low Levels of Ionizing Radiation*

BEIR VII - phase 2 (2005)

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

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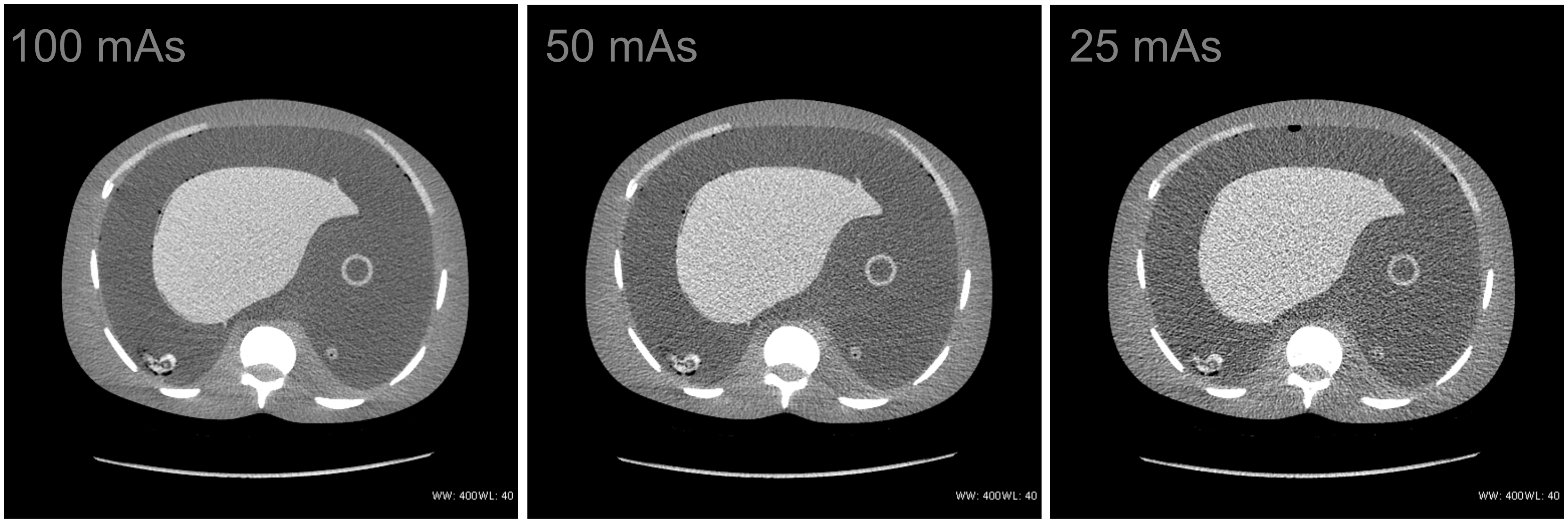
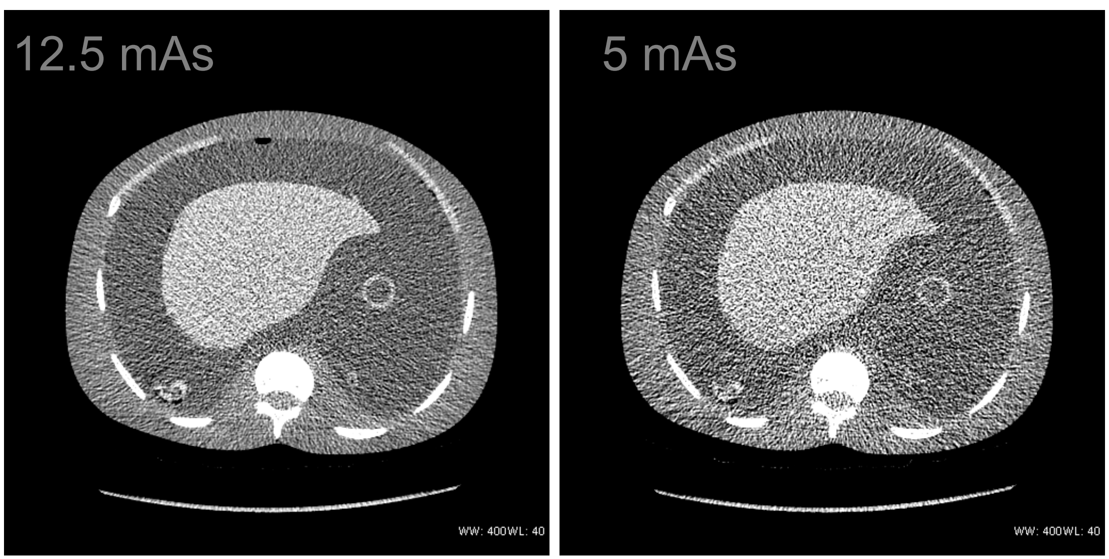
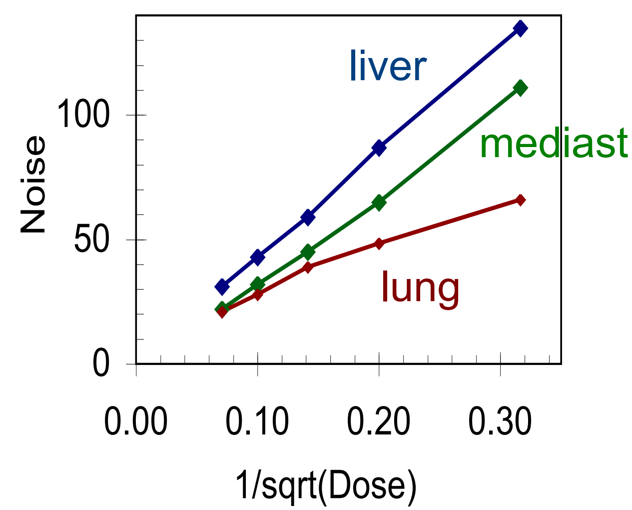
- *The American Association of Physicists in Medicine (AAPM) 2011:*

"... 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

*From Lecture 4*

- 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)

*From Lecture 4*

# 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*** |

*From Lecture 4*

## Effective Dose Comparison with Chest PA Exam

| Procedures | Eff. Dose [mSv] | Equivalent no. of chest x-rays | Approx. period of background radiation |
|---|---|---|---|
| Chest PA *(one 2D projection)* | 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

# 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 <u>contrast agent</u> 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

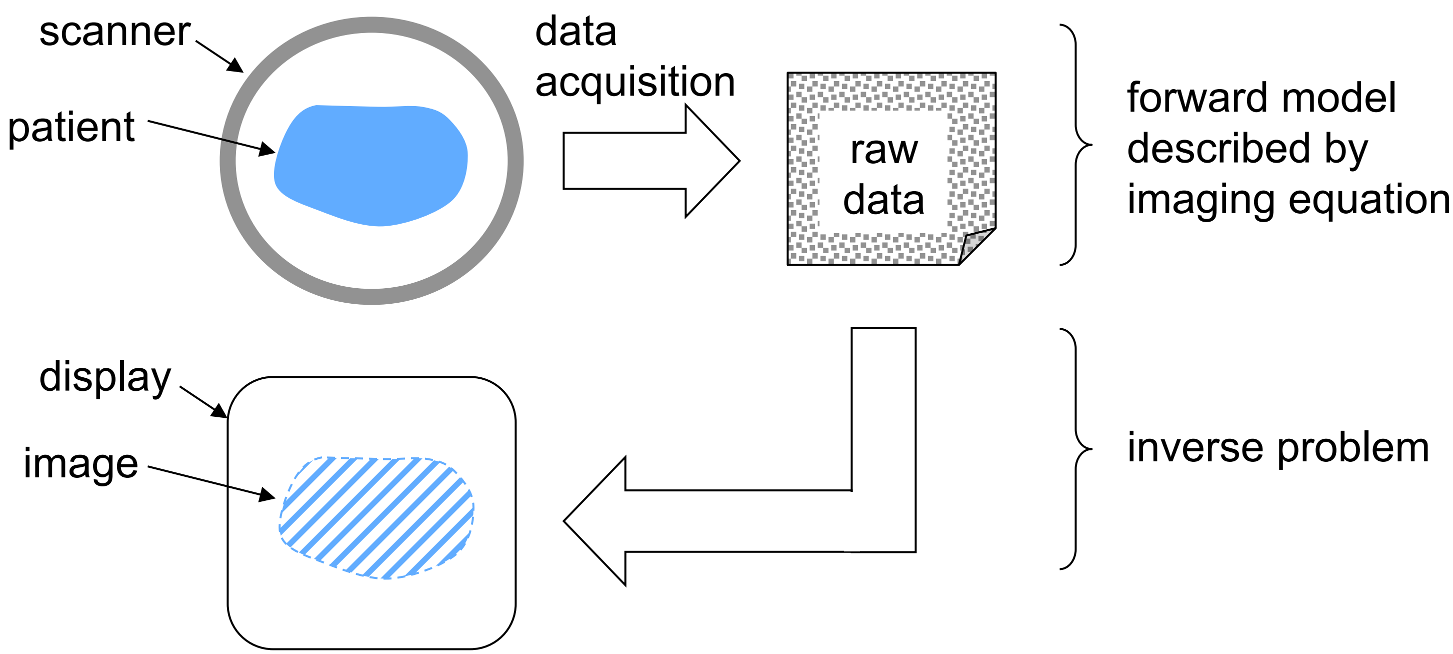
# Contrast / Contrast Agents / Tracers

| 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

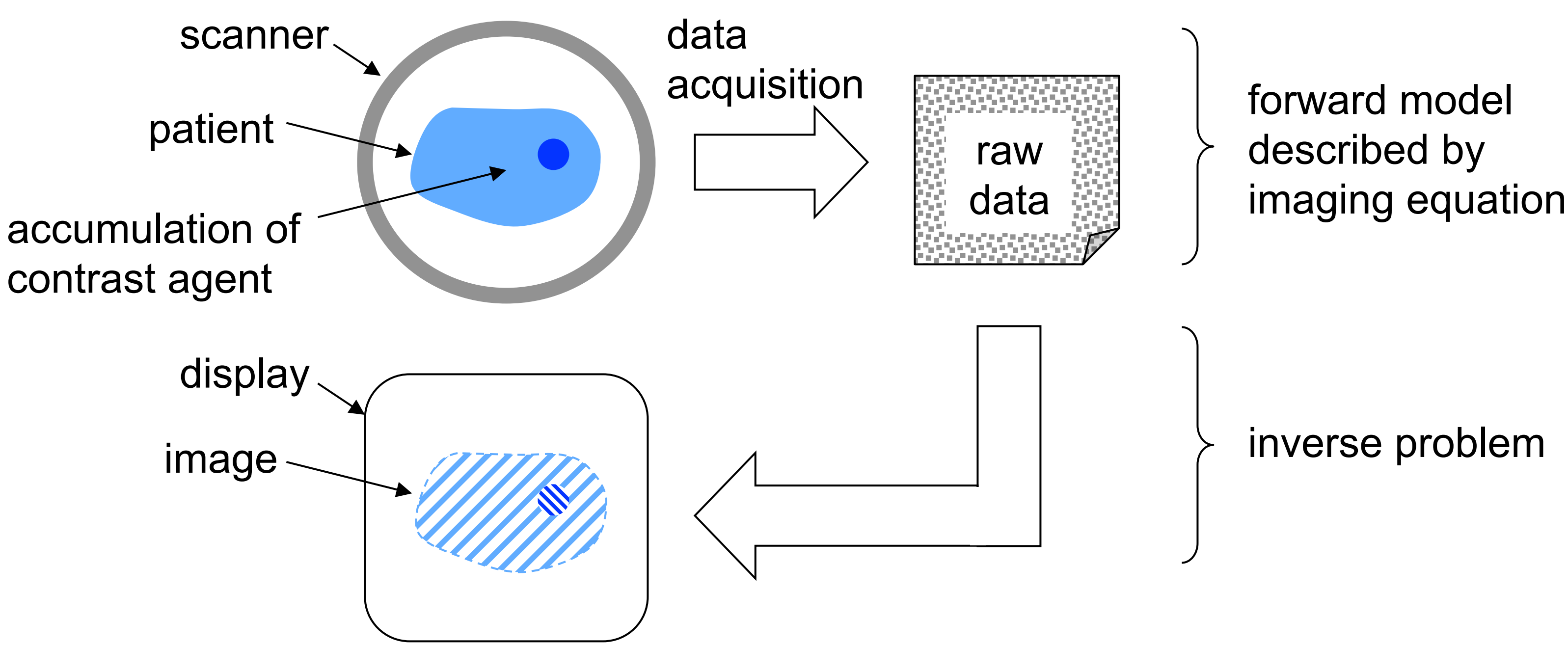
- The differential attenuation of various tissues provides an <u>intrinsic</u> contrast, i.e. we don't need to inject anything into the patient
- Many medical questions, however, can be answered more readily if we could 'amplify' the potential difference we are looking for
- These differences could be 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 <u>extrinsic</u> 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

