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.

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

1+ page outline	**Friday May 10**	**(20%)**
Background summary	Friday May 17	(15%)
Rough draft	Friday May 24	(15%)
Final version	Friday May 31	(30%)
Presentation / slides	Friday June 7	(10%)
Presentation	Thursday June 13	(10%)

Class Project Groups

Group	2	3	4	5	6	7	8	9	10
Project	PET memory disorders	Thyroid cancer	PET Alzheimer's	CT coronary	Barium imaging			Nuclear imaging	
Members	Guertin	Cueva	Destefano	Cooper	Ball	Winslow	Andaz	Boyd	Nelson
	Pedroza	Santos	Morris	Deshmukh	Fuld		Baral	Kiyabu	Piehl
		Alsup	Pletenik	McKay			Burroughs-Heineman	Nebeck	Zhdanov
		Doop	Pourmoghadam	Schasteen				Um	

- Reports
  - 1 person: 10±1 pages
  - 2 people: 18±2 pages
  - 3 people: 24±3 pages
  - 4 people: 28±4 pages
- Presentation
  - 7-10 slides (PDF format please)
  - 10 minute presentation (1 person)

Discussion of Questions from Last Lecture

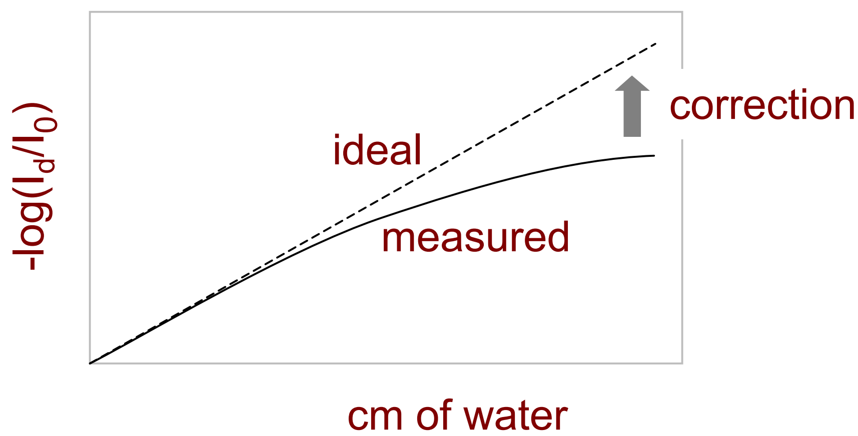
- Are all contrast agents metabolized and excreted in from the body, or do any last in the body for a significant period of time?
  - Currently used iodinated agents are cleared almost completely by glomerular filtration. With reduced renal function, there is vicarious excretion primarily in bile and through the bowel. Circulatory half life is 1–2 hours, assuming normal renal function.
- What are the way(s) to minimize the Beam Hardening effect?

  Water based correction

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

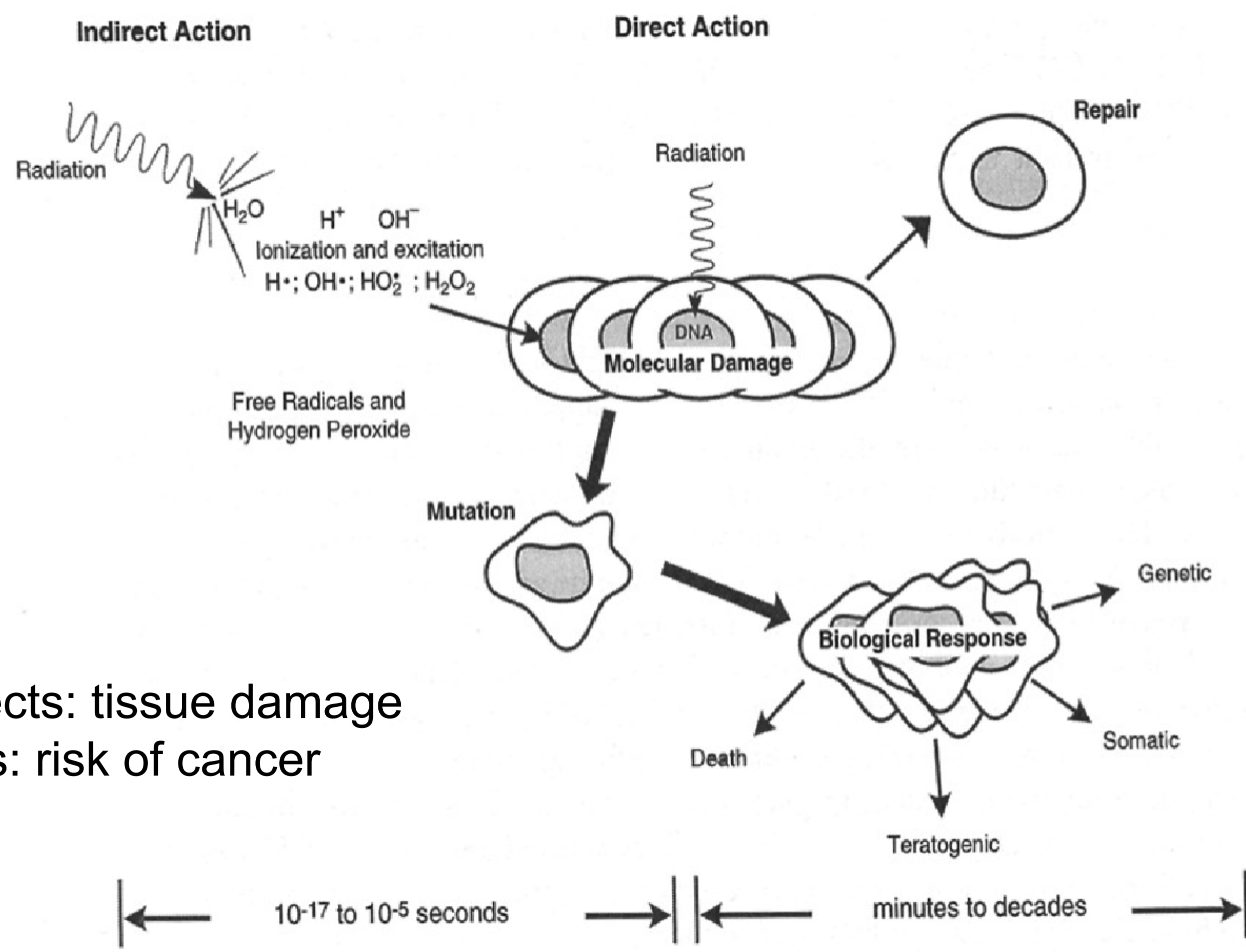
$$\approx I_0 e^{-\mu_W L} \quad \text{(assume all water)}$$

$$\mu_W L = -\log(I_d / I_0)$$



- [what is] the difference between the indirect action and direct action? Also, why is the direct action repairable and indirect not?

Effects of ionizing radiation



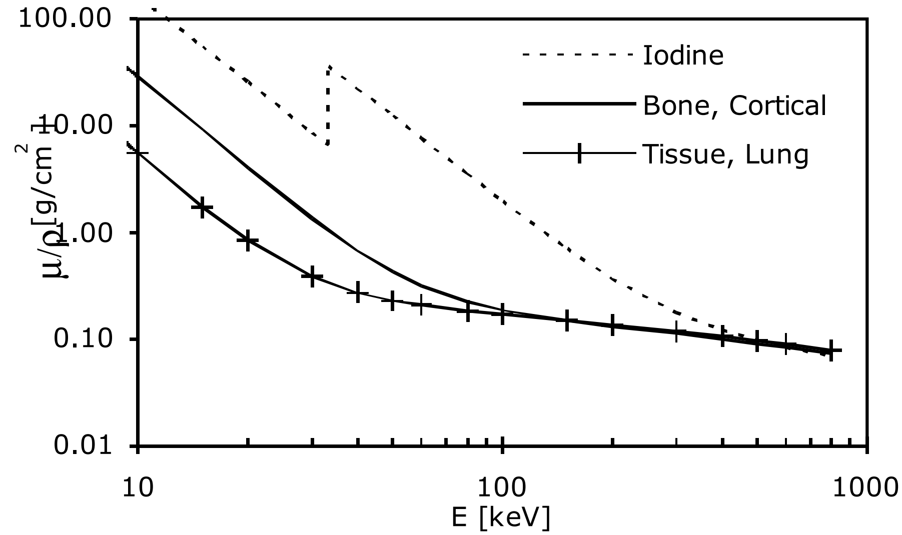
Deterministic effects: tissue damage
Stochastic effects: risk of cancer

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

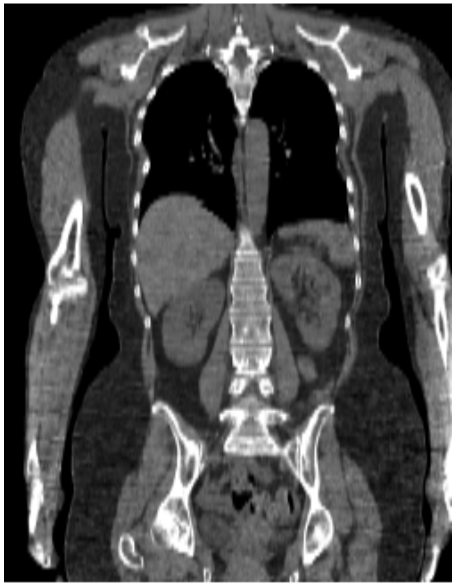
X-ray contrast agents

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



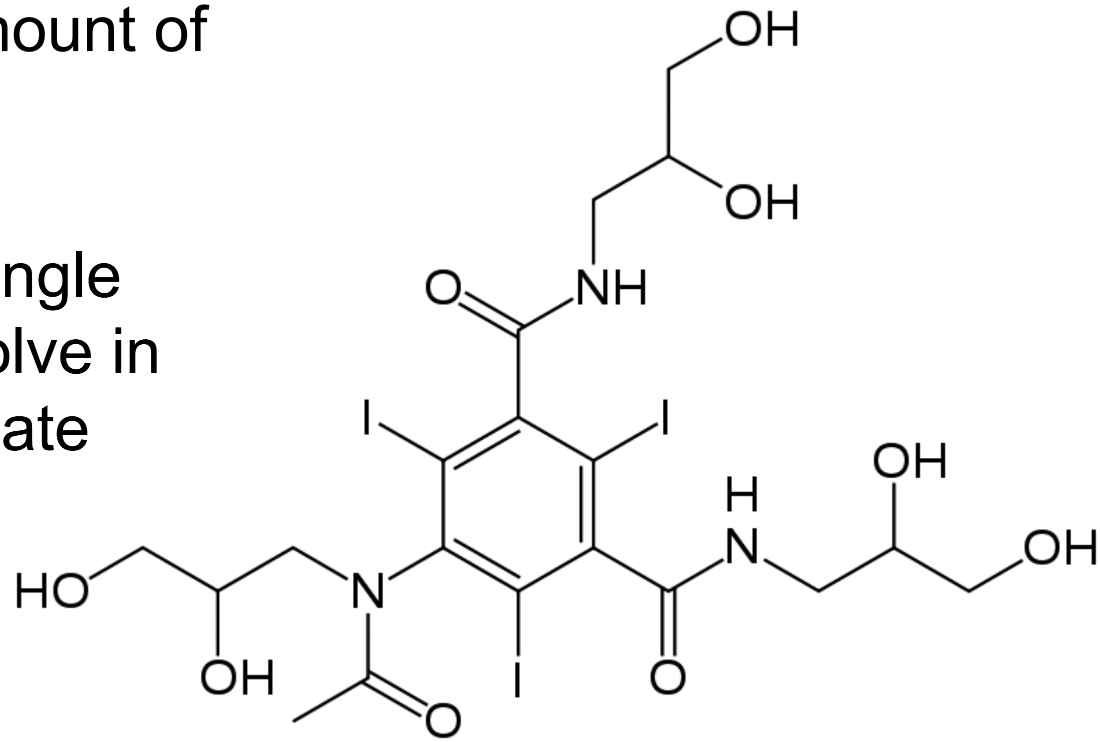
CT scan without contrast showing 'apparent' density



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

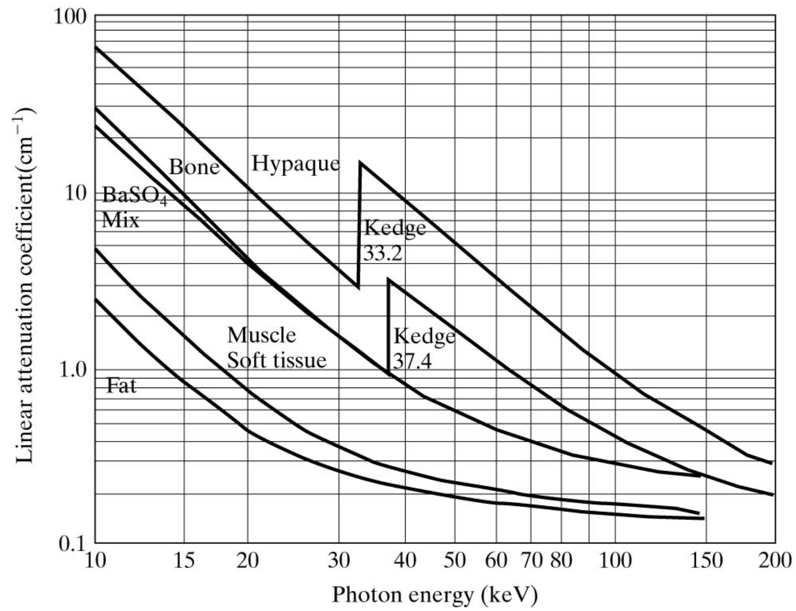


iohexol

- 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

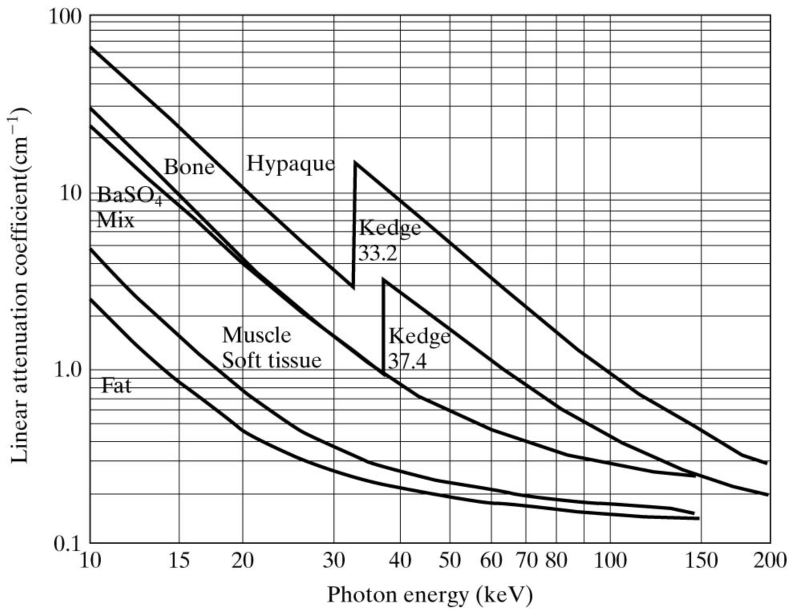
Appendix A–Contrast Media Specifications

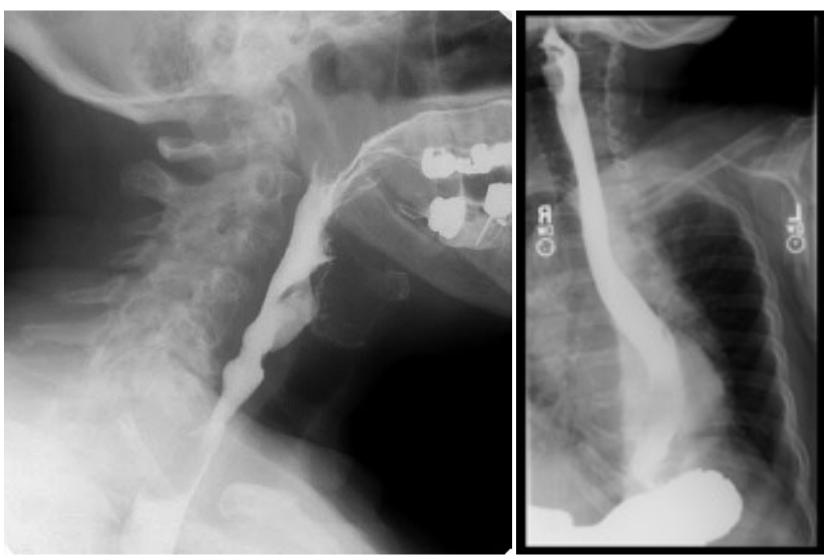
Product	Chemical Structure	Anion	Cation	% Salt Concentration	% Iodine Concentration	Iodine+ (mgI/ml)	Viscosity+ 25° C (cps)	Viscosity+ 37° C (cps)	Osmolality (mOsm/kg H_2O)
INTRAVASCULAR									
Omnipaque®									
140 (GE Healthcare)	Iohexol	Nonionic	Nonionic	None	14	140	2.3*	1.5	322
Conray™ 30 (Covidien)	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

