Development of Complex Curricula for Molecular Bionics and Infobionics Programs within a consortial* framework**

Consortium leader

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**Molekuláris bionika és Infobionika Szakok tananyagának komplex fejlesztése konzorciumi keretben

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BIOMEDICAL IMAGING

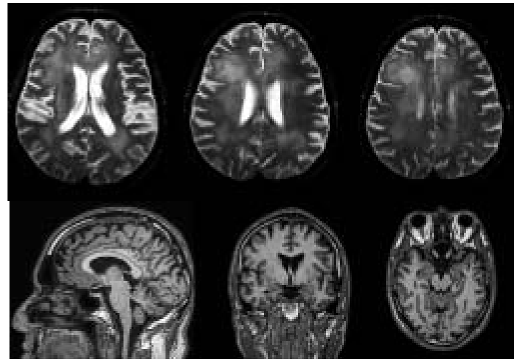
(Orvosbiológiai képalkotás)

MAGNETIC RESONANCE IMAGING (MRI) - BASICS

(Mágneses Rezonancia Képalkotás (MRI) - Bevezetés)

ISTVÁN KÓBOR, GYÖRGY ERŐSS

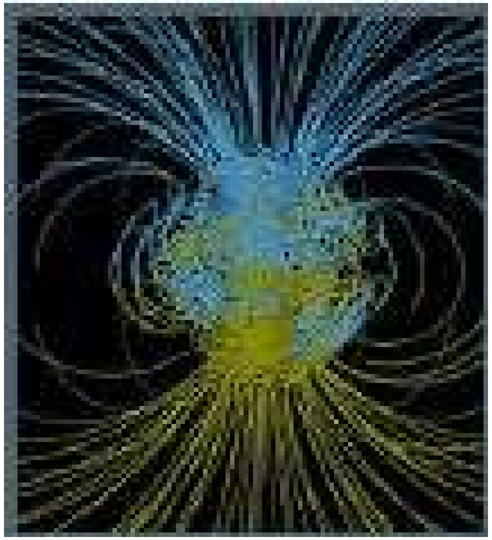
MR Images



Tesla and Gauss are measures of magnetic field strength

- Earth's magnetic field ~0.5 Gauss.
- 1Tesla = 10,000 Gauss.
- Our fMRI system is 3T.

  ~x60,000 earth's field strength



Signal and Field Strength

- Outside magnetic field:
  - Spins randomly oriented
- In magnetic field:
  - Spins tend to align parallel or anti-parallel to magnetic field
  - At room temperature, ~4 parts per million more protons per Tesla align with versus against field
  - As field strength increases, there is a bigger energy difference between parallel and anti-parallel alignment (faster rotation = more energy)
  - A larger proportion will align parallel to field
  - More energy will be released as nuclei align
  - Therefore, MR signal increases with square of field strength

Signal and Field Strength

- Most clinical MRI: 1.5T
- fMRI systems: 3.0T
- Maximum for NbTi MRI ~11.7T
- Field strength influences:
  - Faster Larmor frequency
  - Bigger energy difference between parallel and anti-parallel alignment
    - Larger ratio of nuclei aligned = more signal
    - More signal as nuclei realign
  - Reduced TR and TE: less time to take images

Signal and Field Strength

- In theory:
  - Signal increases with square of field strength
  - Noise increases linearly with field strength
  - A 3T scanner should have twice SNR of 1.5T scanner; 7T should have ~4.7 times SNR of 1.5T

- Unfortunately, physiological artifacts also increase, so advantage is less in practice
- Benefits: speed, resolution
- Costs: artifacts, money, wavelength effects, auditory noise

Electromagnetic Spectrum

- MRI signals are in the same range as FM radio and TV (30-300MHz)
- MRI frequency is non-ionizing radiation, unlike X-rays
- Absorbed RF will cause heating
- Specific absorption rate (SAR): measure of the energy absorbed by tissue
  - Increases ~ with square of field strength
  - Higher SAR = more energy = more signal = more heating
  - FDA limits SAR, and is a limiting factor for some protocols (3 W/kg averaged over 10 minutes)

1 MHz | 1 GHz | 1 THz | 10^{15}Hz | 10^{18}Hz

Power, telephone | FM radio, TV **MR** | microwaves | infrared | UV | X-rays | gamma

MRI terminology

- Orientation: typically coronal, sagittal or axial, can be in-between these (oblique)
- Matrix Size:
  - Voxels in each dimension
- Field of view:
  - Spatial extent of each dimension
- Resolution:
  - FOV/Matrix size

Philips Achieva 3T Scanner

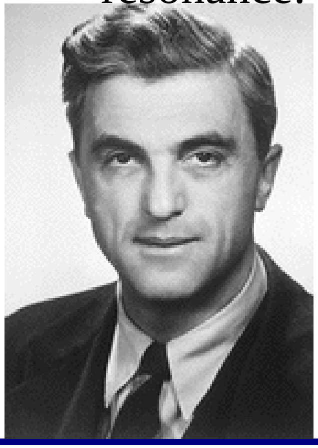
- **MRI** magnetic resonance imaging → images of biological tissues, structural studies
  - static magnetic field + a series of changing magnetic fields and oscillating electromagnetic fields (pulse sequence)
  - depending on frequency of electromagnetic fields, energy is absorbed by hydrogen nuclei (excitation)
  - later the energy is emitted by the nuclei
  - the amount of energy depends on numbers and types of nuclei present
- Advantages of MRI
  - No ionizing radiation exposure
  - Better spatial resolution than CT
- Disadvantages
  - No ferrous metal!

