Biomedical Imaging Methods II: Nuclear Medicine and Magnetic Resonance Imaging

BME 4420/7450

Fall 2022

Biomedical Imaging Methods

- Ultrasound (US)
- Computed Tomography (CT)
- Single Photon Emission Computed Tomography (SPECT)
- Positron Emission Tomography (PET)
- Magnetic Resonance Imaging (MRI)

Nuclear Medicine

"Cat scans are for felines. I will give your dog a pet scan."

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Nuclear Medicine

- Images the distribution of radioactive decay events
  - High energy photons produced by decay of radioactive nuclei
- A *radiopharmaceutical* is a solution containing:
  1. A carrier: specific molecule or microscopic particle
  2. A *radionuclide* (radioactive atom), bound to #1
- The radiopharmaceutical is injected in a vein
- The spatial distribution of the radioactive tracer is measured some time later
  - Displayed as an image
  - Quantitatively analyzed to find uptake rate
- High SNR due to high detection efficiency

Imaging organ function

- Accumulation of radioactive atoms depends on
  - Uptake by tissue
    - Metabolic rate
    - Pathology
  - Radioactive decay rate
    - Half life measures the time in which (on average) half the nuclei decay
  - Excretion by kidneys

Target specific tissues with matching molecules

• Metabolic activity	• Glucose (^{18}FDG)
• Thyroid gland	• Iodine (^{123}I)
• Lung airways	• Noble gas (^{133}Xe)
• Blood	• Albumin (^{99m}Tc)
• Capillaries	• Albumin particles (^{99m}Tc)

- Radioactive atom denoted by

Metastable form

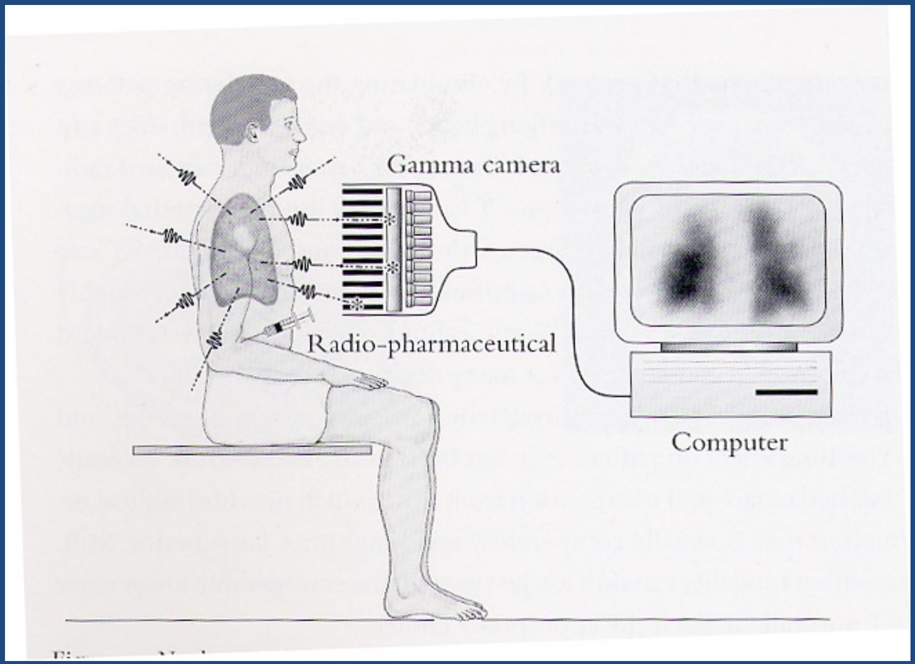
$^{99m}\mathrm{Tc}$

Atomic mass

Symbol for species (# of protons)

The gamma camera

- Measures distribution of radionuclides in 2 dimensions
- Detector has three parts
  - Collimator passes photons traveling perpendicular to detector face
  - Large crystal (NaI) converts a gamma photon to many visible photons ('scintillator')
  - Photomultiplier tubes localize the visible photons
- A computer accumulates the photon positions to make a map of radionuclide activity



What makes a good radionuclide?

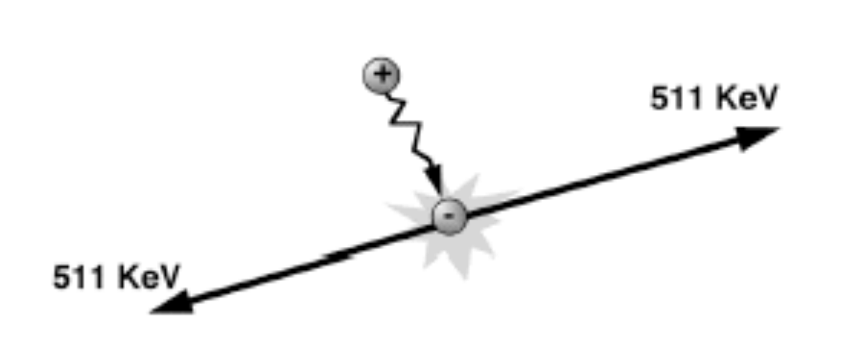
- Half life
  - minutes to hours
- Decay route
  - gamma emission only
- Decay energy
  - High enough to escape body
  - Low enough to be absorbed in scintillator
- Chemistry
  - Biologically active or
  - Easily bound to active molecules

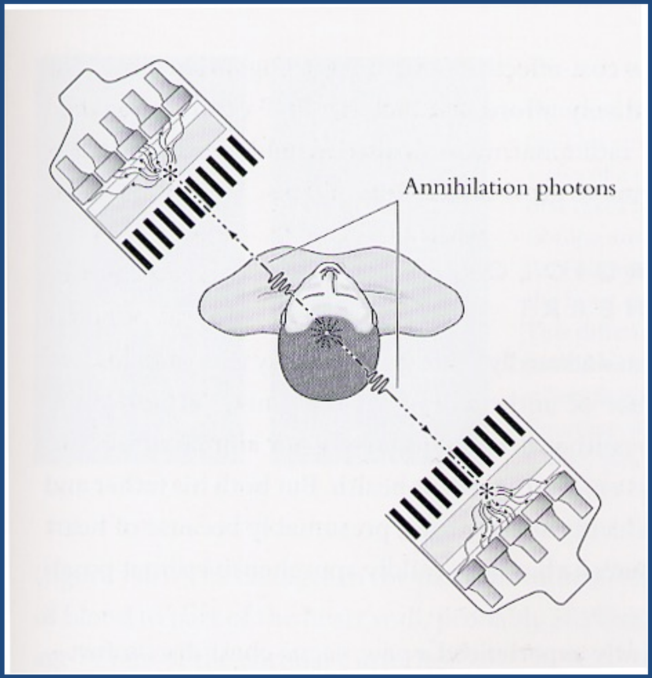
The SPECT camera

- One, two, or three detectors
- Detectors rotate around the subject
- Activity mapped in 2D slices through the subject (tomography)

Positron emission tomography

- Isotopes that emit positrons
  - ^{11}C (CO_2)
  - ^{15}O (H_2O, O_2)
  - ^{18}F (fluorodeoxyglucose)
- Annihilation creates 2 photons
  - Travel in (nearly) opposite directions
  - Coincidence of photons in the two detectors identifies a line on which the source lies
- Detectors encircle the subject
- Image can be reconstructed by backprojection



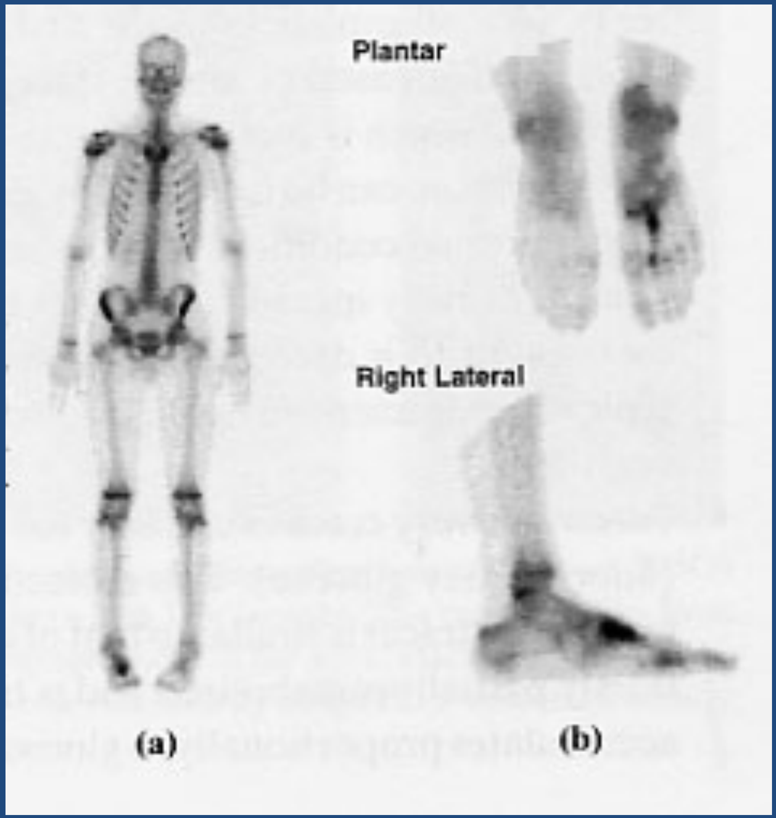


Applications

- Bone metabolism
- Tumor metabolism
- Lung physiology
- Myocardial perfusion
- Receptor density

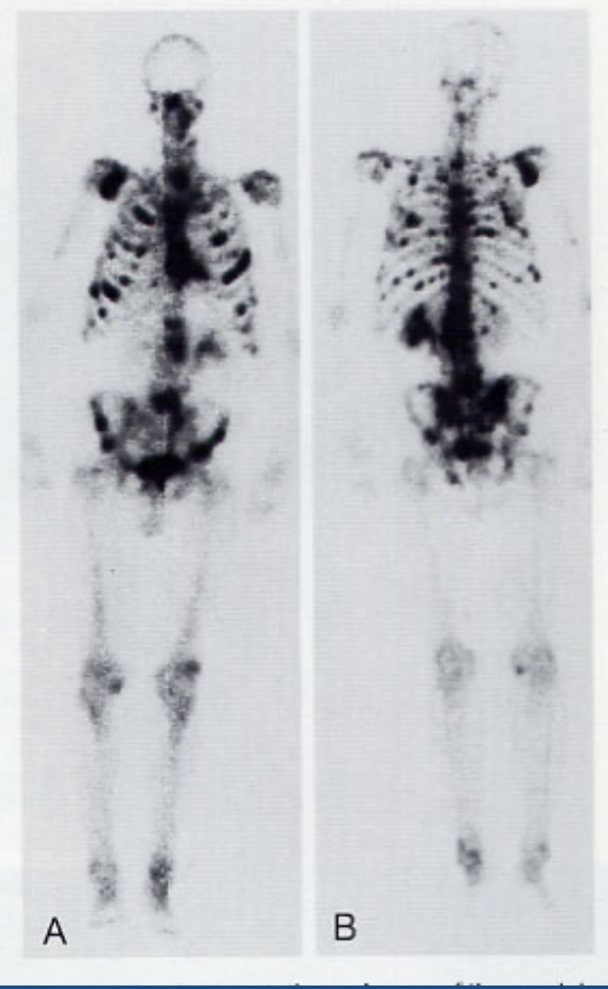
Bone studies

- ^{99m}Tc labeled phosphonate accumulates in proportion to bone turnover
  - Fractures
  - Tumors
  - Inflammation
  - Infection