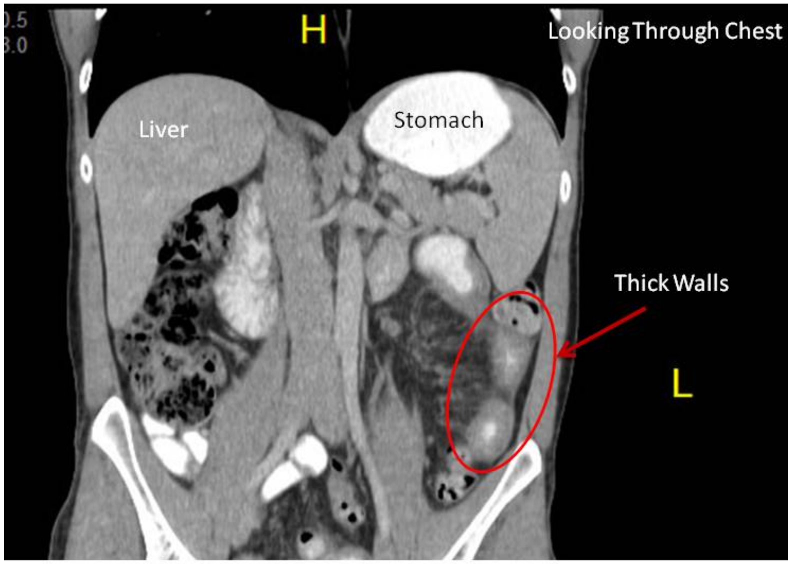
Contrast Agents - Barium

- 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)





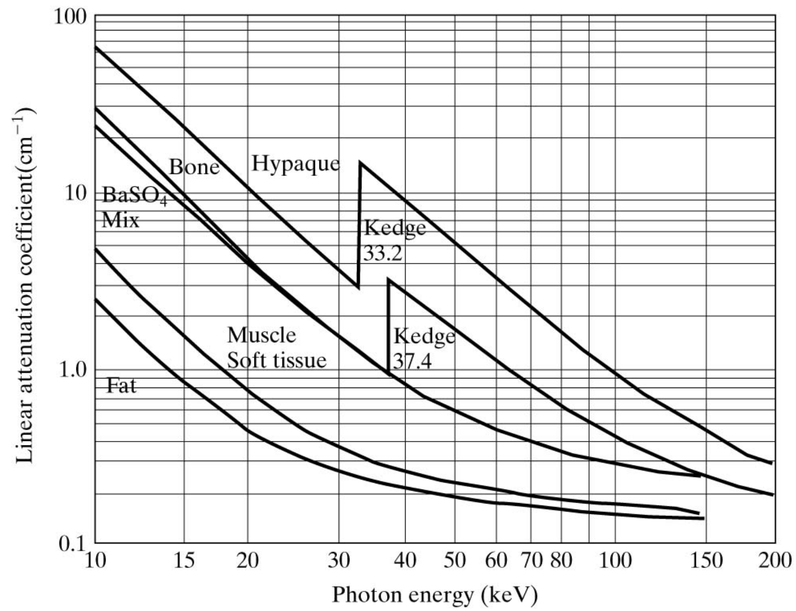
Projection images



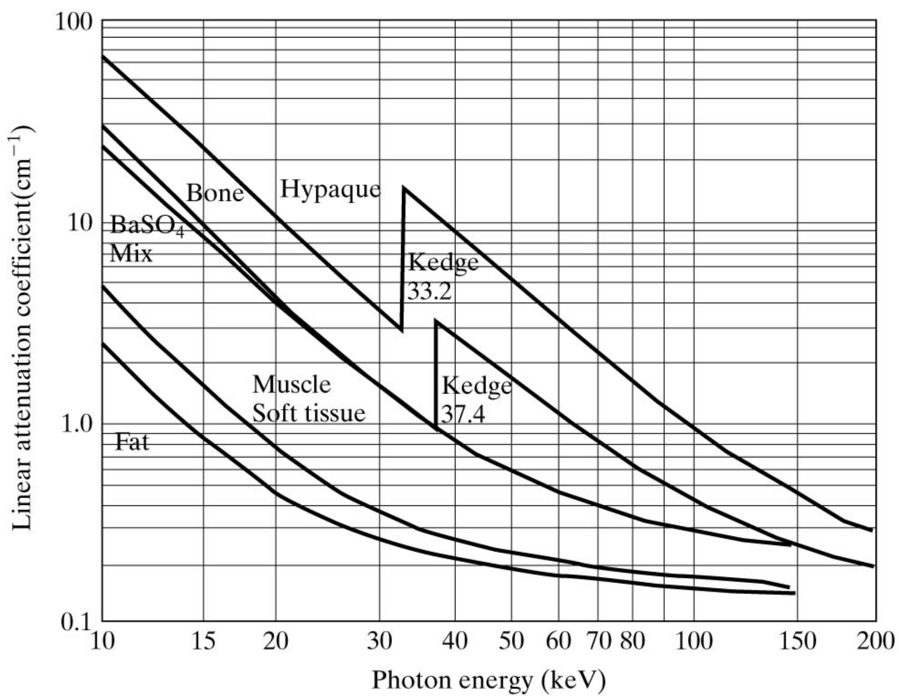
section through a 3D CT image

Contrast Agents - Barium

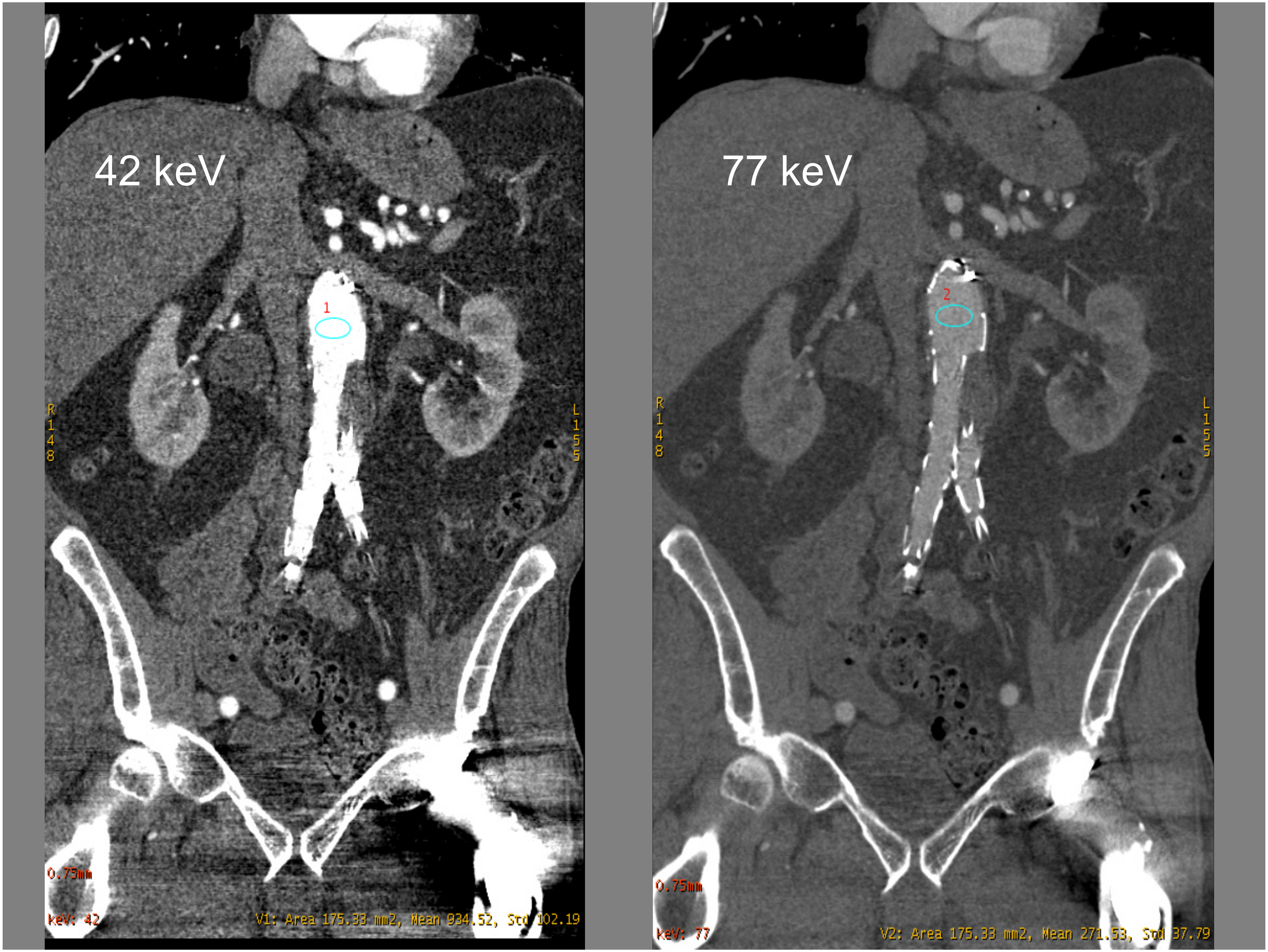
- Example of an combined use of barium and air
- The colon is clearly seen
- The white areas are barium (contrast) and the black regions are air



Contrast Agents - Energy dependence

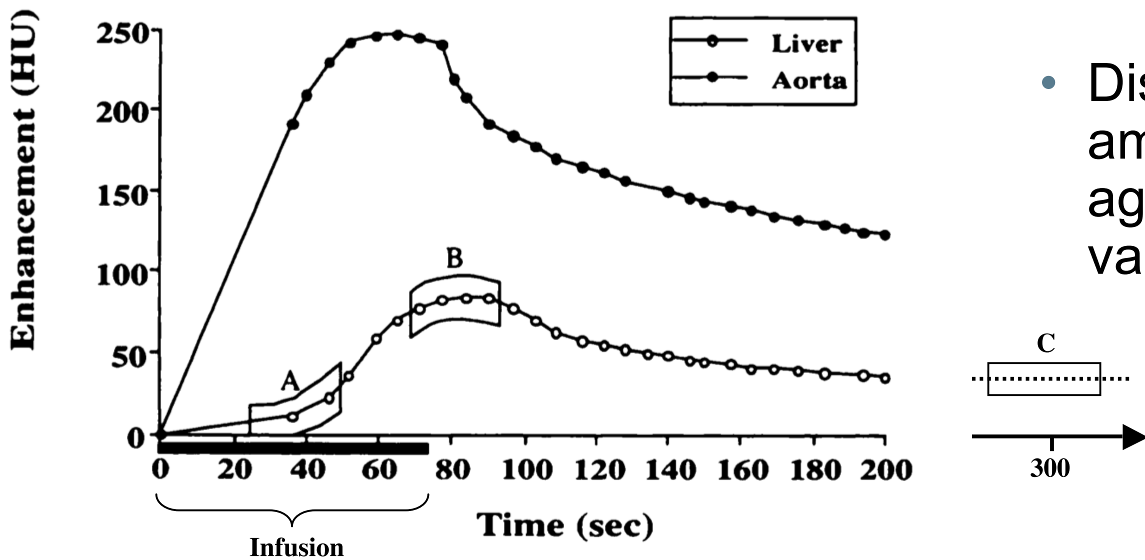


- Reducing energy of photons increases difference in attenuation between contrast agent and tissues
  - and increases difference in attenuation between different tissues
- Reducing energy of photons also increases noise, since fewer photons are transmitted through tissue


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

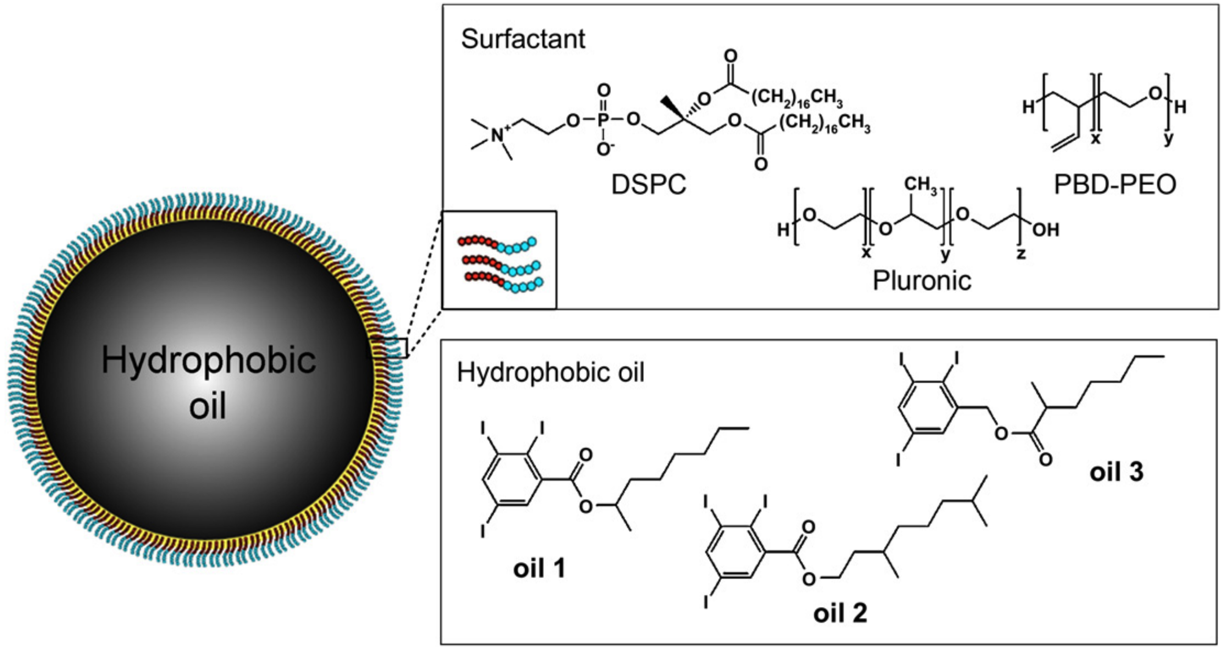
A: 'Arterial'   B: 'Venous'   C: 5 min delay

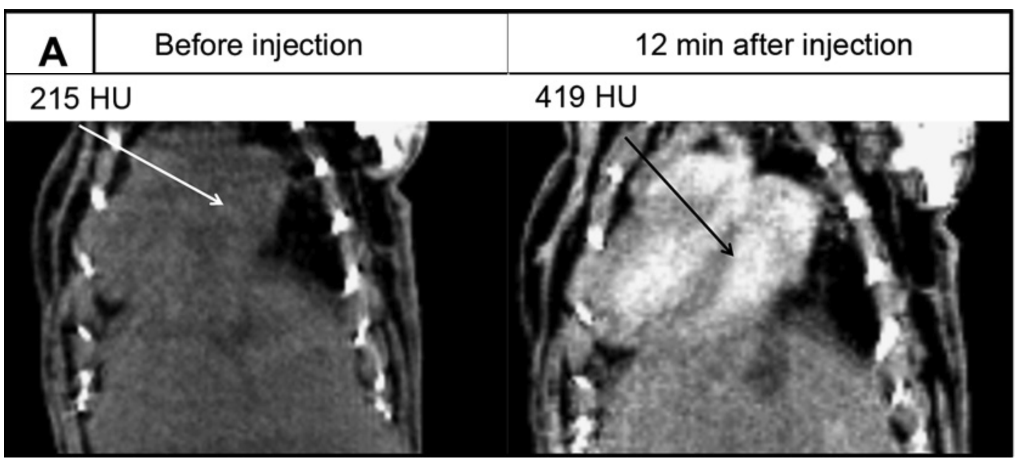


- Distribution and amount of contrast agent enhancement varies with time

Nanoparticle-based iodine contrast agent

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



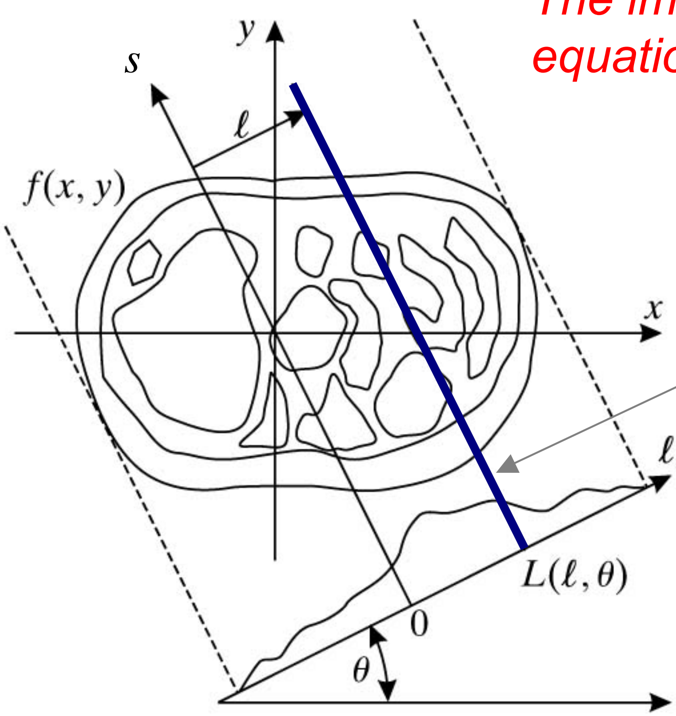


- Nanoparticles having sizes larger than c.a. 5.5 nm (hydrodynamic size) could prohibit rapid renal excretion

2D Image Reconstruction from X-ray Transforms

Mathematical Model

- Many imaging systems acquire *line-integral* data of the object being scanned (or data that can be approximated as line-integrals) often called a line of response