History of MR/ MRI/ fMRI:

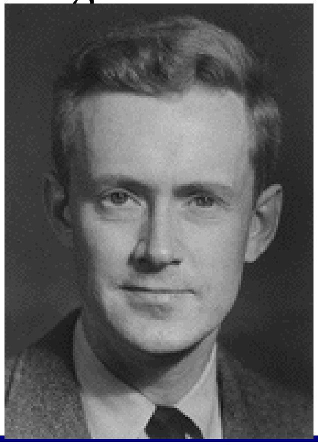
NMR = nuclear magnetic resonance

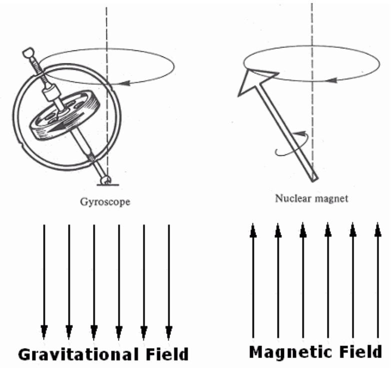
- Felix Block and Edward Purcell
  - 1946: atomic nuclei absorb and re-emit radio frequency energy
  - 1952: Nobel prize in physics
    - nuclear: properties of nuclei of atoms
    - magnetic: magnetic field required
    - resonance: interaction between magnetic field and radio frequency

Felix Bloch



Edward Purcell





History of MR/ MRI/ fMRI:

-1971: MRI Tumor detection (Damadian)

-1973: Lauterbur suggests NMR could be used to form images

-1977: clinical MRI scanner patented

-1977: Mansfield proposes echo-planar imaging (EPI) to acquire images faster

-2003: Nobel prize was awarded to Paul Lauterbur and Sir Peter Mansfield (excluding Damadian – huge controversy)

fMRI

-1990: Ogawa observes BOLD effect with T2*

blood vessels became more visible as blood oxygen decreased

-1991: Belliveau observes first functional images using a contrast agent

-1992: Ogawa et al. and Kwong et al. publish first functional images using BOLD signal

The First ~~ZMR~~ NMR Image

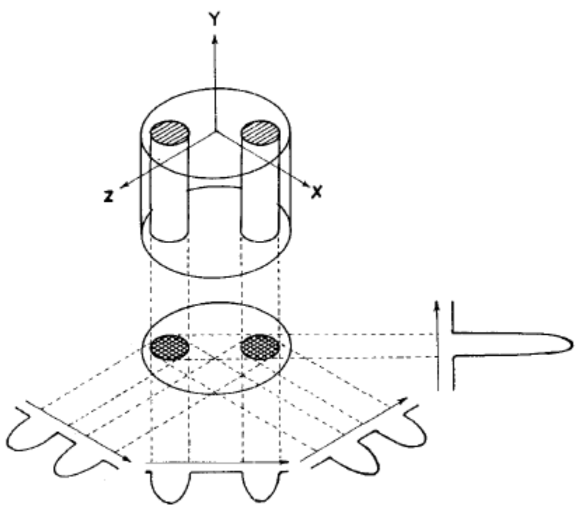


Fig. 1 Relationship between a three-dimensional object, its two-dimensional projection along the Y-axis, and four one-dimensional projections at 45° intervals in the XZ-plane. The arrows indicate the gradient directions.

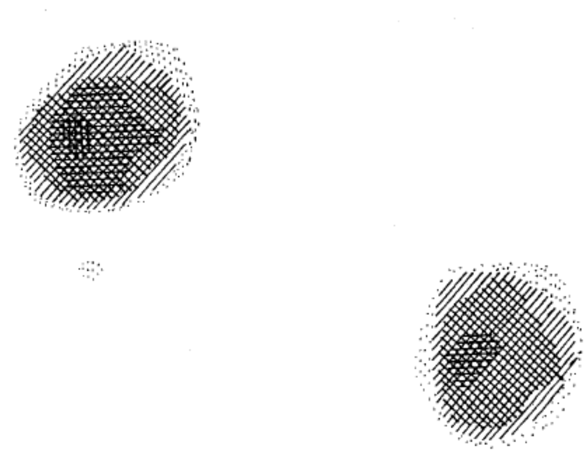


Fig. 2 Proton nuclear magnetic resonance zeugmatogram of the object described in the text, using four relative orientations of object and gradients as diagrammed in Fig. 1.

Lauterbur, P.C. (1973). Image formation by induced local interaction: Examples employing nuclear magnetic resonance. *Nature*, 242, 190-191.