Stress fracture in right foot

Bone Tumor imaging

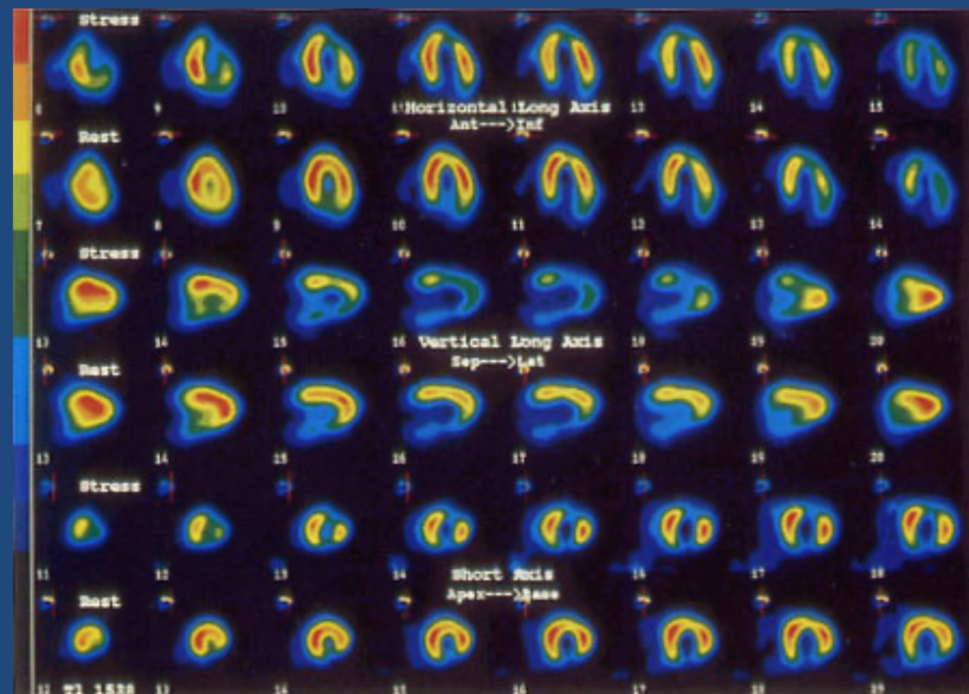


Metastatic carcinoma

^{99m}Tc study

Myocardial perfusion

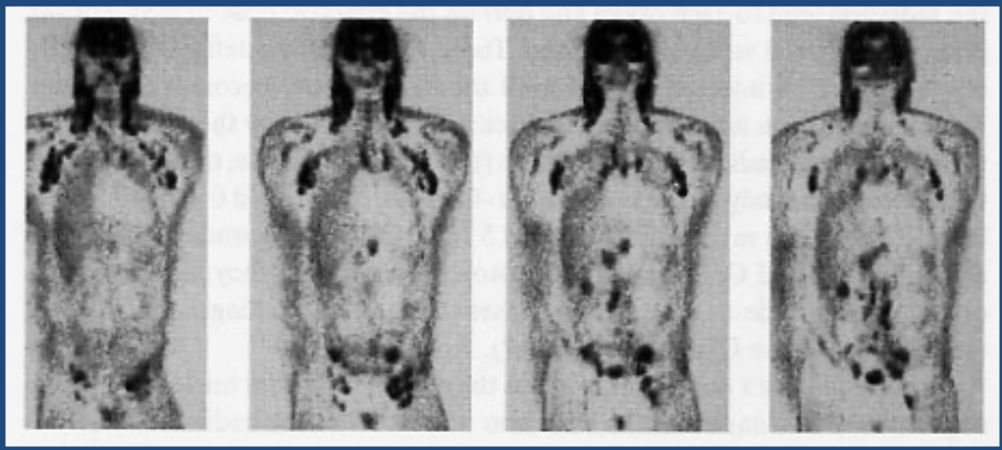
- Thallium (K analog) accumulates in muscle cells
- Uptake in muscle is proportional to blood flow rate
- ^{201}Tl images show ischemic/infarcted myocardium



Cardiac stress test
Stress: rows 1, 3, 5
Rest: rows 2, 4, 6

Tumor growth

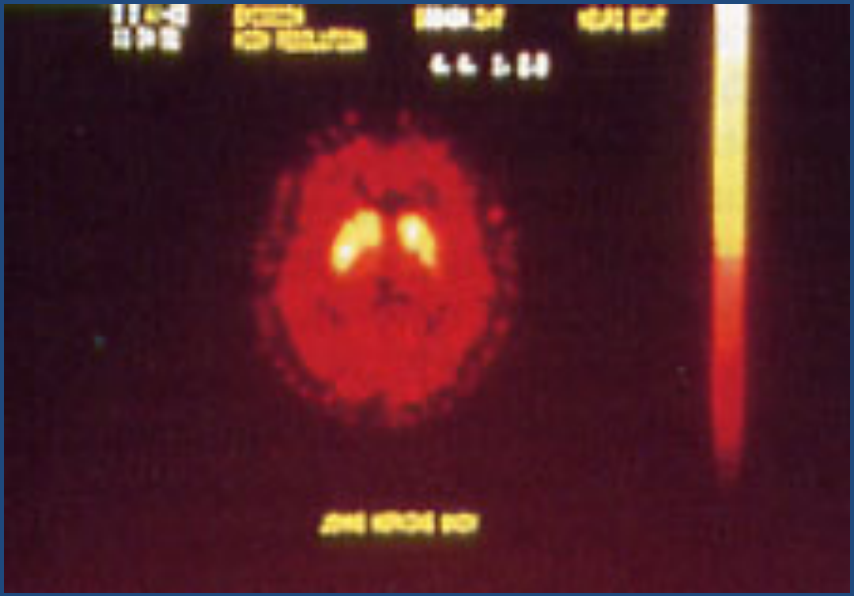
- Fluoro-deoxy-glucose (FDG) is a glucose analogue
- FDG is partially metabolized and trapped in cells
- Accumulates in proportion to glucose consumption
- Indicator of metabolic rate
- Image ^{18}FDG using PET



Hodgkins lymphoma

Receptor density

- Concentration is 10^{-7} to 10^{-10} mol/liter of homogenized tissue
- Need high detection efficiency
- Uptake of radio tracer is proportional to receptor density

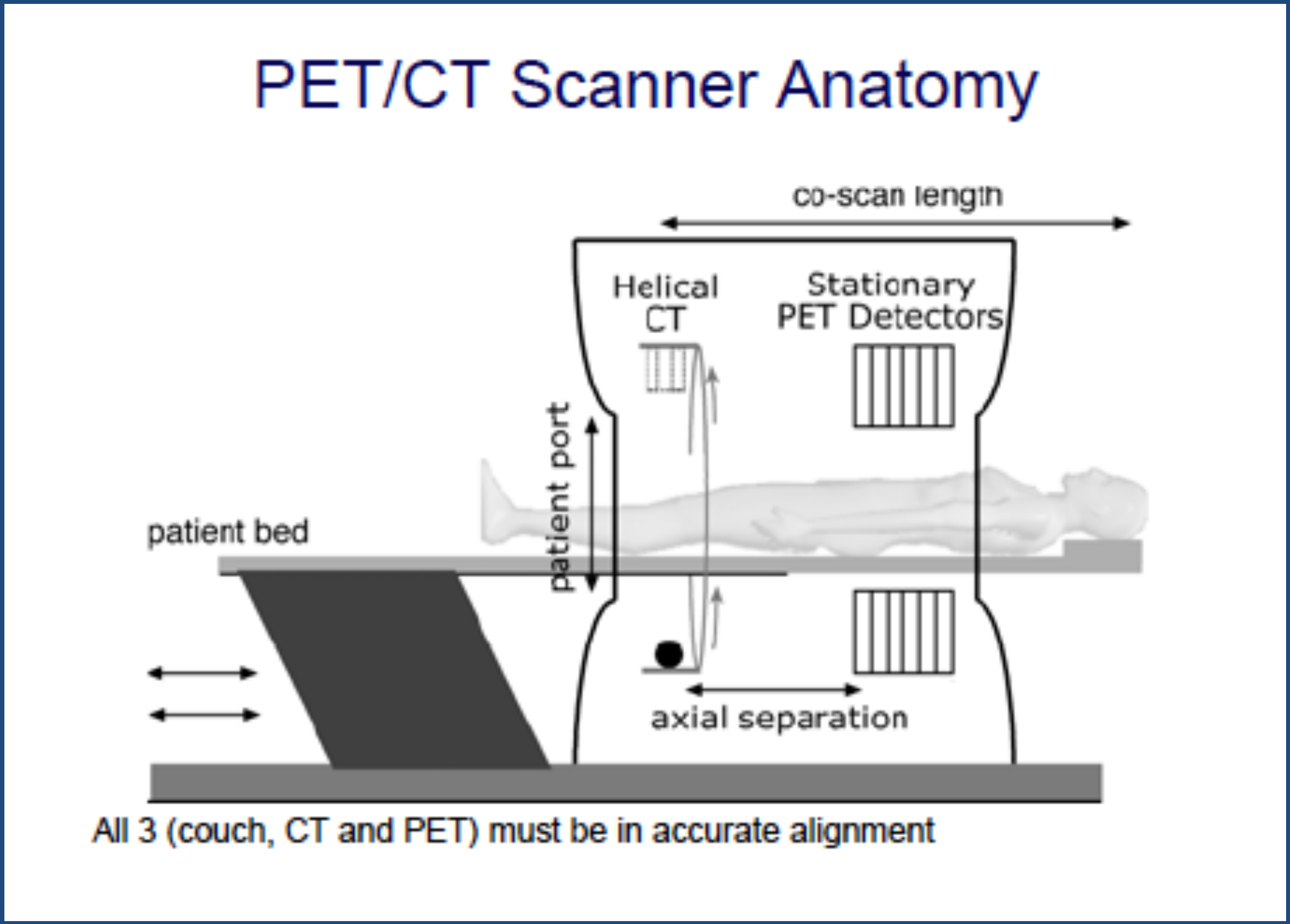


Dopamine receptors imaged with ^{11}C N-methylspiperone PET

Radionuclide imaging

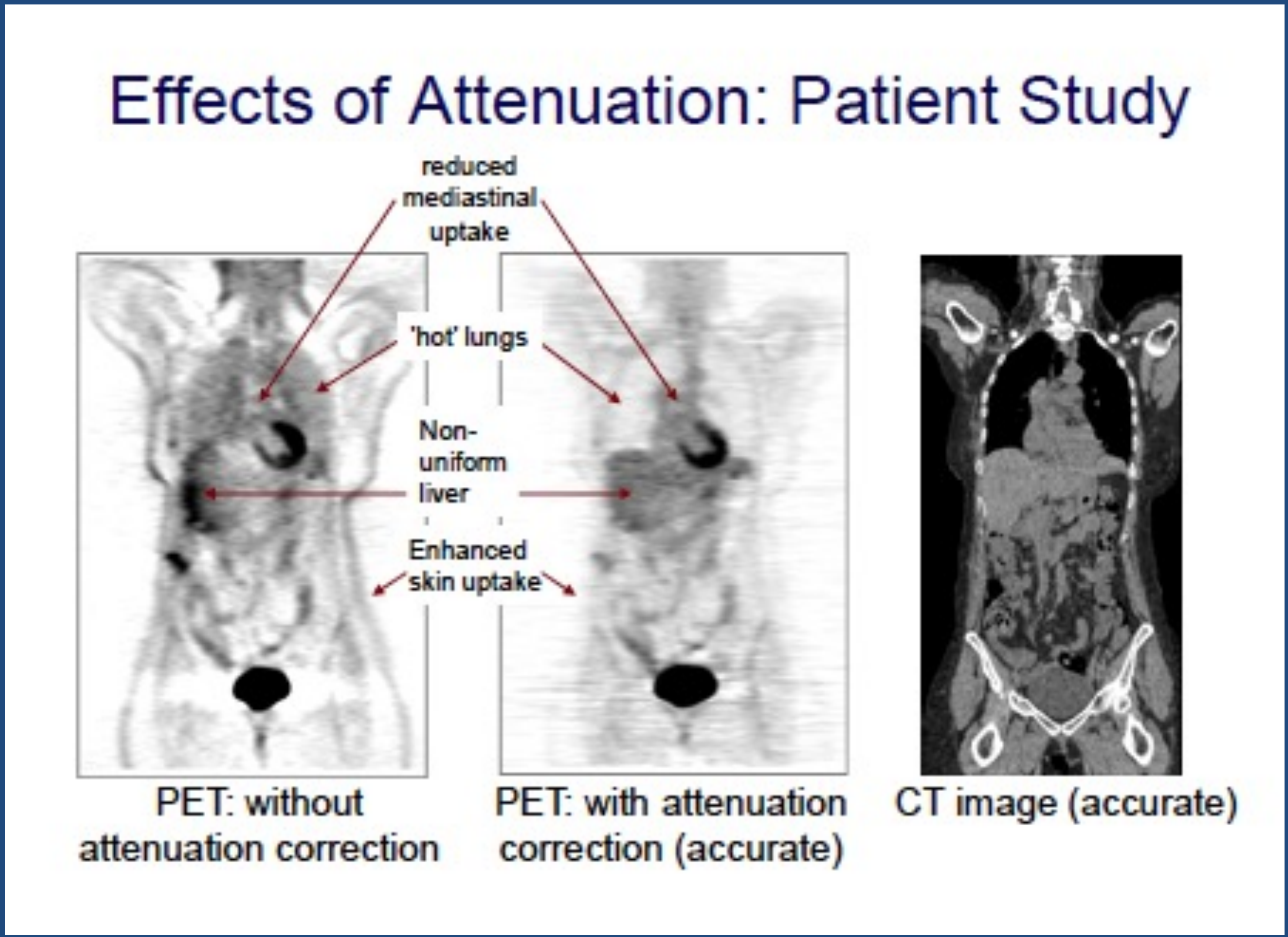
- Most established technique for molecular imaging in humans
- Advantages
  - Sensitive to nano- to femtomolar target concentrations
  - Labeling molecules with a radionuclide does not alter the physical or chemical properties of the molecule
- Disadvantages
  - Time resolution
  - Spatial resolution
  - Requires correction for photon absorption from deep sources
  - Poor structural information
  - Cost
  - Safety
  - Half-life of tracer