The imaging equation

$$\boxed{g(l,\theta) = \int_{-\infty}^{\infty} f(x(s), y(s))\,ds}$$

The integral is along a line

$$L(l,\theta) = \left\{(x,y)\,\middle|\,x\cos\theta + y\sin\theta = l\right\}$$

With rotated coordinates (l,s)

$$x(s) = l\cos\theta - s\sin\theta$$

$$y(s) = l\sin\theta + s\cos\theta$$

Example

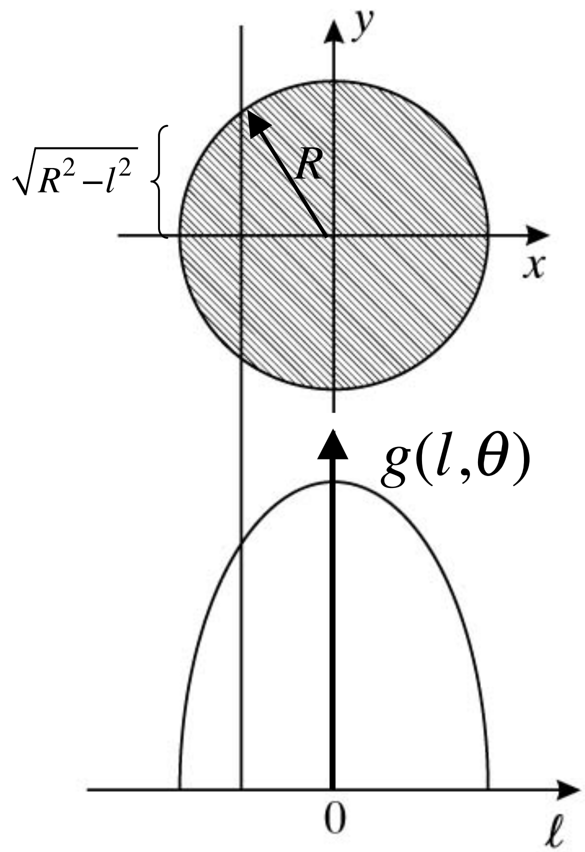
- Consider the unit disk with radius R $\quad f(x,y)=\begin{cases} 1 & x^2+y^2 \le R \\ 0 & \text{otherwise} \end{cases}$

- By geometry

$$g(l,\theta)=\int_{-\infty}^{\infty} f(x(s),y(s))\,ds$$

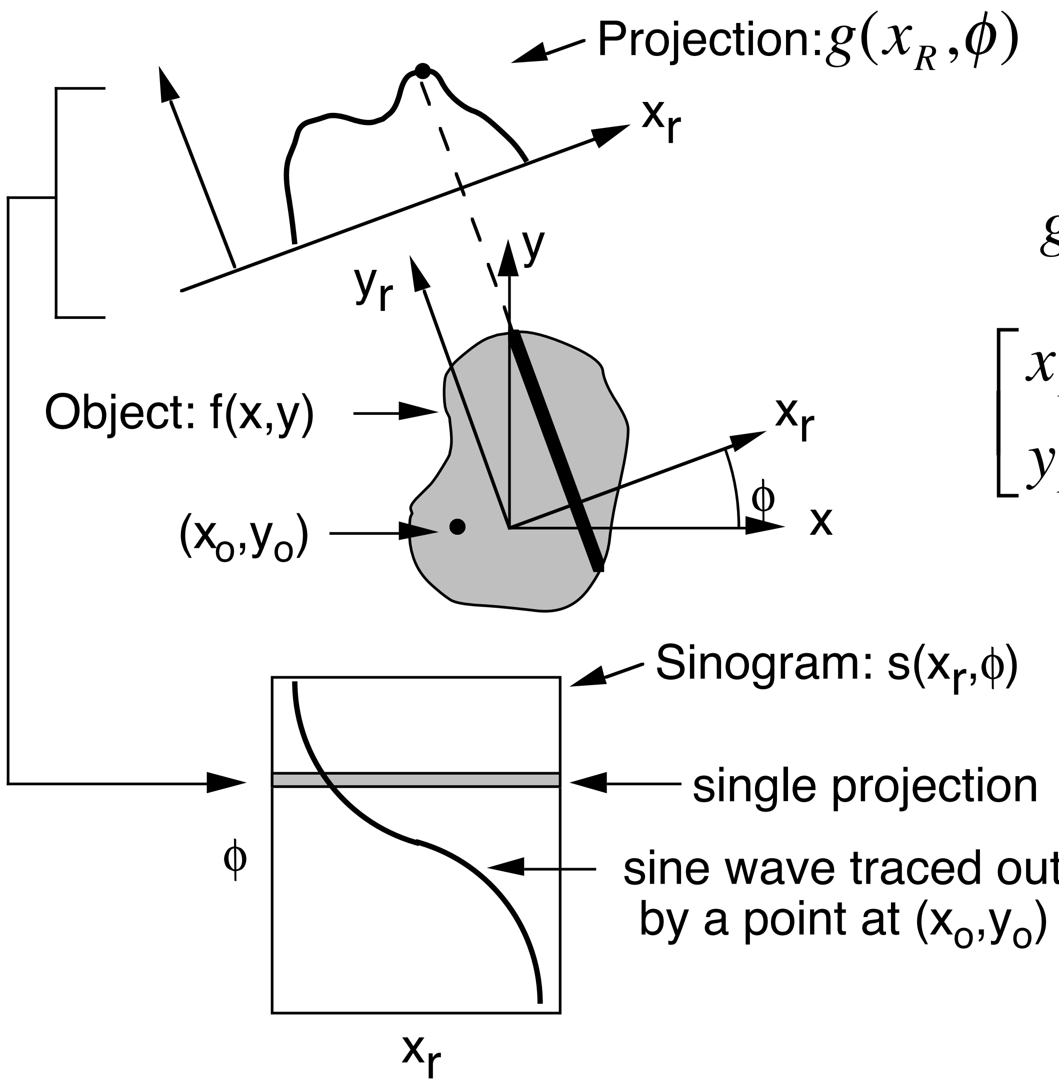
$$=\int_{-\sqrt{R^2-l^2}}^{\sqrt{R^2-l^2}} 1\,ds = 2\int_0^{\sqrt{R^2-l^2}} ds$$

$$=\begin{cases} 2\sqrt{R^2-l^2} & |l|\le R \\ 0 & \text{otherwise} \end{cases}$$



Check: $\quad g(l=0,\theta)=2R, \quad \forall\theta$

One-dimensional projections



$$g(x_R, \phi) = \int_{-\infty}^{\infty} dy_R \, f(x, y)$$

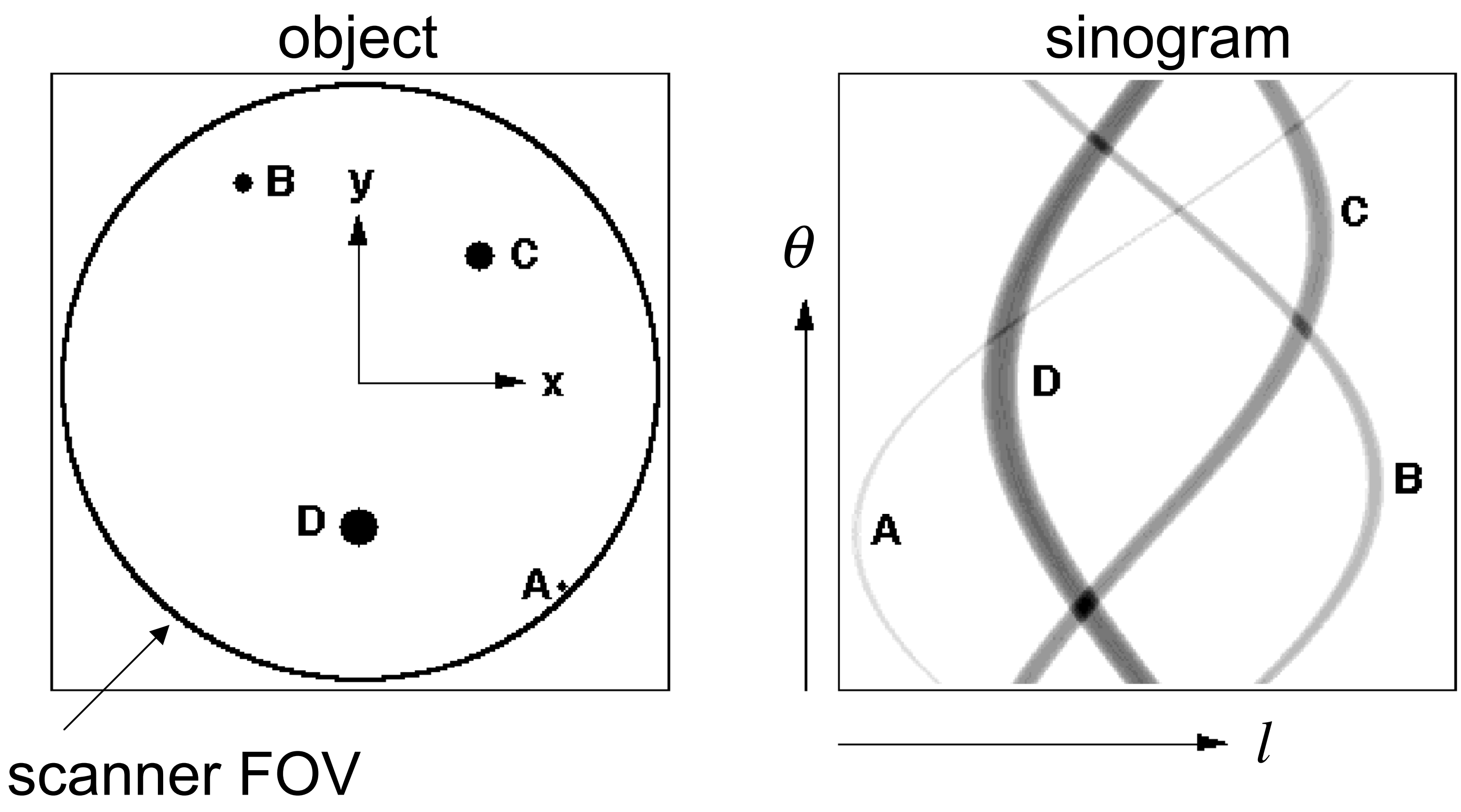
$$\begin{bmatrix} x_R \\ y_R \end{bmatrix} = \begin{bmatrix} \cos\phi & -\sin\phi \\ \sin\phi & \cos\phi \end{bmatrix} \begin{bmatrix} x \\ y \end{bmatrix}$$

To specify the orientation of the line integrals, two parameters are needed, and sets of parallel lines are grouped into projections.

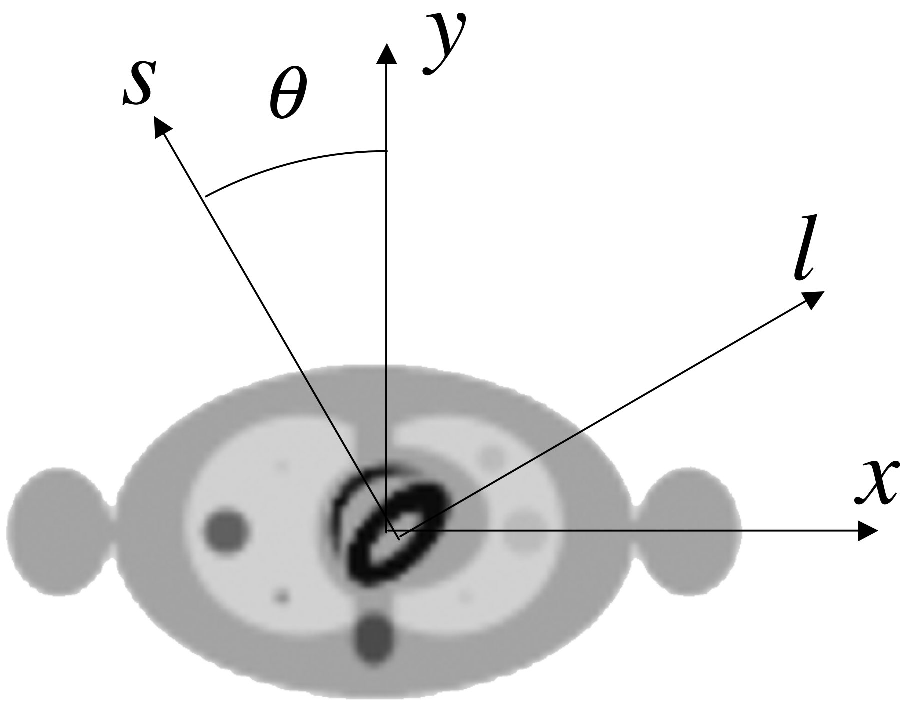
The projections are typically further grouped into sinograms.

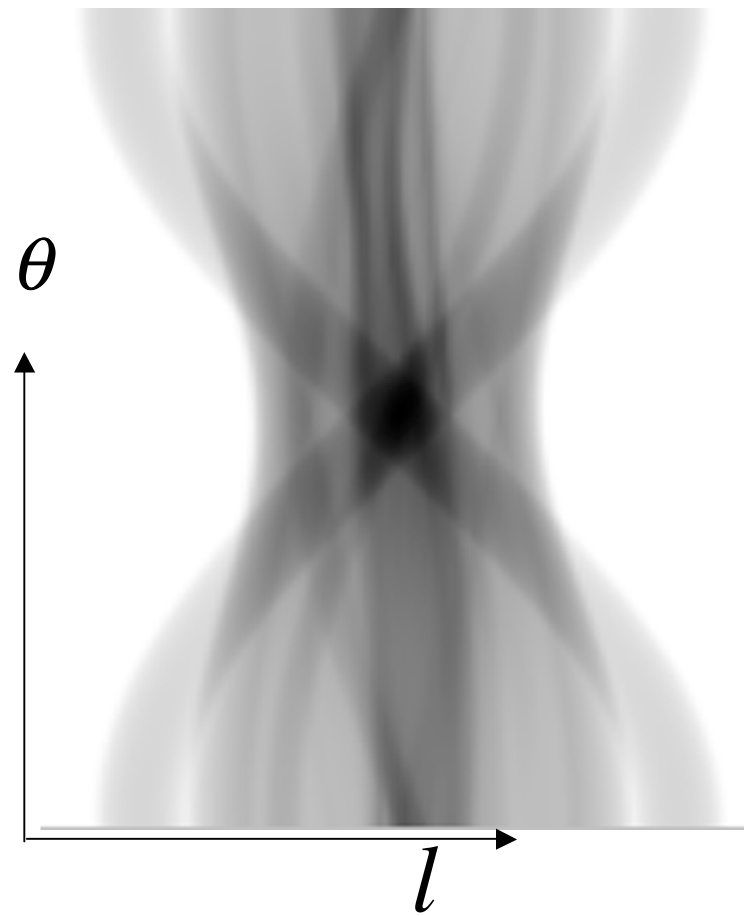
Sinograms

- We can represent the projection data $g(l,\theta)$, as a 2-D image, which is called a sinogram
- Each row is a projection at a fixed angle θ, with an intensity of $g(l,\theta)$
- A point in the object projects to a sine wave in the sinogram



More complex sinogram example





Imaging equation, Inverse Problem, and Image reconstruction

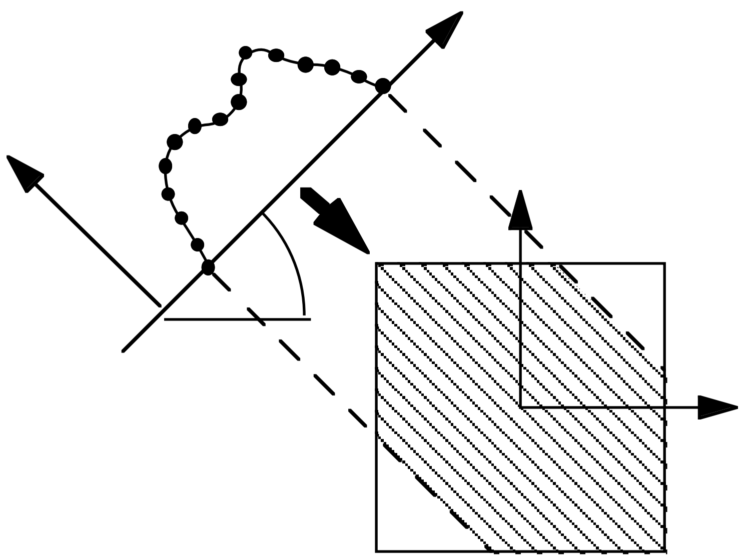
- Our generic imaging system acquires projections, which can be grouped into a sinogram

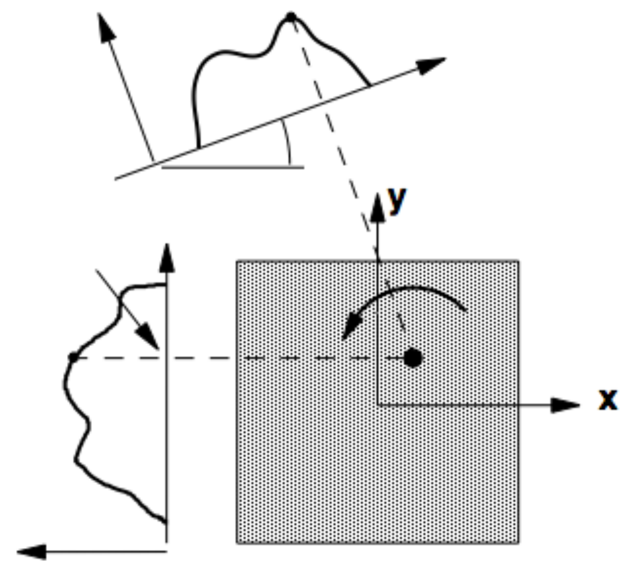
$$g(l,\theta) = \int_{-\infty}^{\infty} f(x(s), y(s))\, ds$$