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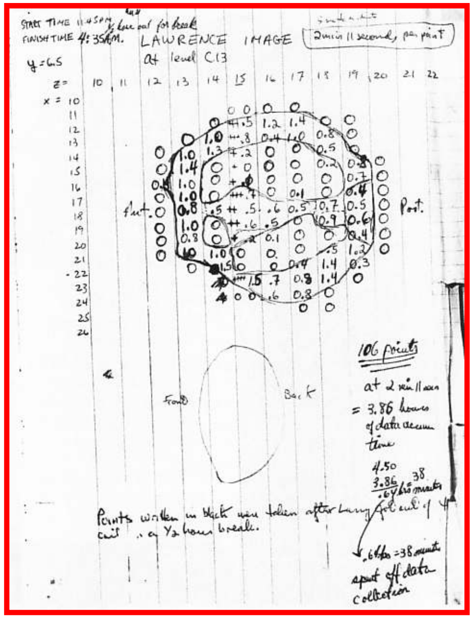
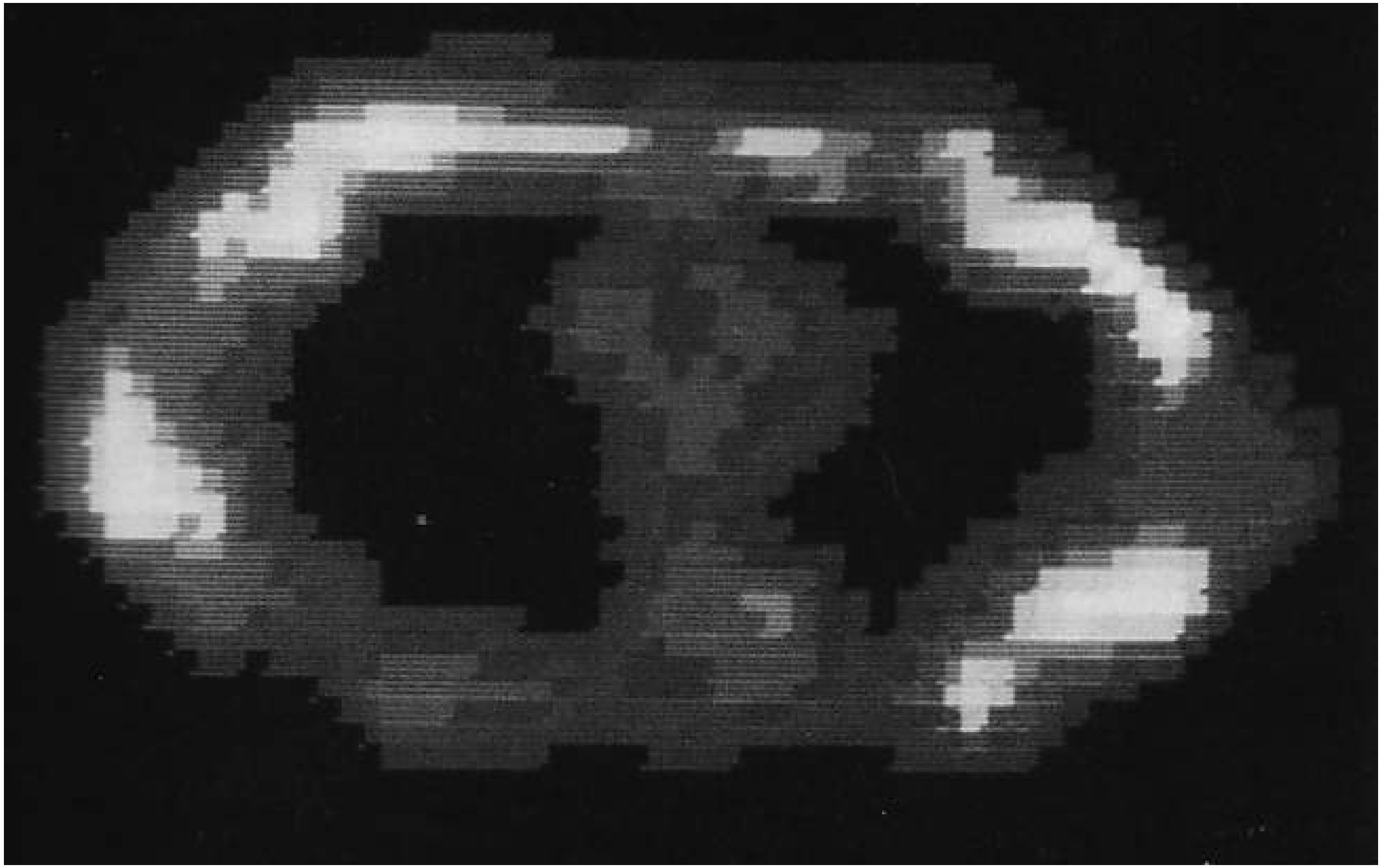
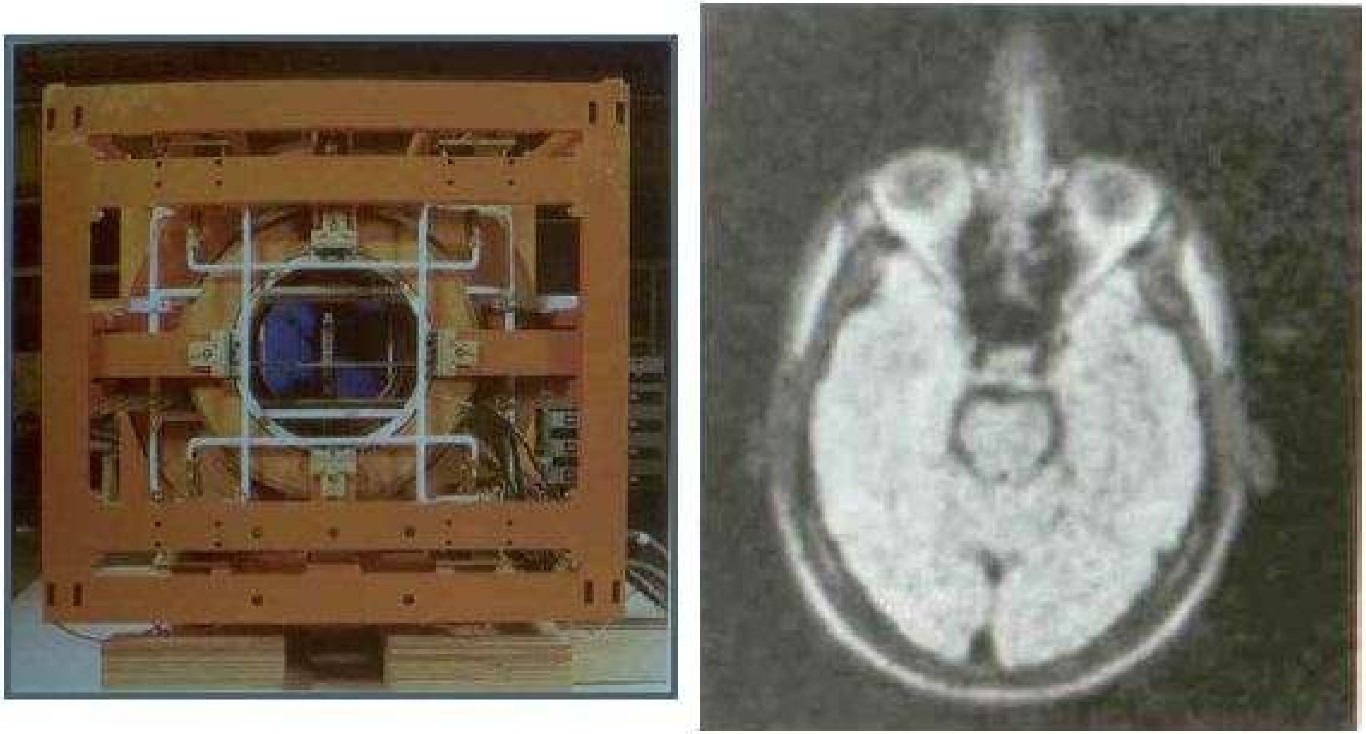
Early Human MR Images (Damadian)

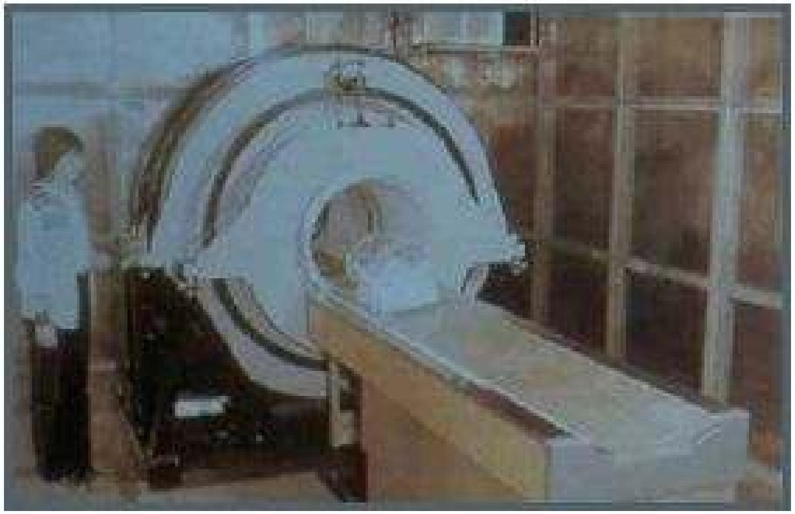




Mink5 Image – Damadian (1977)