Attenuation correction using PET/CT



Kinahan (AAPM)

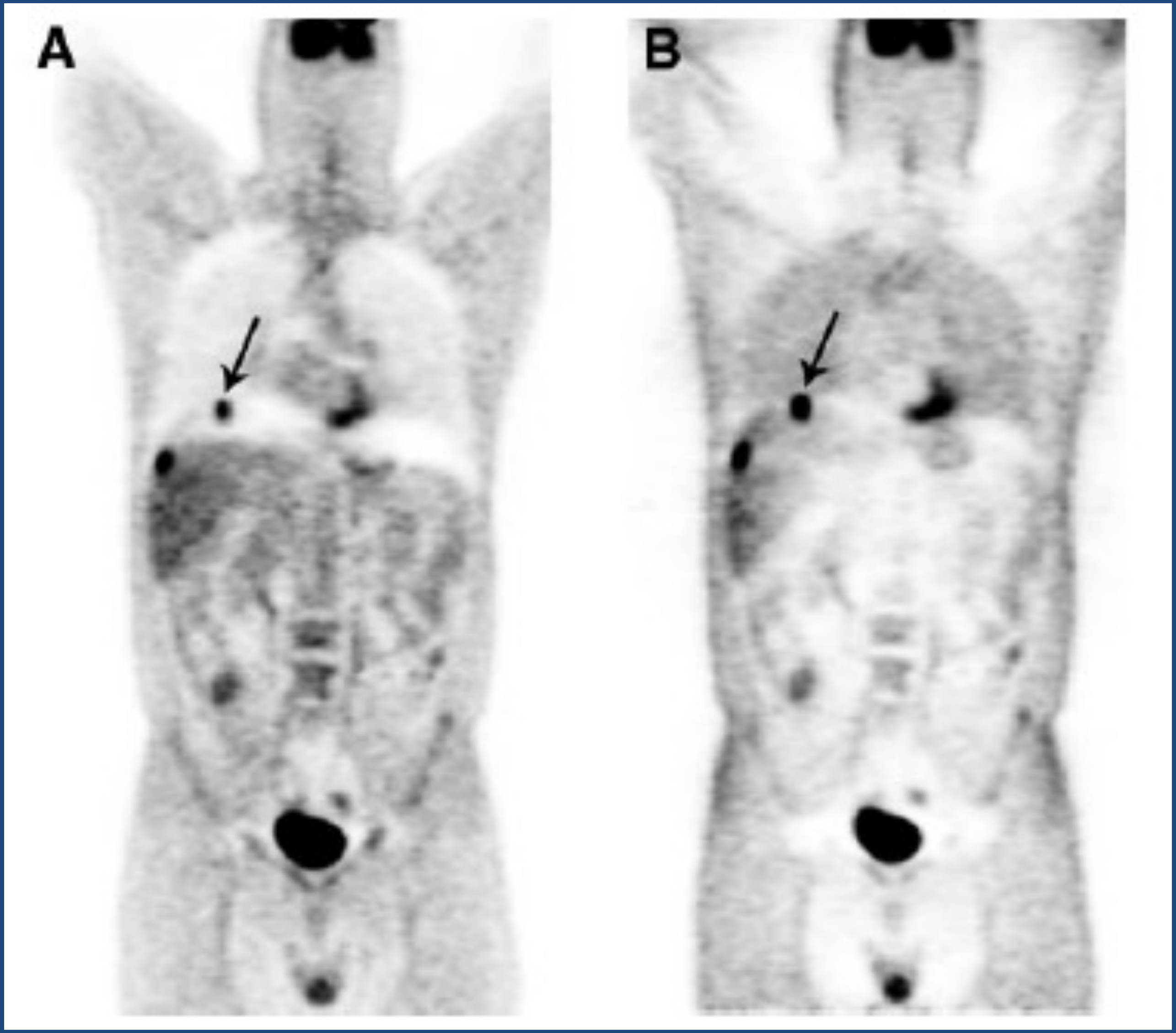
Attenuation correction using PET/CT



Kinahan (AAPM)

In-class exercise: what caused this artifact?

Attenuation -corrected image



Uncorrected image

Sureshbabu, J Nuc Med Tech (2005)

Magnetic Resonance Imaging

"OK, Mrs. Dunn. We'll slide you in there, scan your brain, and see if we can find out why you've been having these spells of claustrophobia."

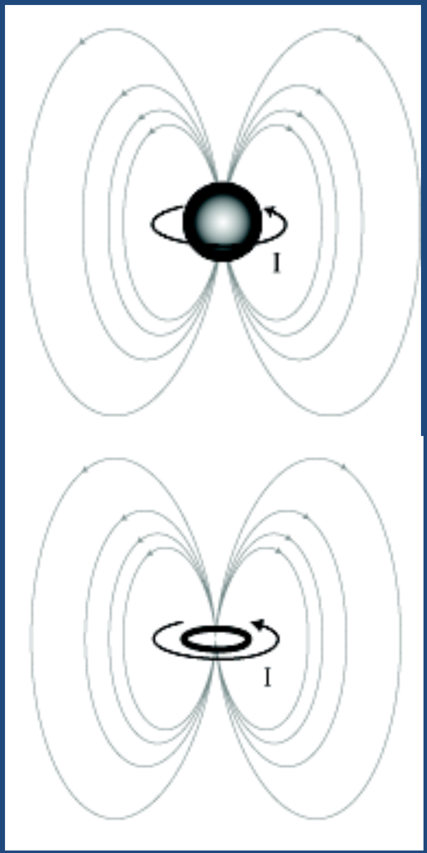
cartoonstock.com

Magnetic Resonance Imaging (MRI)

- MRI maps water in the body
  - (Mobile hydrogen, really)
- Sensitive to interactions of water molecules with their environment
  - *Molecular* environment -> contrast between gray and white matter in the brain
  - *Cellular* environment -> tissue structure
  - *Metabolic* environment -> blood oxygenation
- All possible because the hydrogen nucleus is sensitive to magnetic fields (it's a mini magnetometer!)

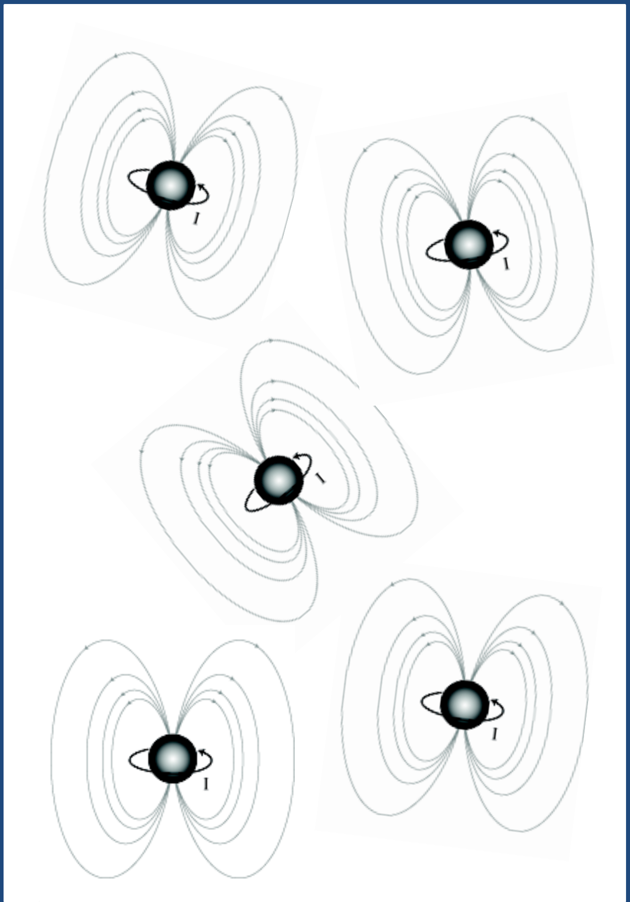
Magnetic moments

- Protons and neutrons
  - Have angular momentum (spin)
  - Generate small magnetic fields
- Magnetic dipole moment
  - Field of a small bar magnet
  - Due to circulating electric charge
  - Allows detection and control of orientation
- Hydrogen nucleus (proton) is most used
  - Relatively large magnetic moment
  - Plentiful in tissues (water)



Magnetization

- Many magnetic dipoles within a volume of tissue
- Net magnetic moment per unit volume:
  - Magnetization, *M*
- Reflects
  - Density of spins <u>and</u>
  - How well they are aligned



MRI in a nutshell

- MRI is a map of magnetization
- To make an image, we need to
  - Create net magnetization
  - Tag it with position information
  - Detect it
- We can do this with 3 magnetic fields
  - *Static field (B_0)*
    - Polarizing spins
    - Detecting spins
  - *Oscillating field (B_1)*
    - Exciting spins
  - *Gradient field (G)*
    - Spatially encoding spins
- Let’s see how these work

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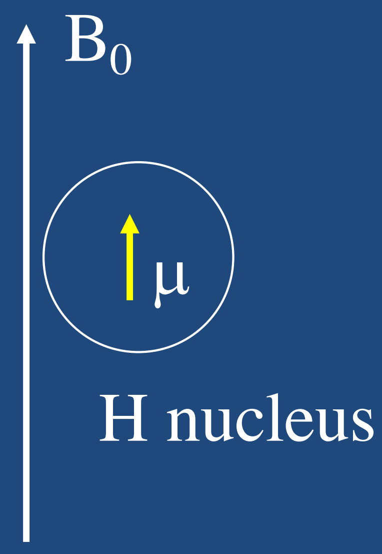
Equilibrium Magnetization

- Sample is placed in a strong polarizing magnetic field, B_0
- Individual nuclear spins preferentially align with B_0
  - Energy:

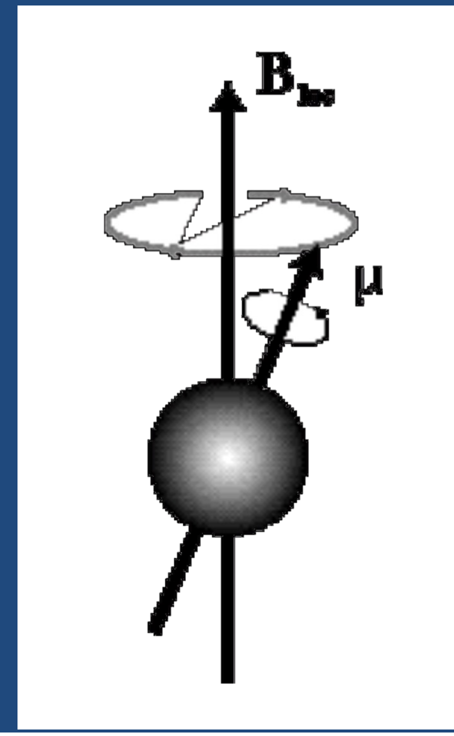
$$E = -\vec{\mu} \cdot \vec{B}$$

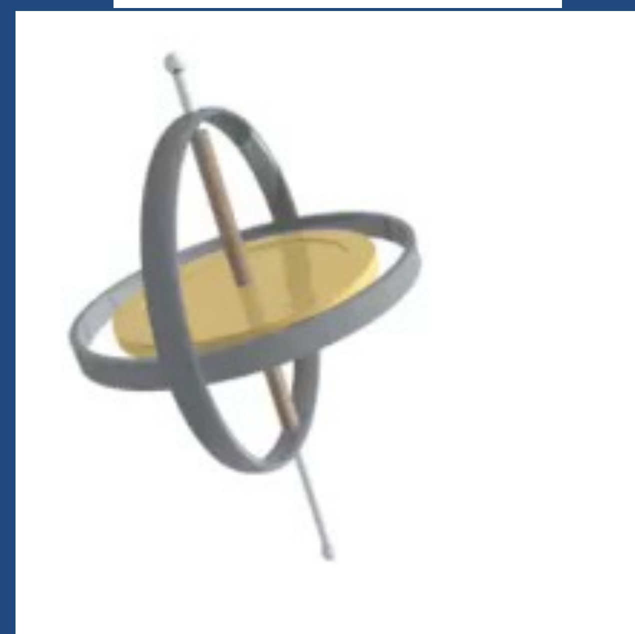
- The net magnetization, M_0, of the sample is parallel to B_0
- Represents an *equilibrium* between
  - The aligning influence of the external (B_0) field
  - The disordering influence of thermal energy (random motion)



