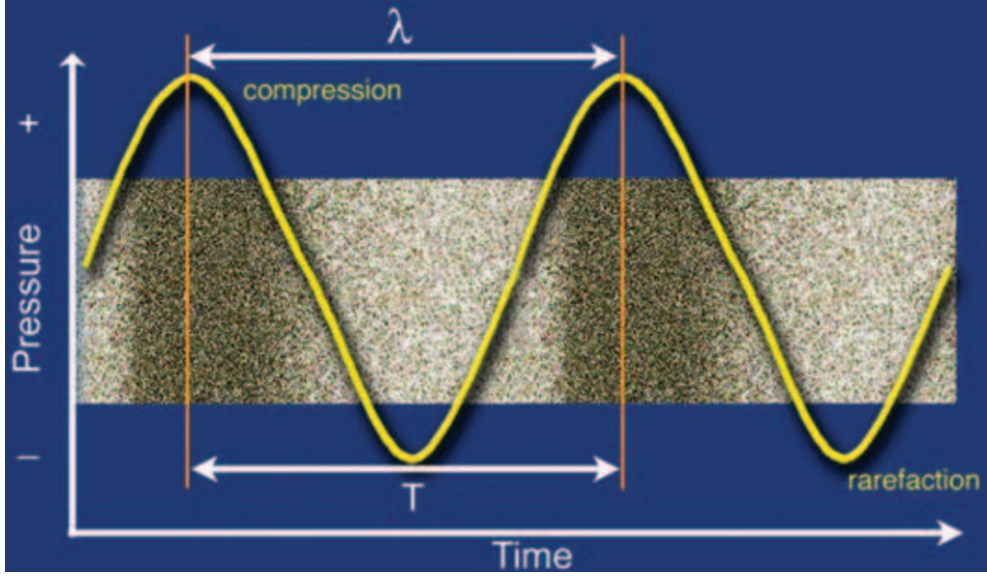
CS463/516

Lecture 7

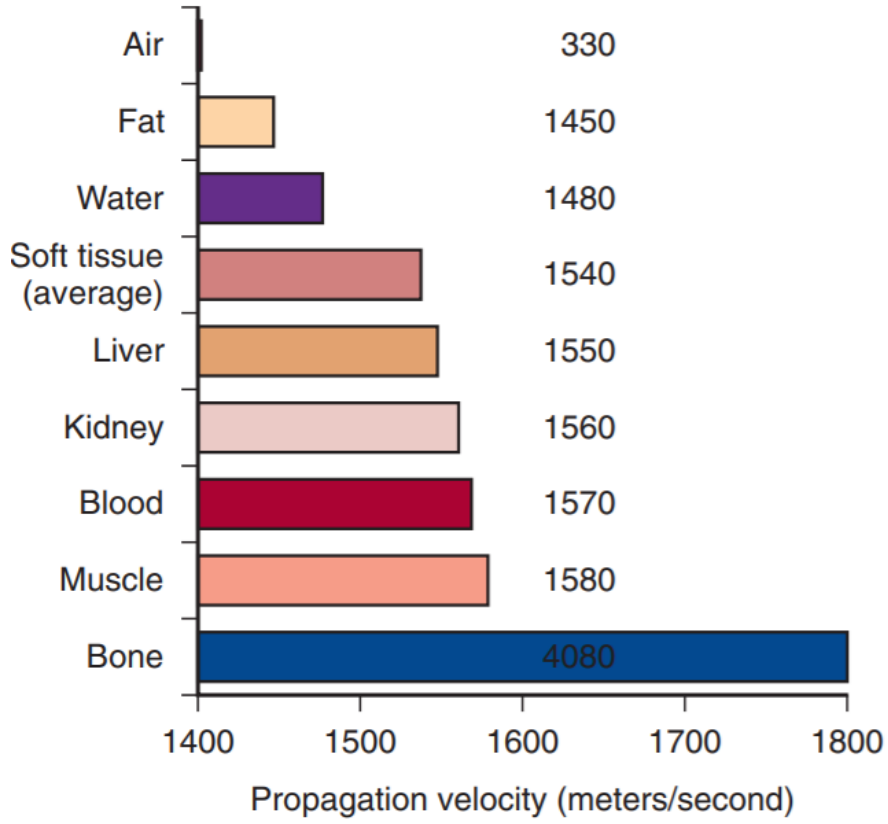
Ultrasound

a)



- Ultrasound imaging is based on scattering of sound energy
- **Basic acoustics:**
  - Sound is result of mechanical energy traveling through matter as a wave producing alternating *compression* and *rarefaction* (a)
  - Distance between corresponding points on time-pressure curve defined as *wavelength* λ
  - Time T to complete a single cycle called *period*
  - number of complete cycles in unit time is *frequency* f of the sound
  - Frequency and period inversely related, $f = 1/T$
  - Unit of *acoustic frequency* is the hertz (Hz)
    - 1 Hz = 1 cycle per second
    - High frequencies expressed in kilohertz (kHz) or megahertz (mHz)
    - Human hearing is limited to 20 – 20,000 Hz
    - Ultrasound differs from audible sound only in its frequency, is 500 to 1000 times higher than audible sound (2-15 MHz)
  - Propagation velocity of sound determined by physical properties of tissue, which varies considerably (b)
  - Propagation velocity of sound related to frequency and wavelength: $c = f\lambda$
  - Thus, 5 MHz wave has wavelength of 0.308 mm in soft tissue
    - $\lambda = \frac{c}{f} = 1540 m/\sec \cdot 5{,}000{,}000\ sec^{-1} = 0.000308\ m = 0.308\ mm$

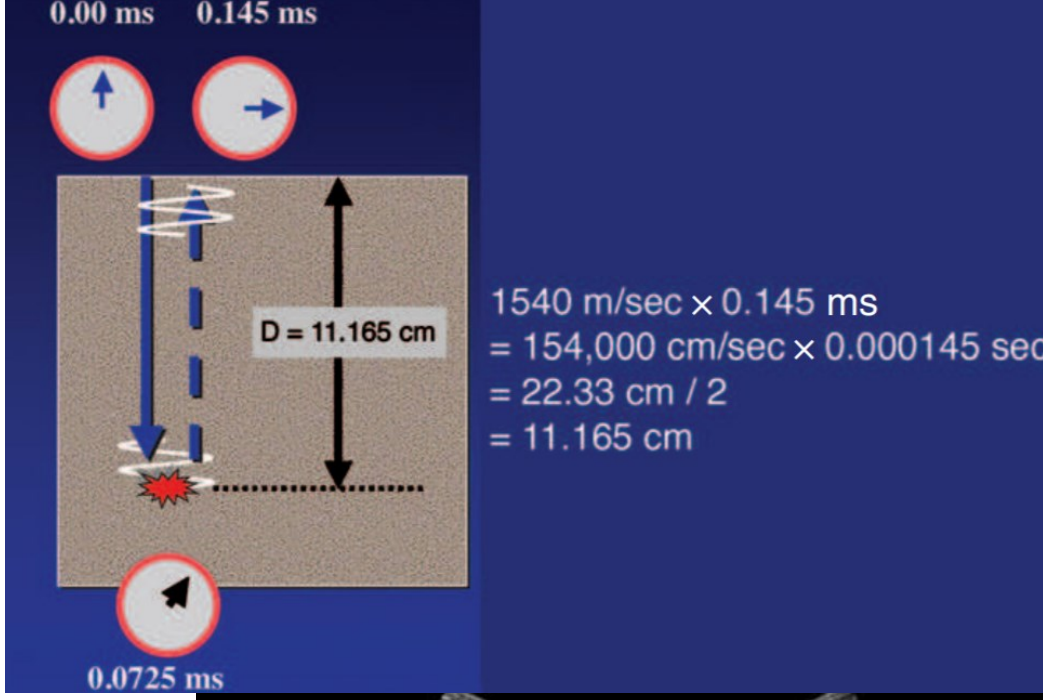
b)



Echo-ranging

- Transmit ultrasound pulse into body, measure time taken for echo to return (a)
- Depth of the tissue interface that generated echo can then be calculated, provided we know the propagation velocity of the tissue
- Example
  - By rapidly repeating this process, a 2d map of reflecting interfaces is created to form the image
  - Accuracy of map highly dependent on how closely presumed velocity of sound corresponds to true velocity in tissue being observed
- Propagation velocity artifact (b)
  - when sound passes through lesion containing fat, echo return is delayed because fat has slower propagation velocity of 1450 m/s
  - Ultrasound scanner assumes sound being propagated at 1540 m/s, so delay in echo is mistakenly interpreted by the scanner as a deeper target

a)