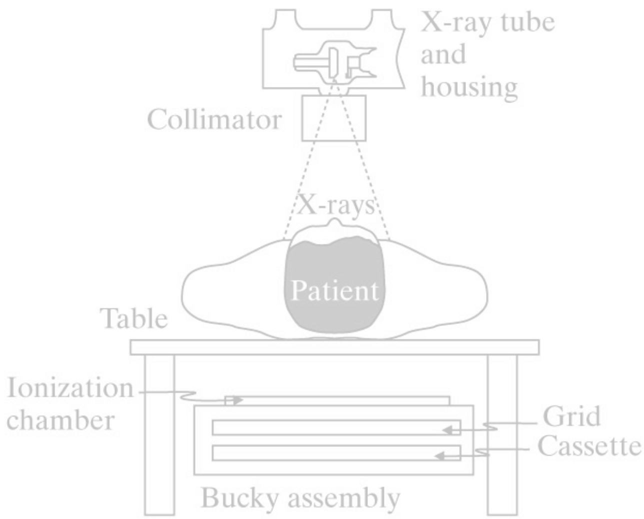
# Imaging Systems + Contrast Agents

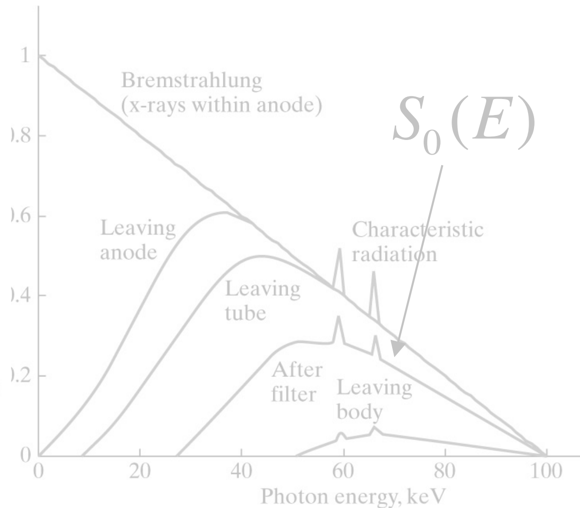


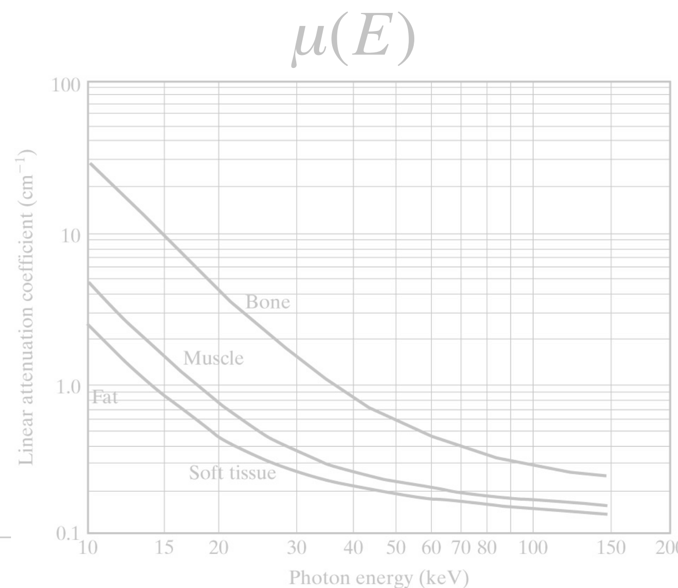

- The use of a contrast agent can amplify the signal of interest, e.g. $\mu$ for iodine is much higher than $\mu$ for tissue.

# 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

*A look back*

# CT Numbers or Hounsfield Units

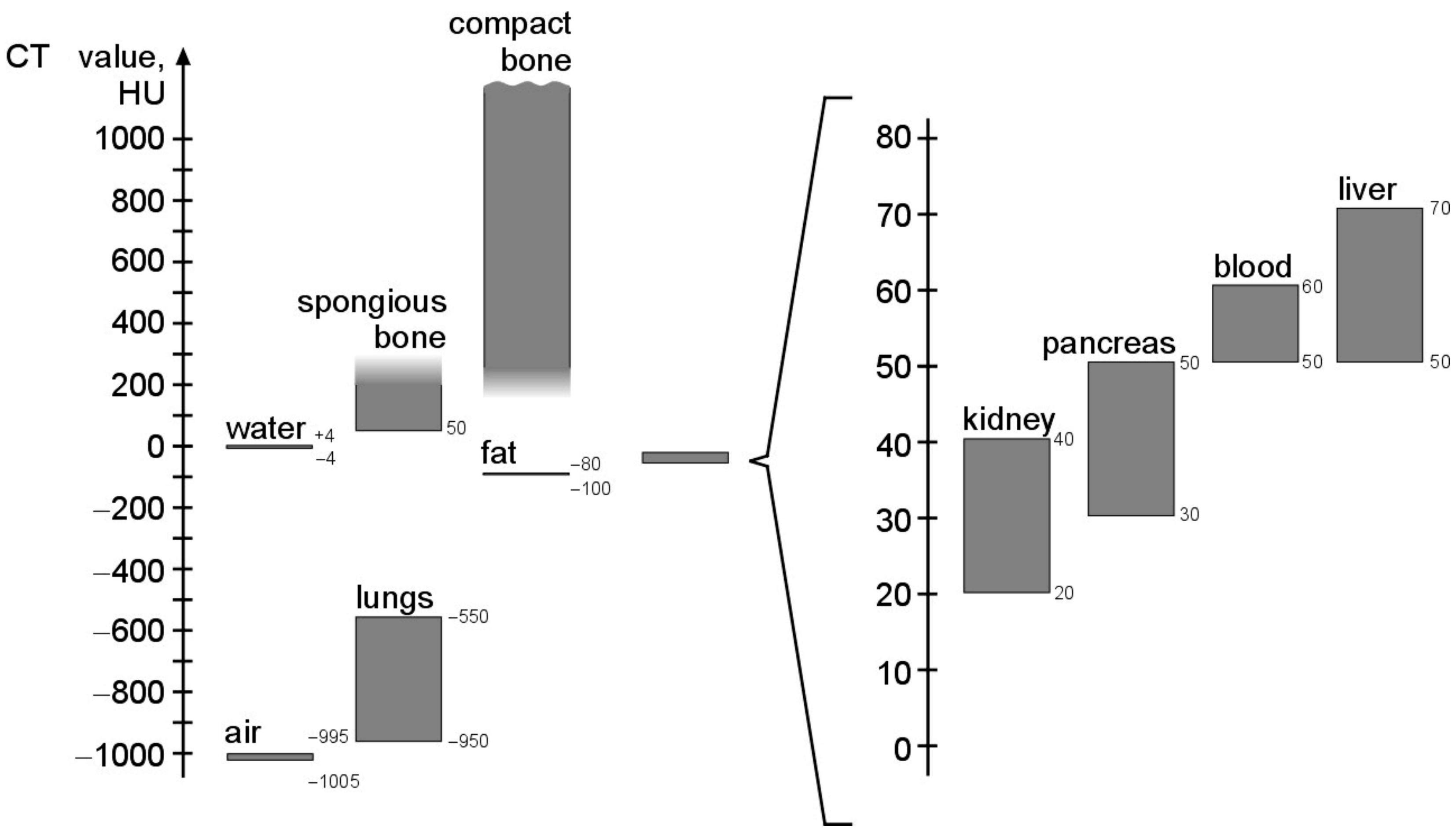
- We can't solve the real inverse problem since we have a mix of densities of materials, each with different Compton and photoelectric attenuation factors at different energies, and a weighted energy spectrum
- The best we can do is to use an *ad hoc* image scaling
- The CT number for each pixel, (x,y) 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, $\mu_{\mathrm{water}}$ 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