The first Philips MR, 1978 (0,15T)



The first Siemens MR, 1980 (0,2T)

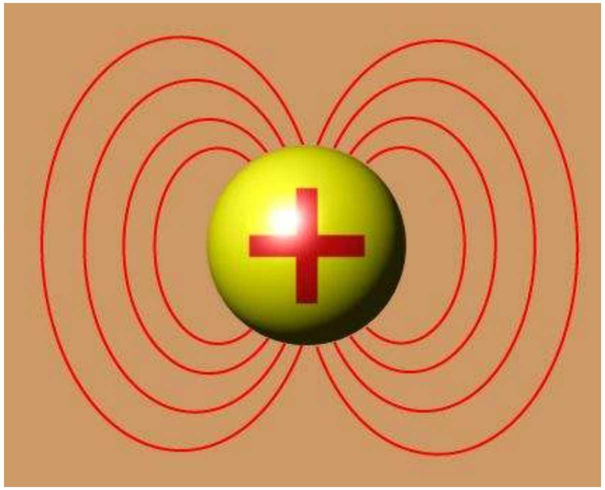
Typical 1.5/3.0T MR system

Special Open-MR system

Nuclear spins

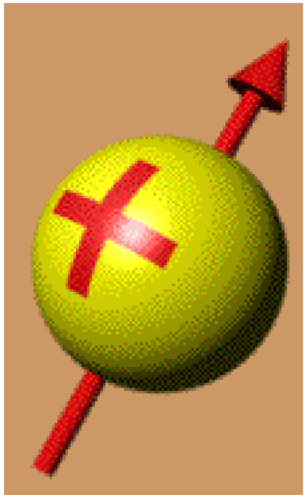
A nucleus of hydrogen

- consists of one proton
- carries a positive charge



- rotates around its axis because of thermal energy

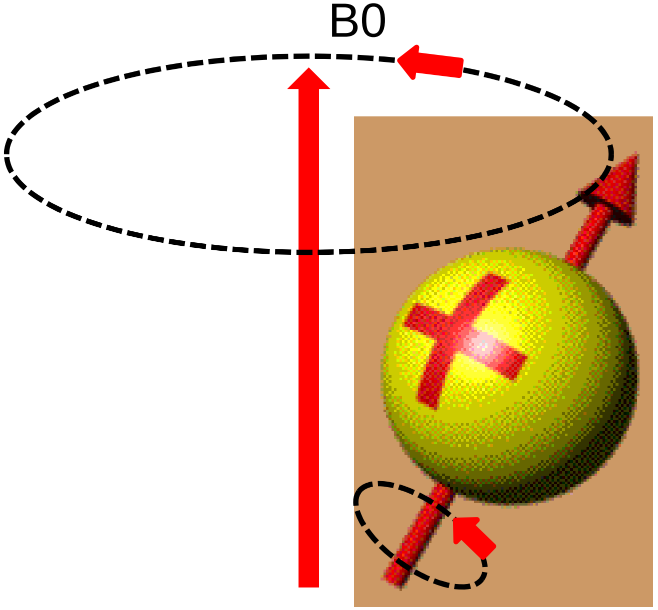
→ electrical current and magnetic source → spin



- Nuclei line up with magnetic moments either in a parallel (low level) or anti-parallel configuration (higher energy level).
- In body tissues more line up in parallel creating a small additional magnetization **M** in the direction of $\mathbf{B}_0$.

Nuclei spin axis not parallel to B_0 field direction.

Nuclear magnetic moments precess about B_0.

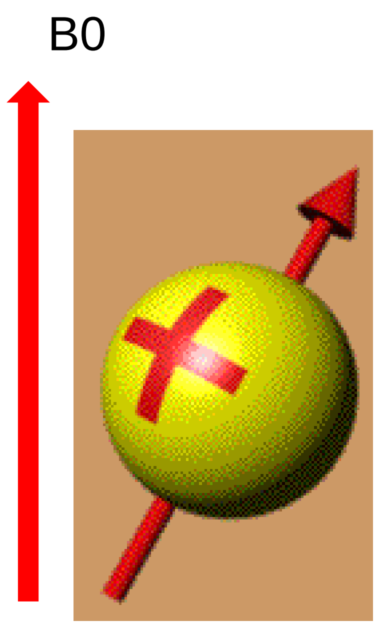


Absorption and Relaxation

- Our RF transmission is absorbed by atoms at Larmor frequency
- After the RF pulse, atoms will begin to realign with the magnetic field: relaxation
- During this period, an RF signal is emitted
- This signal will be at the Larmor frequency
- An antenna can measure this signal

- Frequency of precession of magnetic moments given by **Larmor** relationship

$$f = \gamma \times B_0$$



f = Larmor frequency (mHz)
g = Gyromagnetic ratio (mHz/Tesla)
B_0 = Magnetic field strength (Tesla)