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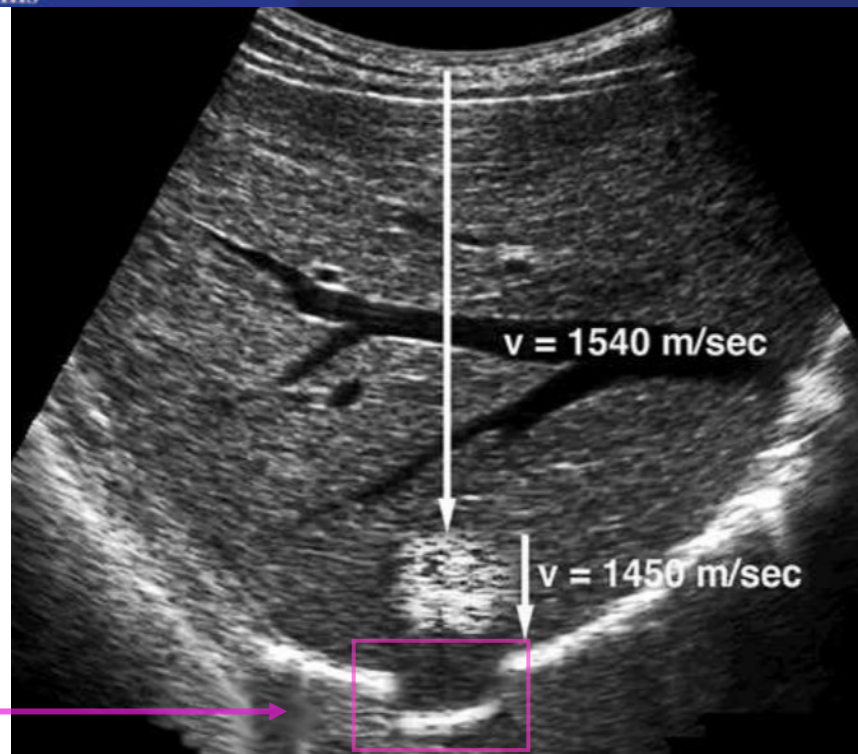
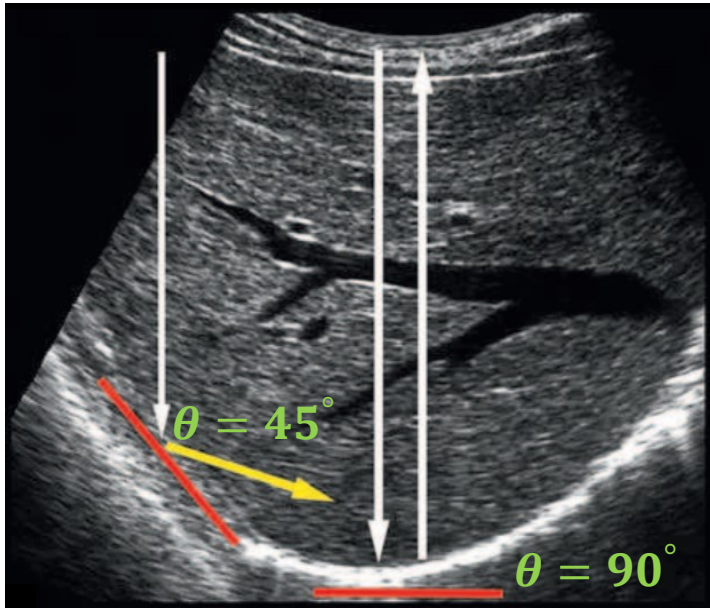


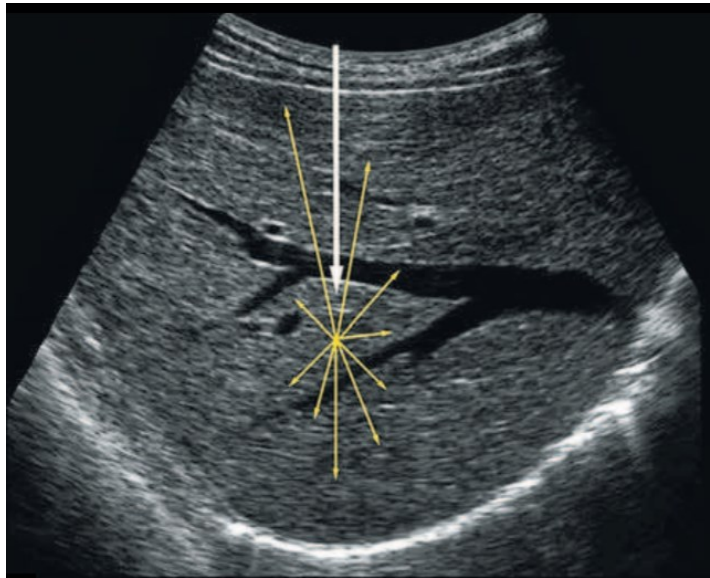
Acoustic impedance and reflection

- Ultrasound relies on detection and display of *reflected sound* or *echoes*
- To produce echo, a reflecting interface must be present
  - Sound passing through completely homogenous medium produces no echoes
- Junction of materials (tissues) with different physical properties produces acoustic interface
  - When sound passes from one tissue to another, some of incident sound energy is reflected
  - Amount reflected (backscatter) determined by differences in *acoustic impedance* of materials forming the interface
- **Acoustic impedance** Z of medium is product of density ρ and propagation velocity c of sound in the medium, $Z = \rho c$
- Interfaces with large differences in acoustic impedance reflect almost all incident energy
  - Example: interface between bone and soft tissue, or between air and bone
- **Reflection:** size and surface features of interface determines how sound is reflected when it strikes the interface
  - large and relatively smooth ⇒ interface reflects sound like mirror reflects light (*specular* reflector)
  - Reflection coefficient $R = (Z_2 - Z_1)^2/(Z_2 + Z_1)^2$ where Z_2, Z_1 are acoustic impedances of media forming the interface
  - *Angle of insonation* θ determines if reflection is detected by ultrasound (should be 90°)
  - **Diffuse reflector** (b): acoustic interface structure much smaller than wavelength of incident sound. Echoes are scattered in all directions.

a) Specular reflector (diaphragm)



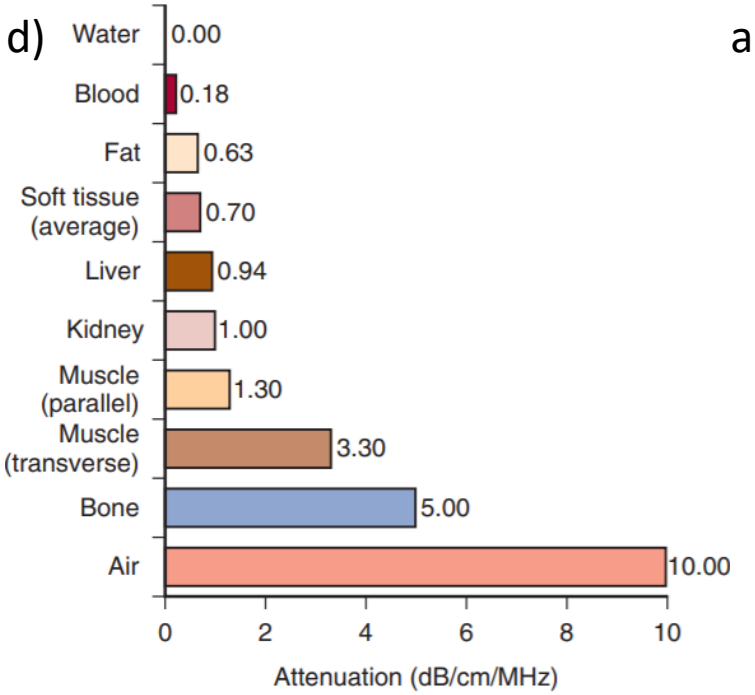
b) Diffuse reflector (most echoes come from this)