Spin precession

- When a magnetic moment μ with spin is placed in an external magnetic field
  - The magnetic moment *precesses*
  - Similar to motion of a spinning top in a gravitational field

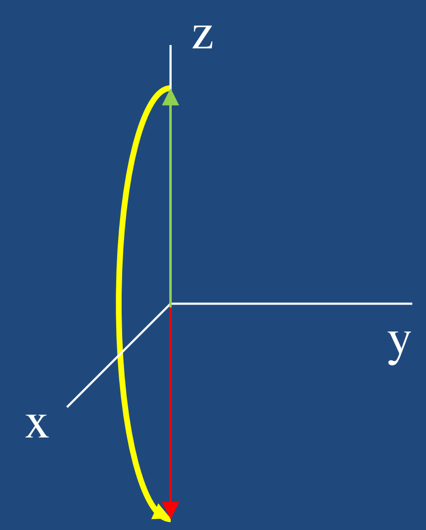




In-class exercise: composite pulses

- Goal: tip spins by 180 degrees
- Rotate spins by π around -y axis: $R_{-y}(\pi)$
  - Apply a constant magnetic field
    - Direction: along -y
    - Duration: ½ period of precession
  - What if the field strength is not uniform?
    - Some spins are over- or under-tipped
- What is the effect of

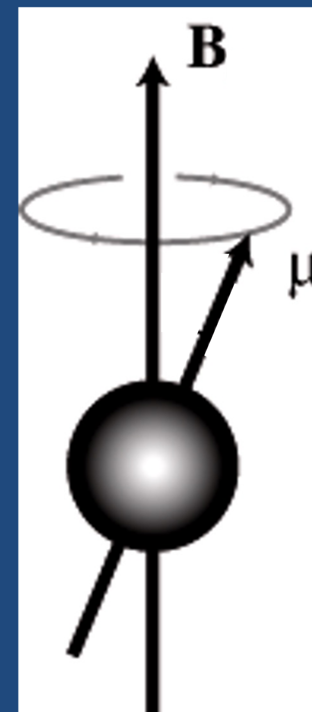
$$R_{-y}(\pi/2)R_x(\pi)R_{-y}(\pi/2)?$$



How can spins be detected?

- Spins precess around an applied field
- Magnetic dipole field precesses also
  - Precession rate
    - Larmor relation: $\omega = -\gamma B$
- Detected by induction

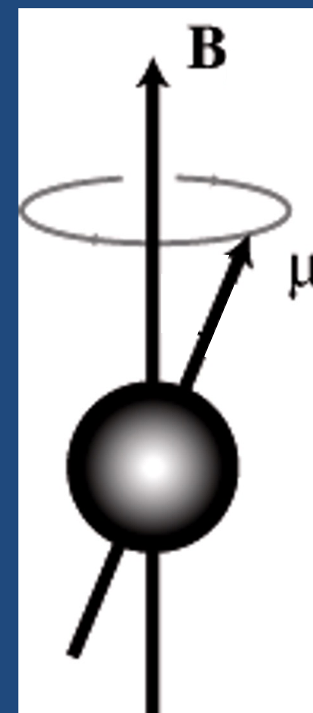
$$V = -\frac{d}{dt}\int_S B_{spin} \cdot da$$



- Frequency of the measured voltage
  - Equals the spin precession frequency
  - Reveals the applied field strength

Spin detection

- If the net B field is different in each position, *x*
  - Frequency of the detected field -> reveals the spin's position
- Spins <u>parallel</u> to *B* don't make a time-varying field and hence are invisible
- Spins <u>perpendicular</u> to *B* produce the largest signals
- In equilibrium, magnetic moments are aligned with *B* on average
  - How can we detect the spins?



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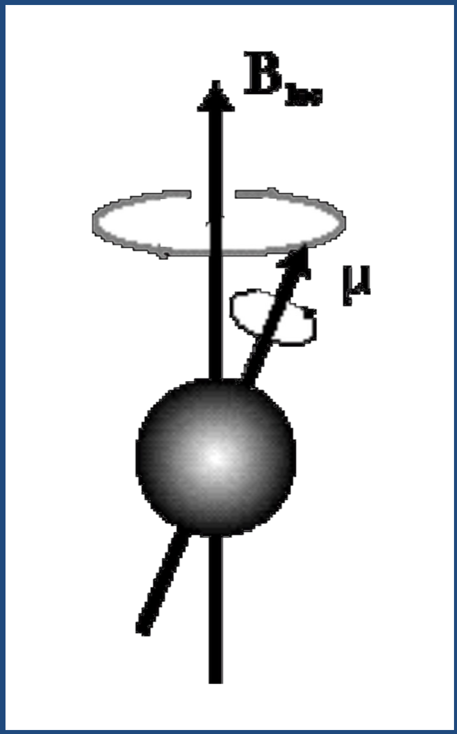
  - *Gradient field (G)*
    - Spatial encoding

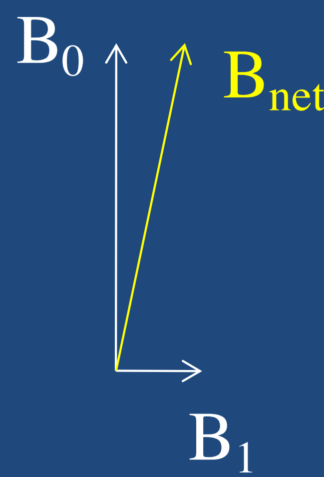
Spin excitation

- To be detectable, spins must be tipped away from the B_0 axis
  - Dipole field precesses
  - Spin ‘excitation’
- Tipping is accomplished with another magnetic field (B_1)
- Spin excitation is the first step in an MR measurement



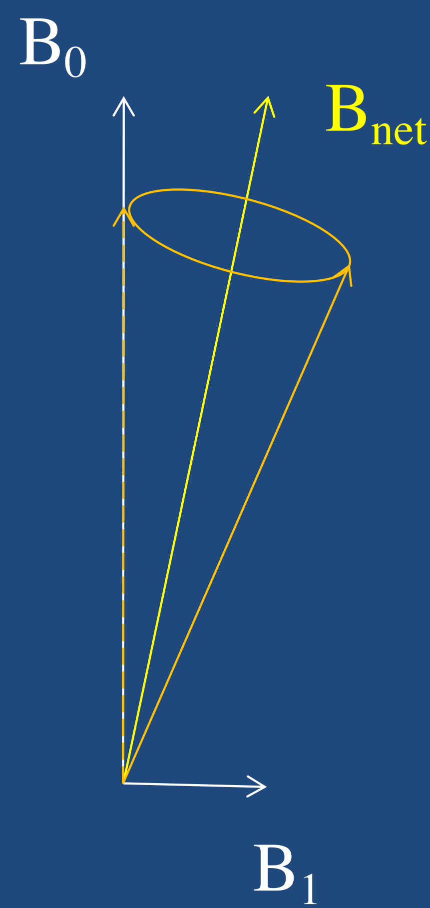
Spin excitation

- B_1 field should be $\perp$ B_0 to tip spins into the transverse plane
- A static B_1 just tilts the polarizing field
  - Does not create large transverse magnetization, $M_\perp$
- A time-varying B_1 field can create large $M_\perp$