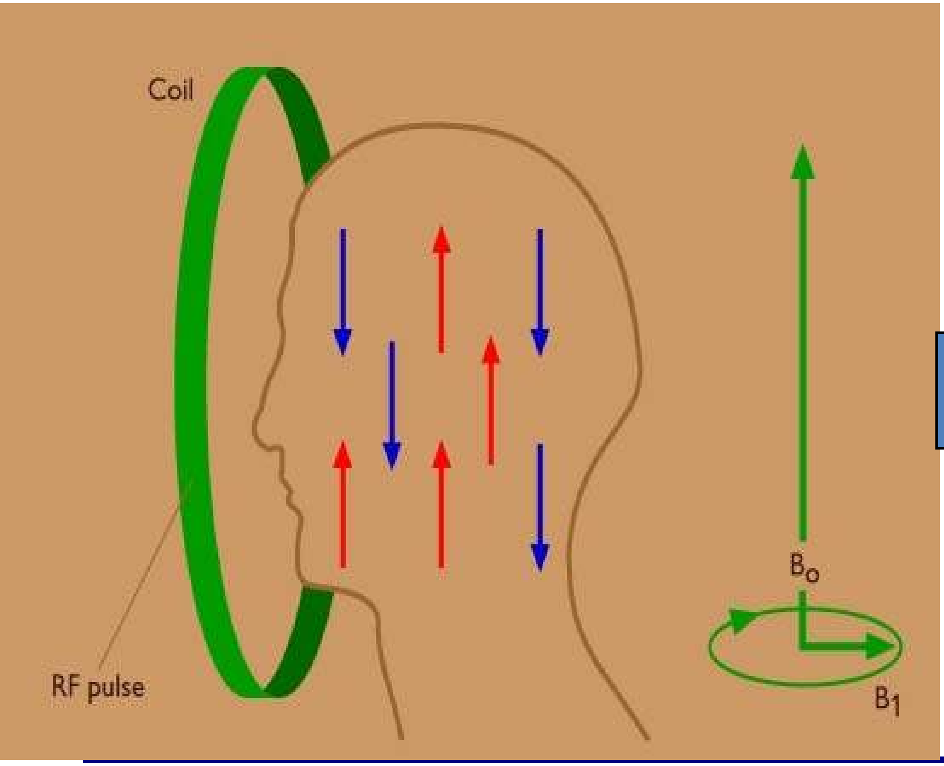
g ~ 43 mHz/Tesla

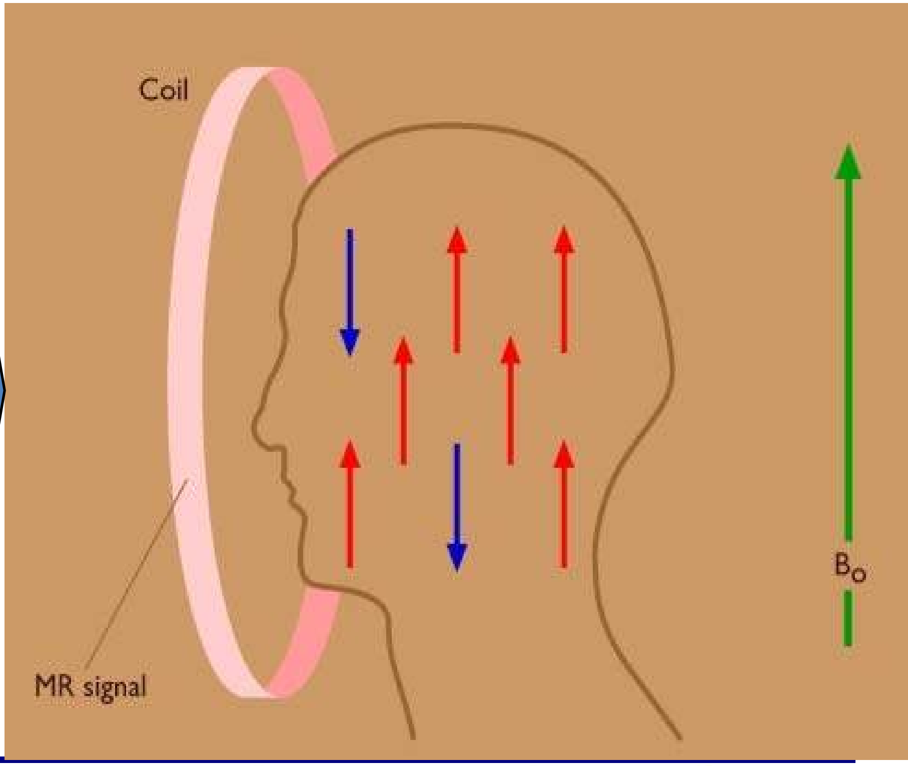
Larmor frequencies of RICs MRIs

3T ~ 130 mHZ
7T ~ 300 mHz
11.7T ~ 500 mHz

Radiofrequency Pulses

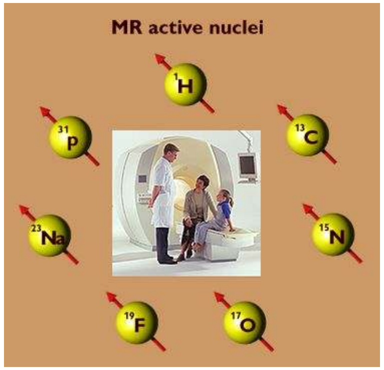
- A radiofrequency (RF) pulse at the Larmor frequency will be absorbed
- This higher energy state tips the spin, so it is no longer aligned to the field
- An RF pulse at any other frequency will not influence the nuclei, only resonance frequency



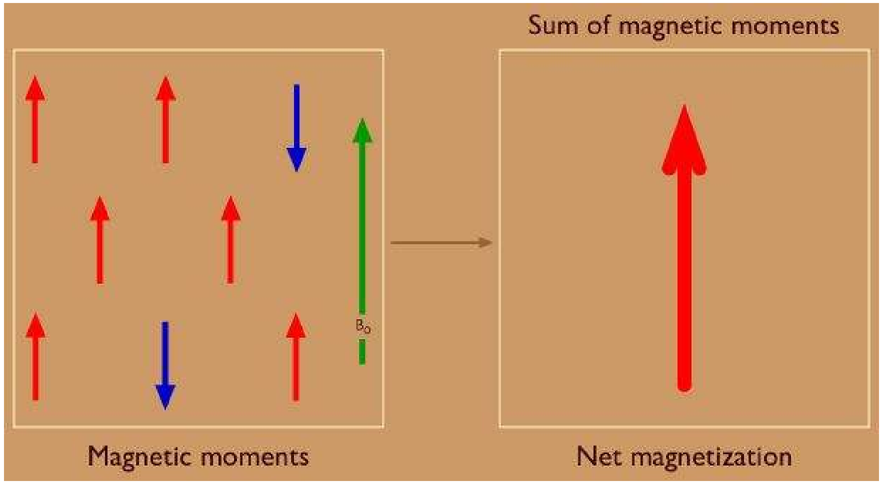


Hydrogen is the mainstay for MRI

- We will focus on Hydrogen
  - Hydrogen abundant in body (63% of atoms)
  - Elements with even numbers of neutrons and protons have no spin, so we can not image them (^{4}He, ^{12}C)
  - ^{23}Na and ^{31}P are relatively abundant, so can be imaged
- Larmor frequency varies for elements:
  - ^{1}H = 42.58 Mhz/T
  - ^{13}C = 10.7 Mhz/T
  - ^{19}F = 40.1 Mhz/T
  - ^{31}P = 17.7 Mhz/T
- Therefore, by sending in a RF pulse at a specific frequency we can selectively energize hydrogen