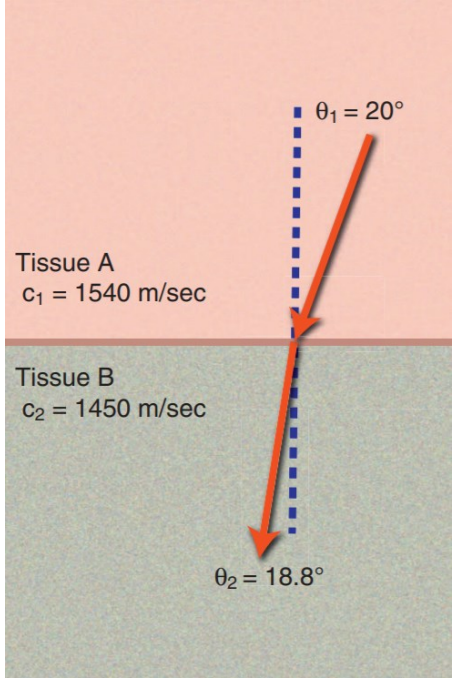
Refraction and attenuation

- Sound wave direction changes when it passes into tissue with different acoustic propagation velocity (a)
  - This is called *refraction* and is governed by Snell law: $sin\theta_1/sin\theta_2 = c_1/c_2$
- Refraction important because it causes *misregistration* of a structure in the ultrasound image
  - b) refraction can cause a *ghost image* (red)
  - c) transabdominal image of uterus showing ghost image (B) and the real image (A)
- As acoustic energy moves through uniform medium, *work* is performed and energy transmitted to the medium as heat.
  - Acoustic *power* (watts W) describes the amount of acoustic energy produced in a unit of time.
  - *Intensity* (I) used to describe spatial distribution of power, obtained by dividing power by area over which power distributed: $I(W/cm^2) = Power(W)/Area(cm^2)$
- *attenuation* of sound energy as it passes through tissue influences *depth* in tissue from which useful information may be obtained
  - Attenuation measured in relative units (decibels dB) rather than absolute units
  - dB is 10 times log_{10} of the ratio of power or intensity values being compared.
  - Example: if intensity measured in tissue is $10\,mW/cm^2$ and at deeper point is $0.01\,mW/cm^2$, difference in intensity is as follows:
  - $(10)(log_{10}\,0.01/10) = (10)(log_{10}0.001) = (10)(-log_{10}1000) = 10(-3) = -30\,dB$
- Attenuation is the result of combined effects of absorption, scattering, and reflection
  - High frequencies attenuated more rapidly than low frequencies
  - Attenuation values for normal tissues show considerable variation (d)

d)



a)



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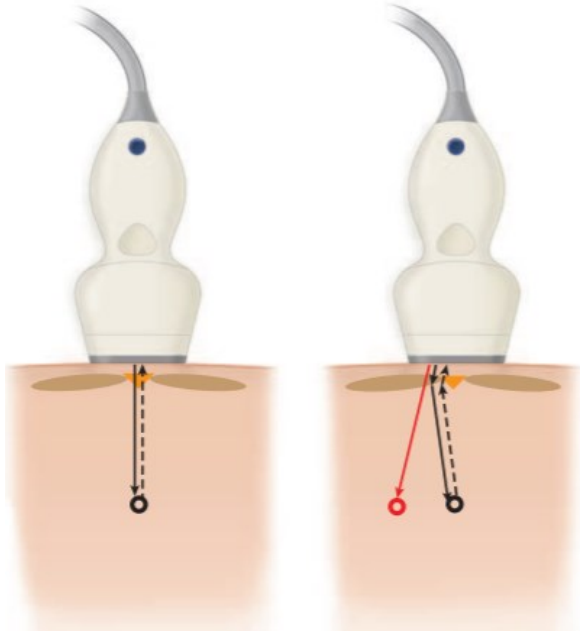

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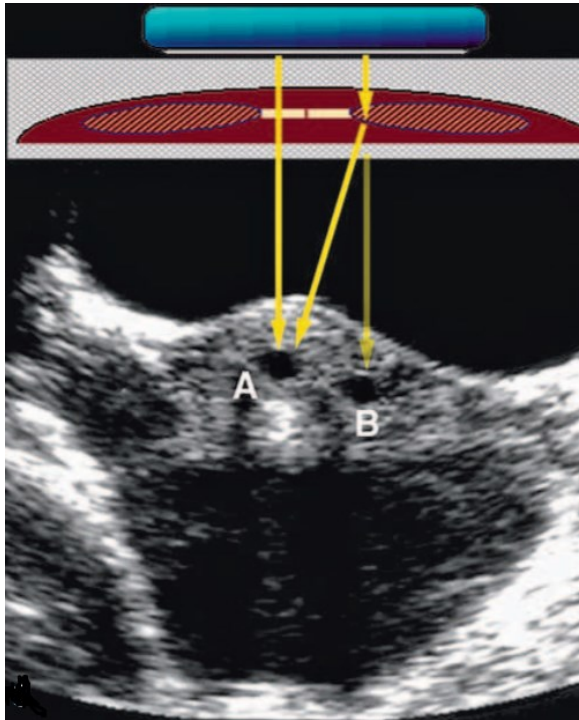
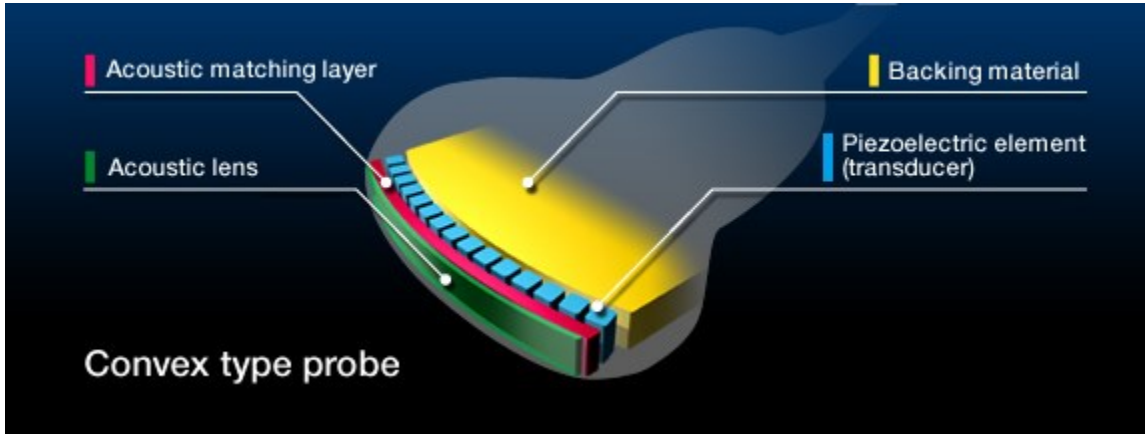


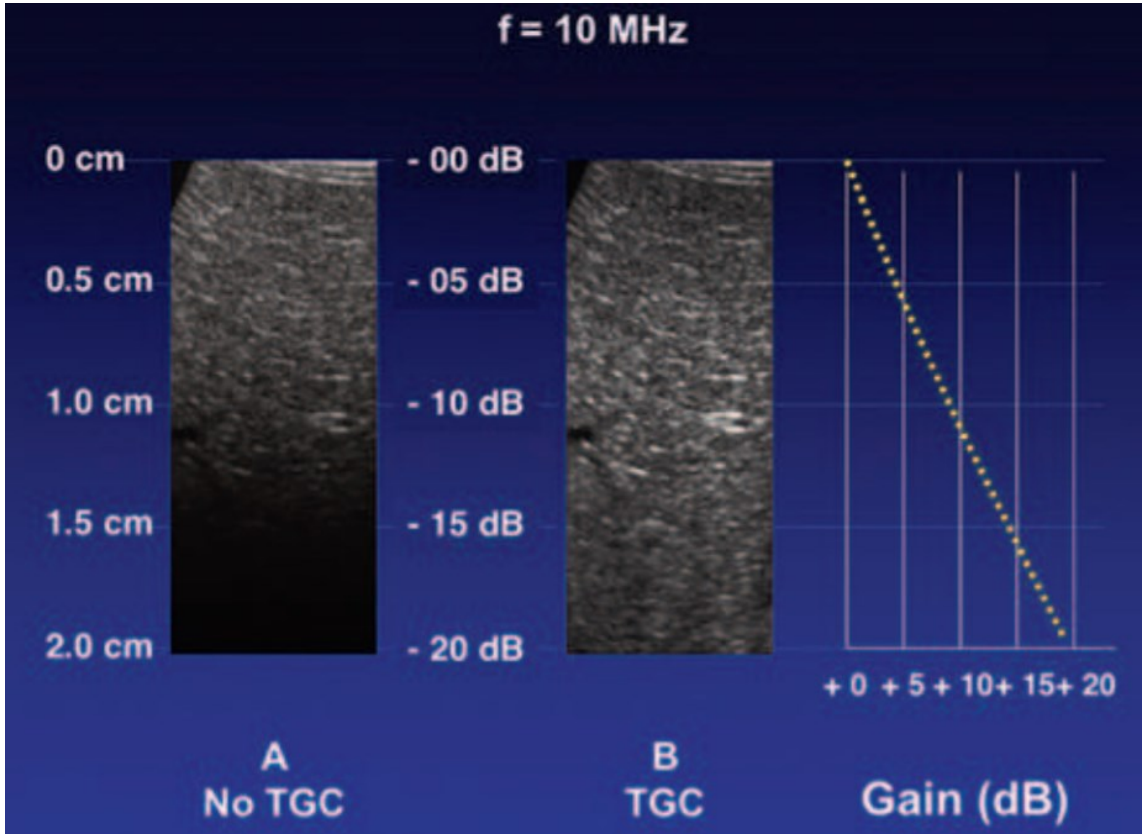
Ultrasound instrumentation

- Transmit sound using ultrasound probe (a)
- Transducer: any device that converts one form of energy into another
- Ultrasound transducer converts electrical energy into mechanical energy and vice versa, has two functions
  - 1) convert electric energy into acoustic pulses directed into the patient
  - 2) receive reflected echoes, converting weak pressure changes into electric signals
  - Uses principle of *piezoelectricity,* which allows certain materials to change shape in presence of electric field, or generate electric potential when compressed
- Ultrasound bandwidth: range of frequencies produced and detected by the probe
  - Broad-bandwidth probes allow to capture signals from many different tissues
- Special gel must be used to ensure efficient transfer of energy from transducer to body
- **Receiver**: when returning echoes strike the transducer face, small voltages produced across piezoelectric elements
  - Receiver detects and amplifies these weak signals
  - Receiver also amplifies later echoes (time gain compensation TGC)
  - User can adjust gain (b) to amplify signals from deeper structures