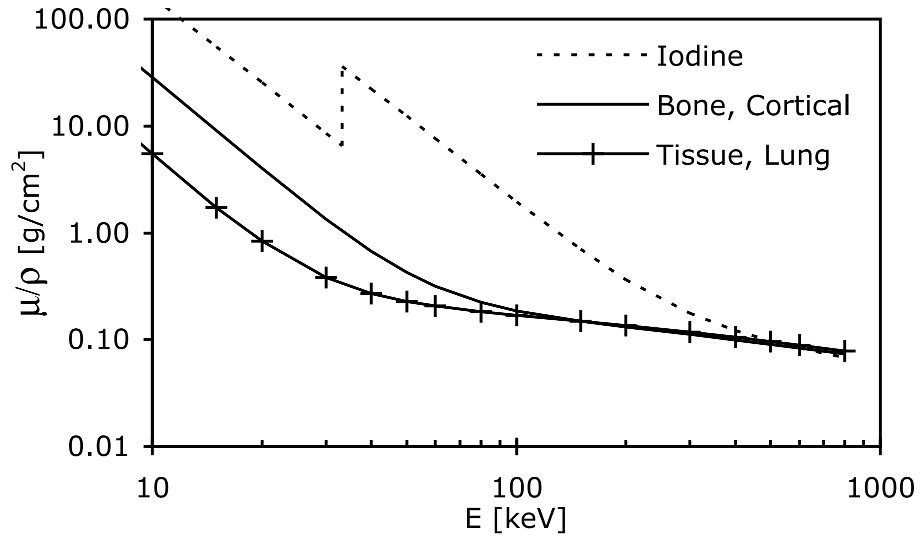
# CT Numbers

- Typical values in Hounsfield Units



# 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

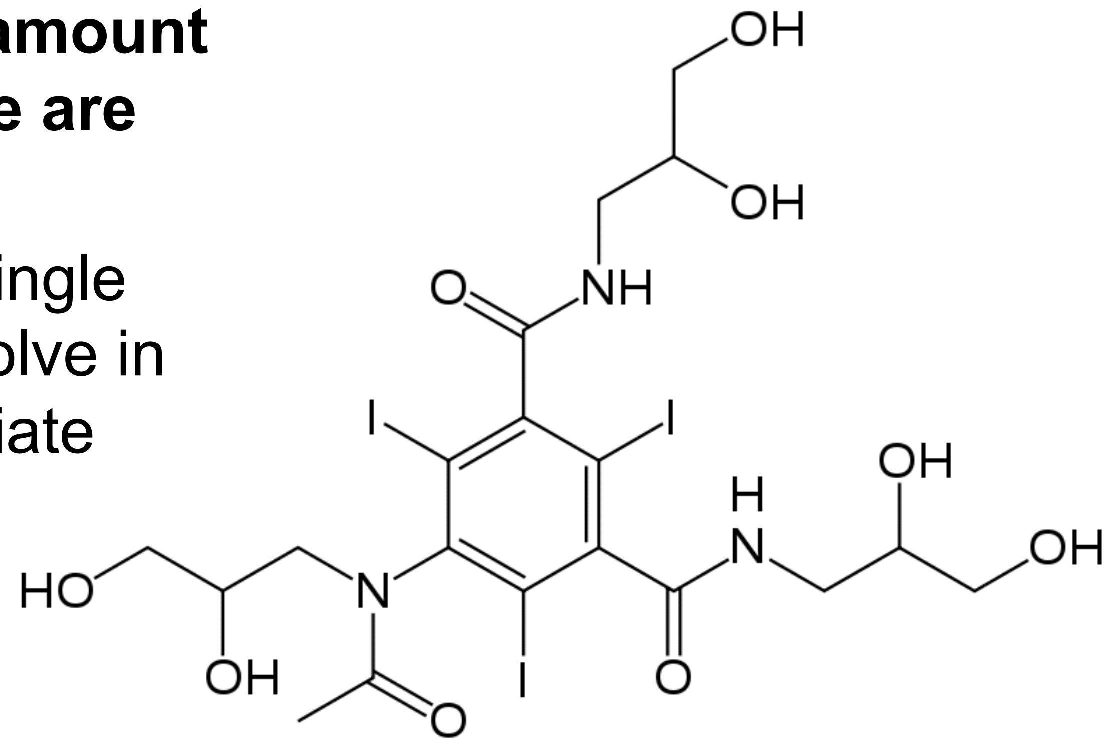



CT scan without contrast showing 'apparent' density

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

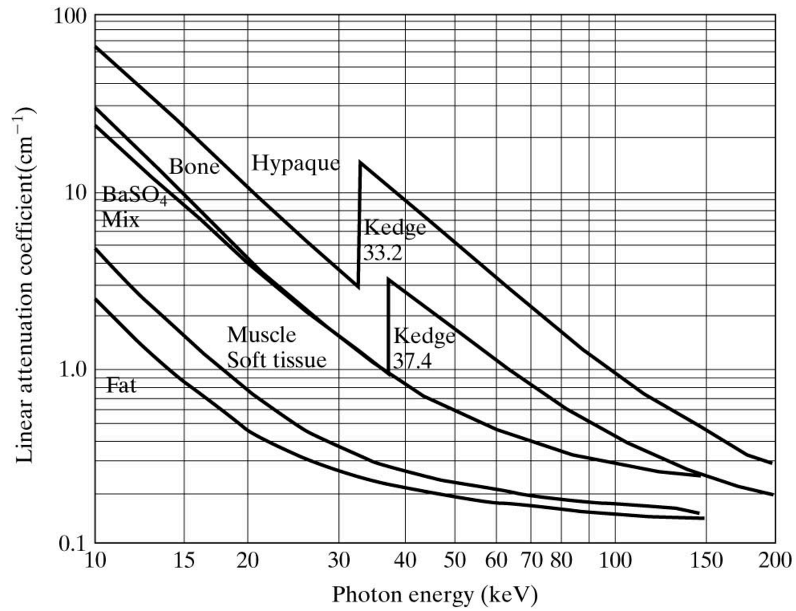



iohexol

- 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

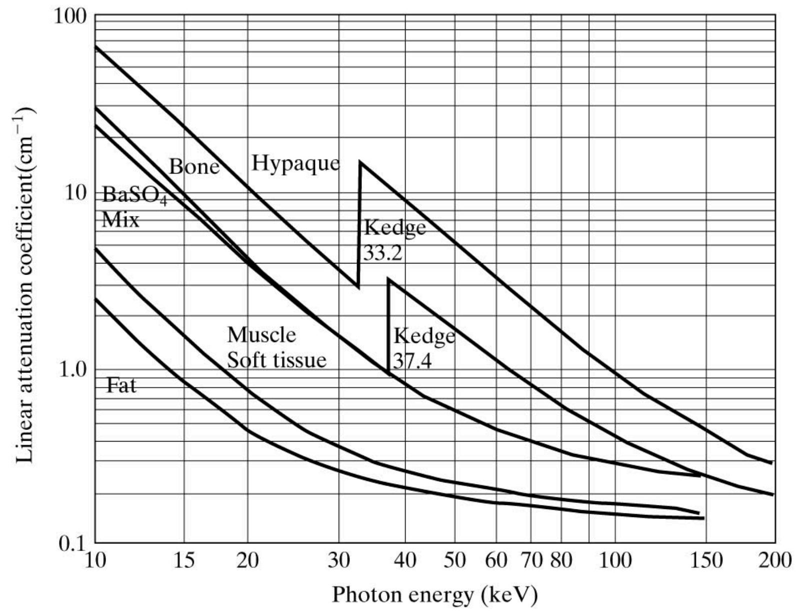
## Appendix A–Contrast Media Specifications

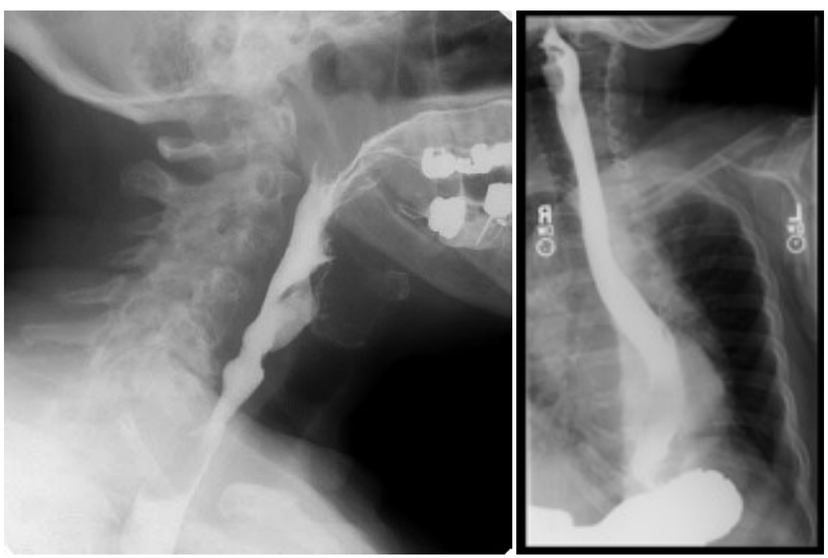
| Product | Chemical Structure | Anion | Cation | % Salt Concentration | % Iodine Concentration | Iodine+ (mgI/ml) | Viscosity+ 25° C (cps) | Viscosity+ 37° C (cps) | Osmolality (mOsm/kg $H_2O$) |
|---|---|---|---|---|---|---|---|---|---|
| INTRAVASCULAR | | | | | | | | | |
| Omnipaque® | | | | | | | | | |
| 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

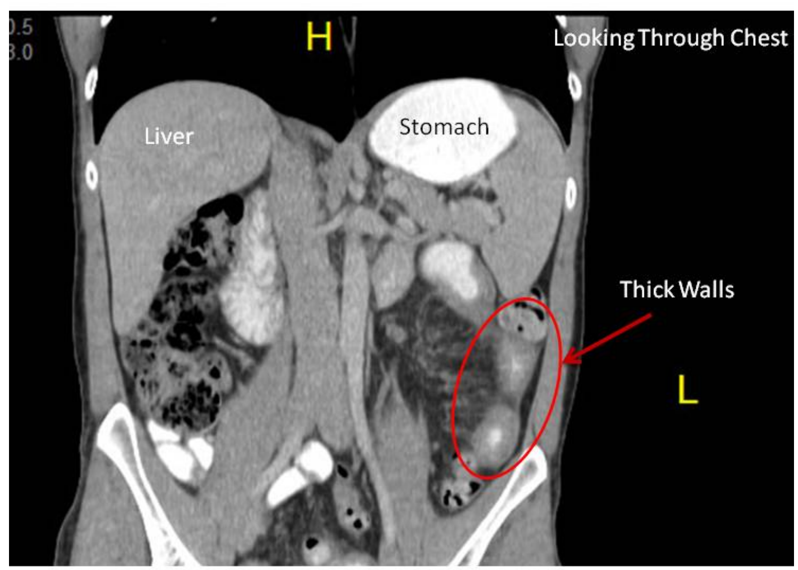
# Contrast Agents - Barium

- 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)