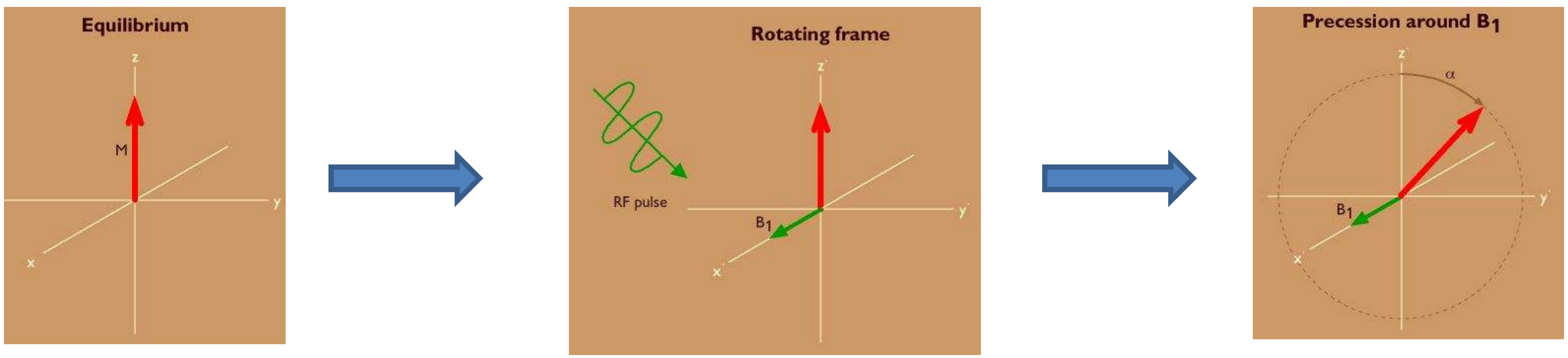


- **M** is parallel to $\mathbf{B}_0$ since transverse components of magnetic moments are randomly oriented
- The difference between the numbers of protons in the parallel and anti-parallel states leads to the ***net magnetization*** (**M**)
- Proton density relates to the number of parallel states per unit volume
- Signal producing capability depends on proton density



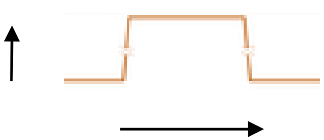
RF Pulse

Frequency of rotation of **M** about B_1 determined by the magnitude (strength) of $\mathbf{B}_1$

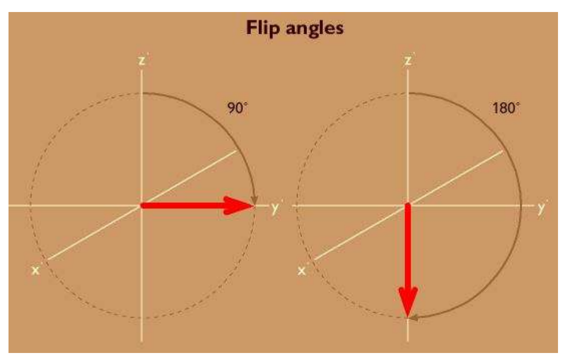


RF Pulse

strength

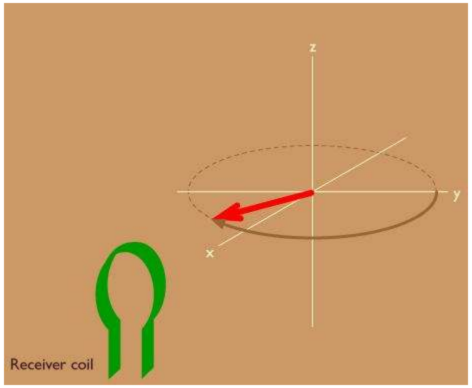


duration



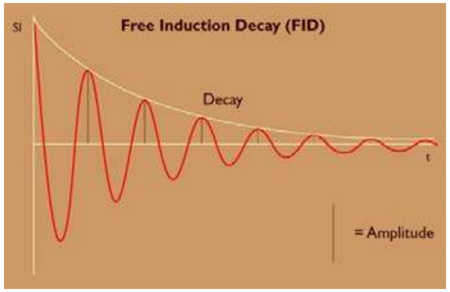
RF pulse duration and strength determine flip angle

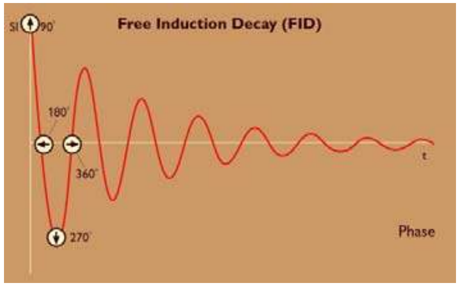
- 90° RF pulse rotates M into transverse (x-y) plane
- Rotation of M within transverse plane induces **signal** in receiver coil at Larmor frequency
- Magnitude **signal** dependent on proton density and $\mathbf{M}_{xy}$

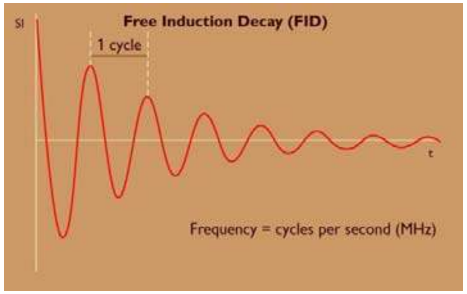


FID = Free Induction Decay

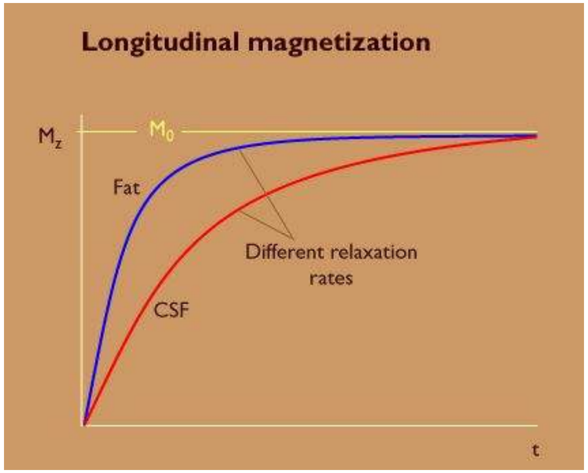
- FID magnitude decays in an exponential manner with a time constant T2. Decay due to spin-spin relaxation