a) Ultrasound probe



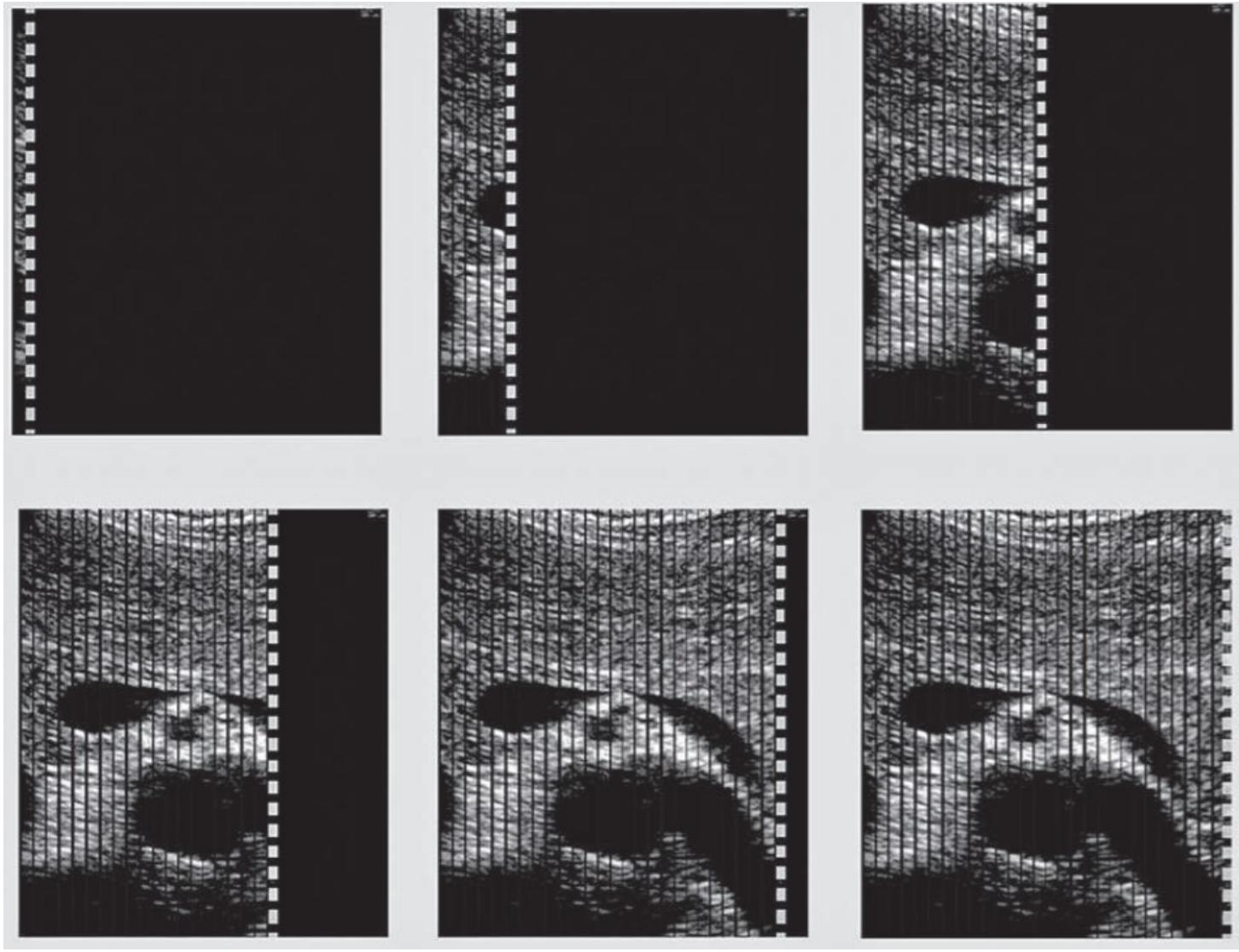
b) Time gain amplification



B-mode imaging

- B-mode display most common way to view ultrasound images in real time
- Variations in display intensity indicate reflected signals of differing amplitude
- To generate 2d image, multiple ultrasound pulses sent down series of successive scan lines (a) building a 2d representation of object being scanned
  - Signals of greatest intensity appear white
  - Absence of signal shown in black
- B-mode imaging is real time, can generate 2d images at up to 60 frames per second!
  - Good for visualizing moving structures (such as the heart)
    - This is called *echocardiography*

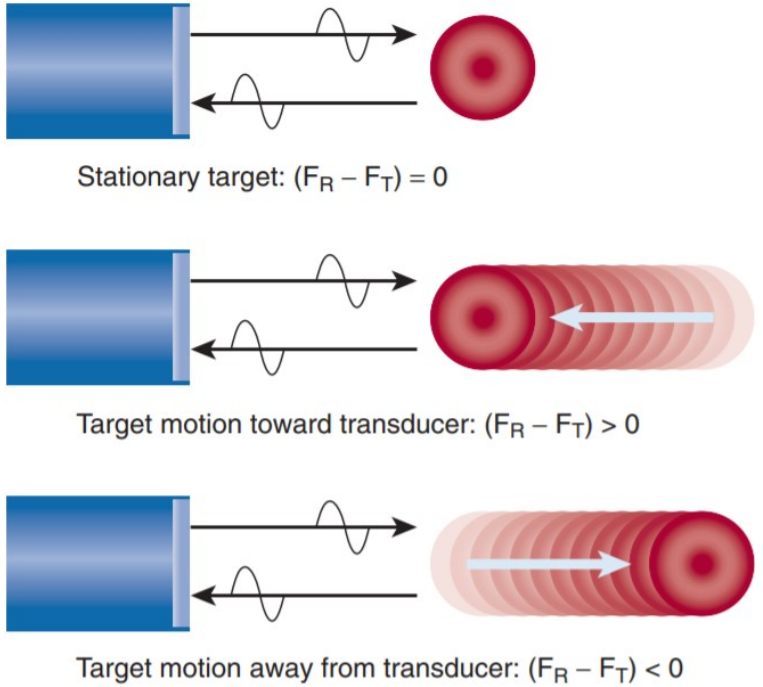
a) B-mode imaging



Applications, strengths and weaknesses of ultrasound

- Excellent temporal resolution
  - Can acquire up to 60 images per second
- Good spatial resolution
  - Up to 0.4 mm pixels if using a 5 MHz transducer (resolution depends on frequency of emitted sound wave, higher frequency = smaller pixels)
- Weaknesses:
  - Operator dependent – improper use of instruments causes artifacts
  - Limited depth, can't penetrate through bone (skull)
- Application: Doppler imaging
  - *Doppler effect:* if reflecting interface is moving w.r.t sound beam emitted by transducer, there is a change in frequency of sound emitted by moving object (a)
  - Relationship of returning ultrasound frequency to velocity of reflector described by Doppler equation:
    - *Doppler frequency shift* $\Delta F = (F_R - F_T) = 2 \cdot F_T \cdot v/c$
    - Where F_R is frequency of sound reflected from moving target, F_T is frequency of sound emitted from transducer, v is velocity of target towards transducer, and c is velocity of sound in medium
    - Doppler imaging used to estimate **blood flow velocity**

a)



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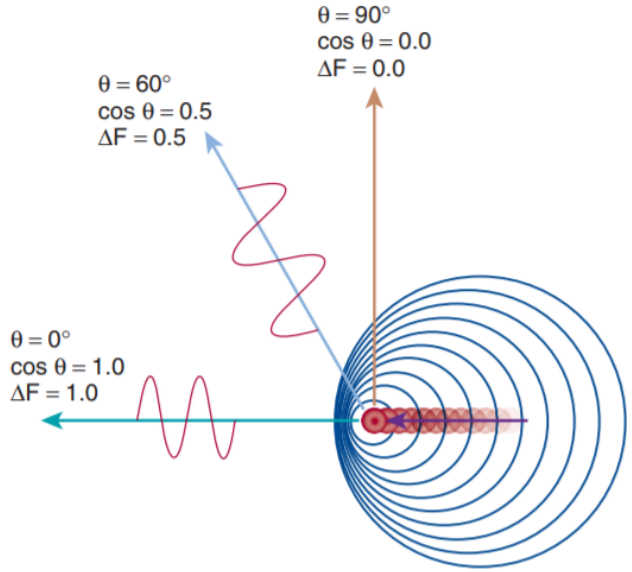