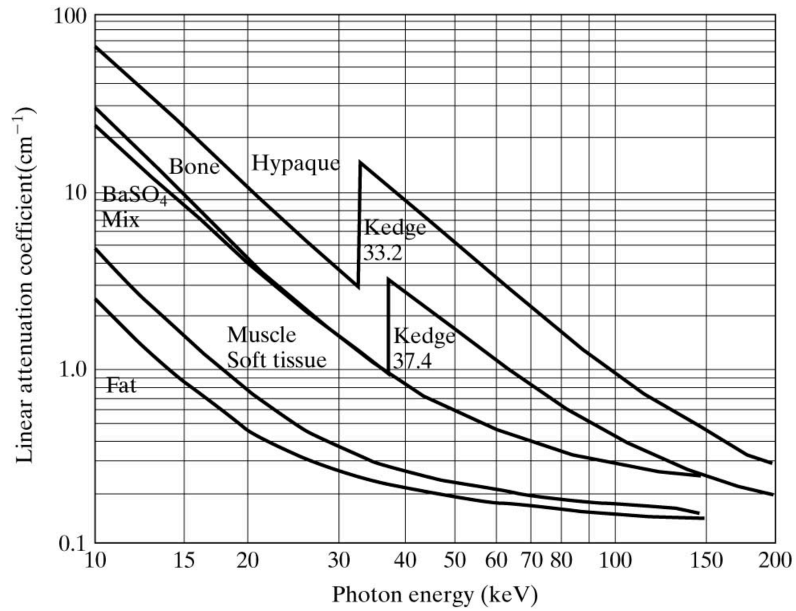
Projection images



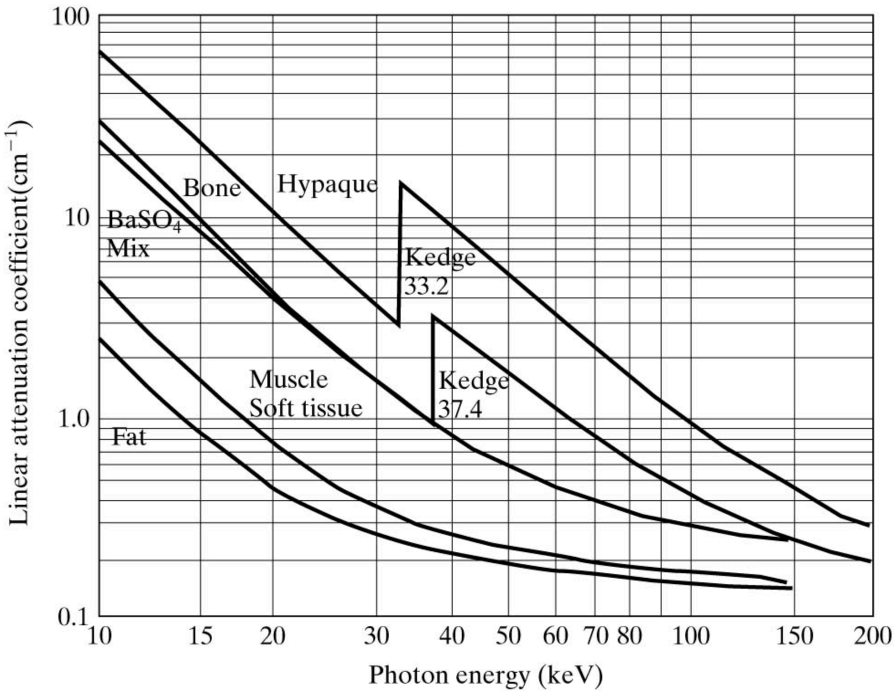

section through a 3D CT image

# Contrast Agents - Barium

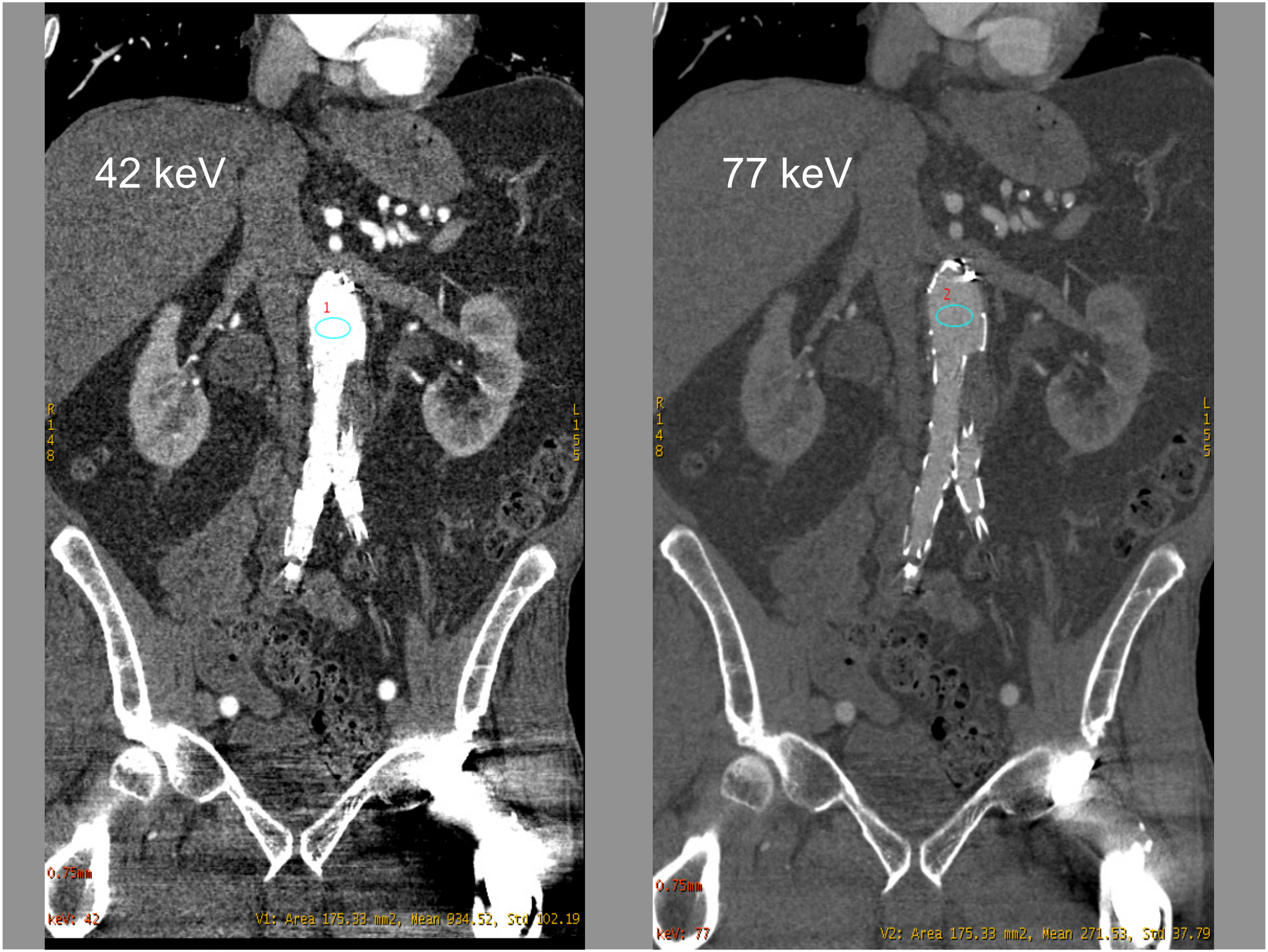
- Example of an combined use of barium and air
- The colon is clearly seen
- The white areas are barium (contrast) and the black regions are air




# Contrast Agents - Energy dependence

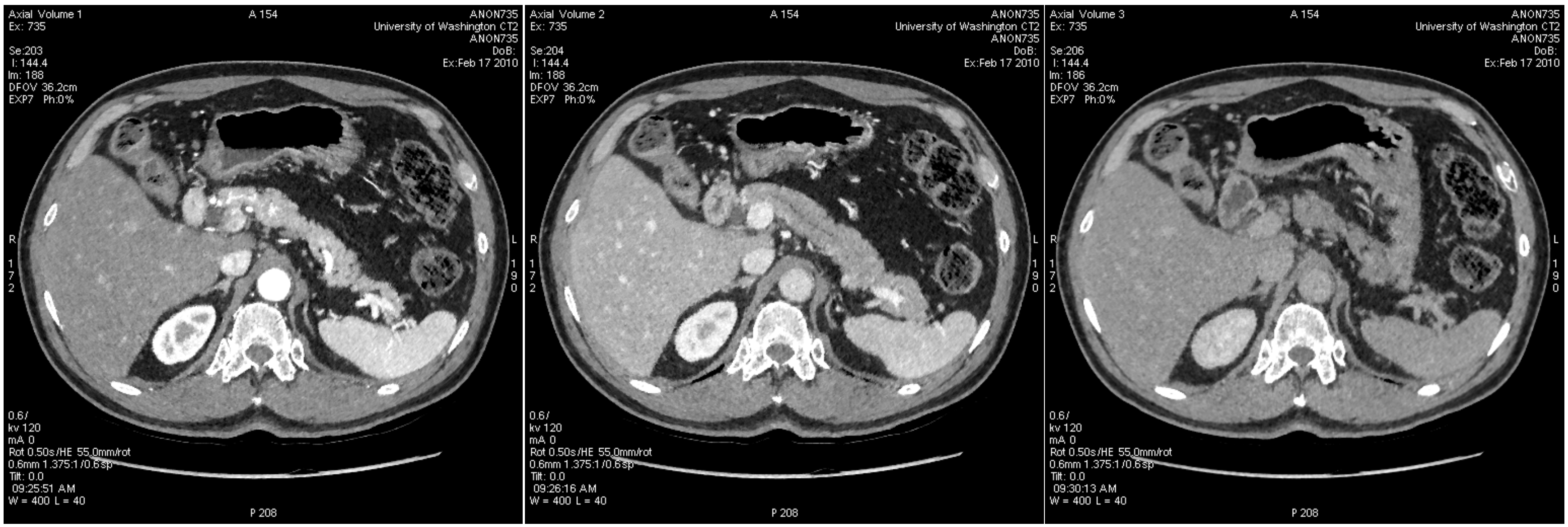


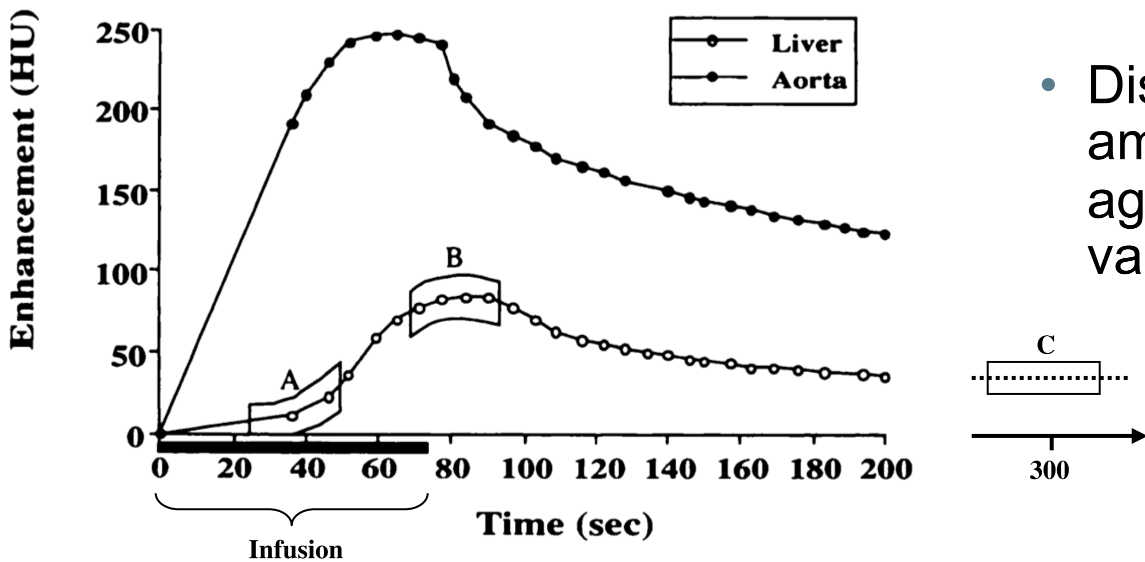

- Reducing energy of photons increases difference in attenuation between contrast agent and tissues
  - and increases difference in attenuation between different tissues
- Reducing energy of photons also increases noise, since fewer photons are transmitted through tissue