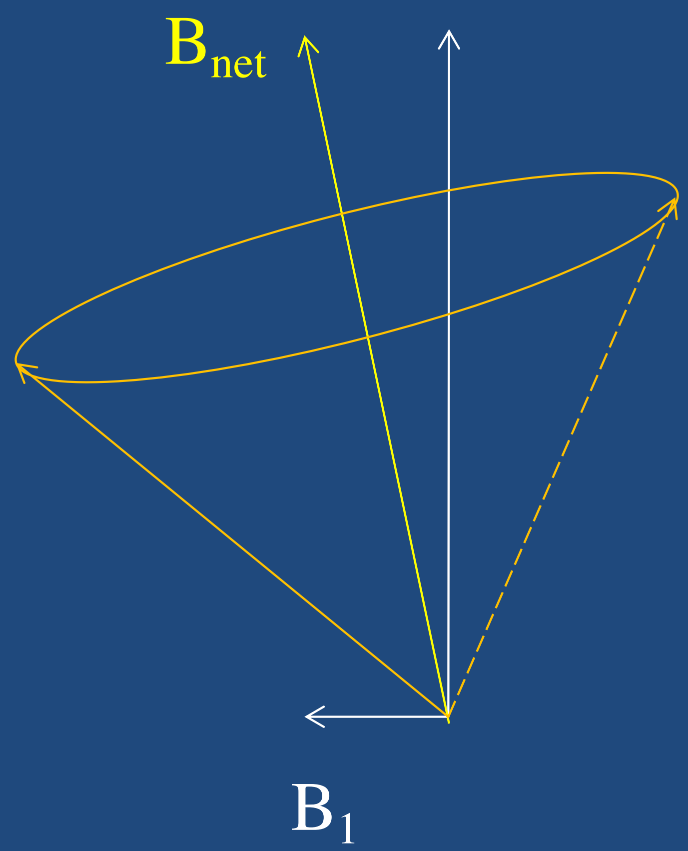


At time = 0

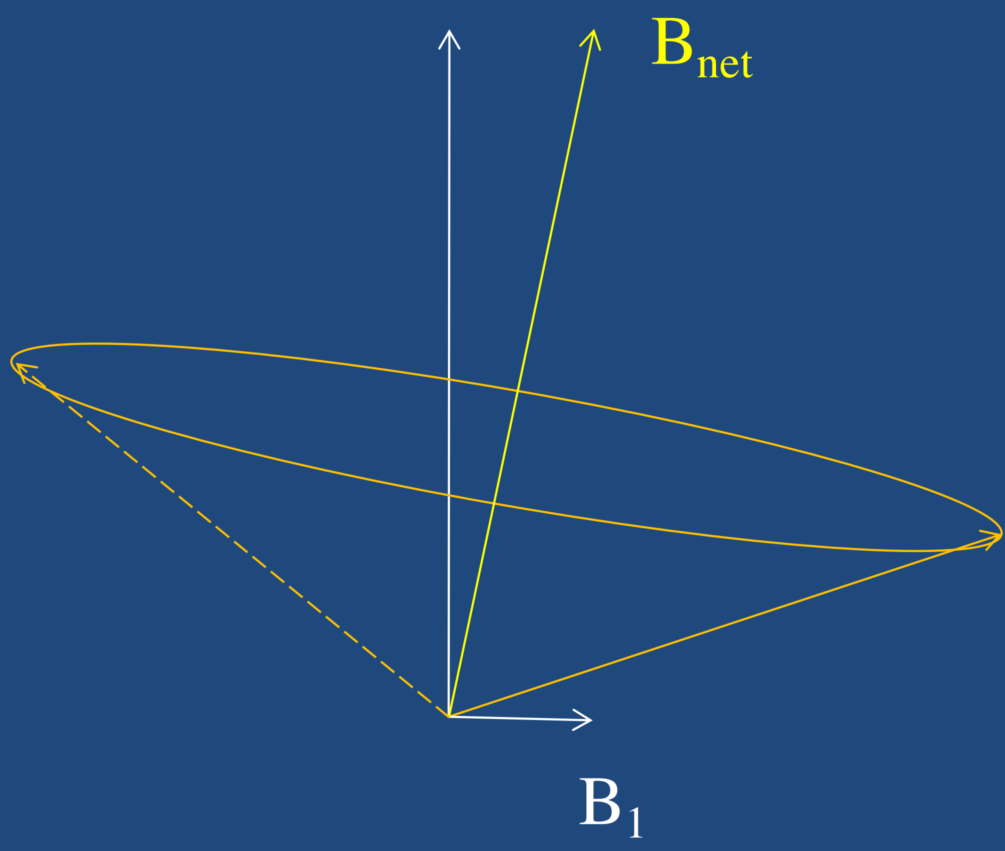
At time = $\tau/2$



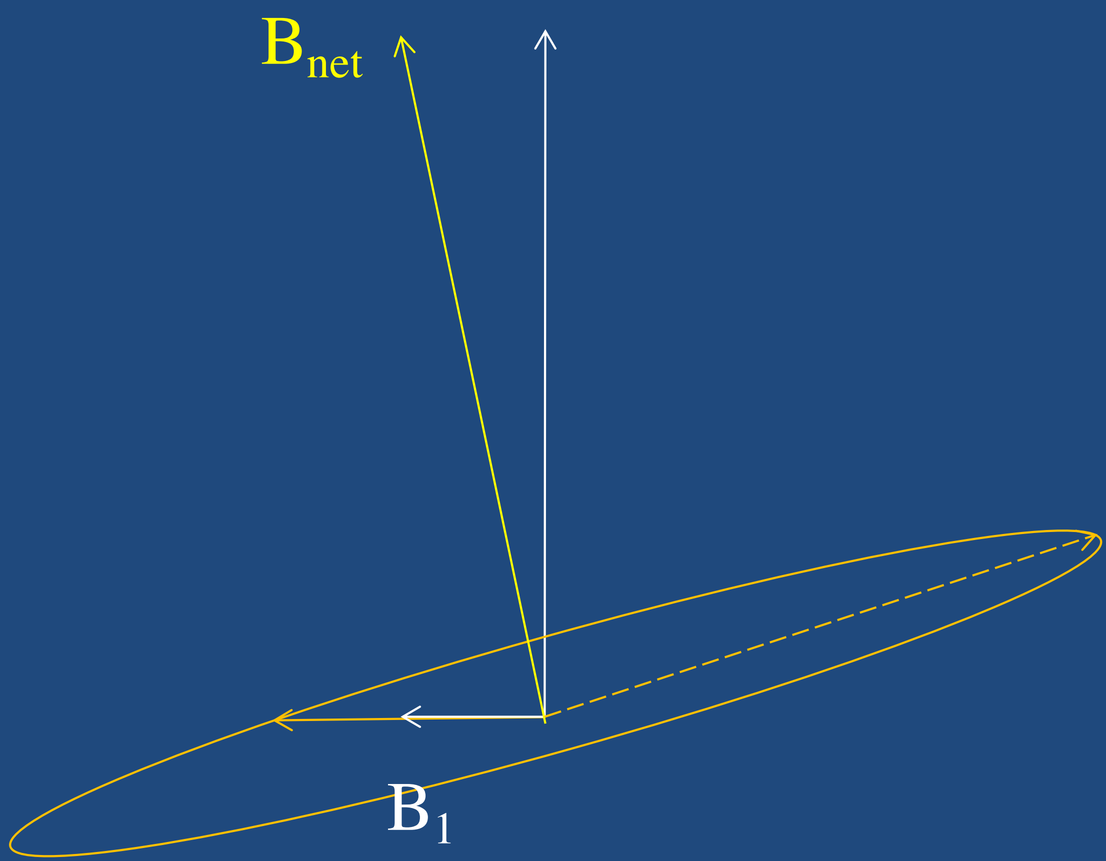
At time = τ



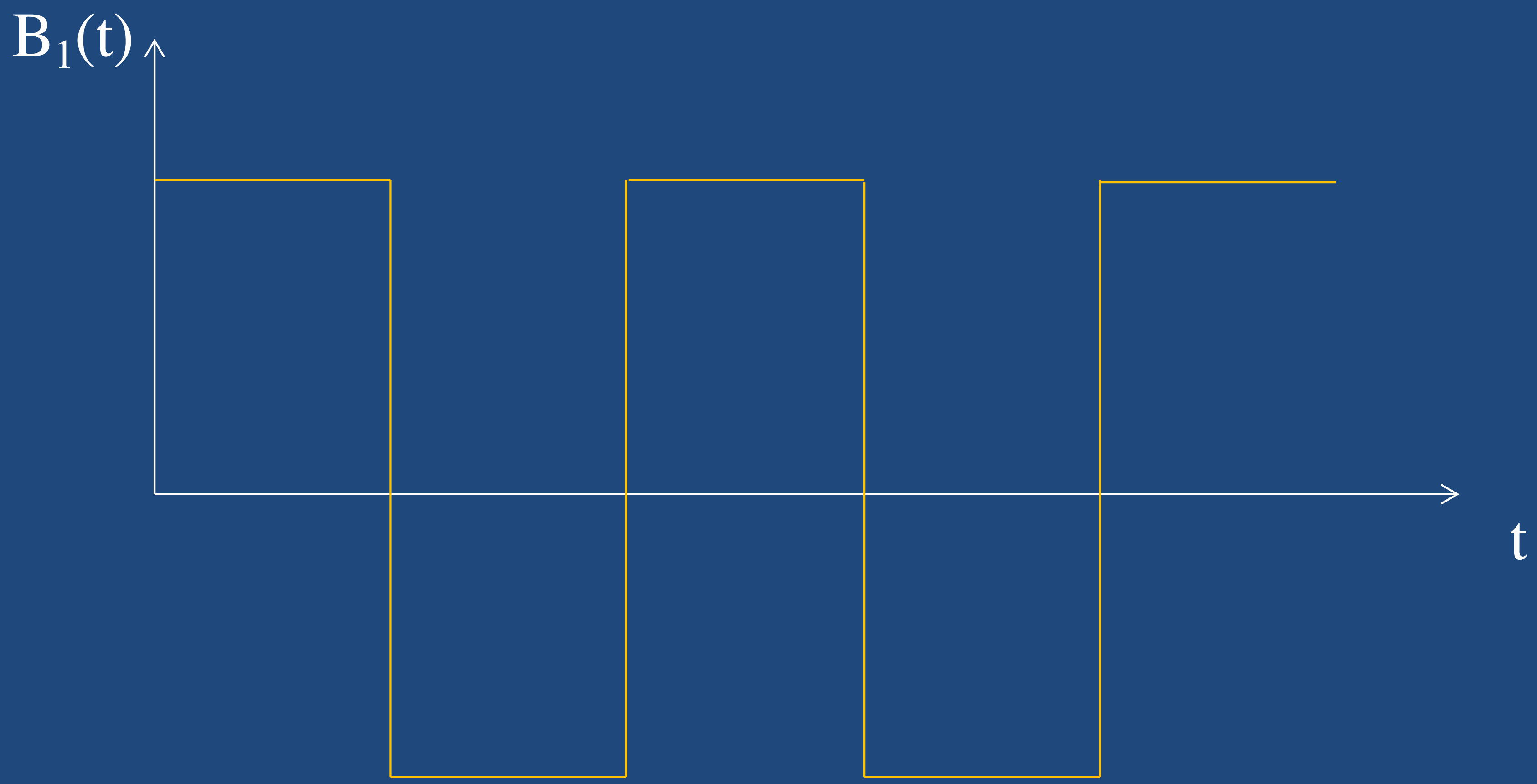
At time = 3τ/2



Tip angle = 90°



Time dependence of B_1 field



Frequency = $\omega = \gamma B_0$

Spin excitation

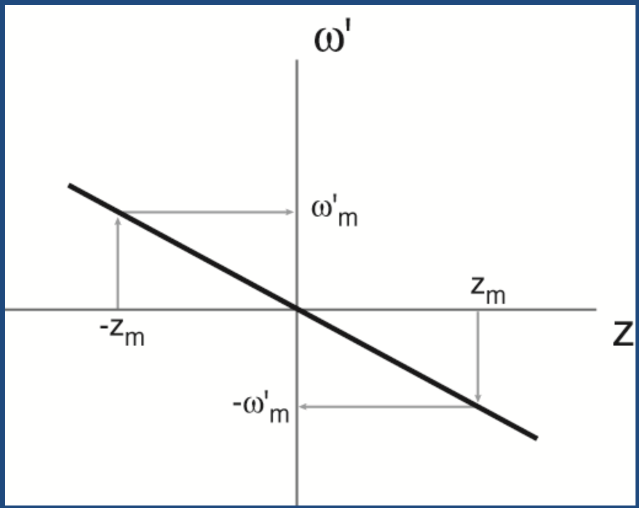
- A time-varying B_1 field can create large $M_{\perp}$
  - If the B_1 field precesses with the spins, slow tipping can accumulate over time
- Frequency of B_1 field must match spin precession frequency to have a significant effect
  - B_1 must be resonant with spin precession

MRI in a nutshell

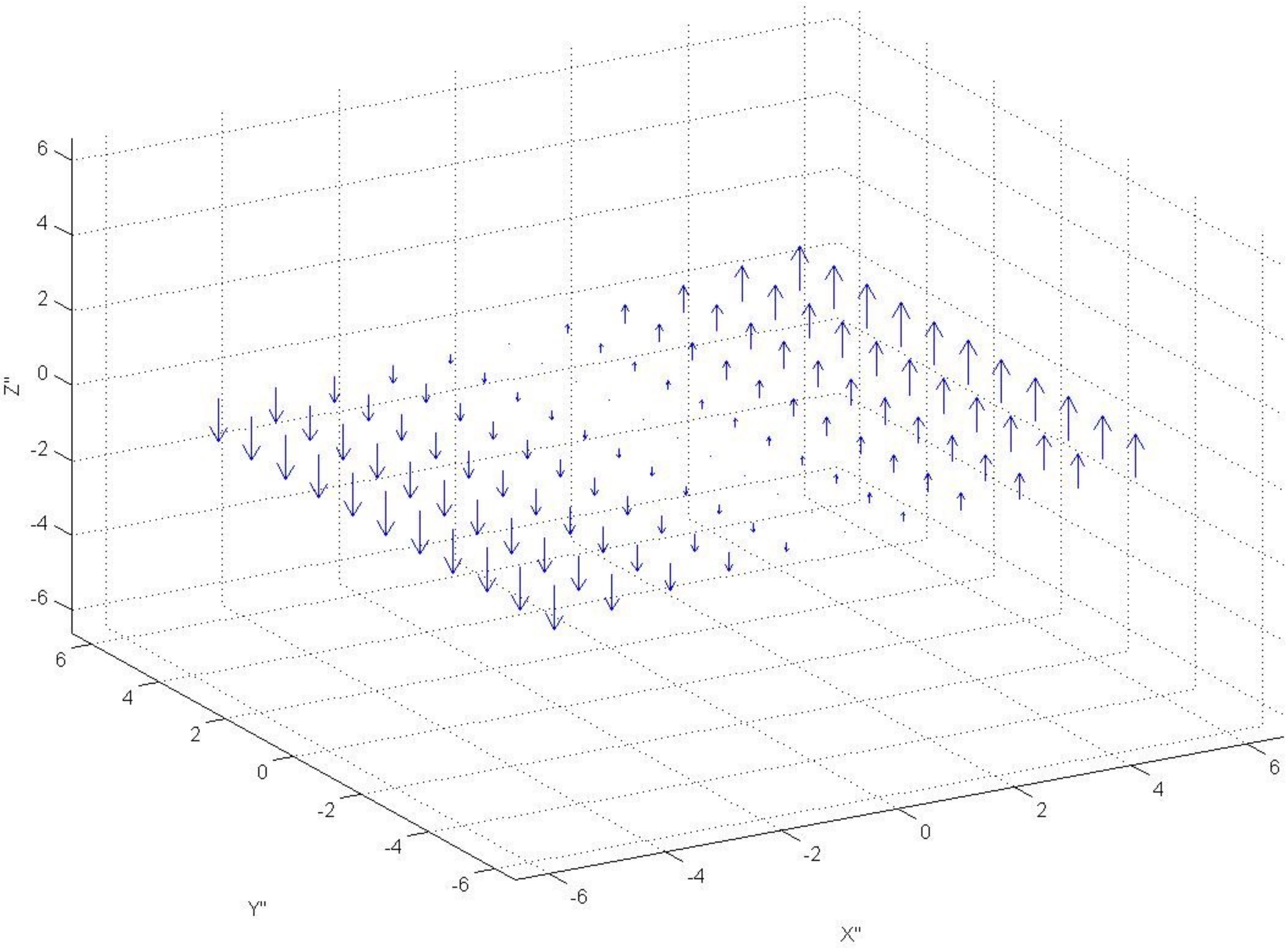
- MRI is a map of magnetization
- To make an image, we need 3 magnetic fields
  - *Static field (B_0)*
    - Polarization
    - Detection
  - *Oscillating field (B_1)*
    - Excitation
  - *Gradient field (G)*
    - Spatial encoding