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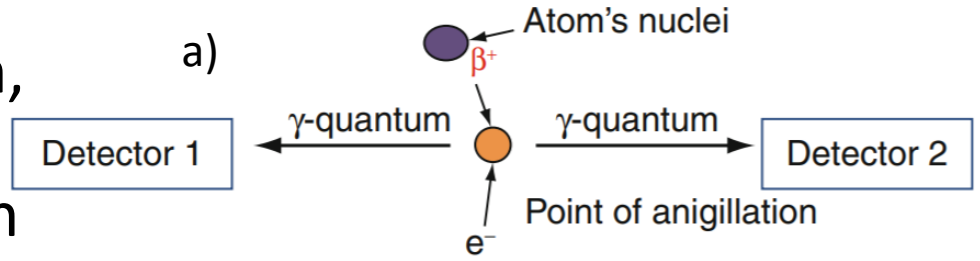
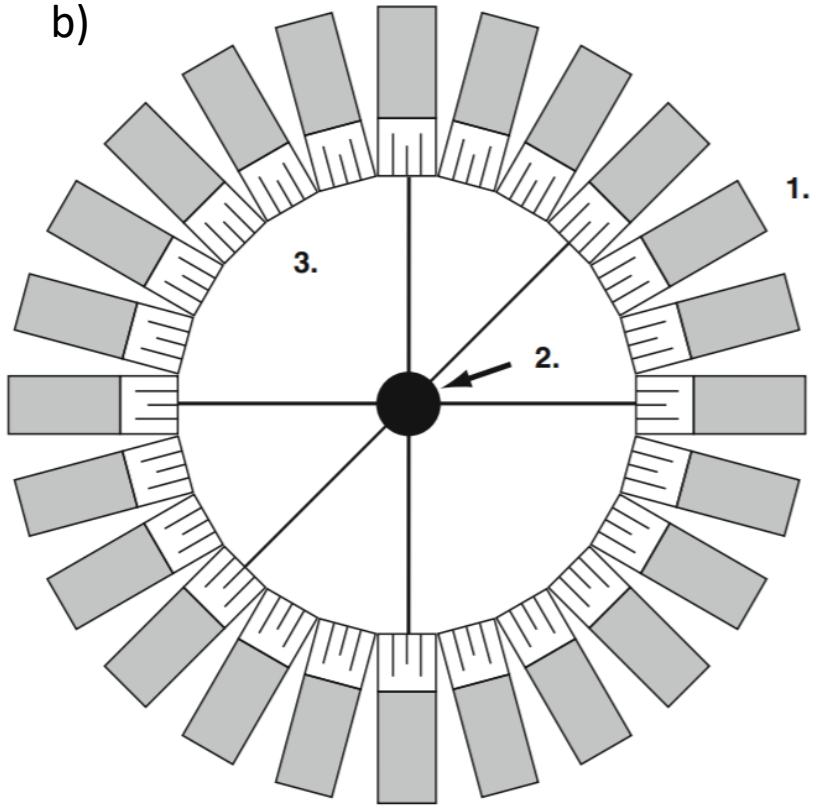
Positron emission tomography (PET)

- **Positron**: subatomic particle equal in mass to electron, but with positive charge
- PET is based on phenomenon of spontaneous positron emission by nuclei of unstable ultra-short lived radionuclides (a)
  - Radioactive isotopes of atoms such as oxygen or fluoride emitting positrons are injected into the body
  - Positron annihilates with electron, releasing two gamma-photons having equal energy moving in opposite directions (180° apart)
- PET scanner: highly sensitive detectors housed in rings work to detect coincident photons (b)
  - 1. ring of detector blocks
  - 2. some radiation source in the body
  - 3. lines going through radiation source, connecting pairs of detector-blocks
- 'coincidence window' of 4.2-12 nanoseconds





Coincidence detection

- Black circle indicates site of positron annihilation
- a) true coincidence
  - Derives from single positron-electron annihilation. Two annihilating photons both reach detectors on opposite sides without interacting significantly with surrounding atoms
- b) scattered event where one or both photons undergo a Compton interaction (open arrow)
  - Compton scattering causes loss in energy of photon and change of direction. Leads to decreased contrast and inaccuracies in final image
- c) multiple coincidence arising from two positron annihilations in which three events are counted
- d) random/accidental coincidence arising from two positrons in which one of the photons from each positron annihilation is counted

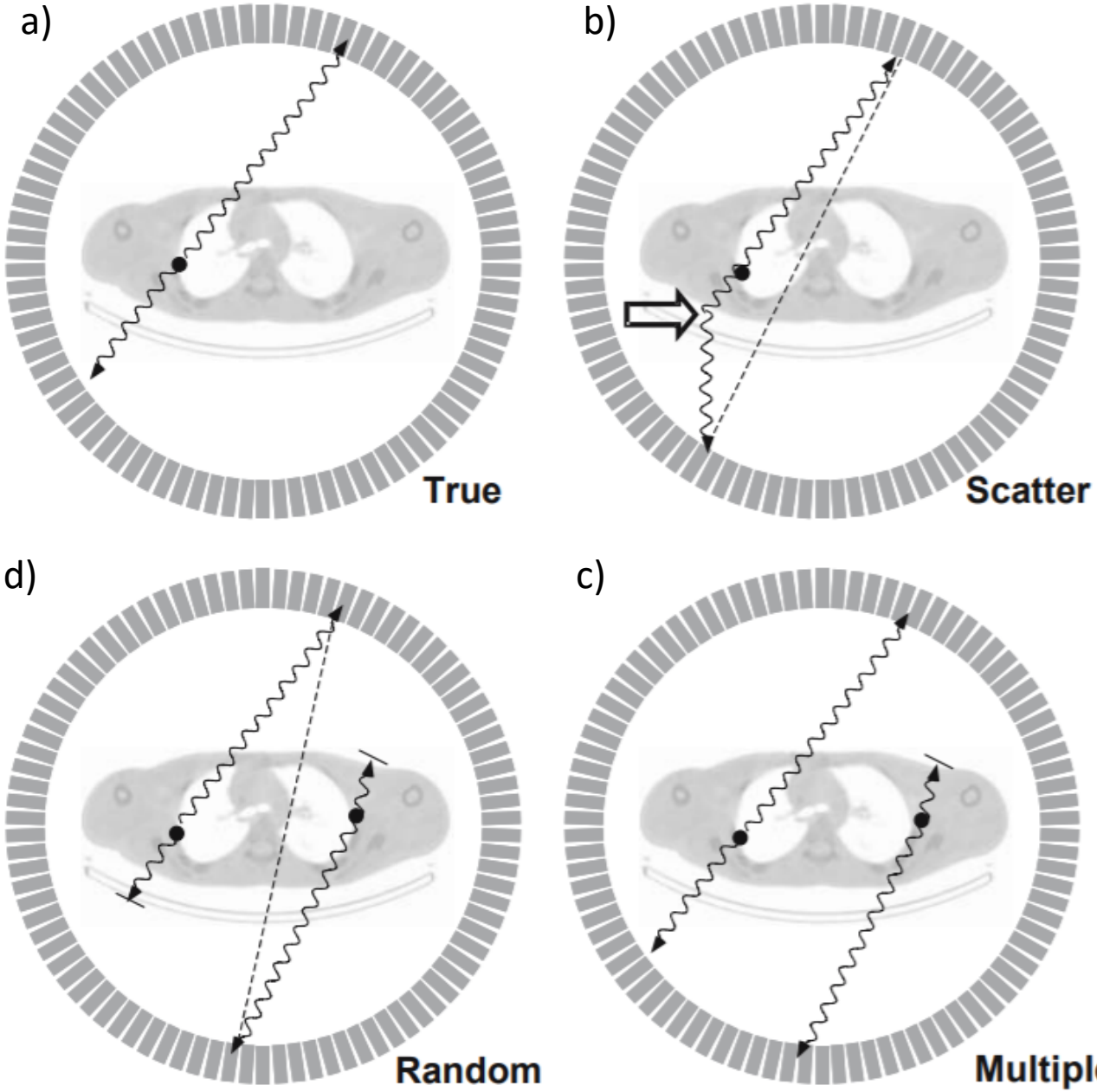
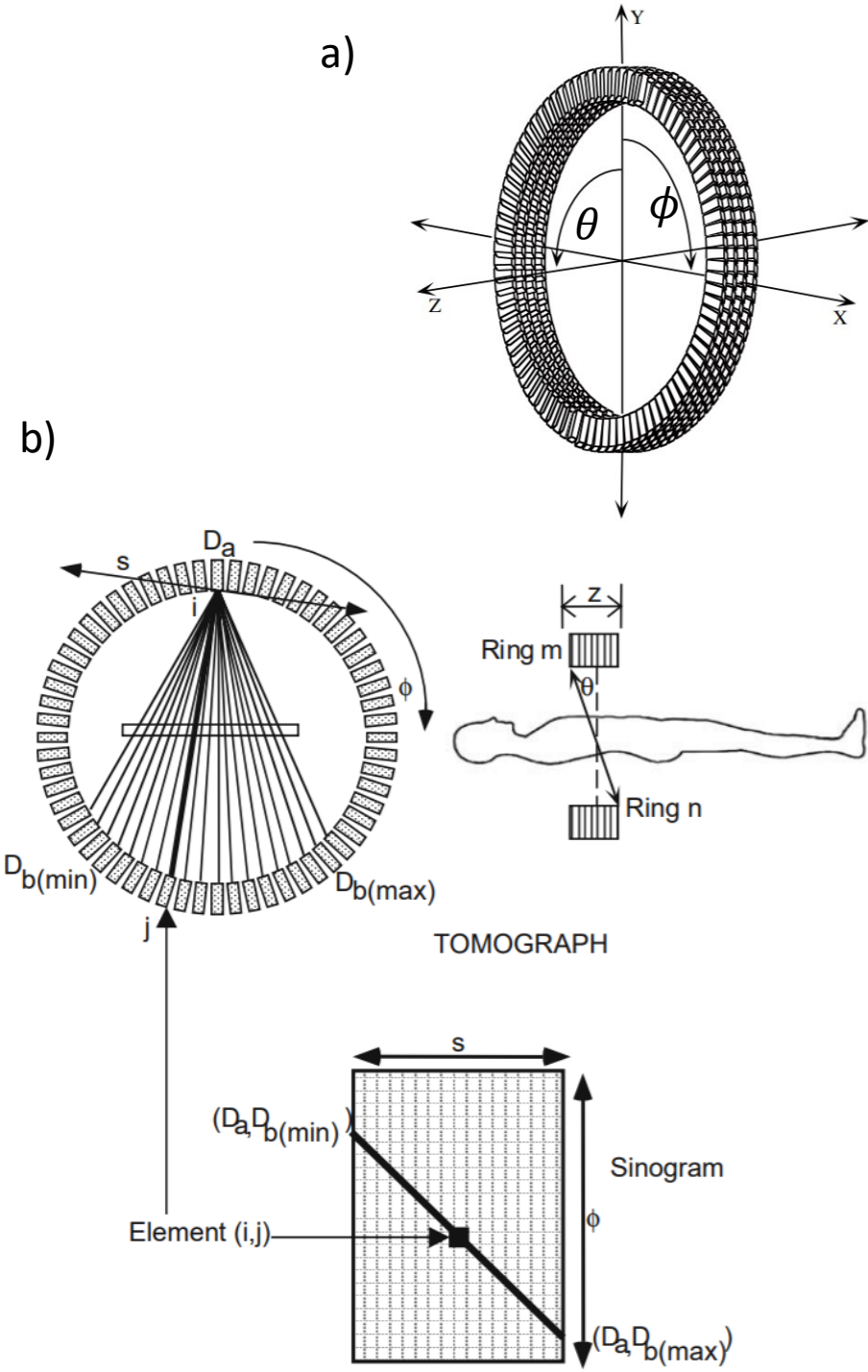