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

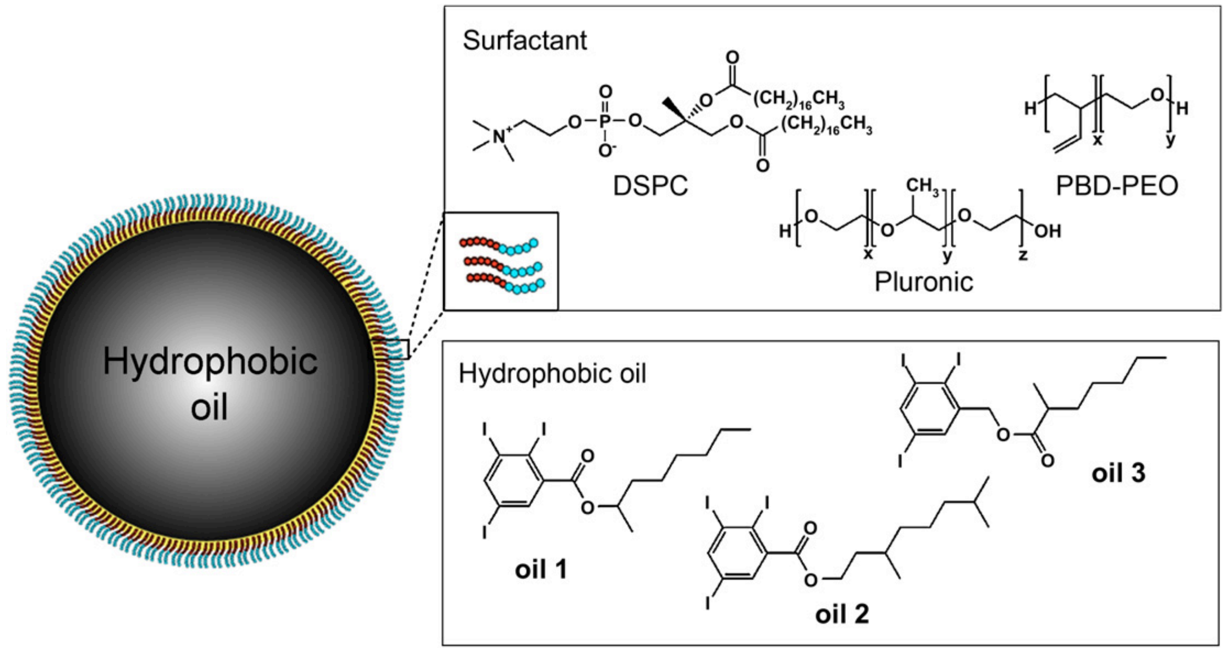


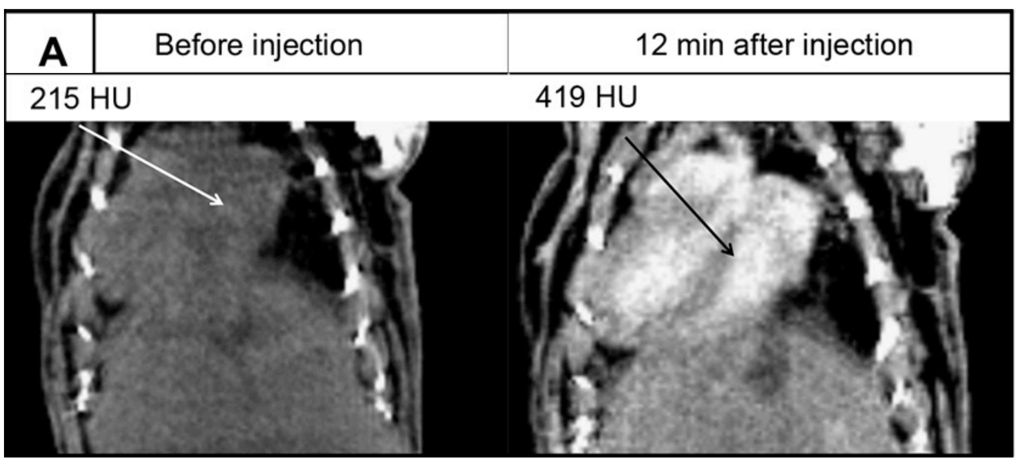



- Distribution and amount of contrast agent enhancement varies with time

# Nanoparticle-based iodine contrast agent

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

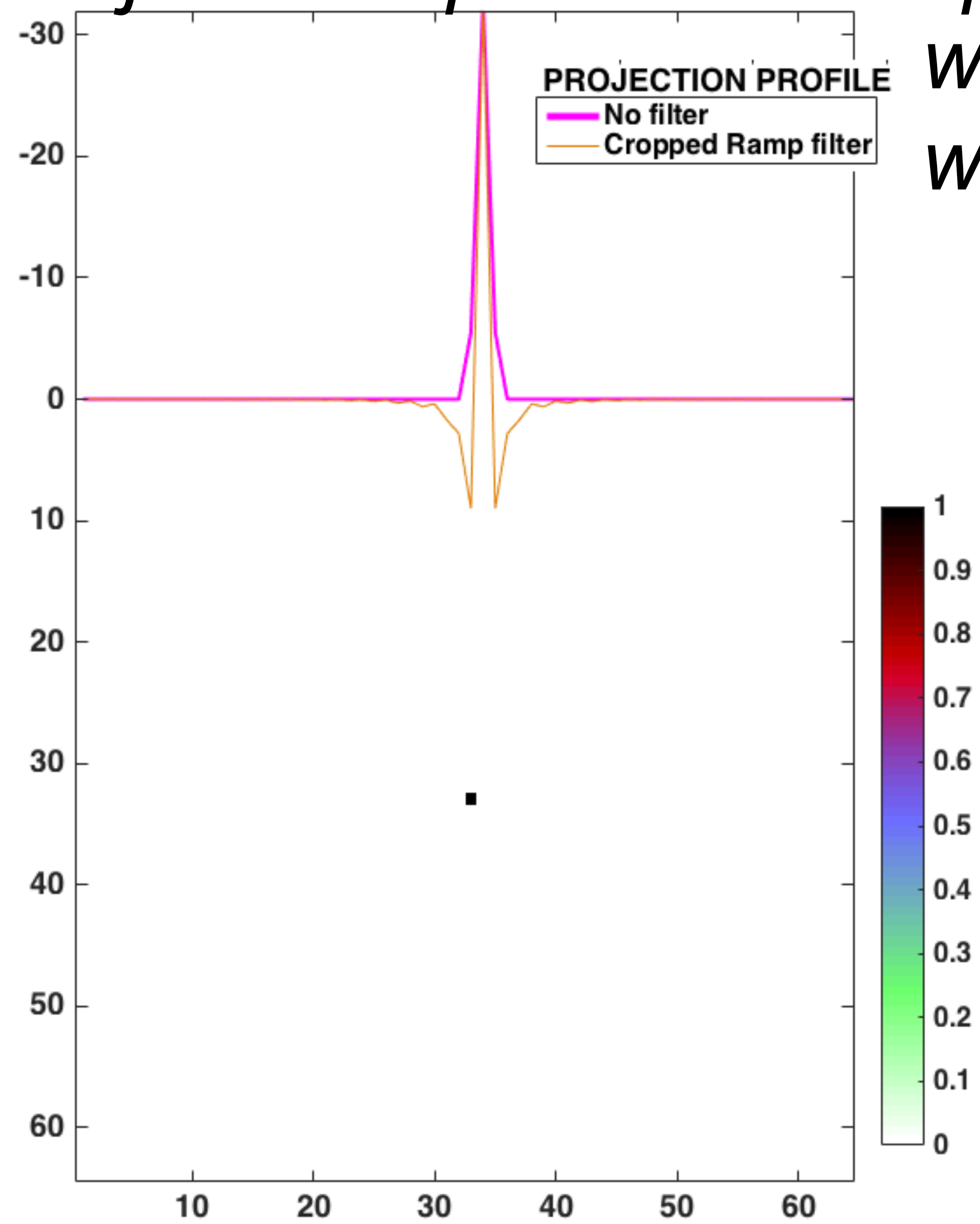


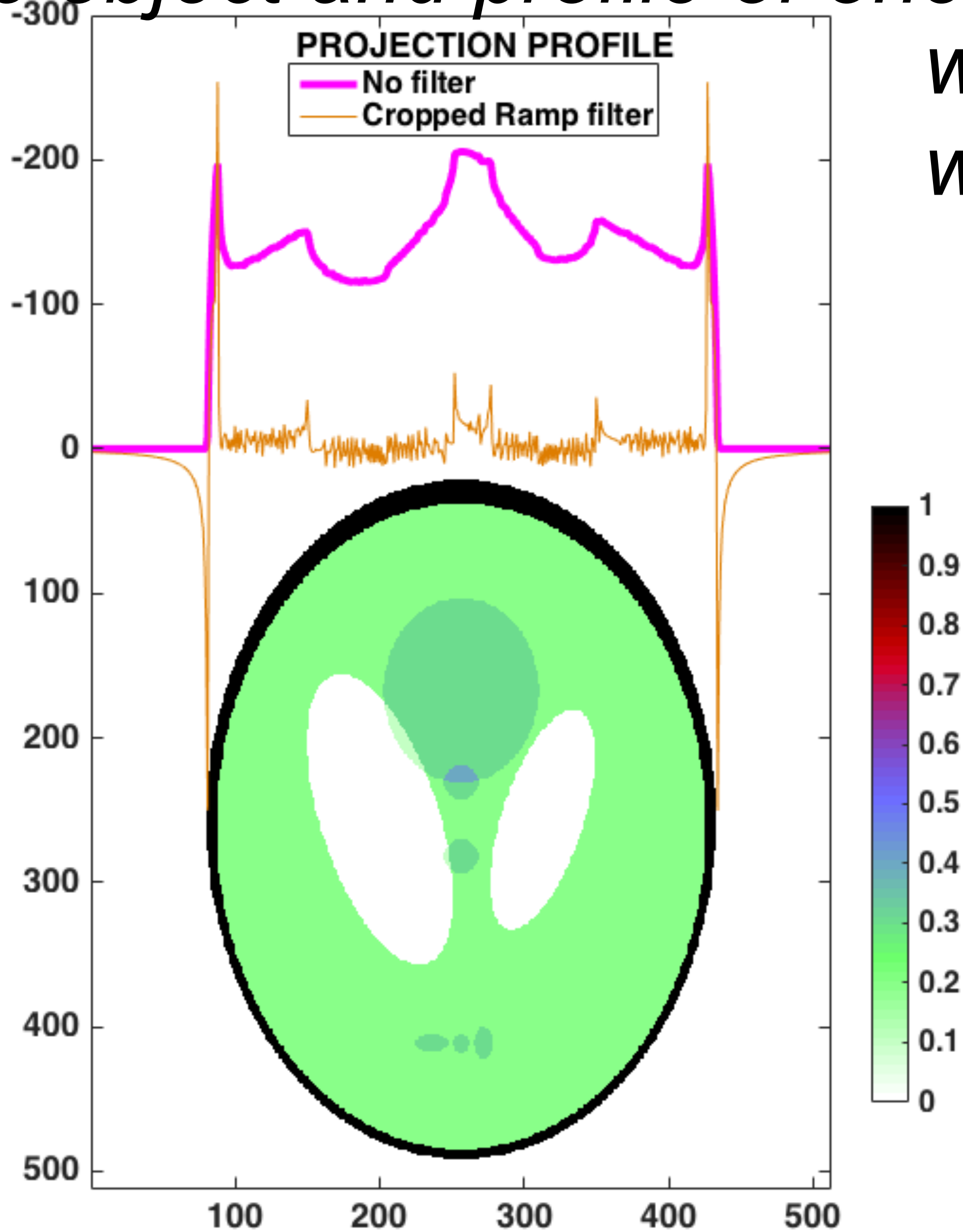

- Nanoparticles having sizes larger than c.a. 5.5 nm (hydrodynamic size) could prohibit rapid renal excretion

# Filtered-Backprojection Reconstruction

*Point-like object and profile of one project with and without filter*



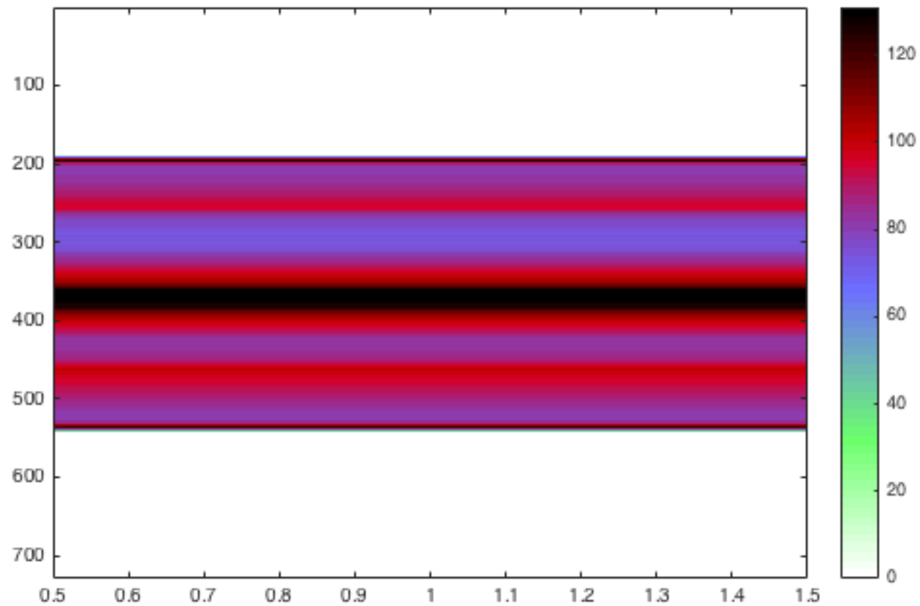
*Anthro-like object and profile of one project with and without filter*