Magnetic Field Gradients

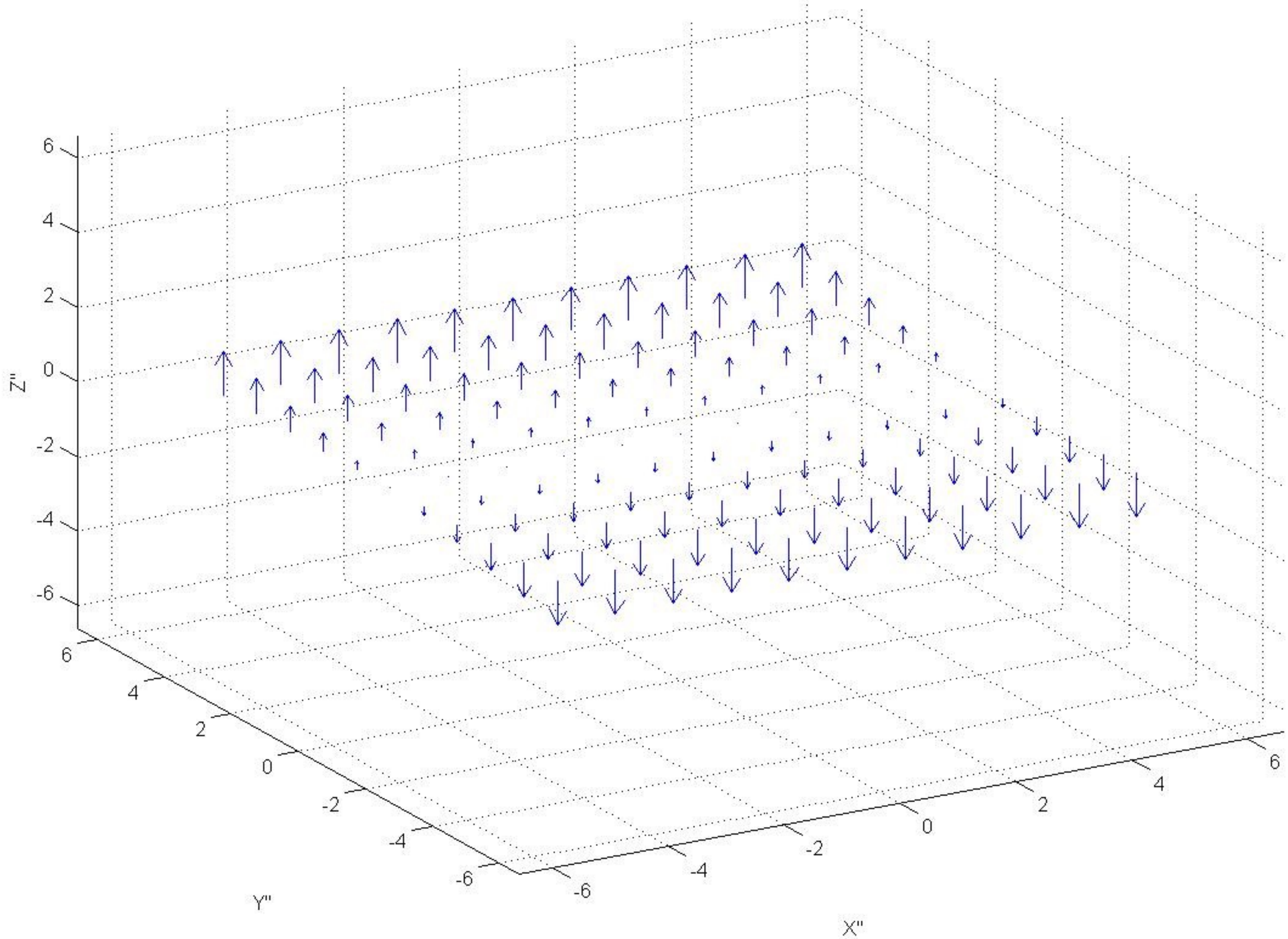
- Spin precession frequency depends on the local field strength ($\omega = -\gamma B_z$)
- If the local field strength varies with position, then so will precession frequency
- Simplest position dependence => linear
  - Precession frequency proportional to spin's displacement from origin



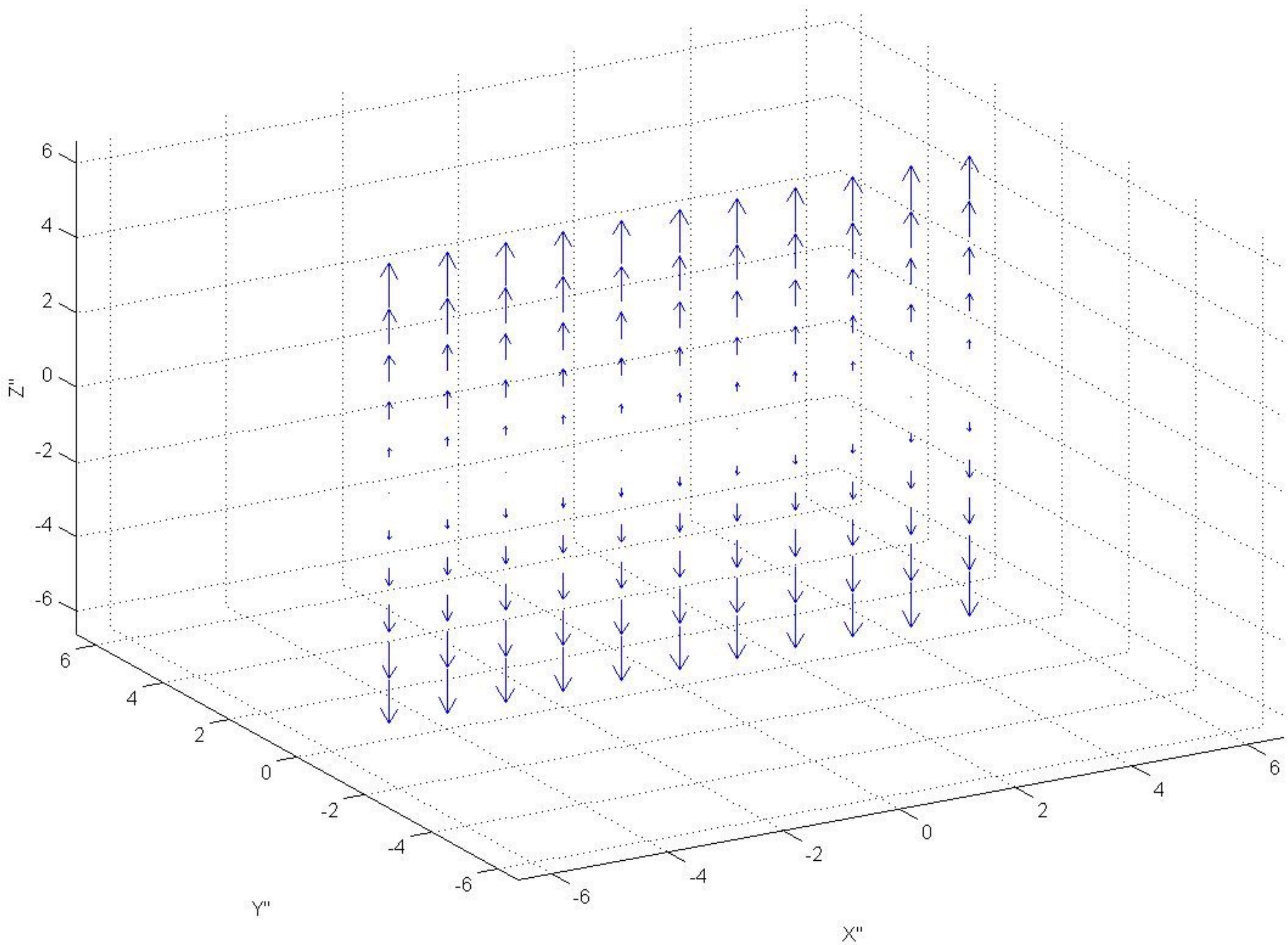
A gradient of B_z in the x direction



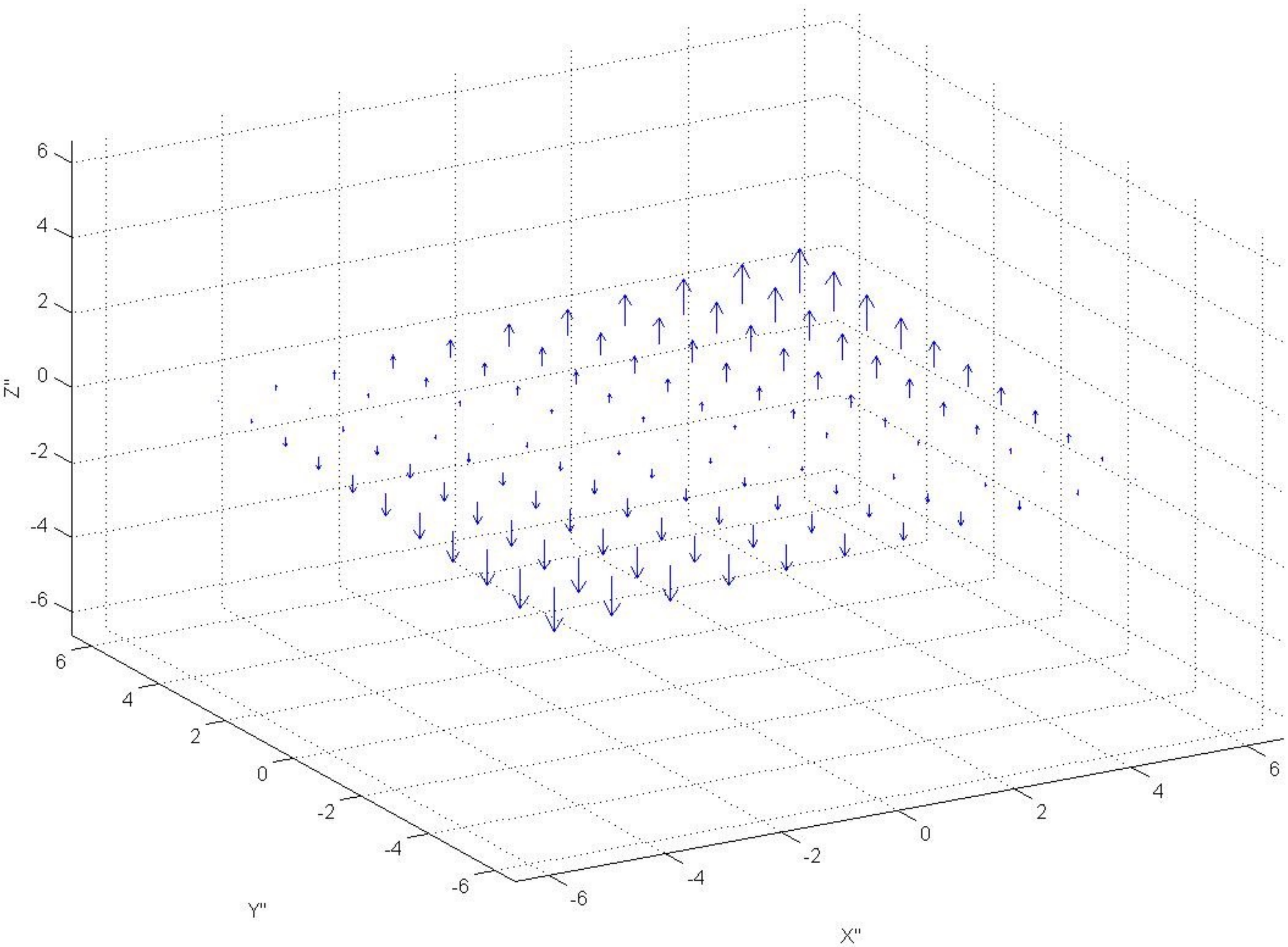
A gradient of B_z in the y direction



A gradient of B_z in the z direction

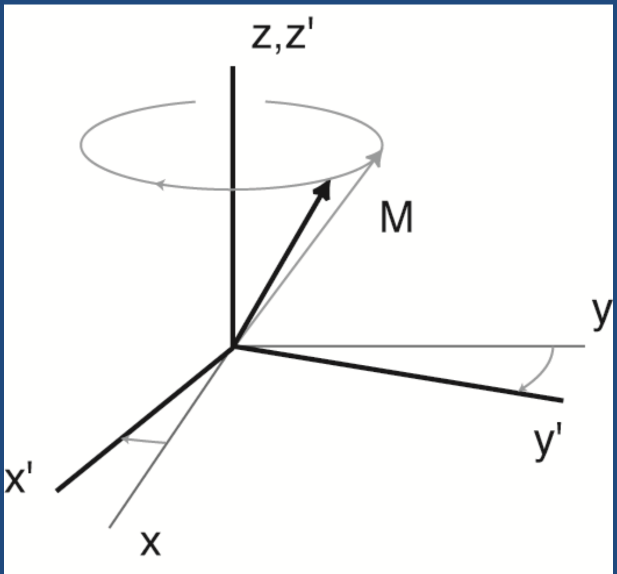


A gradient of B_z in the x+y direction



The rotating frame

- Analyze spin motion in a coordinate frame (x',y',z') precessing around z at the Larmor frequency $-\gamma B_0$
- Spin motion is simpler in the rotating frame
  - If $B_z=B_0$, spins are motionless in the rotating frame
  - If $B_z=B_0+dB_z$, spins precess at frequency $\omega' = -\gamma \cdot dB_z$
- In the rotating frame, we can ignore the effect of B_0