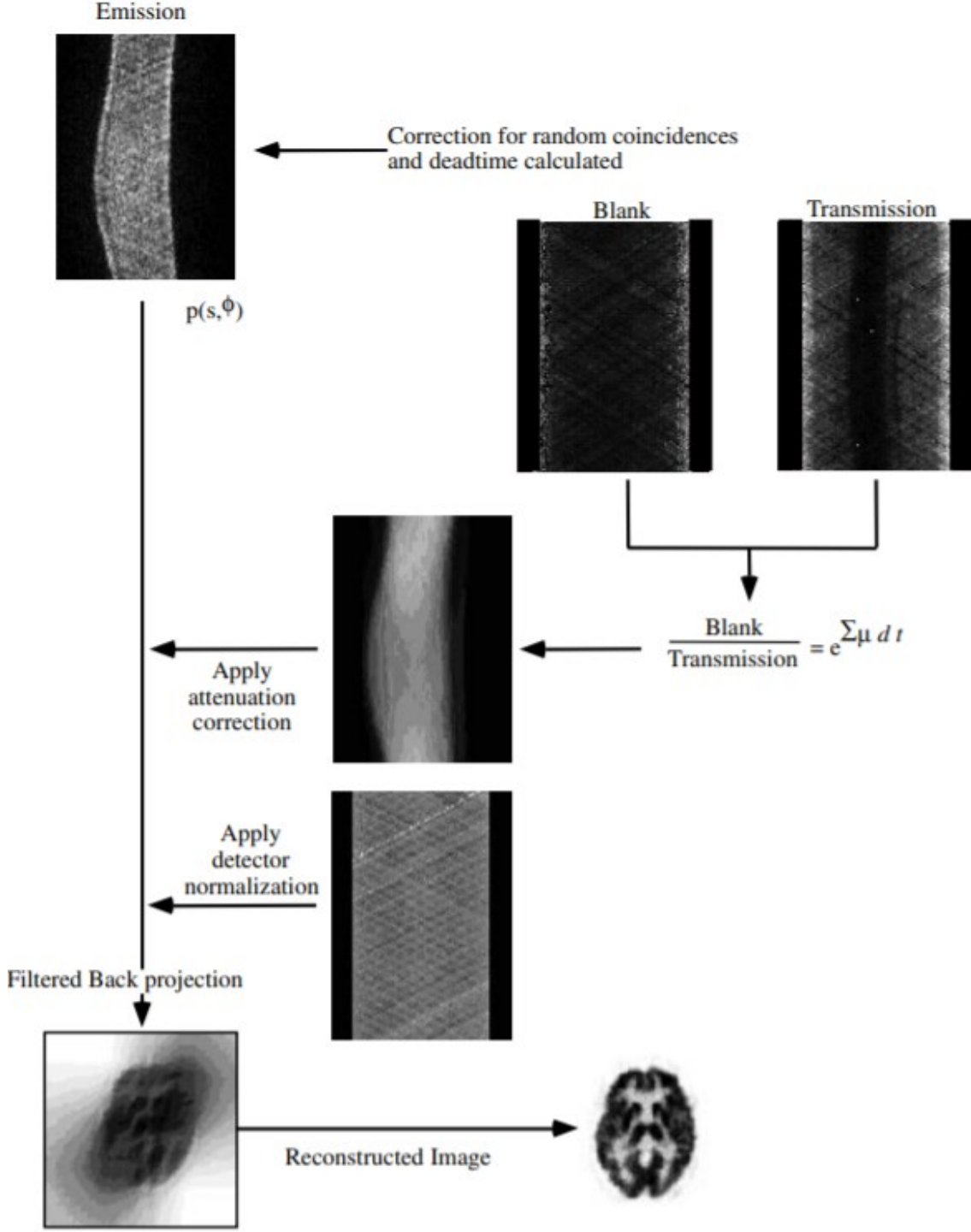
Image formation in PET

- PET systems use 360° rings for full coincidence detection
  - a) Full-ring gamma camera with coordinate system describing orientation of camera
    - Azimuthal angle ϕ measured *around* the ring
    - Polar angle θ measures angle *between* the rings
    - in 2d PET, data acquired for $\theta = 0$ while in 3d PET polar angle can be increased as desired
- Individual detector elements form coincidence pairs with opposing detectors and are mapped to sinogram space
  - b) mapping from sampling projections to sinograms
  - Fan angles map to a diagonal line in the sinogram



From projection to reconstructed image

- In addition to the emission sinogram, a set of normalization sinograms is needed to correct for differential detector efficiencies and geometric effects related to the ring detector
- A set of sinograms of *attenuation correction factors* to correct for photon attenuation (self absorption or scattering) by the object is also required
  - These are derived from a *transmission scan* of the object, and a transmission scan without the object in place (also called a 'blank' or reference scan).