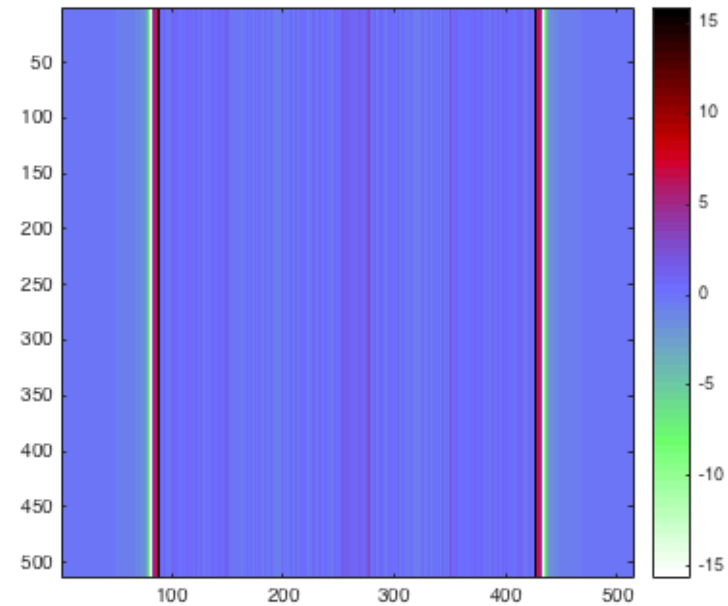
# Filtered Back Projection Image of Anthro-like object

## 1 projection

Sinogram

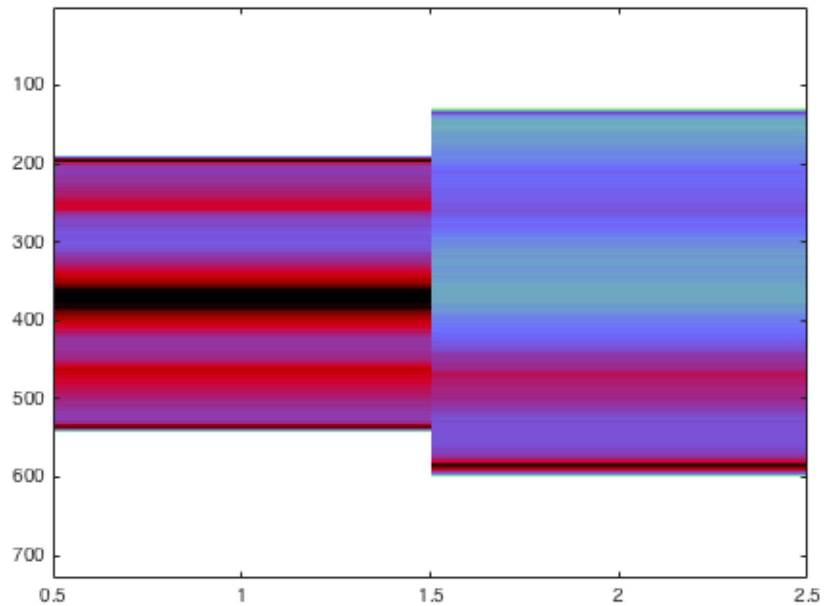



Image

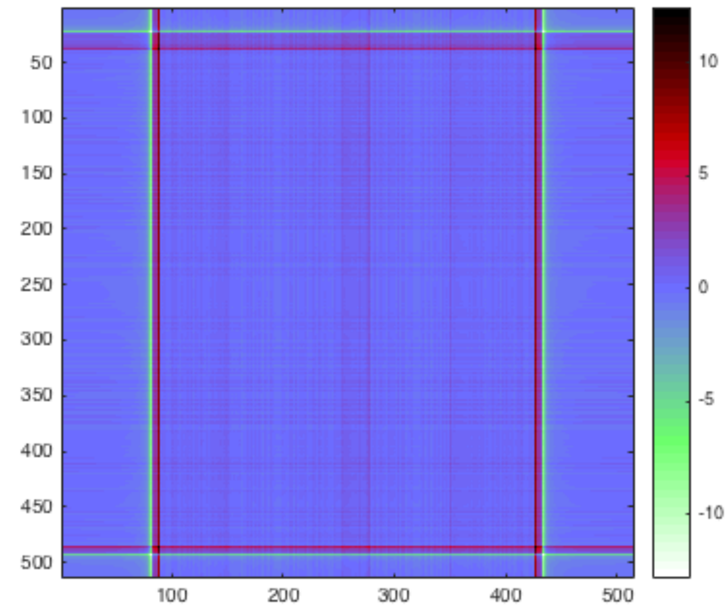


# Filtered Back Projection Image of Anthro-like object 2 projections

Sinogram



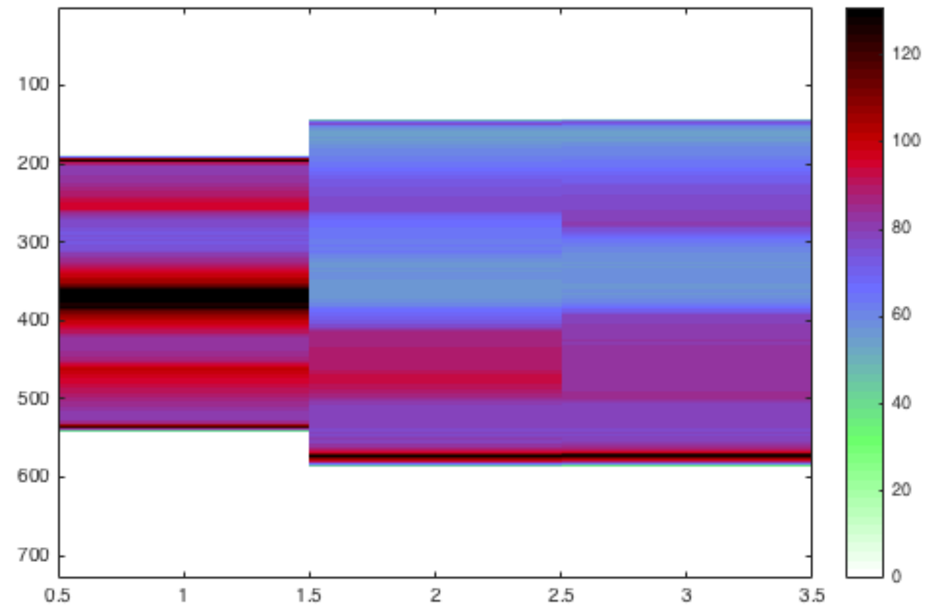

Image



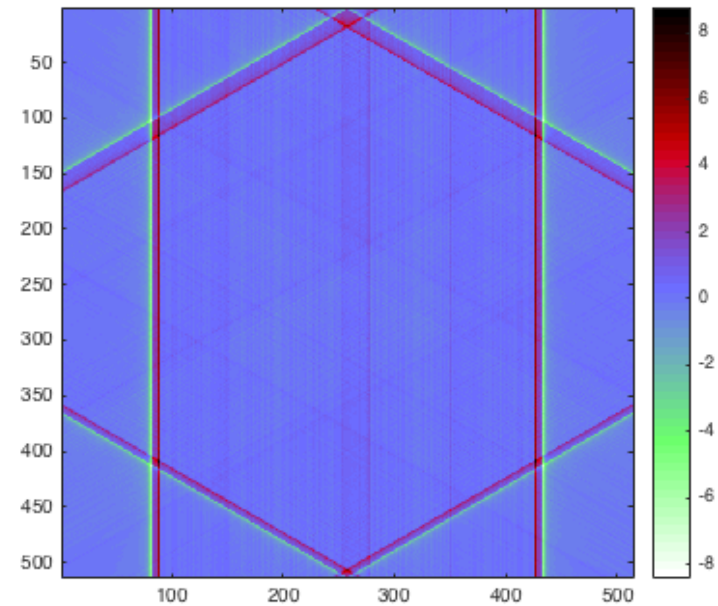
# *Filtered Back Projection Image of Anthro-like object*

## *3 projections*

### *Sinogram*



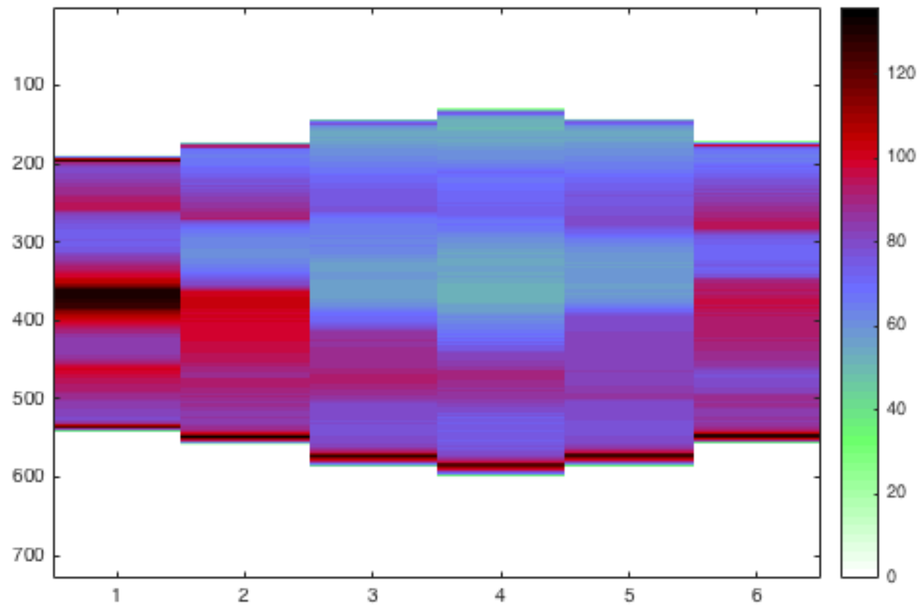

### *Image*



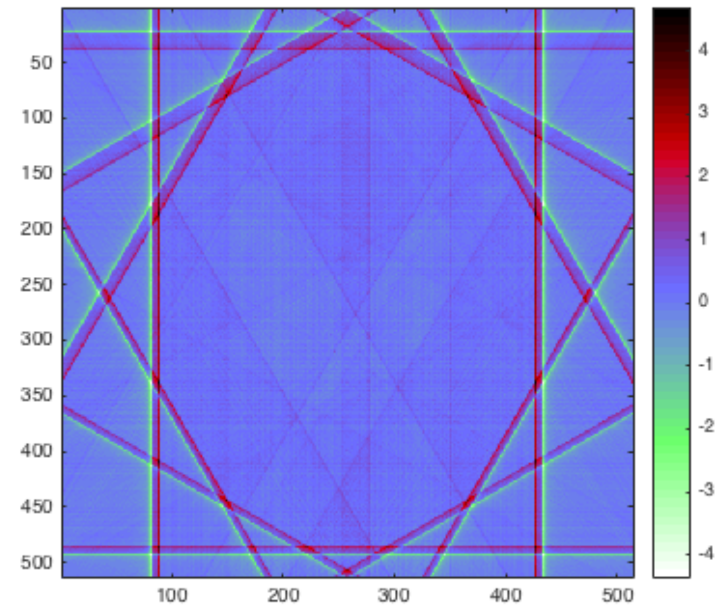
# *Filtered Back Projection Image of Anthro-like object*