- The above is an imaging equation
- This is an inverse problem: given $g(l,\theta)$, what is $f(x,y)$?
- In medical imaging this is called image reconstruction

Back-projection (or Backprojection)

- First idea - try the *adjoint* operation to the x-ray transform to see if it gives us the inverse operation (adjoint ~ reverse)
- If the initial operation is integration along a line (2-D to 1-D), then the 'opposite' operation is to spread values back along a line (1-D to 2-D)
- This is called backprojection

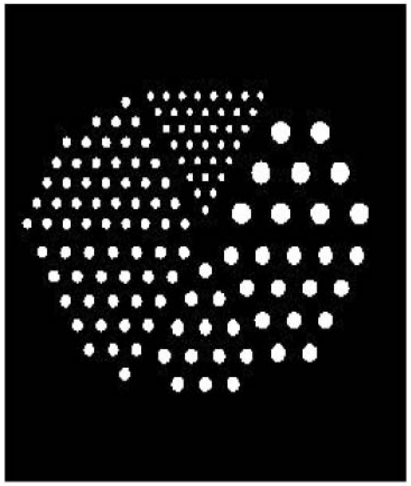


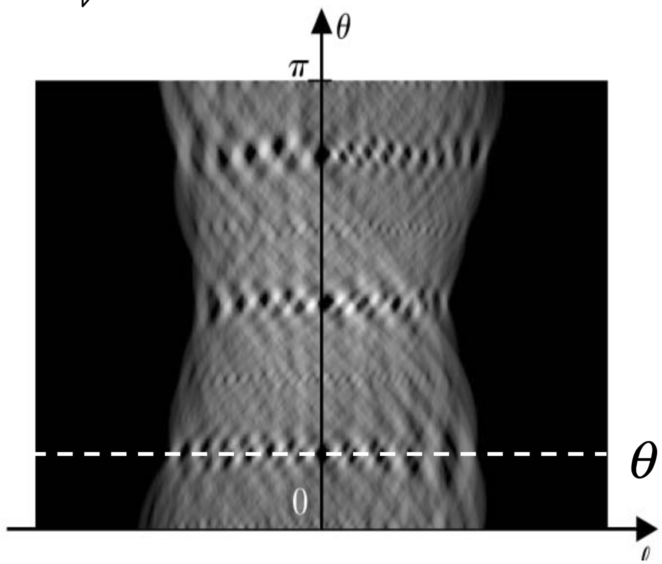


alternative mode of calculation

Backprojection does not work

Original object ⇨ sinogram

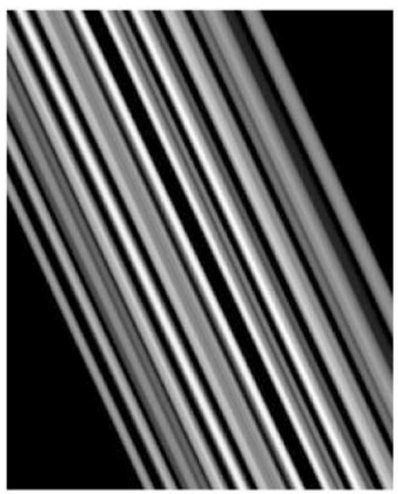




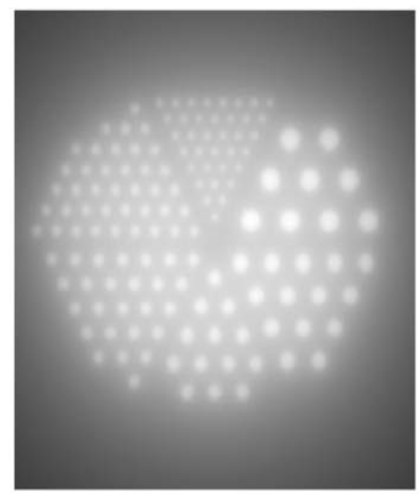
backprojection of $g(l,\theta)$ along angle θ

backprojection for all θ

image matrix

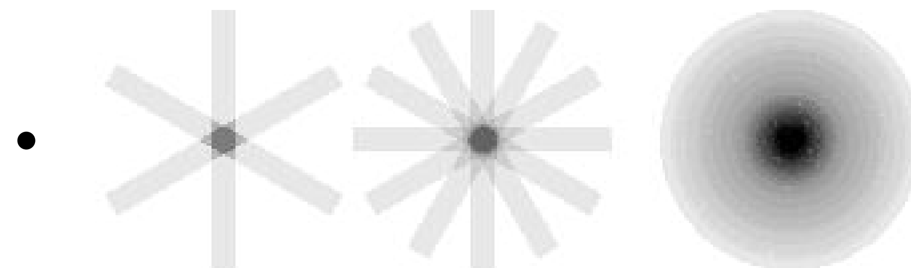


⇨



Backprojection Reconstruction

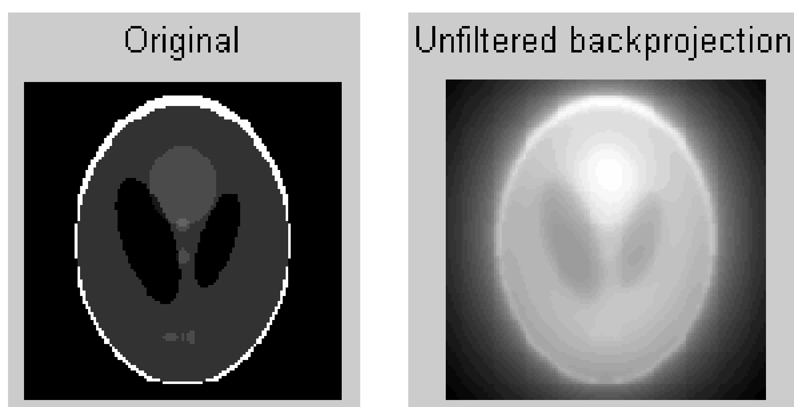
- Backprojection leads to a $1/r$ low-pass filter, so backprojected images are very blurry, and are typically unusable
- Examples
  - illustration for a small source



object 3 6 many

# of projections

  - for a more realistic object

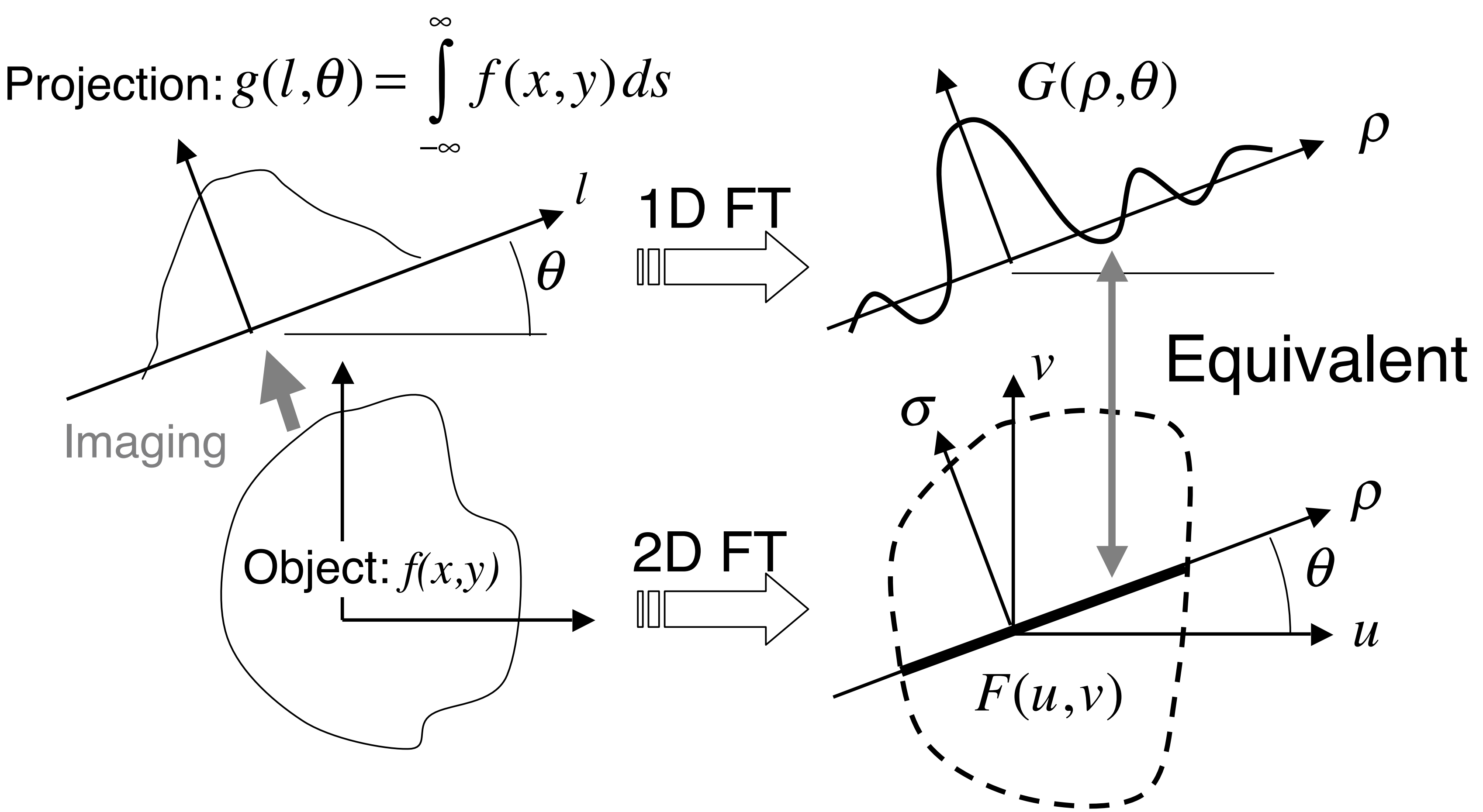


Shepp-Logan
head phantom

Projection-Slice Theorem

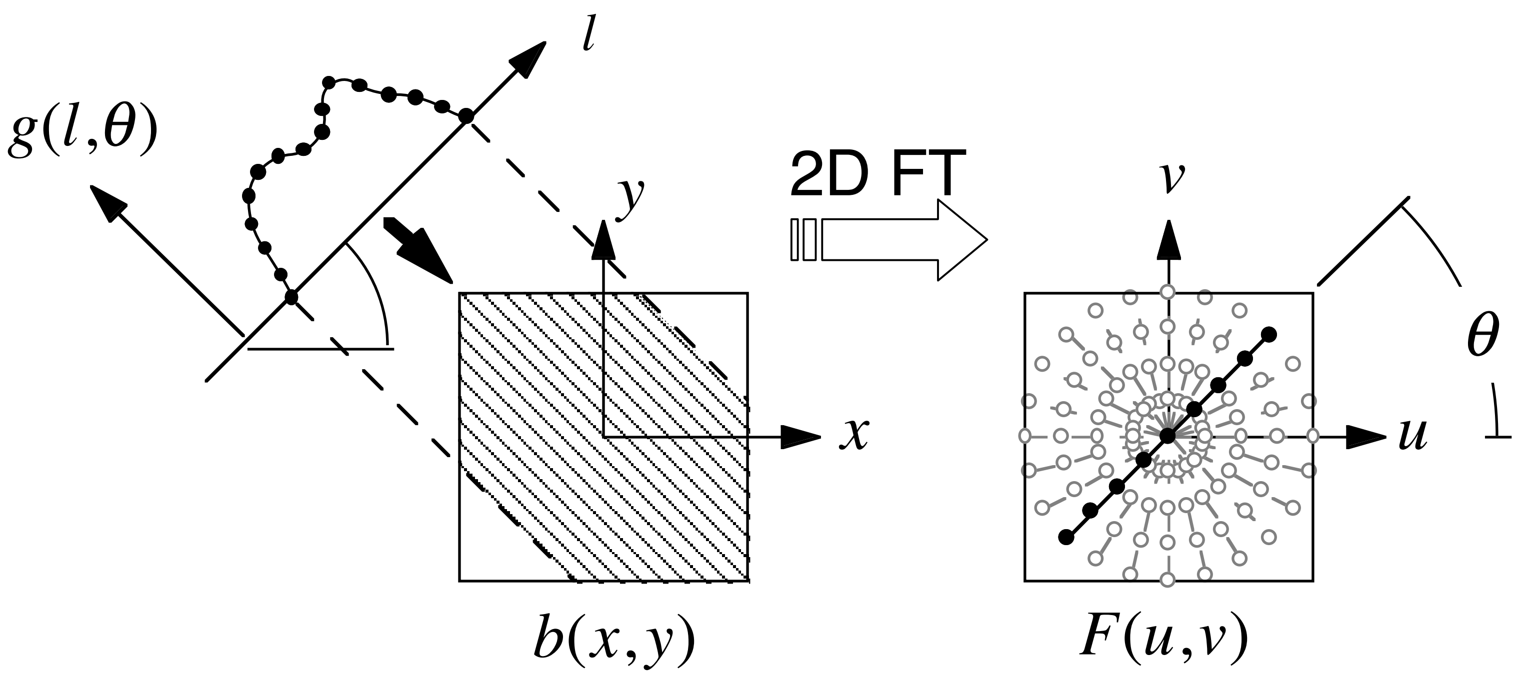
Projection-Slice Theorem

- The simplest way to understand 2-D image reconstruction, and a good way to start understanding 3-D image reconstruction.



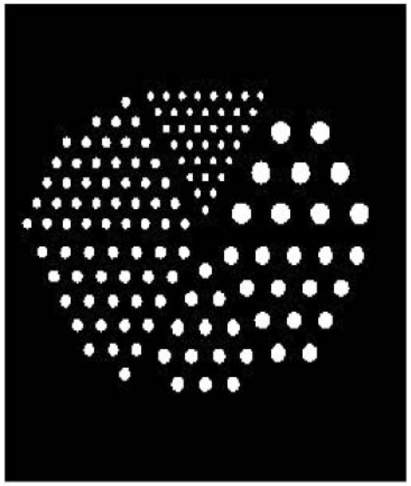
Backprojection Revisited

- By a corollary of the projection-slice theorem, backprojection is equivalent to placing the Fourier transformed values into an array representing $F(u,v)$, as shown

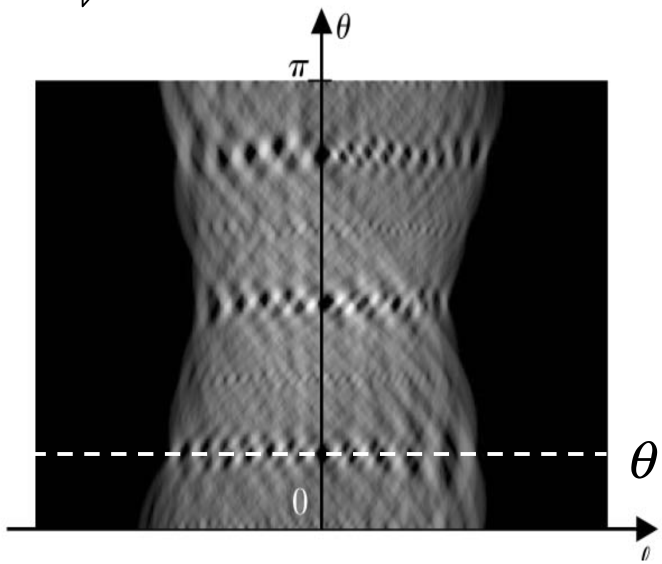


This is why backprojection does not work

Original object



sinogram



$$
\begin{aligned}
b(x,y) &= f(x,y) * h(x,y) \\
&= f(x,y) * \frac{1}{r} \\
&= f(x,y) * \frac{1}{\sqrt{x^2 + y^2}}
\end{aligned}
$$

backprojection of $g(l,\theta)$ along angle θ

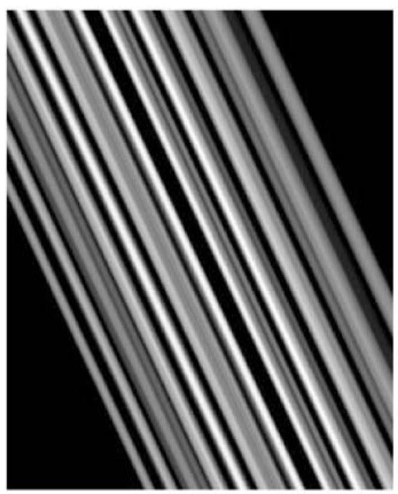
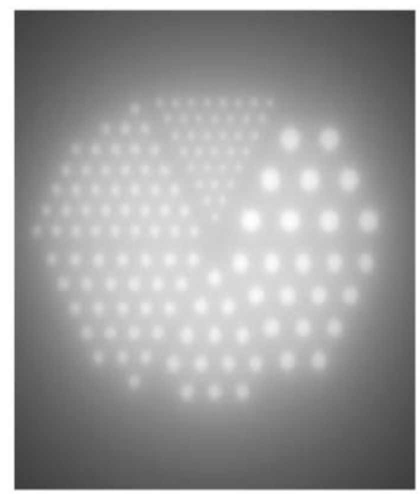