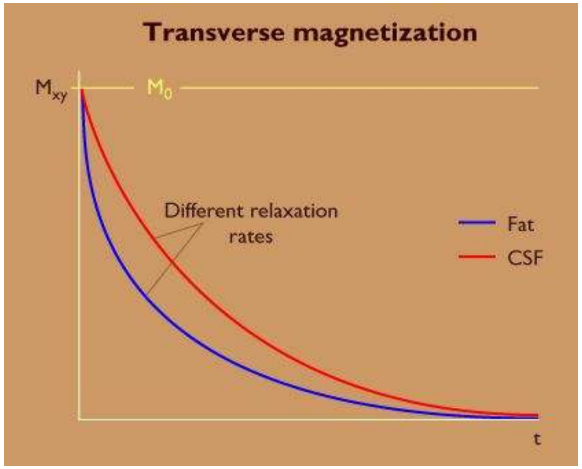




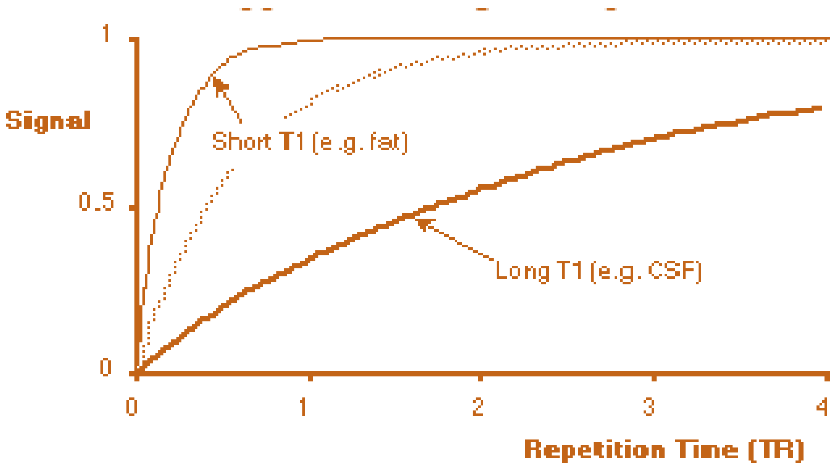
- T1-Relaxation: Recovery
  - Recovery of longitudinal orientation of **M** along z-axis
  - ‘T1 time’ refers to time interval for 63% recovery of longitudinal magnetization
  - **Spin-Lattice interactions**



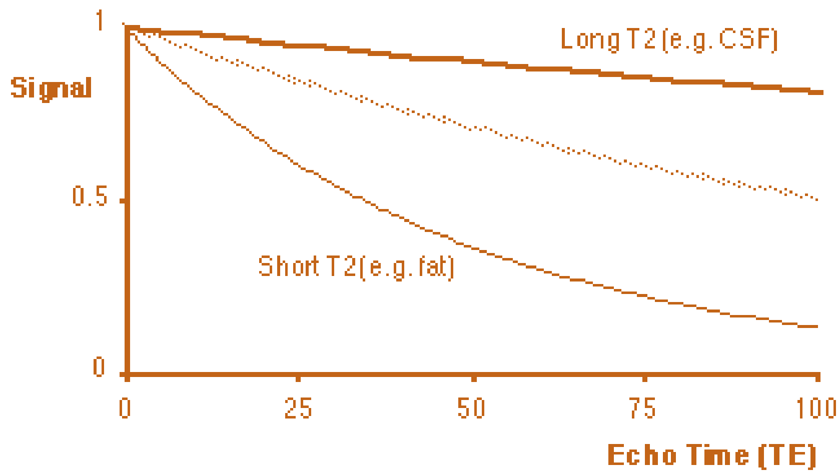
- T2-Relaxation: Dephasing
  - Loss of transverse magnetization $\mathbf{M}_{xy}$
  - ‘T2 time’ refers to time interval for 37% loss of original transverse magnetization
  - **Spin-spin interactions, and more**



- T1 is shorter in fat (large molecules) and longer in cerebrospinal fluid (CSF) (small molecules). T1 contrast is higher for lower TRs



- T2 is shorter in fat and longer in CSF. Signal contrast increased with TE



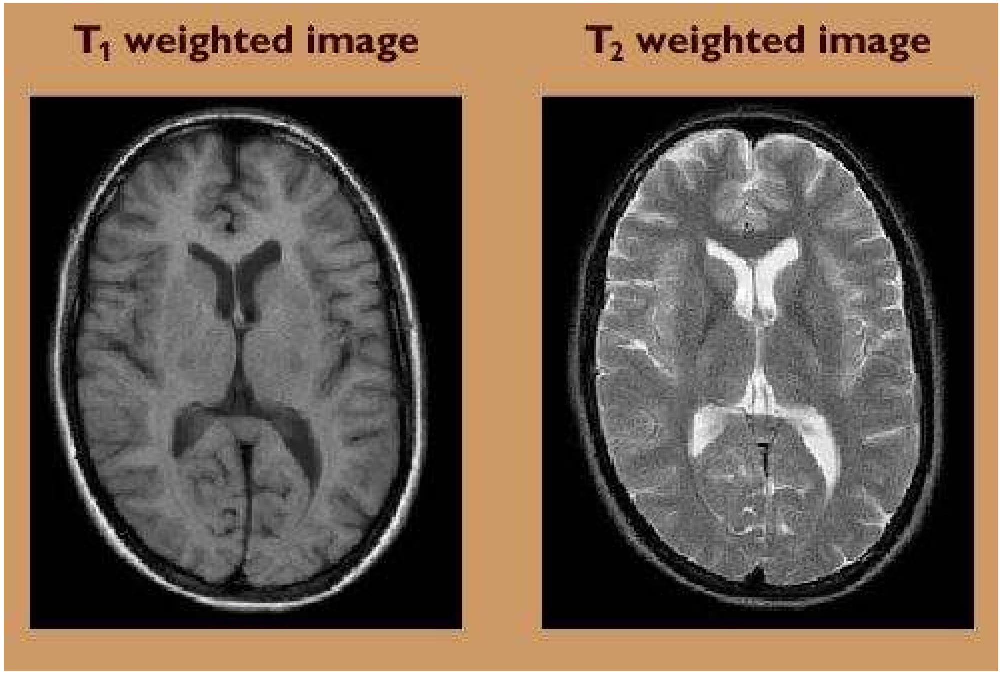
- **TR determines T1 contrast**
- **TE determines T2 contrast**