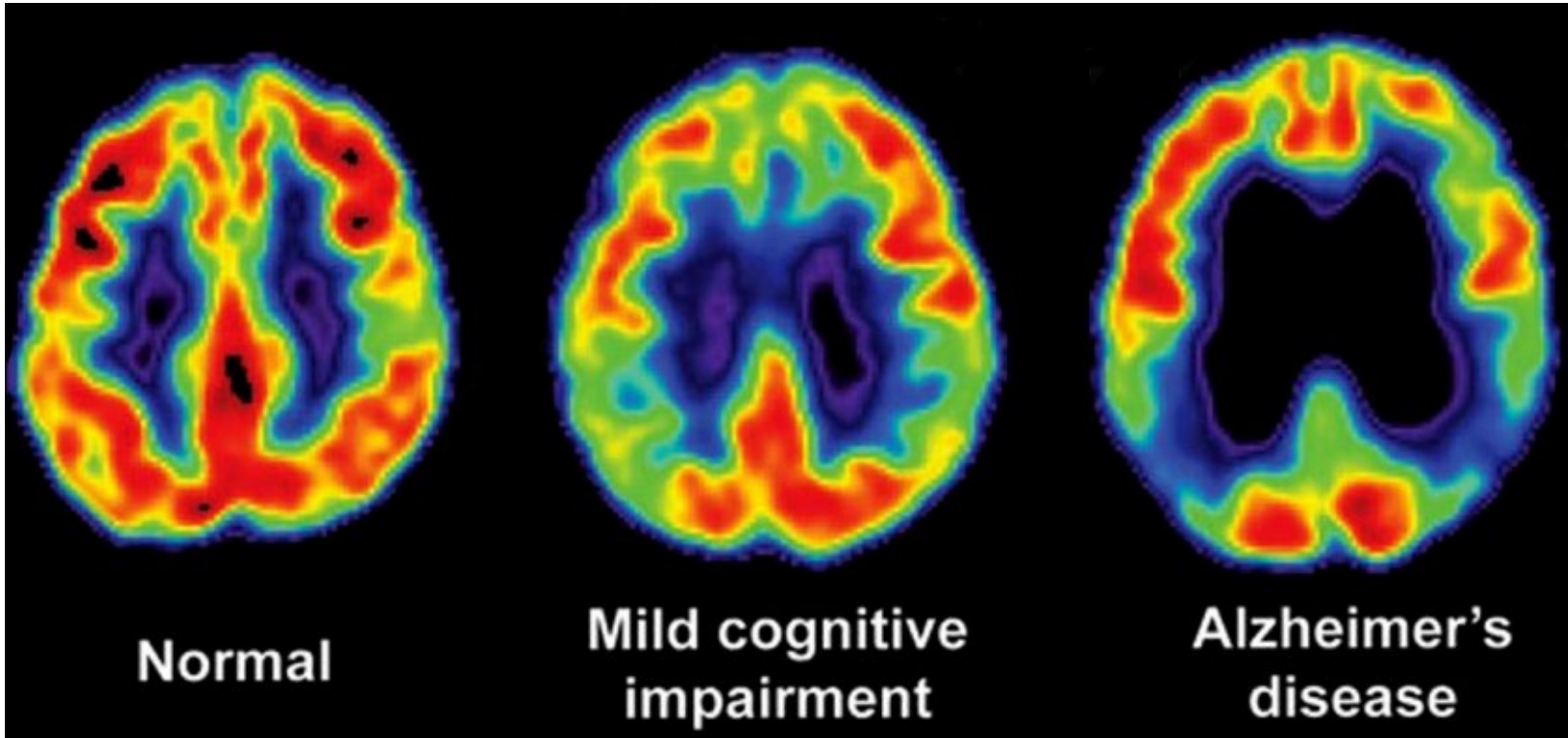


Interpreting PET image

- Is PET quantitative? What does image intensity mean?
  - PET images are often assessed visually by a trained clinician (semi-quantitative)
  - Example: using FDG-PET for early diagnosis of dementia
    - The PET tracer 18F-FDG allows the in-vivo study of glucose metabolism and is the most widely used PET tracer in both clinical and research setting.
    - Differences in intensity indicate differences in tracer uptake. More red = more tracer deposited in region

Typical PET experiment:

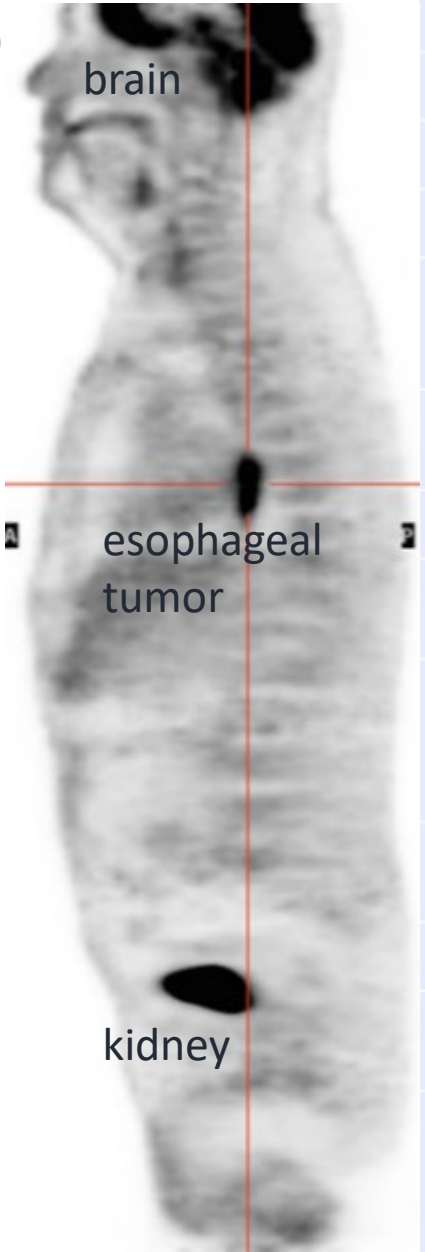
1) Patient fasts (doesn't eat) for 4-6 hours prior to experiment
2) Patient is connected to an intravenous line (prepare for injection)
3) Radioactive tracer is injected into patient's bloodstream. Wait 30 minutes.
4) Acquire image. During acquisition, the patient's body or head is stabilized to minimize motion artifacts
5) Image is reconstructed



Applications, strengths, weaknesses of PET

- The primary application of PET imaging is in cancer diagnosis
- Main strength: flexibility
  - Diagnostic capability of PET determined not just by scanner hardware, but by the radiopharmaceutical (RP) used in the experiment (injected into patient)
  - Currently, hundreds of different RPs have been developed for use in PET imaging, 15 common RPs shown in (a)
    - The two most widely used are *methionine* and *fluorine desoxyglucose (FDG)*, for imaging brain tumors and glucose metabolism, respectively
  - Example: FDG PET scan of patient with esophageal cancer (red crosshair).
    - Note how the brain and kidney are darkest, meaning they consume the most glucose. The esophageal tumor is also dark because tumors consume lots of energy

b)



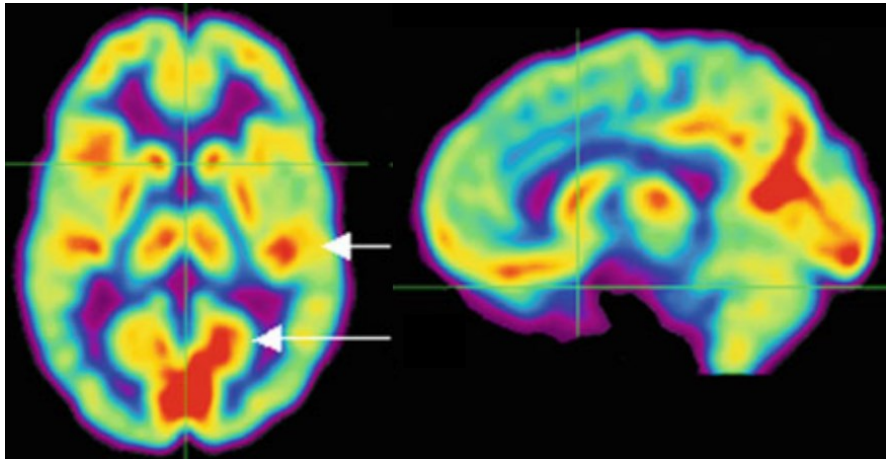
a)

nuclide	Substance	RP description	its range of application
[^{15}O]	Water	^{15}O-water	Speed of regional blood flow (in brain)
[^{82}Rb]	Rubidium chloride	^{82}Rb chloride	Speed of regional perfusion (in myocardium)
[^{13}N]	Ammonium	^{13}N-ammonium	Speed of regional perfusion (in myocardium)
[^{11}C]	**Methionine**	^{11}C-methionine (^{11}C-MET)	Speed of protein synthesis (in brain tumors)
[^{11}C]	Tyrosine	^{11}C-tyrosine	Speed of protein synthesis (in brain tumors)
[^{11}C]	Thymidine	^{11}C-thymidine	Speed of proliferative activity in tumor cells
[^{11}C]	Choline	^{11}C-choline	Speed of phospholipid synthesis – marker of membrane-forming (prostate cancer and its metastases)
[^{11}C]	Acetate	^{11}C-acetate	Speed of oxidative metabolism (in myocardium and brain)
[^{11}C]	Palmitic acid	^{11}C-palmitic acid	Speed of fatty acid metabolism (in myocardium)
[^{18}F]	**Fluorine desoxyglucose**	2-[^{18}F]-fluorine-2-desoxy-D-glucose (^{18}F-FDG)	Speed of the metabolism of (transmembrane transfer) of glucose
[^{18}F]	DOPA	^{18}F-fluorine-dihydroxyphenylalanine (^{18}F-DOPA)	Concentration of dopamine receptors in brain and in some tumors (mebullary thyroid cancer, pancreas tumors, GIST, brain tumors)
[^{18}F]	Thyrosine	^{18}F-fluoro-ethyl-tyrosine (^{18}F-FET)	Speed of transmembrane transfer of amino acids (in tumors)
[^{18}F]	Fluoride	^{18}F-ion (fluoride)	Speed of calcium metabolism (revealing bone metastases)
[^{18}F]	Thymidine	3-deoxy-3-[^{18}F]-fluorothymidine (^{18}F-FLT)	Speed of proliferative activity in tumor cells
[^{18}F]	Choline	^{18}F-choline	Speed of phospholipid synthesis – membrane-forming (prostate cancer and its brain metastases, oesophagus tumors)