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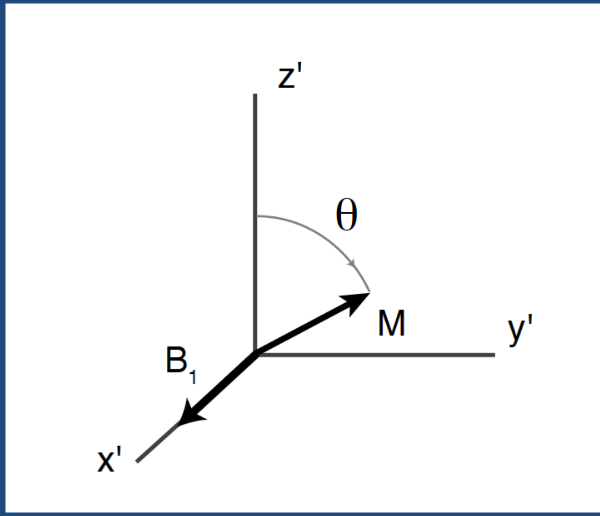
- In the rotating frame, we can ignore the effect of B_0
  - A B_1 field rotating in the lab frame at the frequency $-\gamma B_0$ is stationary in the rotating frame



Effects of a field gradient

- If the applied field, B_z, depends linearly on position

$$B_z(\vec{r}) = B_0 + \vec{G} \cdot \vec{r}$$

then it has a constant gradient

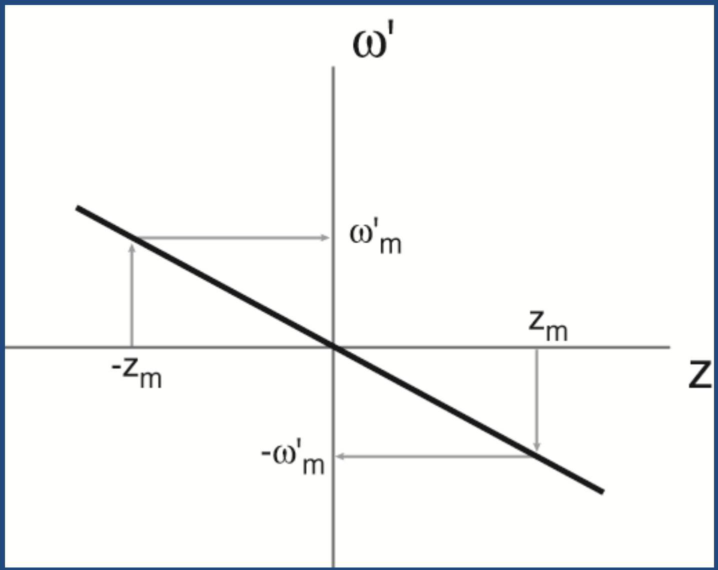
$$\vec{G} = \nabla B_z$$

- In the rotating frame, the field is

$$B'(\vec{r}) = \vec{G} \cdot \vec{r}$$

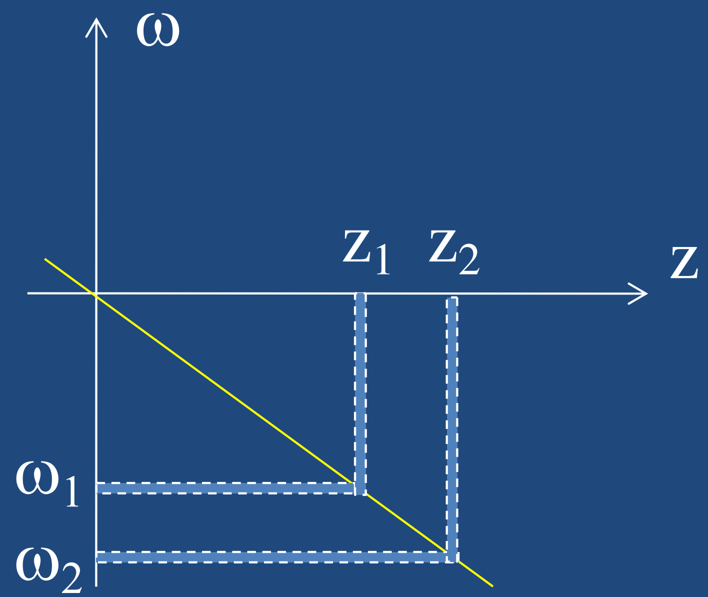
which implies the precession frequency in this frame is

$$\omega' = -\gamma \vec{G} \cdot \vec{r}$$



Application 1: Selective Excitation

- To excite spins uniformly in the range $z=z_1$ to z_2, apply a $B_1(t)$ pulse that covers the frequency range $\omega=\omega_1$ to ω_2 uniformly.
- What function of time has a uniform spectrum over a finite frequency range?



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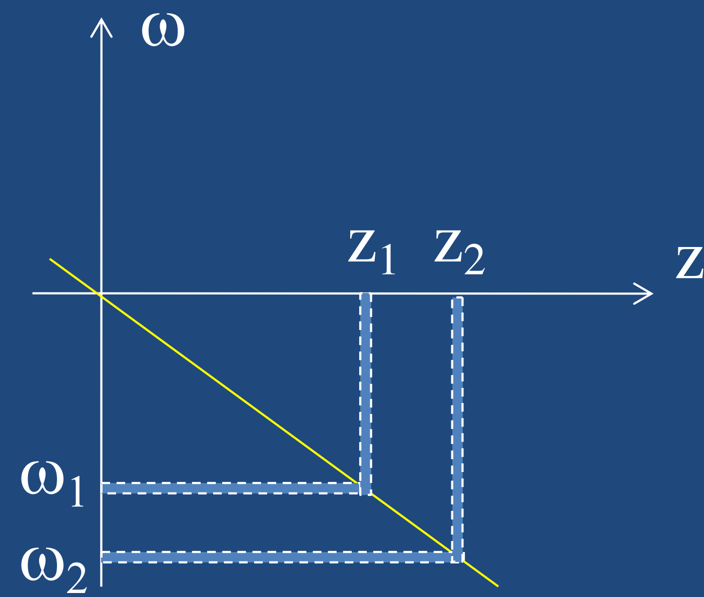
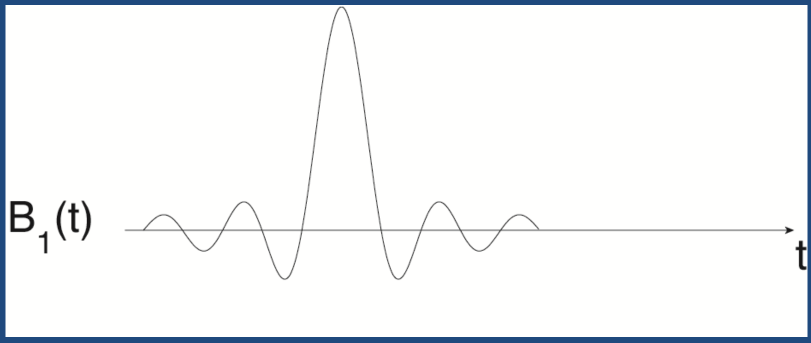
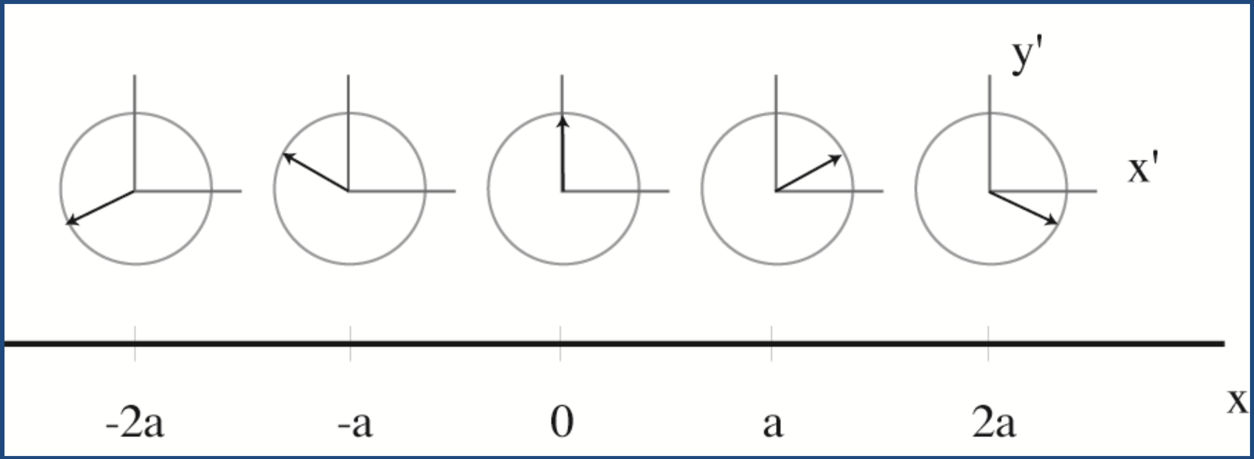


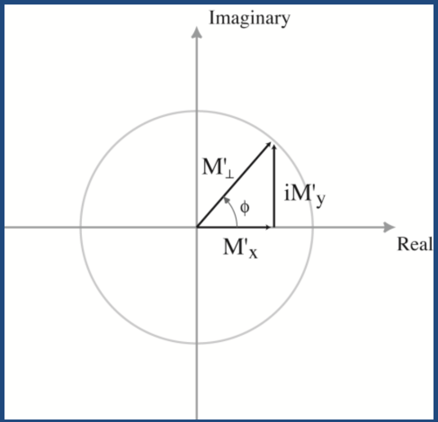


Application 2: Spatial encoding



- Spin orientation in a gradient field is proportional to position
- The proportionality constant is -k

- Define the transverse magnetization as a complex quantity:



$$M_\perp \equiv M_x + iM_y$$
$$= \rho \cdot e^{i\varphi}$$

- The signal voltage is proportional to the net magnetic moment of the sample. Define the signal:

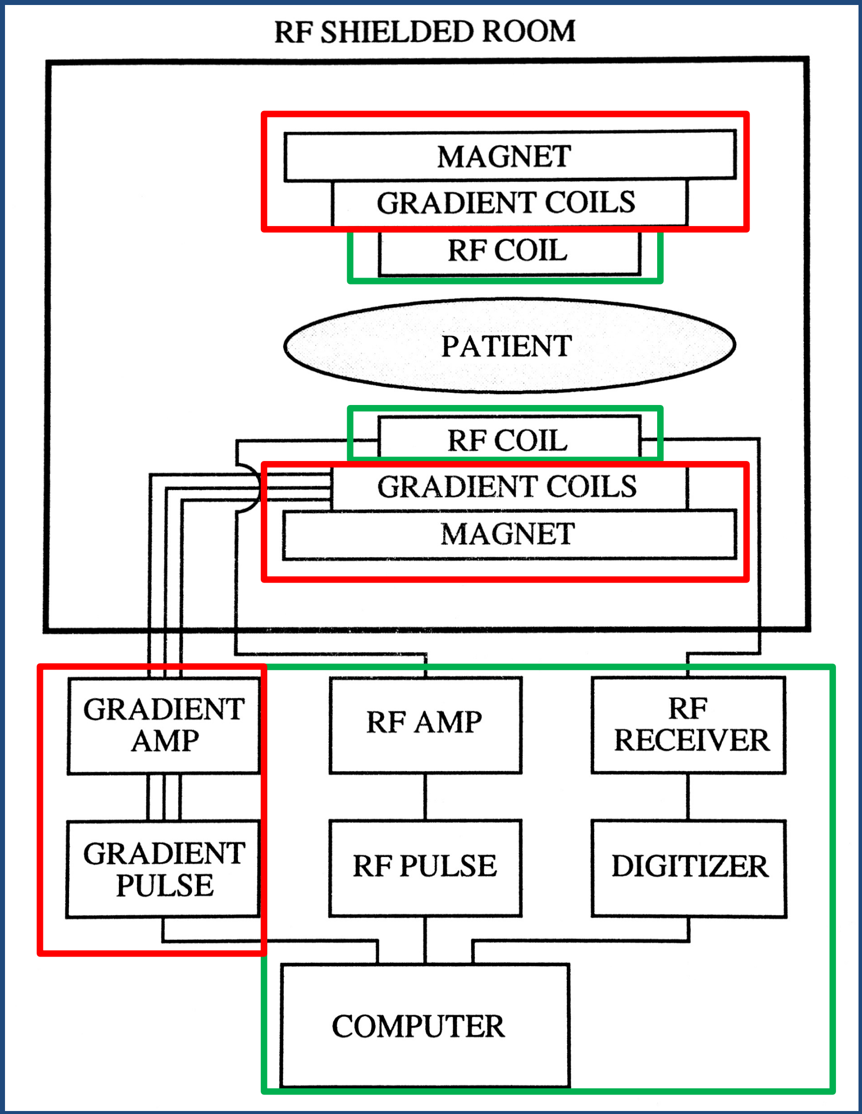
$$S = \int M_\perp(x)dx = \int \rho(x)\, e^{i\varphi(x)}dx = \int \rho(x)e^{-ikx}dx$$