## *6 projections*

*Sinogram*

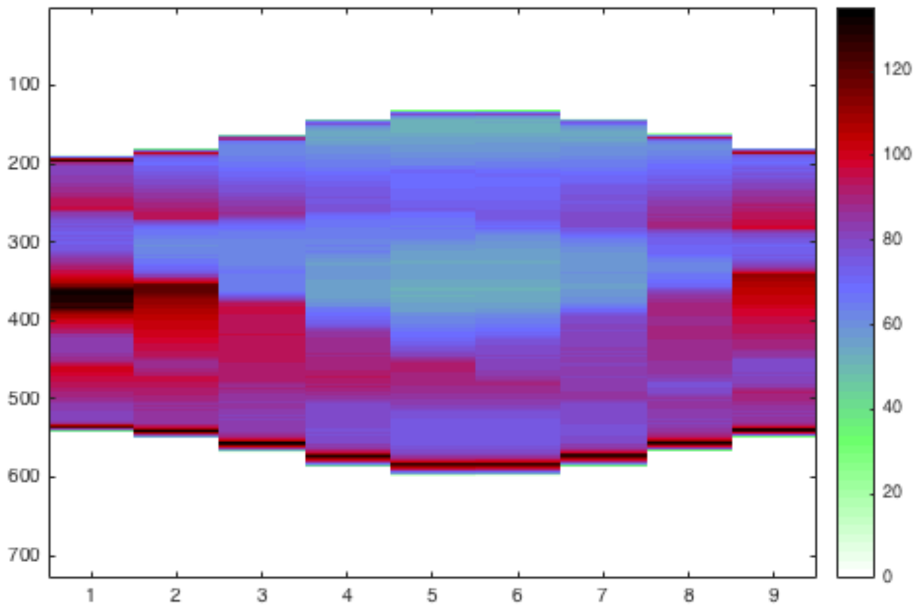



*Image*

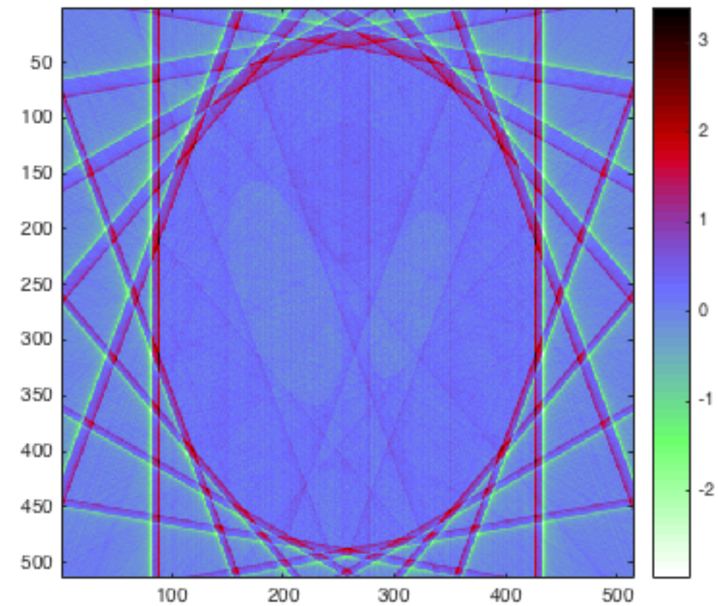


# Filtered Back Projection Image of Anthro-like object
# 9 projections

Sinogram

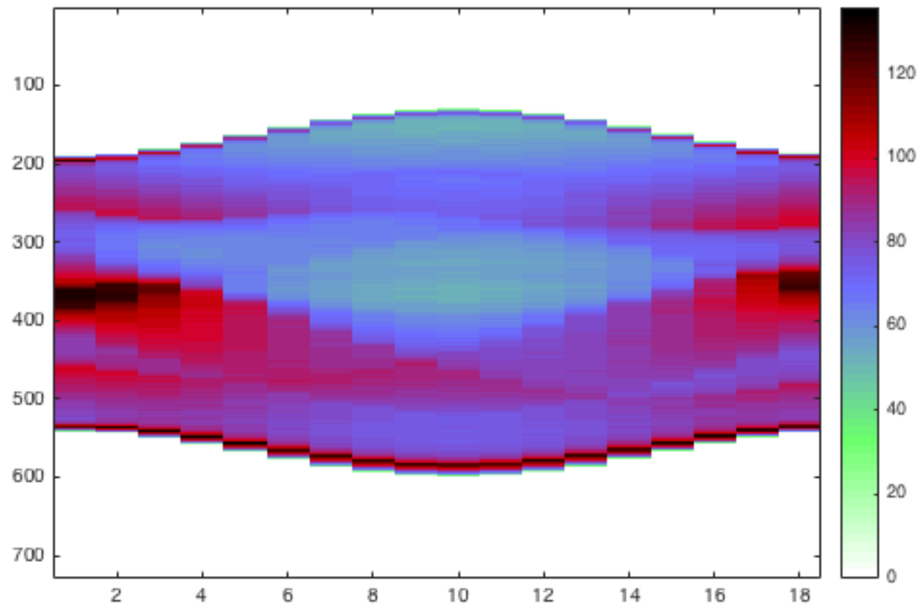



Image

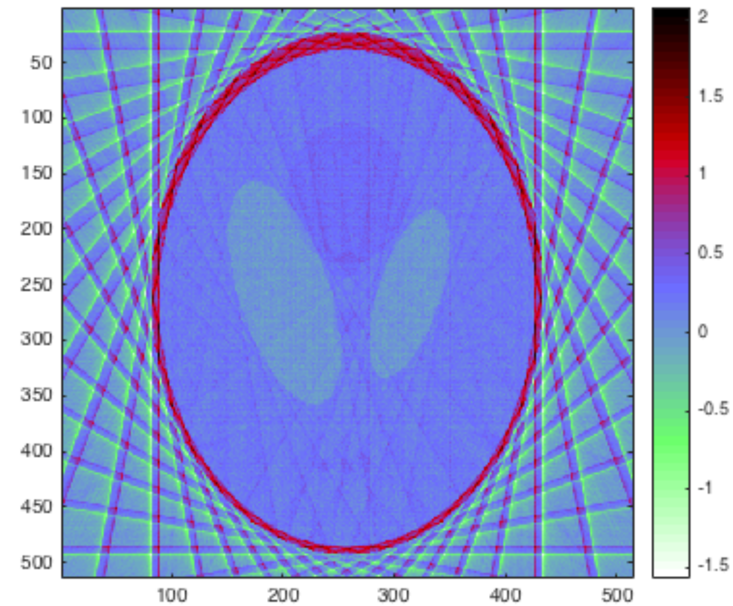


# Filtered Back Projection Image of Anthro-like object 18 projections

Sinogram

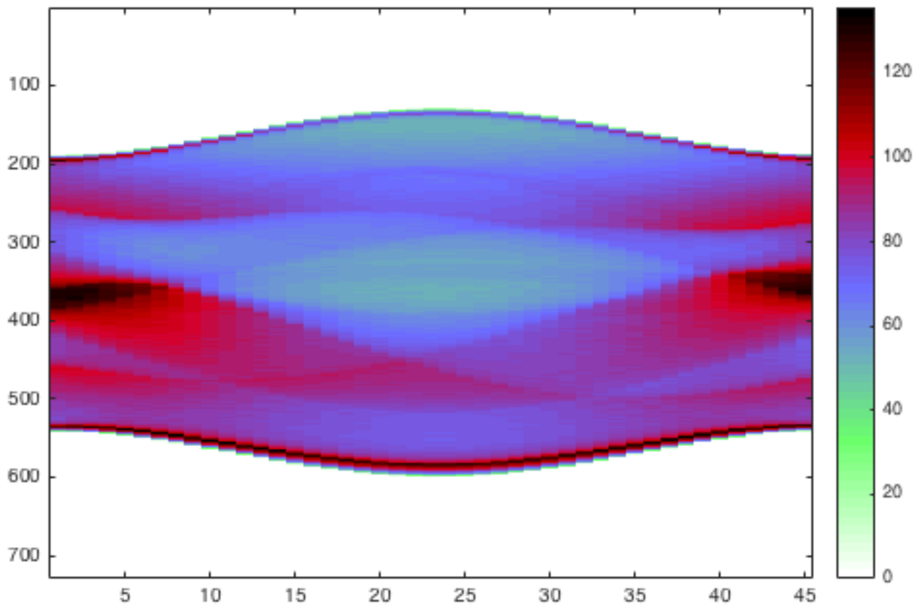



Image

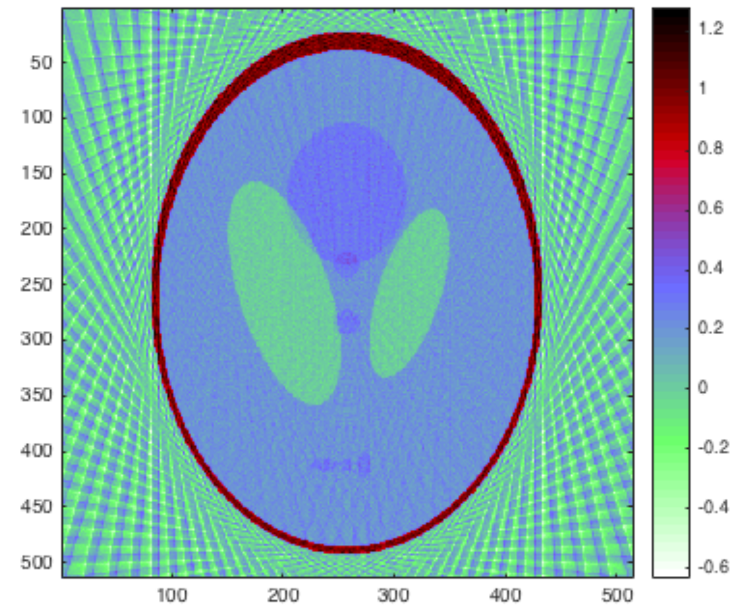


# Filtered Back Projection Image of Anthro-like object 45 projections

Sinogram

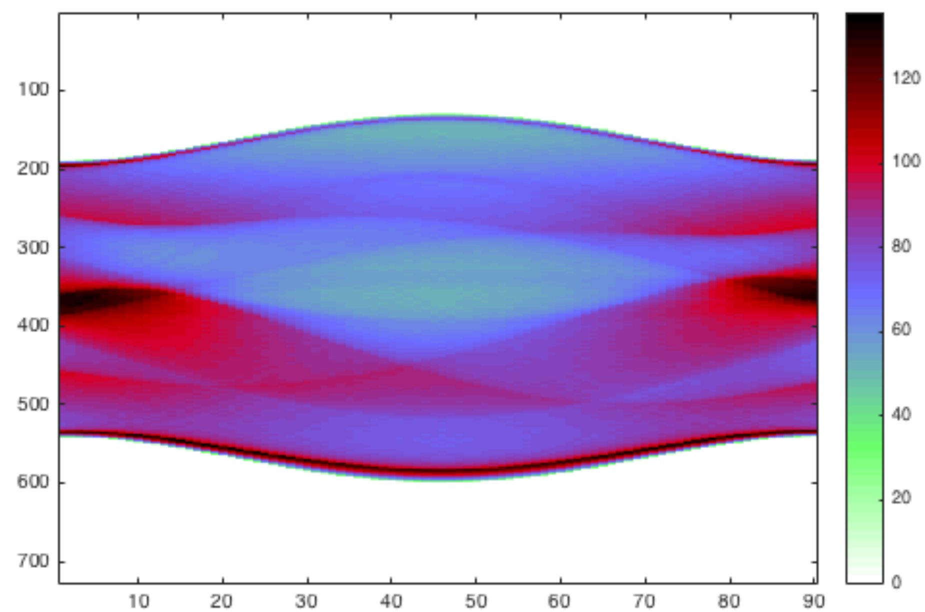



Image

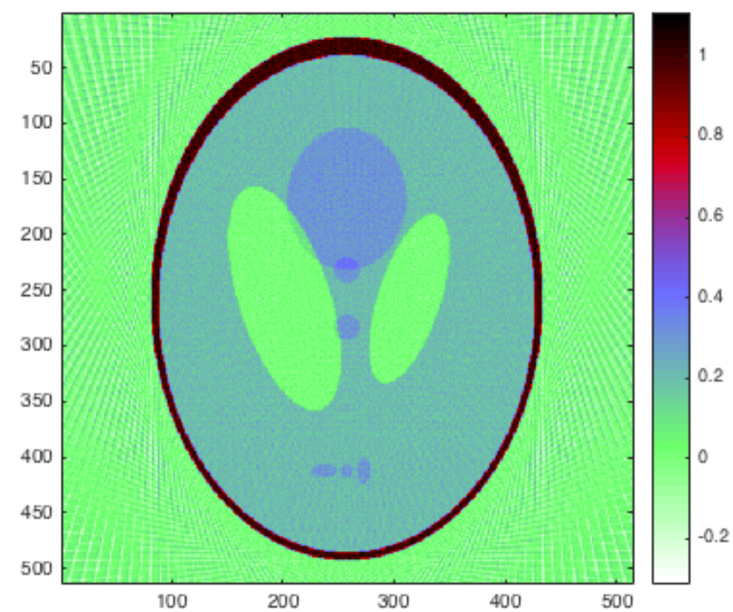


# Filtered Back Projection Image of Anthro-like object 90 projections

Sinogram

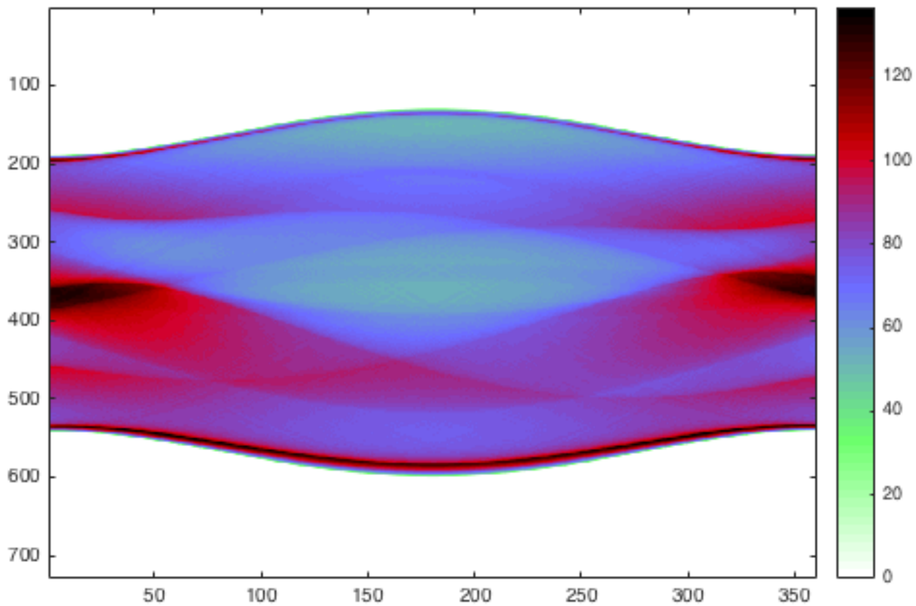