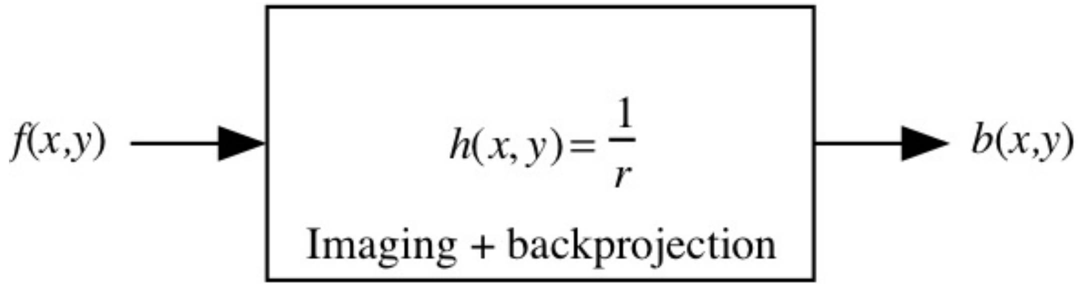
image matrix

backprojection for all θ

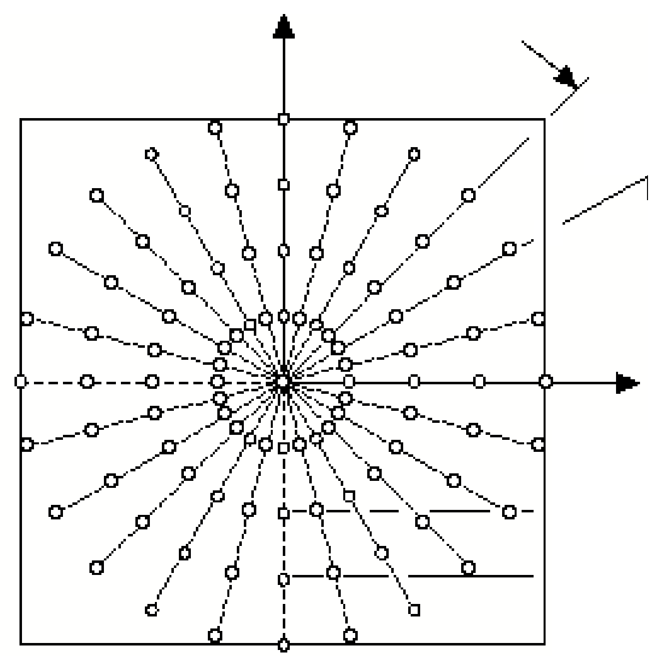


Backprojection Reconstruction

- Thus the backprojection of X-ray transform data comprises a shift-invariant imaging system blurred with a $1/r$ function

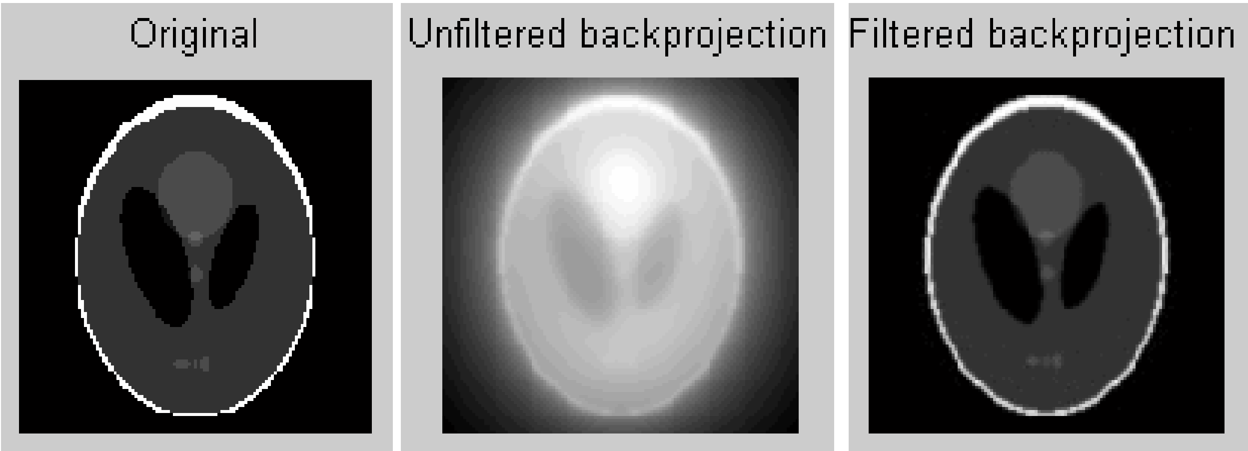


- This can also be seen intuitively by considering the sampling of the Fourier transform of the backprojected image
- In the limiting case the sampling density in frequency space is proportional to $1/q$



Backprojection Filtering

- We can fix this! Recall that $B(u,v) = F(u,v)/q$
  so very simply $F(u,v) = qB(u,v)$
- *Backprojection Filtering Algorithm*
  - for each θ, backproject measured data $g(l,\theta)$ into image array $b(x,y)$
  - compute the 2-D Fourier transform $B(u,v)$
  - multiply by 2-D 'cone' filter $q = \sqrt{u^2 + v^2}$ to get $F(u,v)$
  - compute the inverse 2-D Fourier transform to get $f(x,y)$

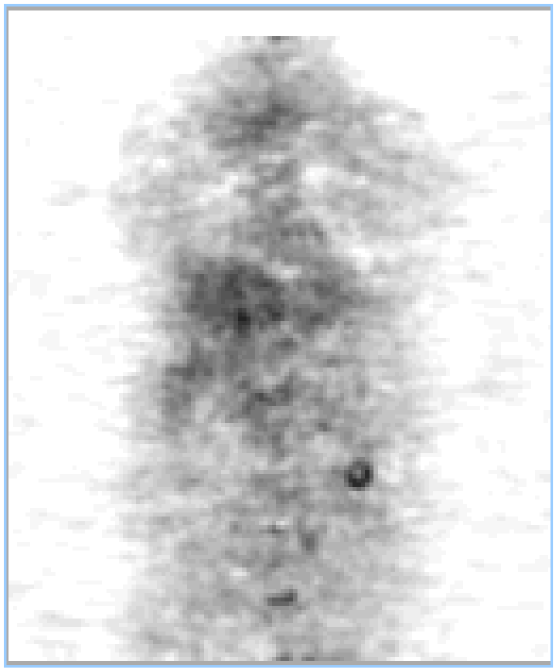


Challenges with Backprojection Filtering

- The low-pass blurring operation of $1/q$ has very long tails, so backprojection must be done on a much larger array than is needed for just the image
- Backprojection filtering is computationally very expensive
  - CT images are typically 512 x 512, and a typical factor of 4 needed will bring backprojection image size to 2048 x 2048, and another factor of 2 for zero padding for FFTs gets us to 4096 x 4096, per image
- An alternative solution is to interchange order of filtering and backprojection
  - the proof that we can do this is a bit complex

Image Quality

Image quality assessment



Question: which is a better image?

Answer: what are you trying to do?

Image Quality

Image quality, for the purposes of medical imaging, can be defined as the ability to extract desired information from an image

- Harrison H. Barrett *PNAS, 1993*

- "Task-based" definition of Image quality

Methods of determining imaging quality

- Six important factors
  1. Contrast
  2. Resolution
  3. Noise
  4. Accuracy
     a) quantitative accuracy
     b) diagnostic accuracy
  5. Artifacts
  6. Distortion

Contrast

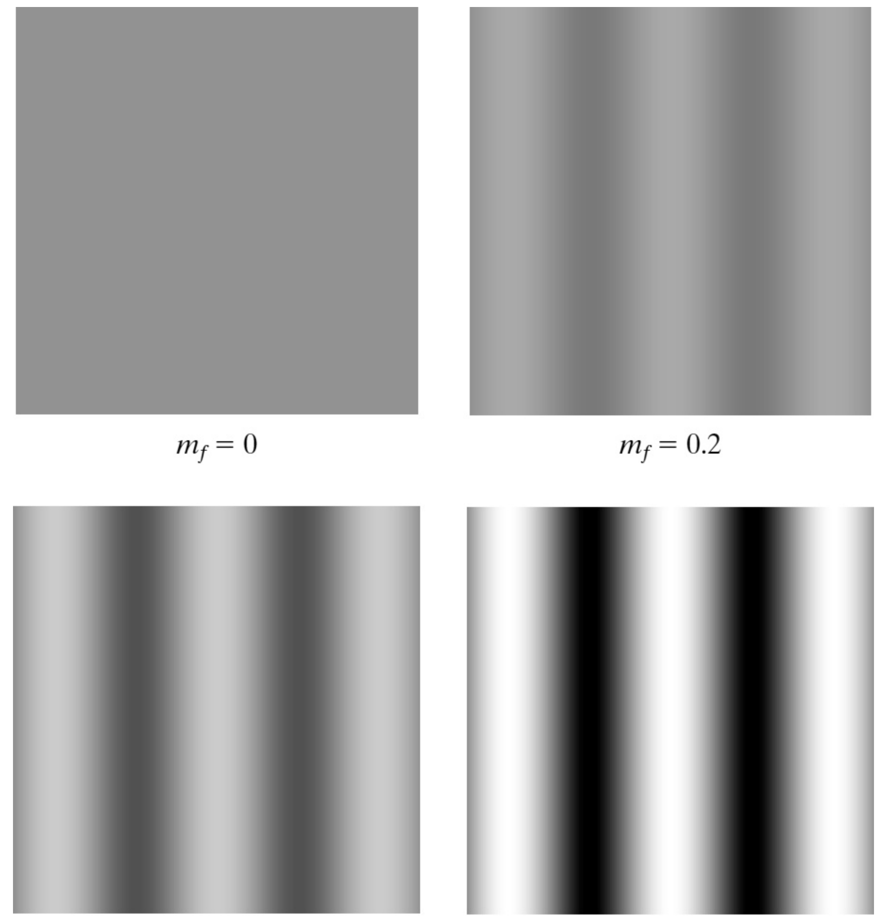
- Define modulation $m_f = \dfrac{f_{\text{MAX}}(x,y) - f_{\text{MIN}}(x,y)}{f_{\text{MAX}}(x,y) + f_{\text{MIN}}(x,y)}$

- Suppose

$$f(x,y) = A + B\sin(2\pi u_0 x)$$

$$\text{if } A \geq B > 0, \quad \text{then} \quad m_f = \frac{B}{A}$$

- Increasing modulation
  = increasing contrast



$m_f = 0$ $m_f = 0.2$

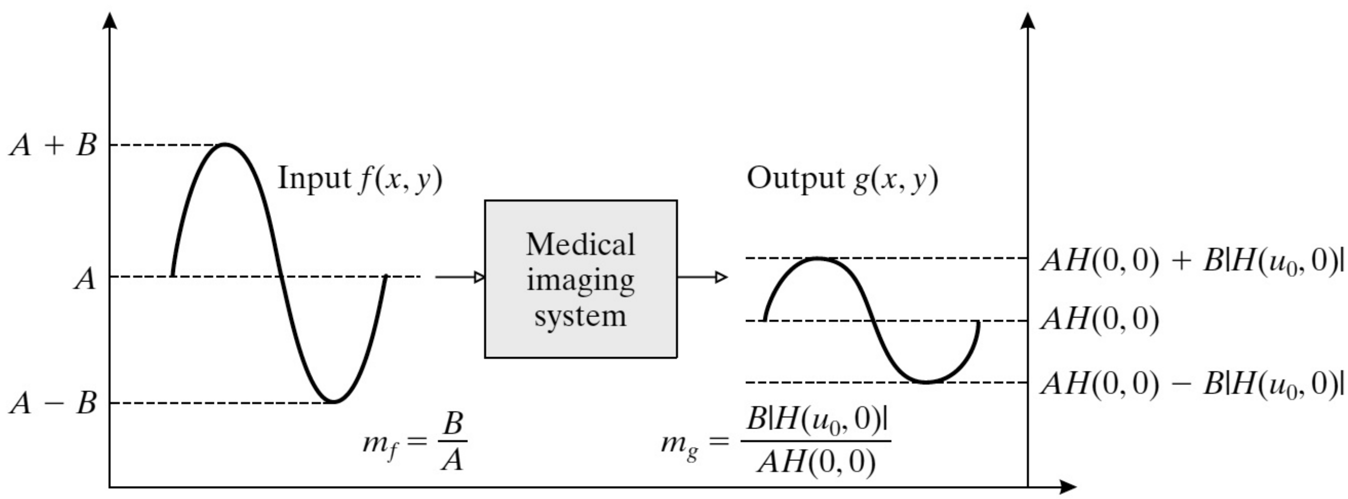
$m_f = 0.5$ $m_f = 1$

Modulation Transfer Function

- For a linear shift-invariant (LSI) system, define the Modulation Transfer Function (MTF) as the ratio of the output modulation to the input modulation

$$\mathrm{MTF} = \frac{m_g}{m_f}$$

- If the PSF is $h(x,y) = \mathscr{F}_{2D}^{-1}\{H(u,v)\}$
- Then $\mathrm{MTF}(u,v) = \dfrac{m_g}{m_f} = \dfrac{|H(u,v)|}{H(0,0)}$

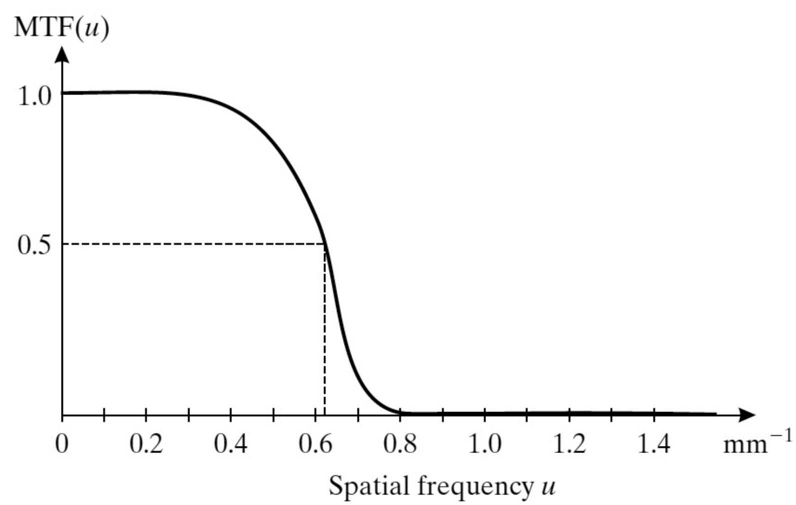


Modulation Transfer Function

- The Modulation Transfer Function quantifies the degradation in contrast as a function of frequency

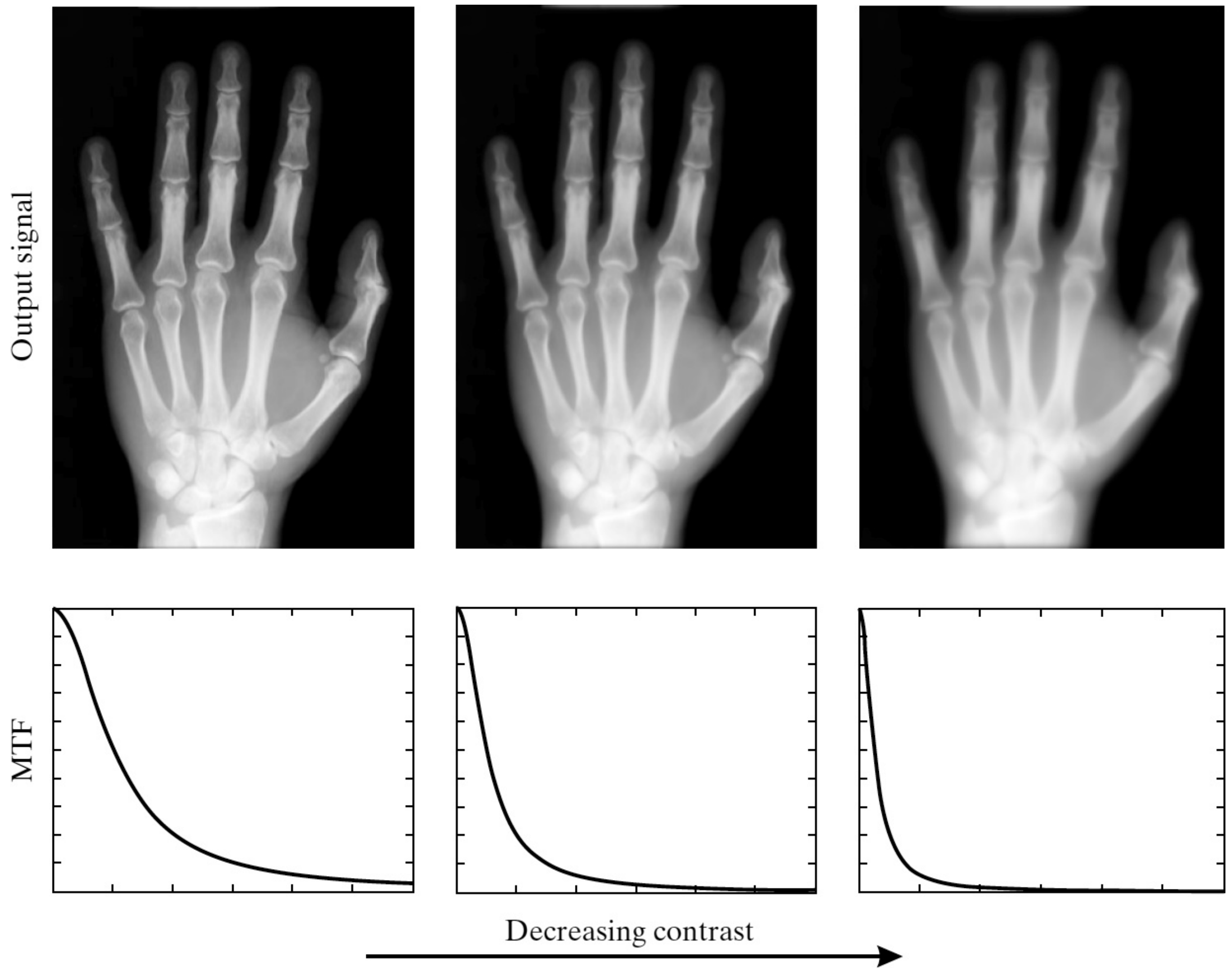
- Typically $0 \leq \mathrm{MTF}(u,v) \leq \mathrm{MTF}(0,0) \leq 1$