Example: 4 different radiopharmaceuticals (tracers)

- The contrast obtained from PET depends on the type of radiopharmaceutical injected into the patient:
  - a) FDG PET scan shows how much glucose the tissue is consuming, which is closely correlated with energy consumption
  - b) 11C-SB PET can be used for early detection of Alzheimer's or differentiation of tumor type
  - c) 11C-MET PET scan, can be used to differentiate between tumor type and cancer progression stage
  - d) uptake of DOTATOC, used for in-vivo diagnosis of neuroendocrine tumors

a)



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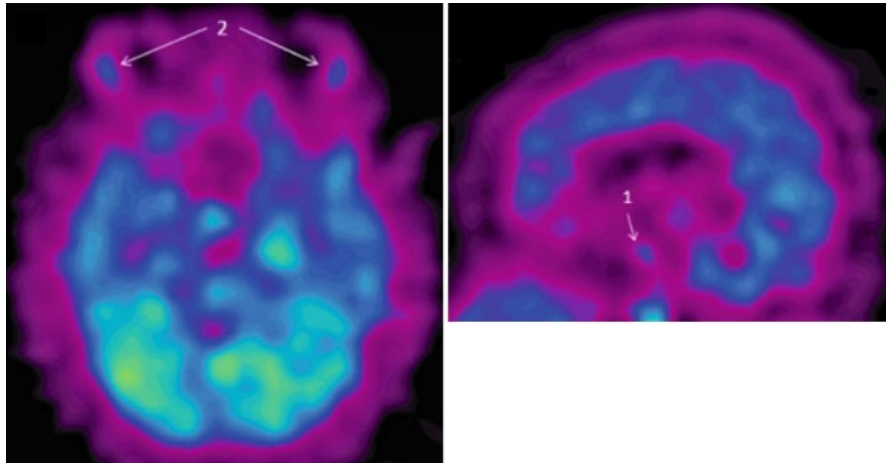

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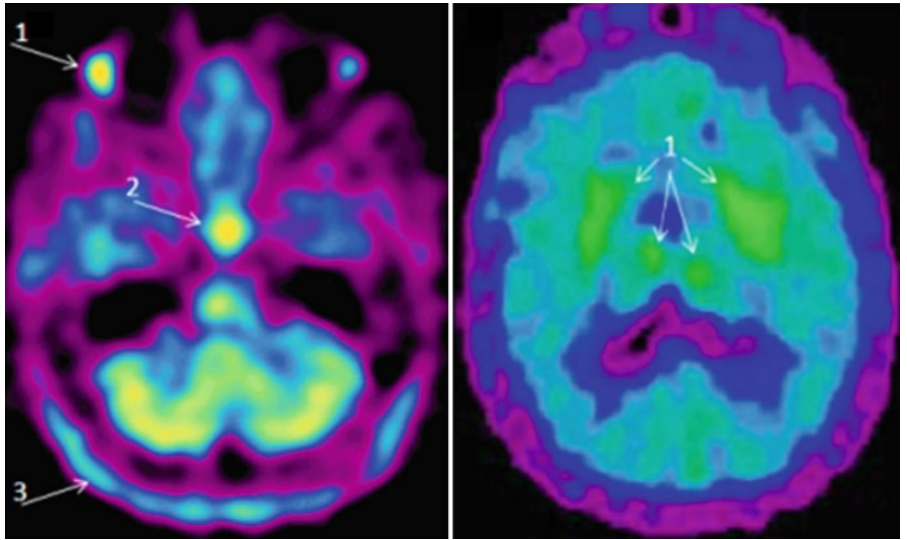

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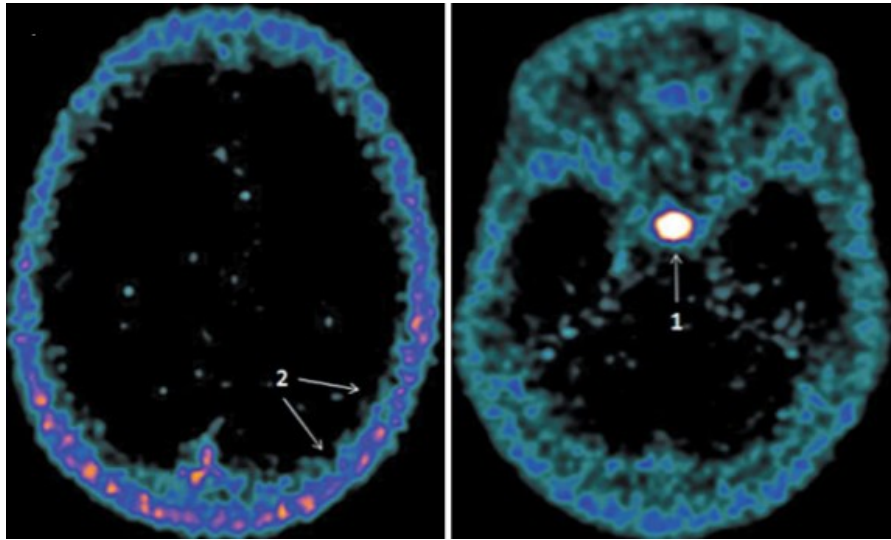
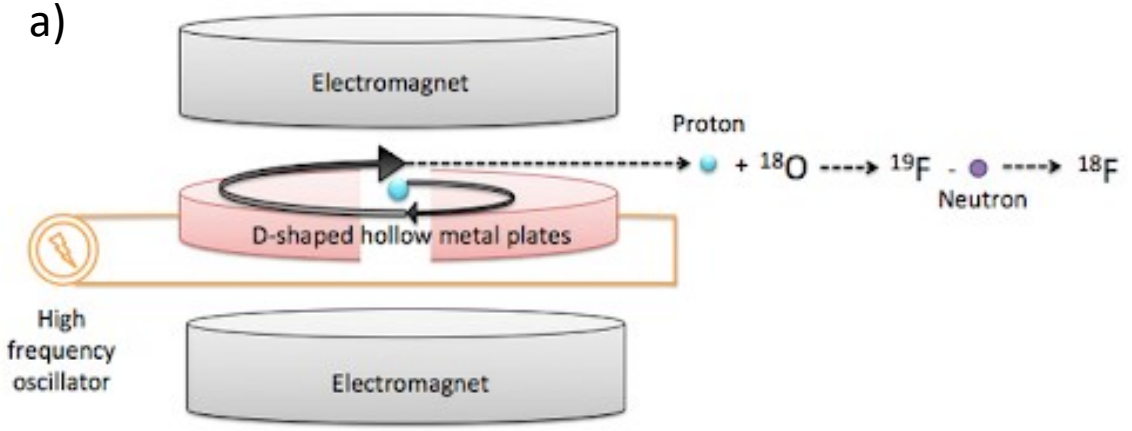


Applications, strengths, weaknesses of PET

- Weakness: expensive and inconvenient
  - PET requires injection of radiopharmaceuticals (RPs) labeled with positron emitters, some of which have very short half-life, such as ^{15}O and ^{11}C.
    - Therefore, usage of PET is restricted to hospitals and research centers with on-site cyclotron (a) to synthesize these RPs (not feasible to transport over large distance)
  - RPs also expensive to synthesize
  - Radioactive tracers are by definition radioactive, releasing gamma rays. Cannot do too many PET scans on same patient (similar to CT in this regard)
  - Requires some other type of scan (CT or MRI) to get the anatomical underlay (b)
    - Example of coronal, sagittal, and axial PET-CT fusion images of patient with gastric cancer and distant metastasis (FDG-PET)

a)



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