Image

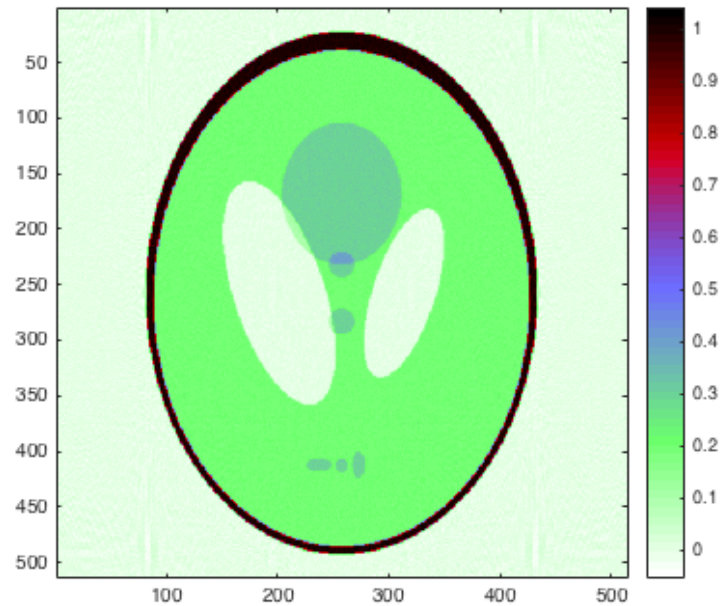


# *Filtered Back Projection Image of Anthro-like object 360 projections*

*Sinogram*

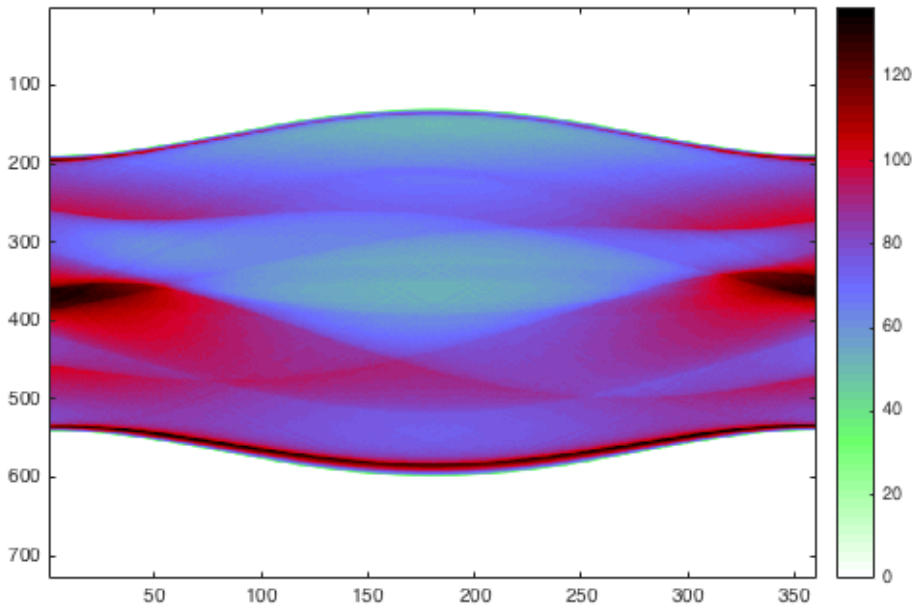



*Image*

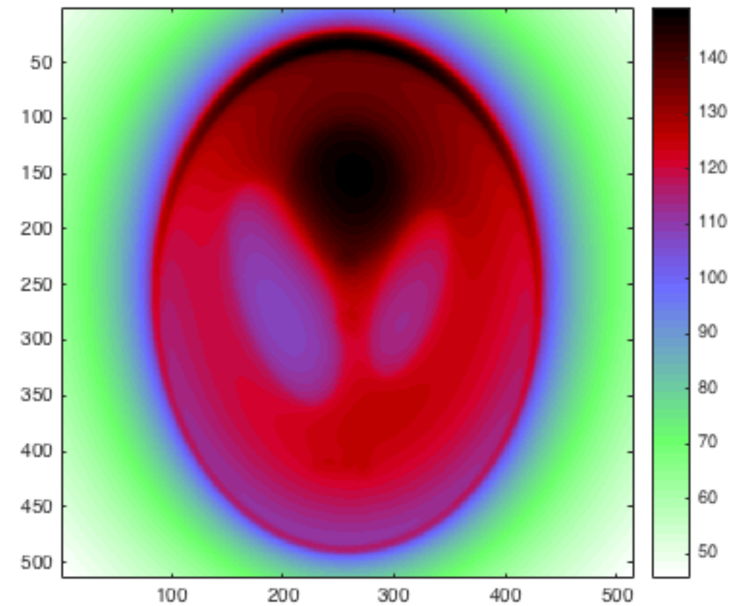


# *NON-Filtered* *Back Projection Image of Anthro-like object* ***projections***

*Sinogram*




*Image*

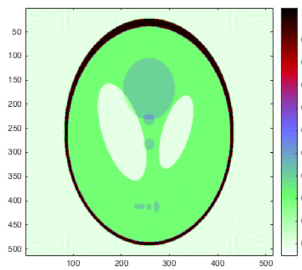



*Loss of resolution*

# *Filtered Back Projection Image of Anthro-like object*

## *Difference of 360 and 180 projections*

*360*



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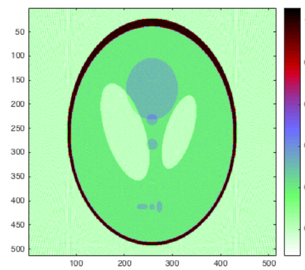
*180*



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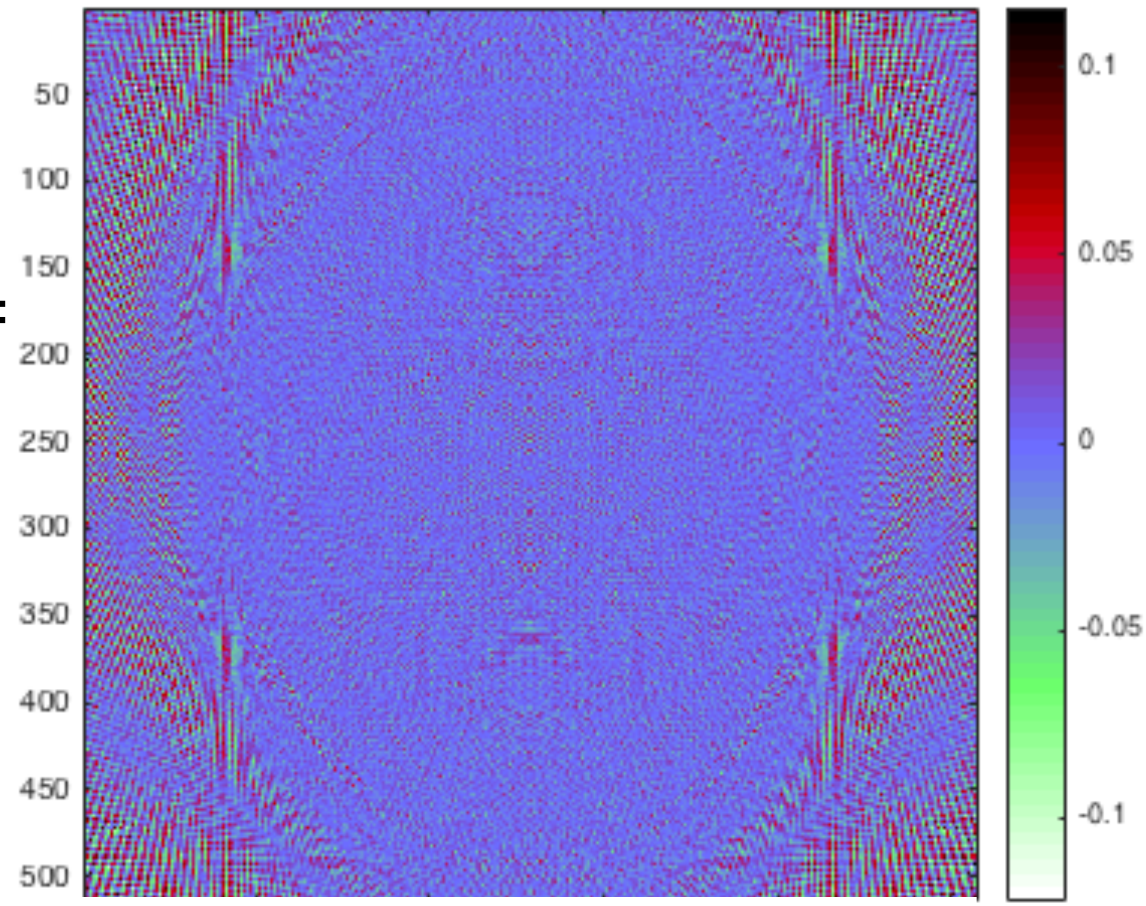


*Improving fine structure*