- I.e. as frequency increases there is less contrast information transferred



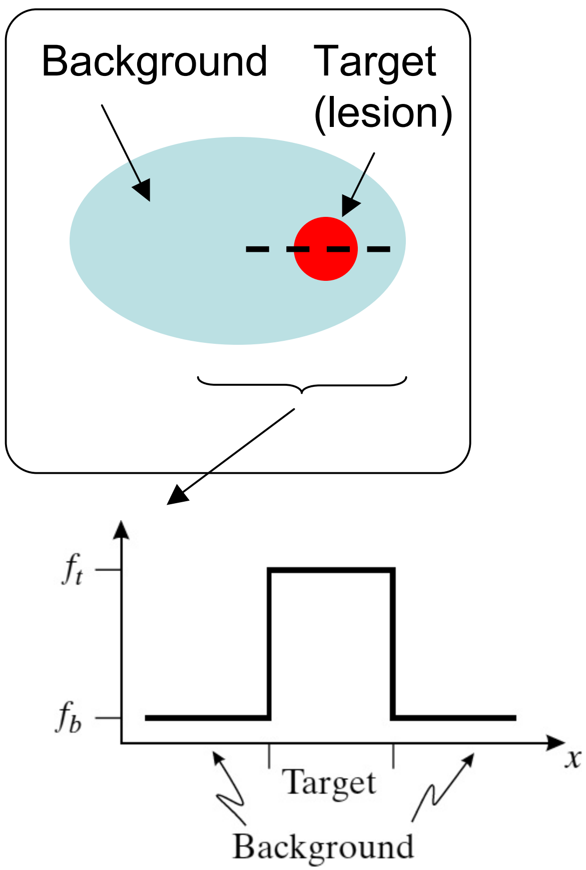
Modulation Transfer Function

- Loss of contrast at higher frequencies is equivalent to blurring



Local Contrast

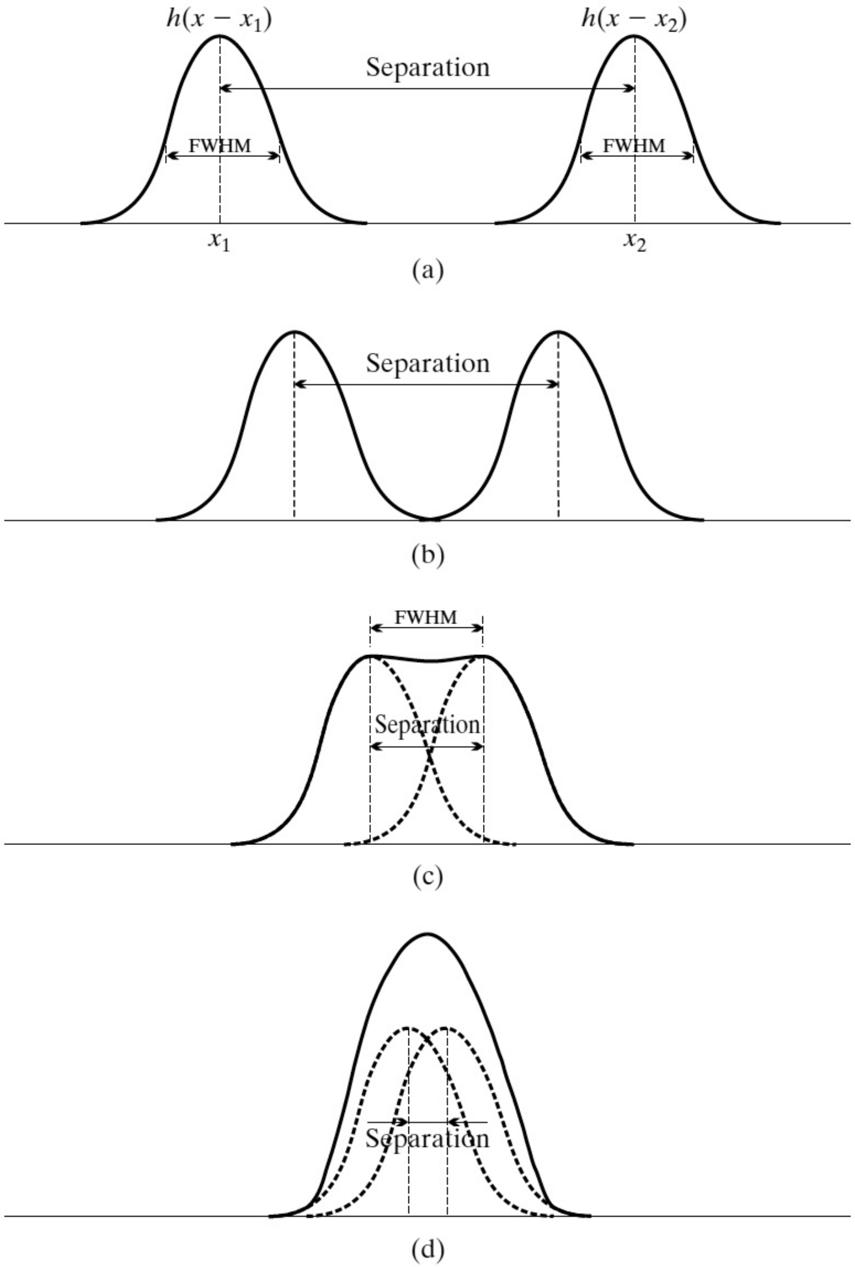
- MTF is valid for sinusoidal objects
- For localized objects, we can use <u>local contrast</u>



$$C = \frac{f_T(x,y) - f_B(x,y)}{f_B(x,y)}$$

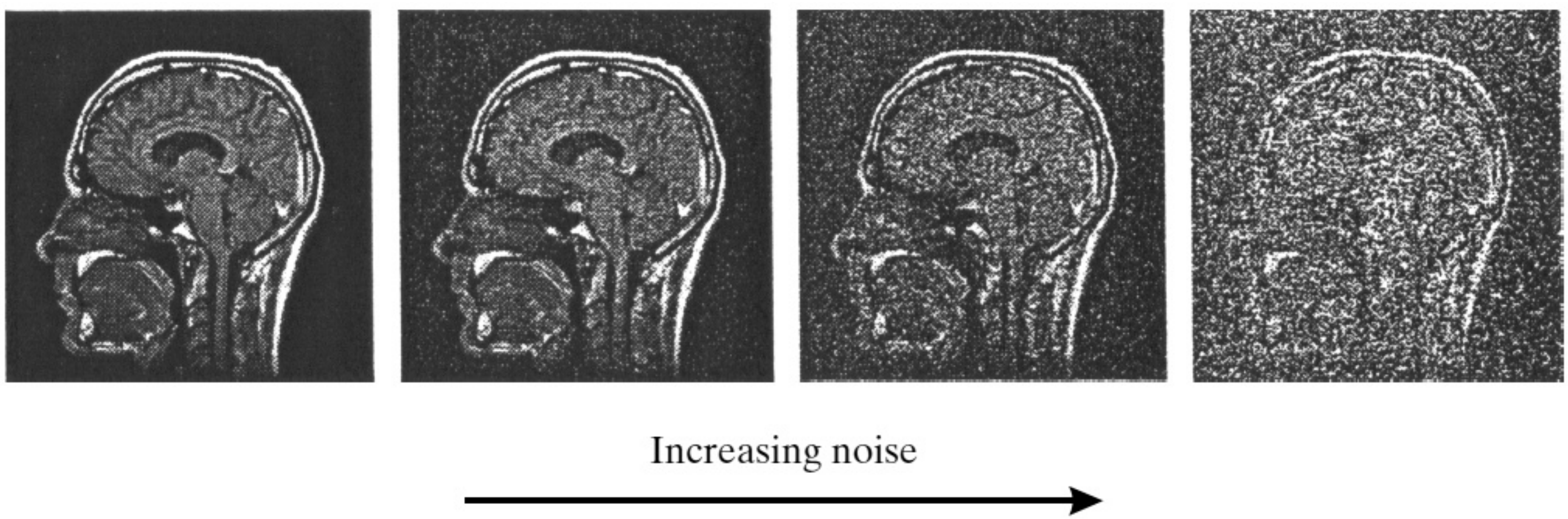
Resolution

- Defined as the ability to accurately depict two distinct events in space, time, or frequency as separate
- The full-width at half-maximum (FWHM) is the minimum distance for the two points to be separable
- A decrease in FWHM is an increase in resolution



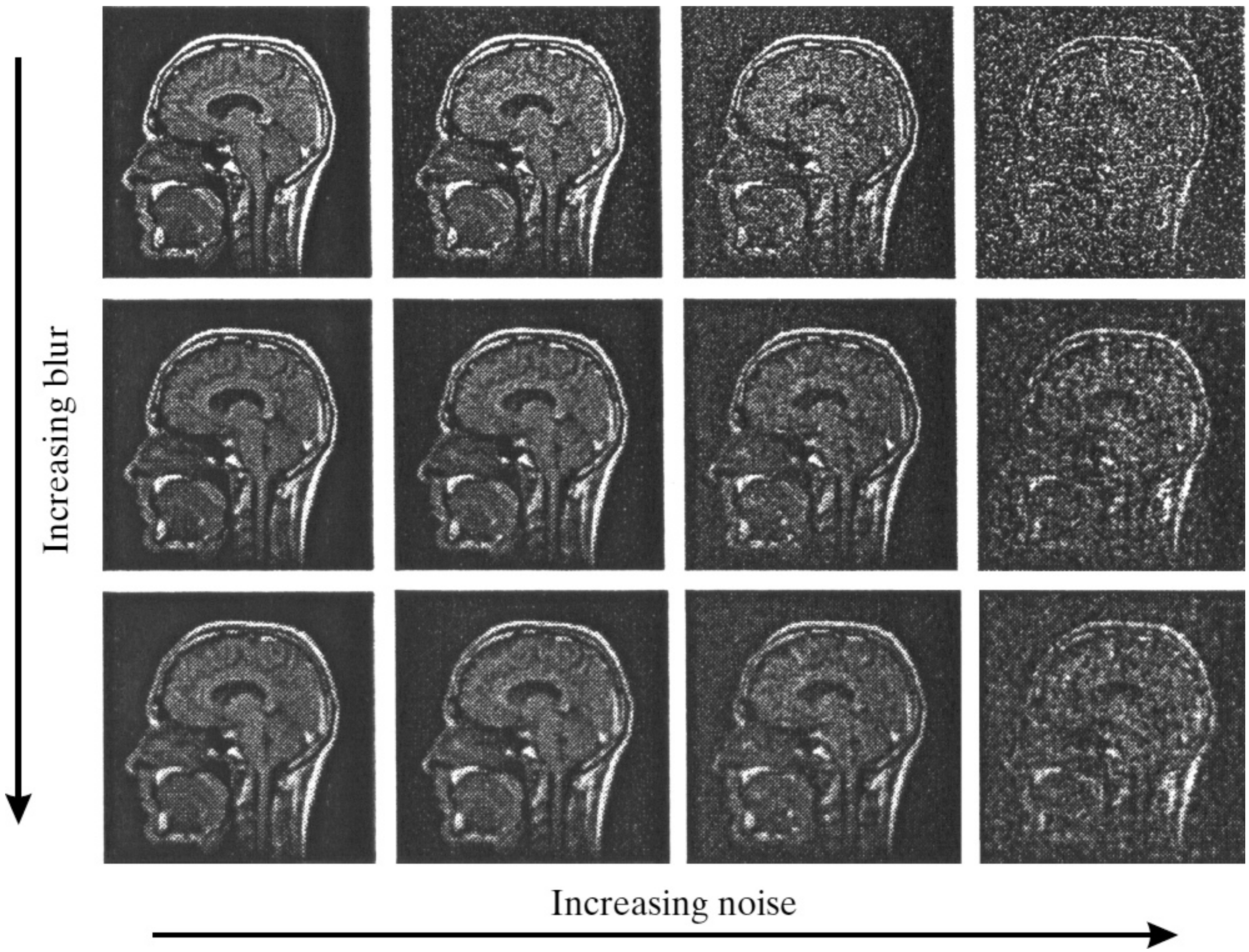
Noise

- Source and type of noise depends on the physics of the imaging system
- Noise is a degrading effect



Signal to Noise Ratio

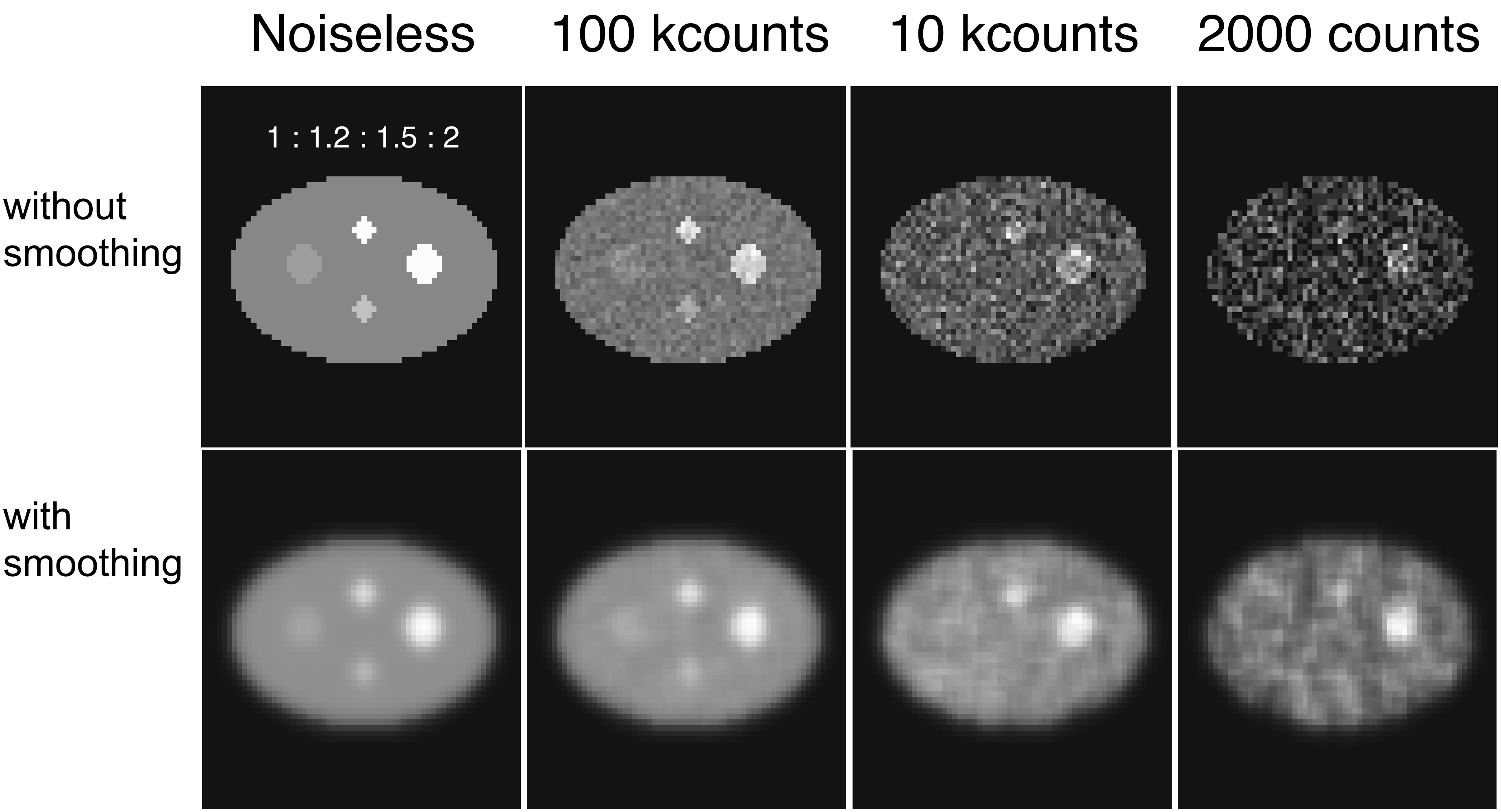
- When we reduce noise, we reduce contrast (or resolution)
- Evaluate overall effect through the signal-to-noise ratio (SNR)



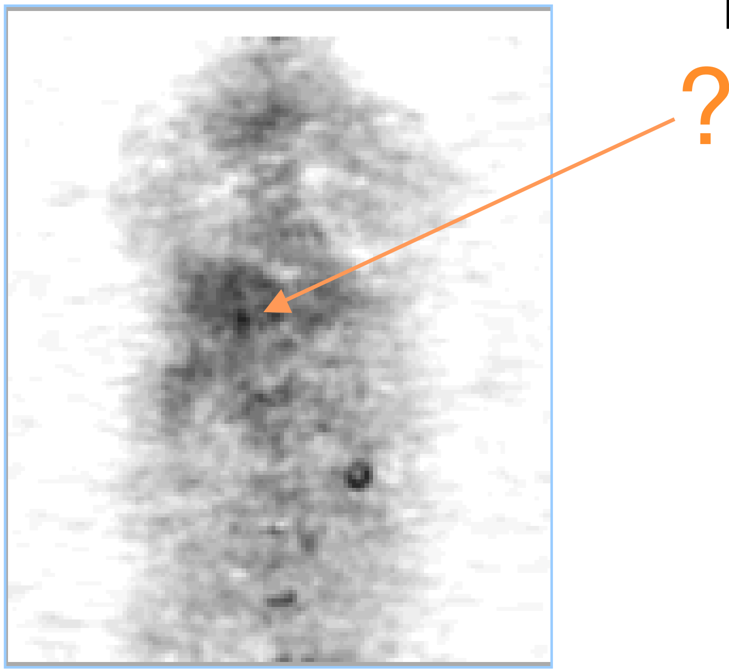
Signal to Noise Ratio

- Exact form of SNR depends on the physics of the imaging system (since noise does)
- Two common forms:
  - Amplitude SNR $$SNR_A = \frac{\text{Amplitude}\{f(x,y)\}}{\text{Amplitude}\{N(x,y)\}}$$
  - Power SNR $$SNR_P = \frac{\text{Power}\{f(x,y)\}}{\text{Power}\{N(x,y)\}}$$

Detectability: Is it there?