- The (inverse) Fourier Transform gives the spatial distribution of magnetization

$$\rho(x) = F^{-1}\{S(k)\}$$

MRI System Design

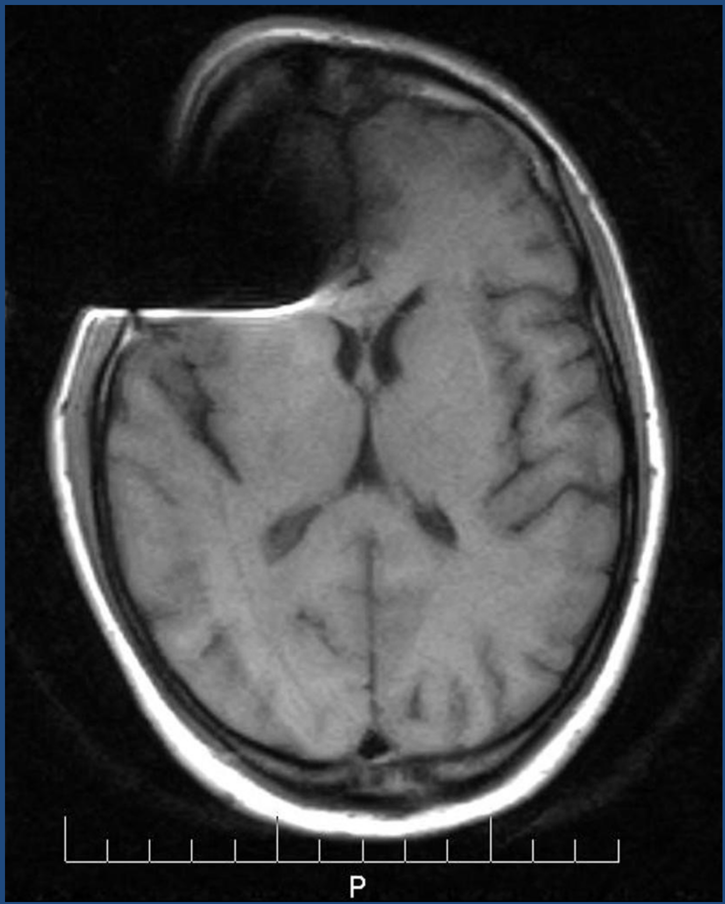
- Static magnet
  - Uniform B_0
- Gradient subsystem
  - Spatially dependent B_z
- Radio frequency (RF) subsystem
  - RF pulse generator
  - RF receiver



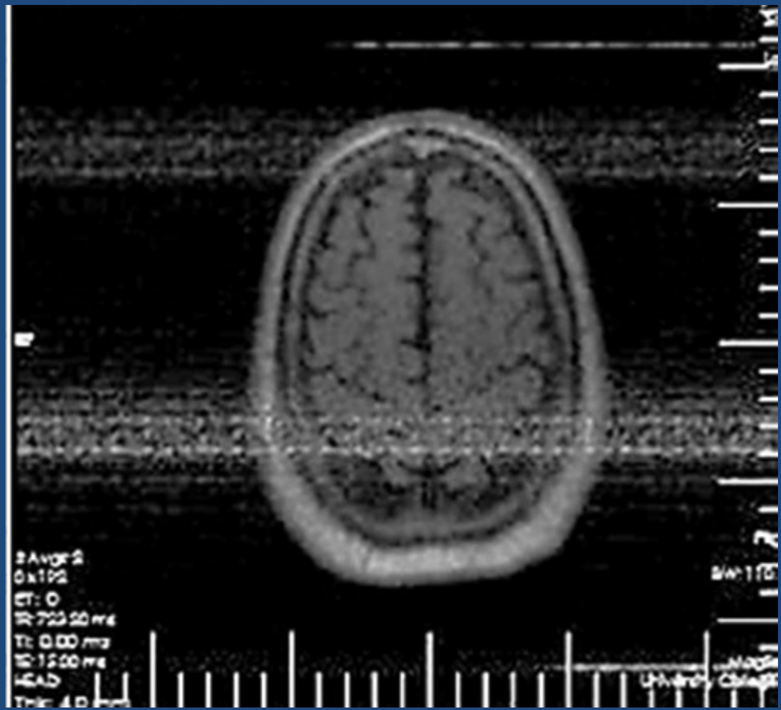
Jin (1999)

Patient handling

What caused these artifacts?



Case courtesy of Dr Ayush Goel, Radiopaedia.org



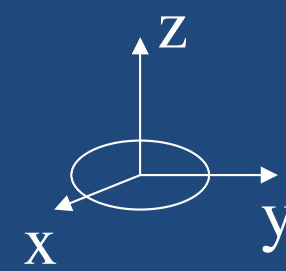
Ogbole et al, Niger Postgrad Med J (2017)

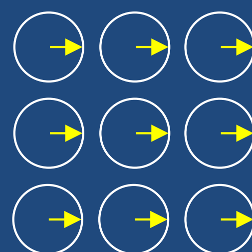
MRI in a nutshell

- MRI is a map of magnetization
- To make an image, we need 3 magnetic fields
  - *Static field (B_0)*
    - Polarization
    - Detection
  - *Oscillating field (B_1)*
    - Excitation
  - *Gradient field (G)*
    - Spatial encoding
- What determines the brightness of the image at each point?

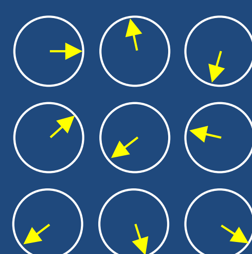
Transverse relaxation

- No net M_x or M_y in equilibrium state
- After spins are put in the xy plane, large transverse magnetization:





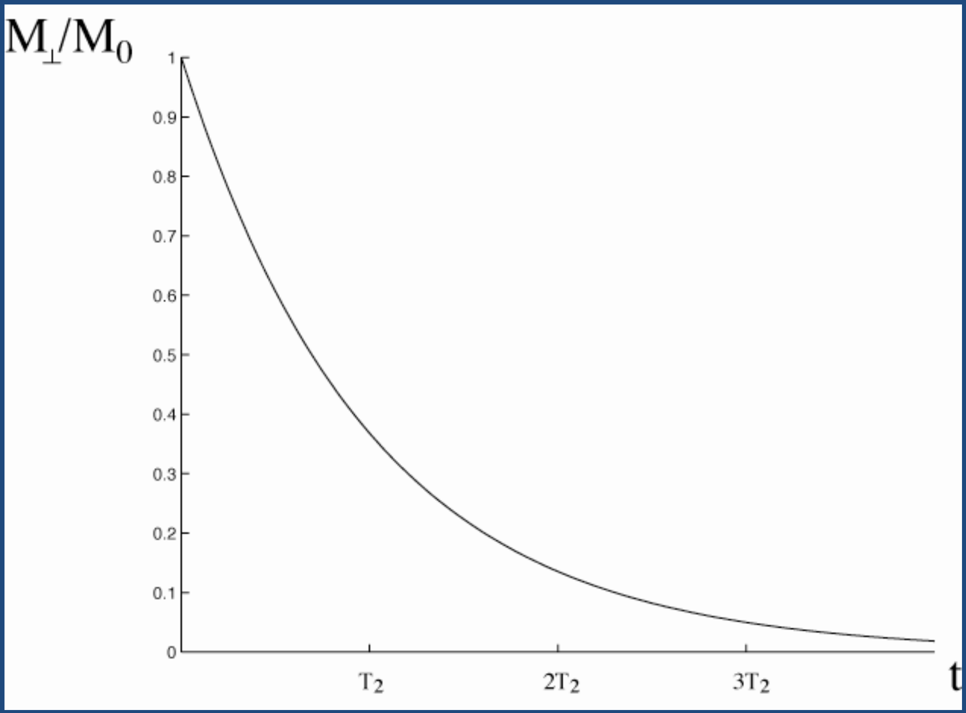
- Over time, spin orientations become randomized:



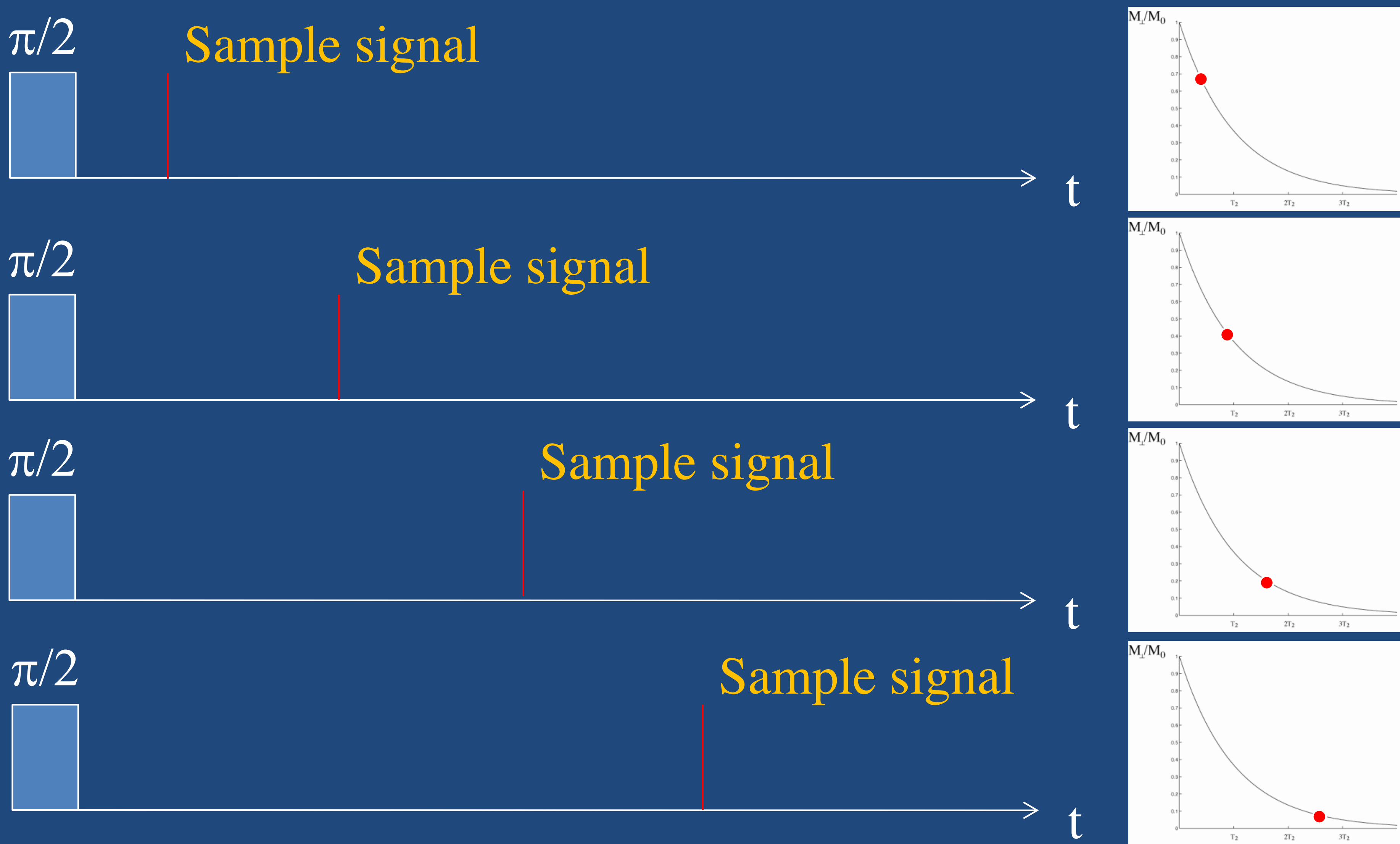
- Occurs at rate $R_2 = 1/T_2$

Multiple decay time measurements of T_2

- Acquire a series of images, each at a different time after the tipping B_1 pulse
- Signal intensity decays exponentially with rate constant $1/T_2$



T_2 measurement



Magnetic Resonance Imaging (MRI)

- MRI maps water in the body
  - (Mobile hydrogen, really)
- Pros
  - Diverse sources of contrast
    - Soft tissue contrast
    - Structure and function
  - Non-ionizing radiation
- Cons
  - Cost
  - Safety for metal objects

For more information

- Spin precession and Nuclear Magnetic Resonance (NMR)
  - https://youtu.be/TQegSF4ZiIQ

Summary of medical imaging methods

- Each method relies on mapping the interaction of tissues with some form of energy or material
  - Acoustic (US)
  - Electromagnetic
    - Radiofrequency (MRI)
    - X-ray (CT)
  - Radiopharmaceutical (SPECT and PET)
- Each method has advantages and disadvantages
  - Understand these in terms of image resolution, sensitivity (the topics we’ll turn to next…)

Sources

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