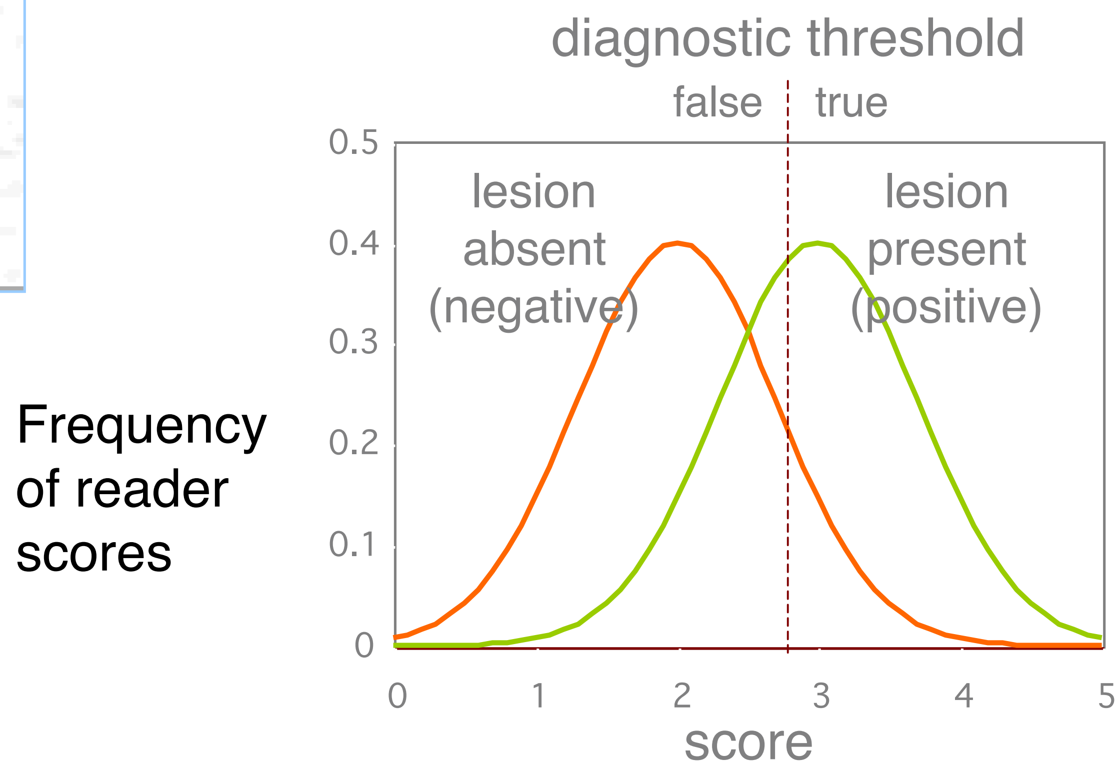


Quantifying Detection Performance

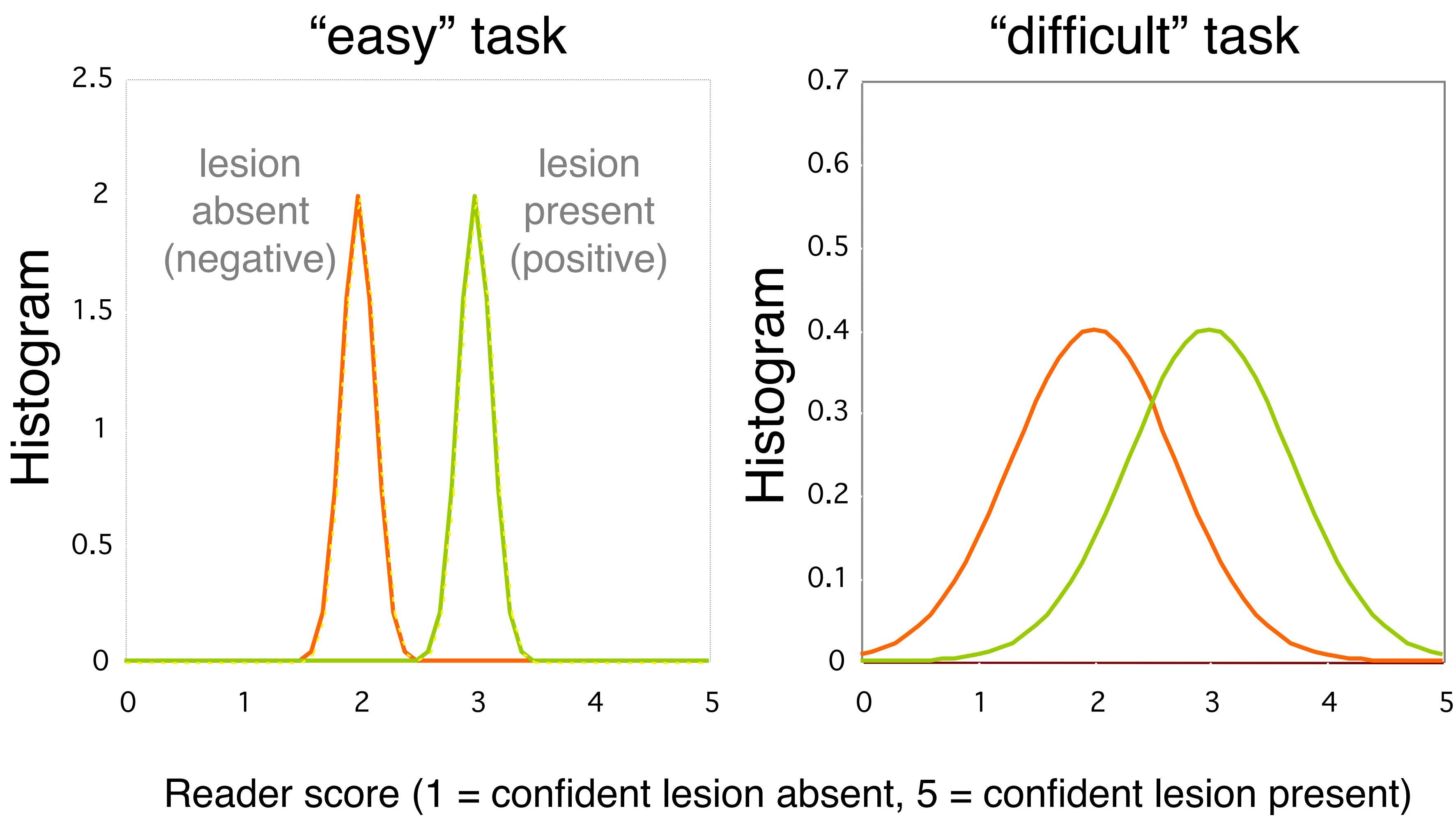


Possible method of reader scoring:

1 = confident lesion absent
2 = probably lesion absent
3 = possibly lesion absent
4 = probably lesion present
5 = confident lesion present



Class Separability (e.g. detectability)



Quantifying Detection Performance

Is the object present?

Does the observer say the object is present?		Positive	Negative
	True	True Positive (TP)	False Positive (FP)
	False	False Negative (FN)	True Negative (TN)

Key concepts

- Sensitivity: True positive fraction

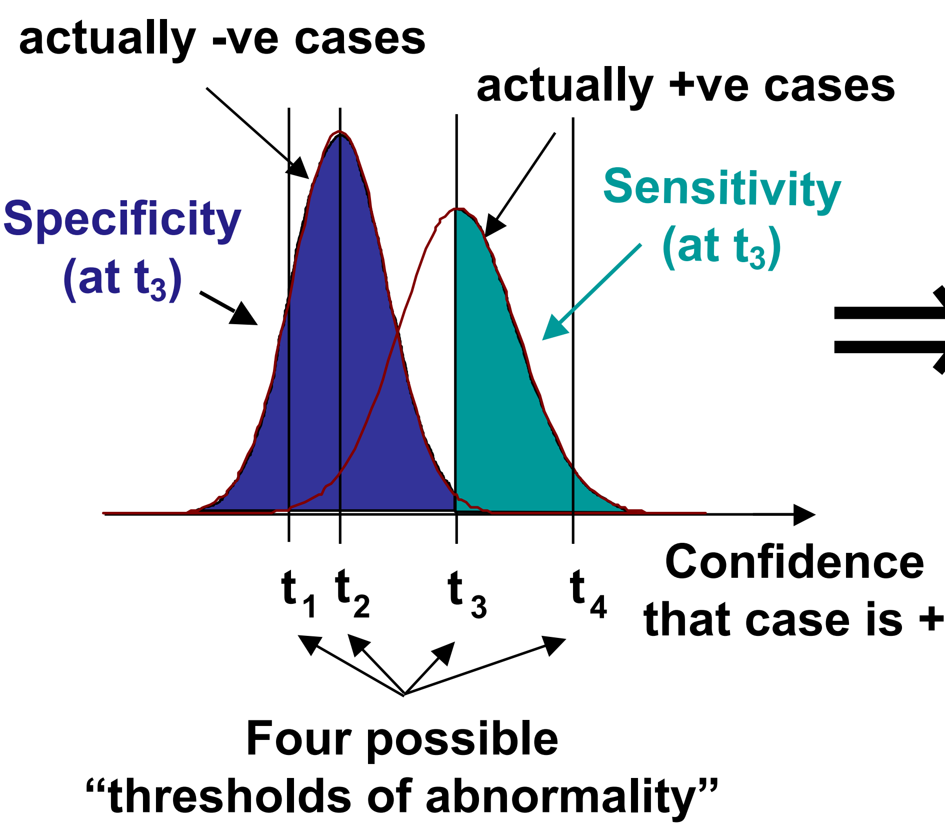
  (TPF) = TP/(TP + FN) = TP/P
- Specificity: True negative fraction

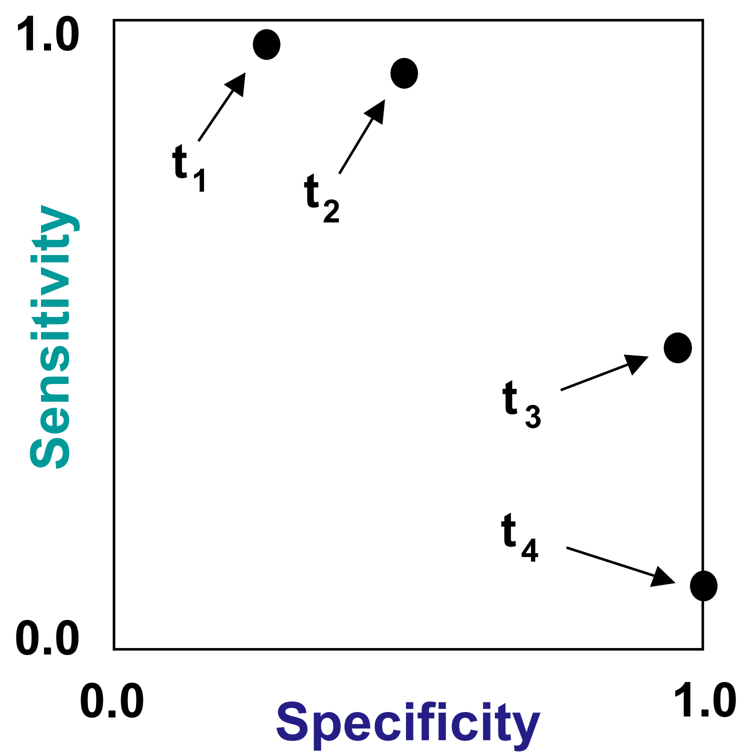
  (TNF) = TN/(TN + FP) = TN/N
- Accuracy = (TP + TN) / (P + N)

Is the object present?

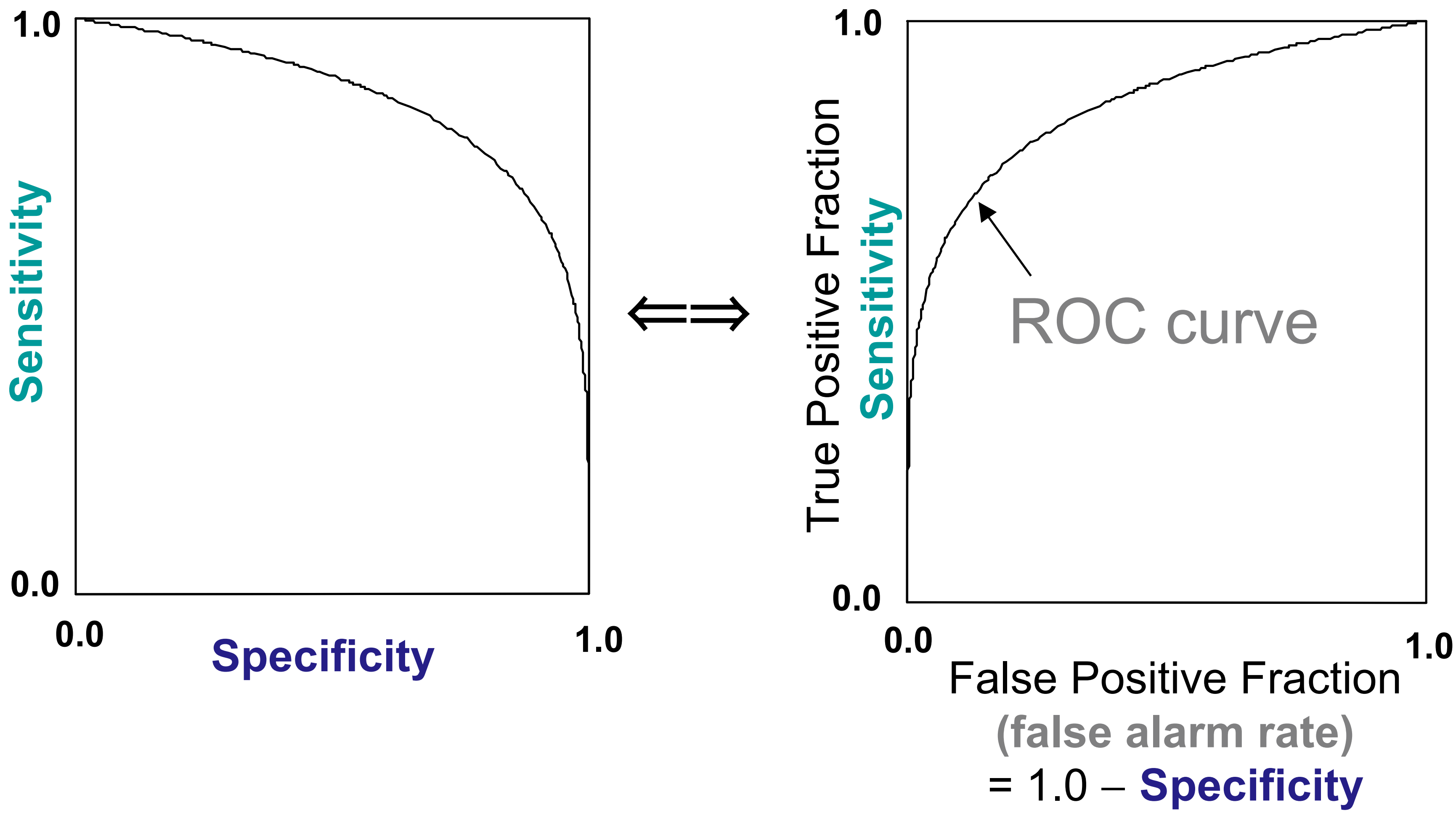
	Positive	Negative
True	True Positive (TP)	False Positive (FP)
False	False Negative (FN)	True Negative (TN)

Dependence of Sensitivity and Specificity on “threshold of abnormality”:

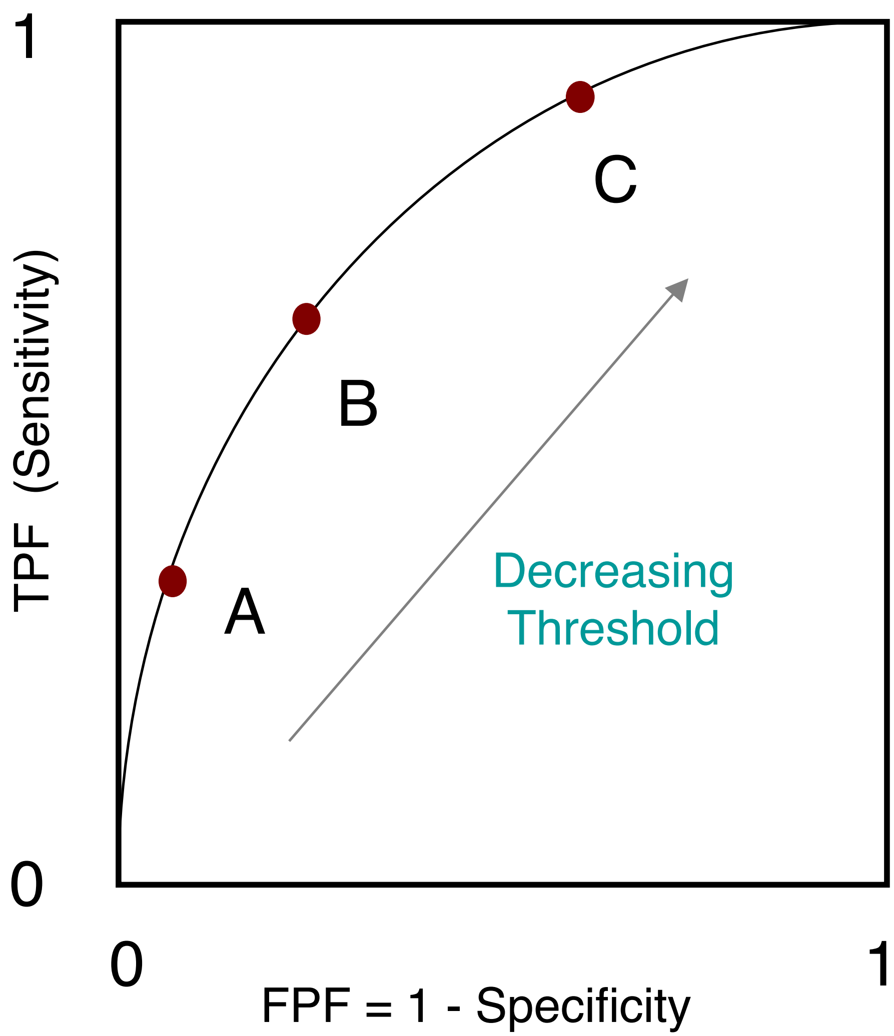




Reciever Operating Characteristic (ROC) Curve

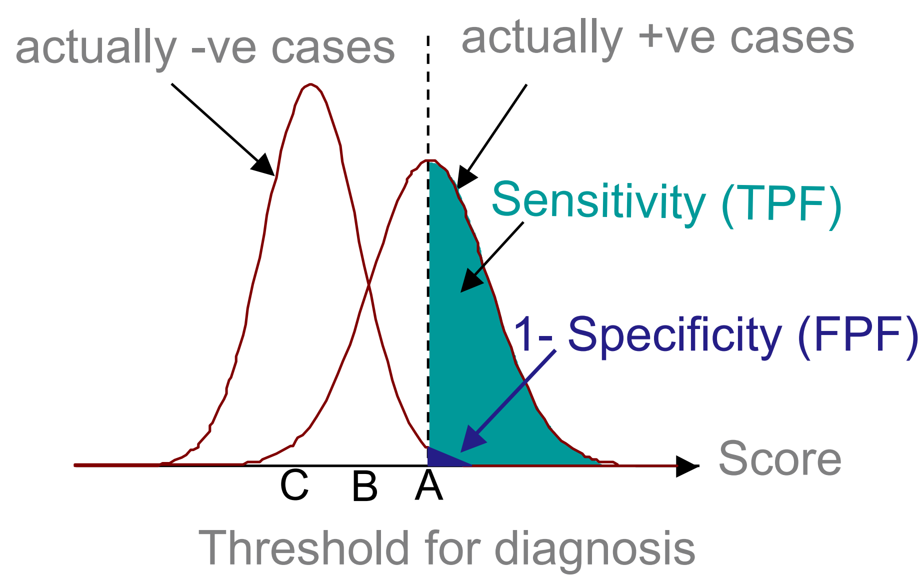


The ROC Curve

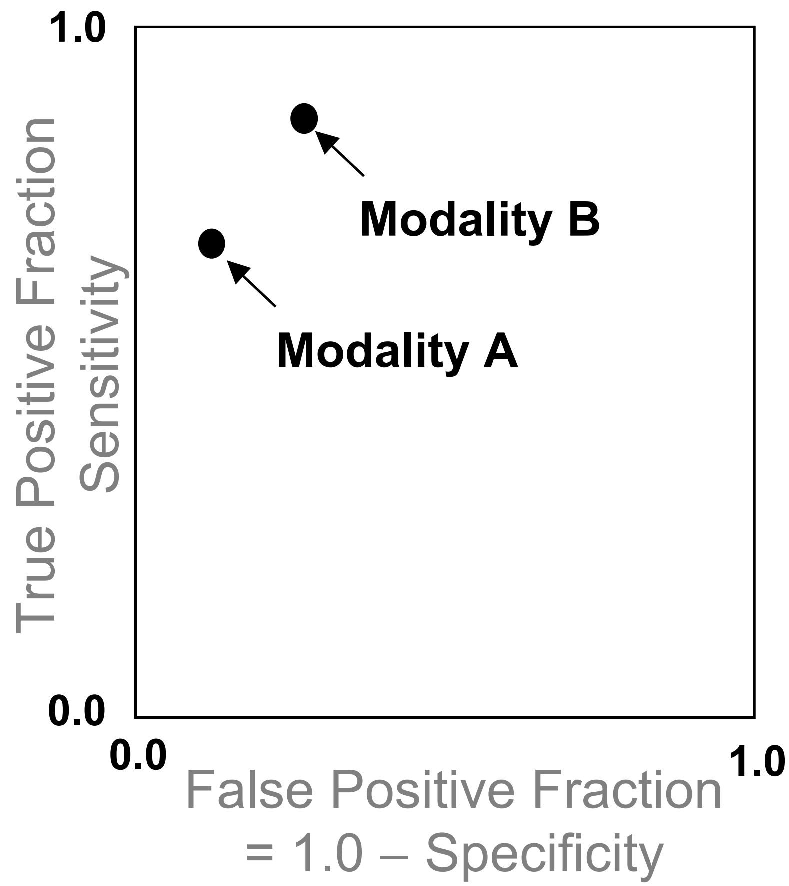


Points A, B, & C correspond to different thresholds

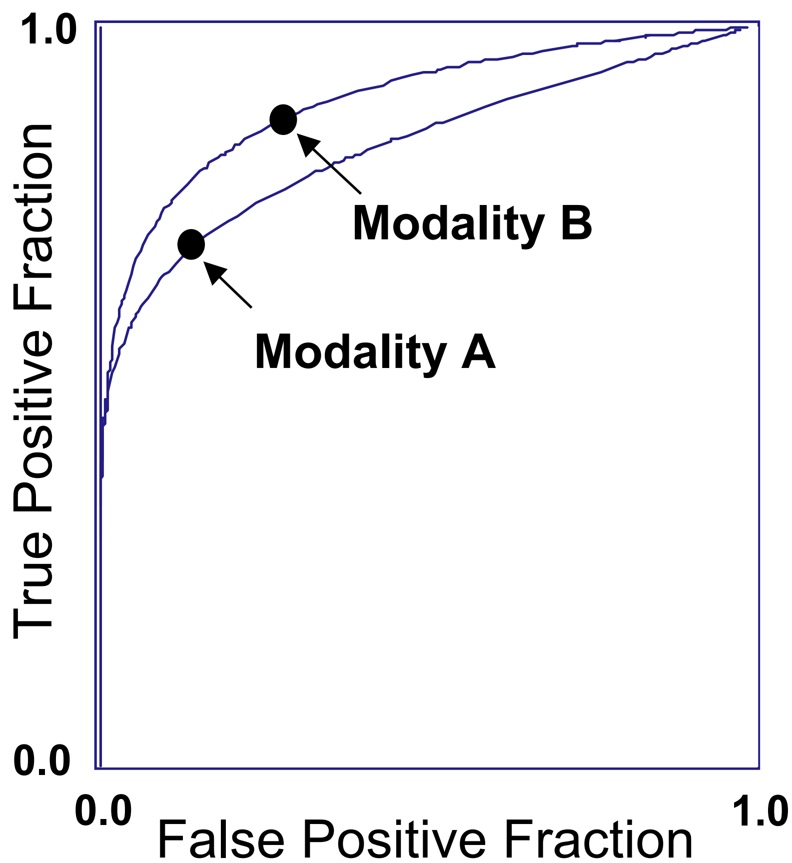
Note, for example, it is always possible to make sensitivity = 1 if the threshold is low enough!



A dilemma: Which modality is better?



The dilemma is resolved after ROCs are determined (one possible scenario):

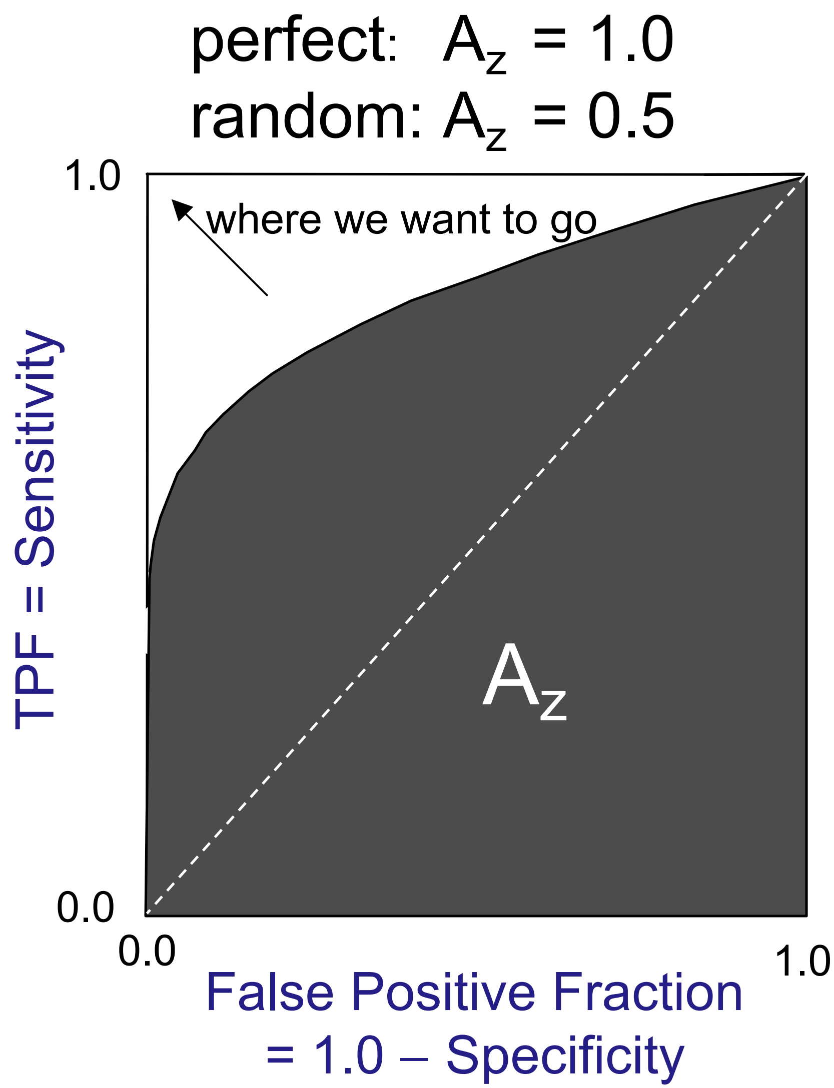


Conclusion:

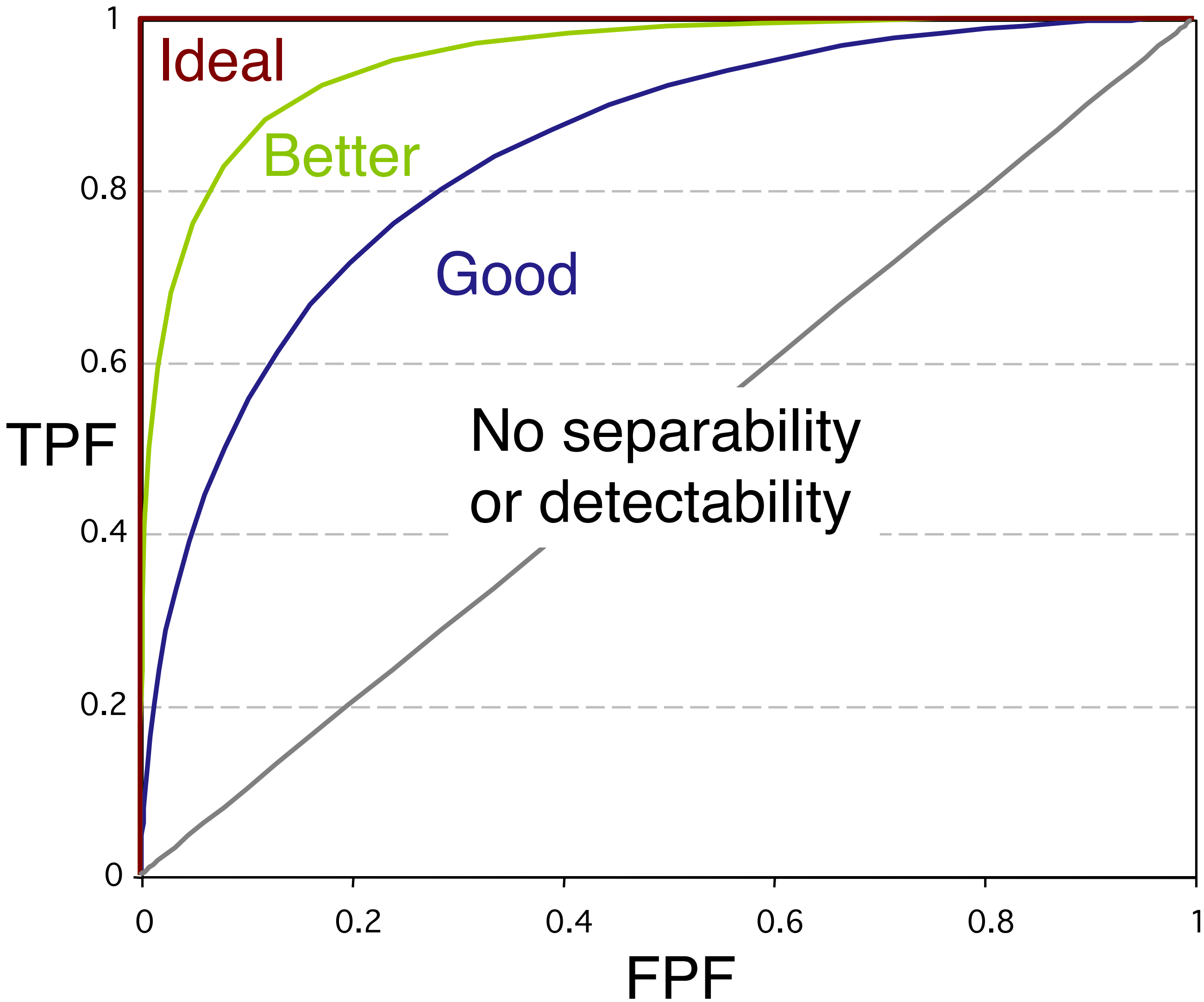
Modality B is better, because it can achieve:

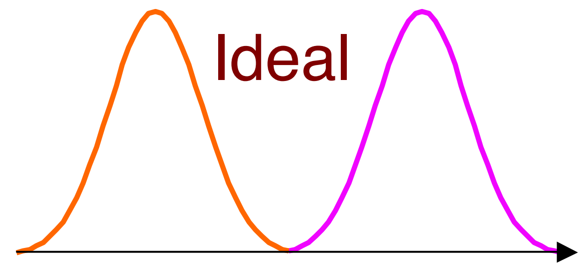
- higher TPF at same FPF, or
- lower FPF at same TPF

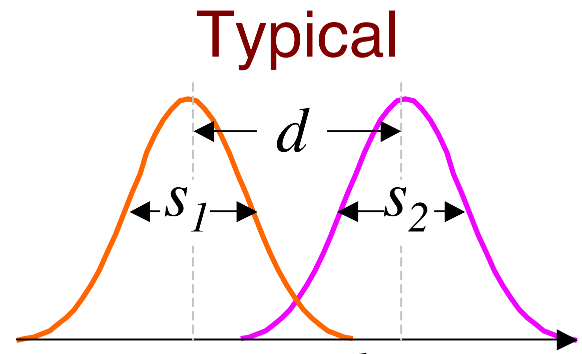
The ROC Area Index (A_z)



Comparing Imaging Systems







$$SNR = \frac{d}{\sqrt{\left(s_1^2 + s_2^2\right)/2}}$$

(SNR for detection task)