Properties of Body Tissues

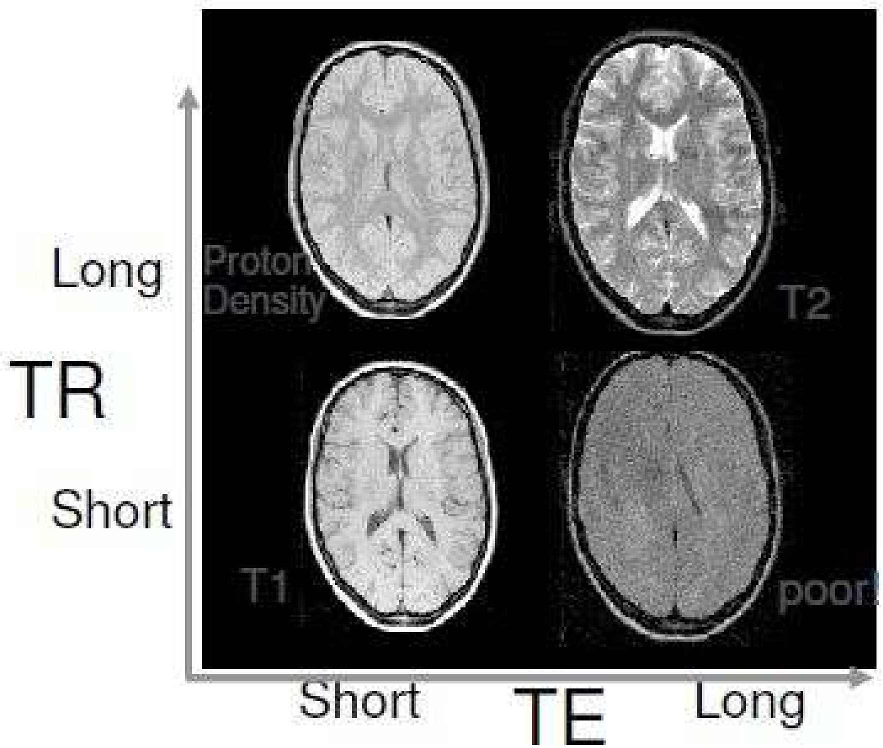
	T1 (msec)	T2 (msec)
Grey Matter	**950**	**100**
White Matter	600	80
Fat	250	60
Blood	1200	100-200
Cerebrospinal Fluid	4500	2200
Muscle	900	50

T1 values for B_0 ~ 1Tesla.
T2 ~ 1/10th T1 for soft tissues

T1/T2 weighted images:



Contrast, Imaging Parameters:



- Short TEs reduce T2W
- Long TRs reduce T1W

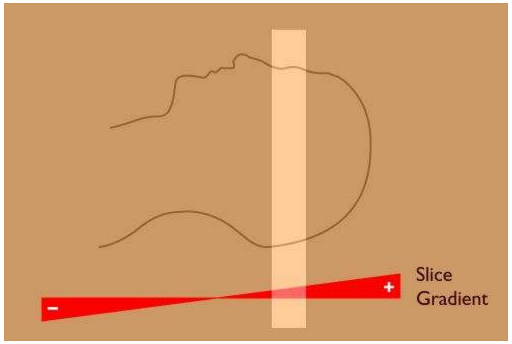
Making a spatial image

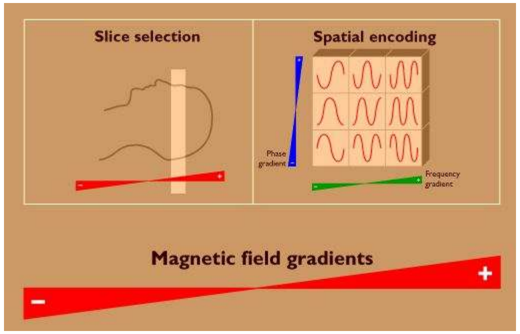

Lauterbur

- To create spatial images, we need a way to cause different locations in the scanner to generate different signals
- To do this, we apply gradients
- Gradients make the magnetic field slightly stronger at one location compared to another
- Lauterbur: first MRI: 2003 Nobel Prize

Slice Selection Gradient

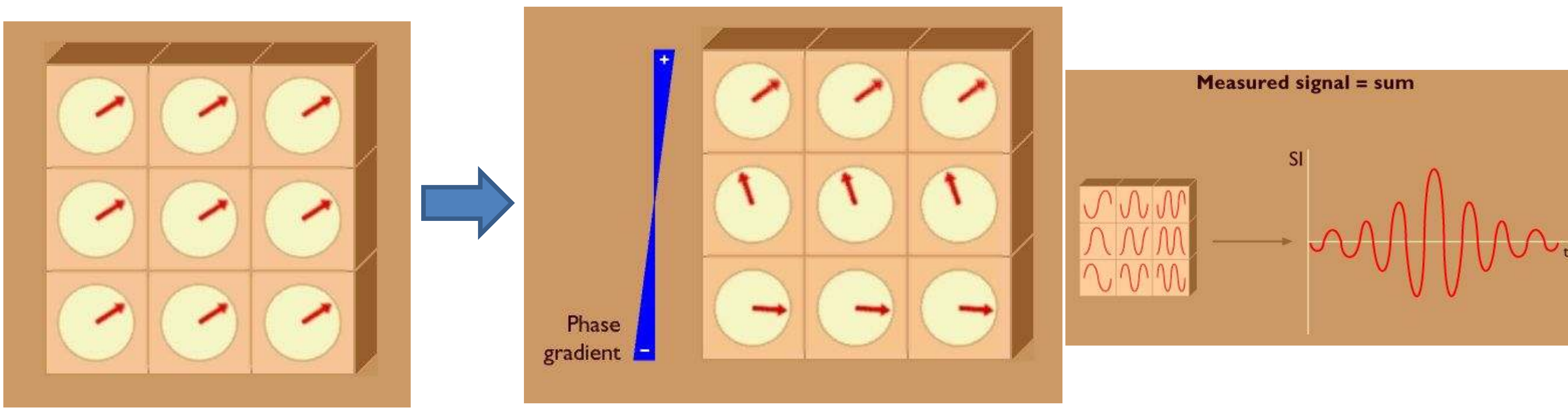
- Gradients make field stronger at one location compared to another
- Larmor frequency different along this dimension
- RF pulse only energizes slice where field strength matches Larmor frequency
- Gradual slice selection gradients will select thick slices, while steep gradients select thinner slices
  - The strength of your scanner's gradients can limit minimum slice thickness
  - FDA limits speed of gradient shift (dB/dt) and some of our protocols can elicit slight tingling sensation or brief muscle twitches
- Position of gradient determines which 2D slice is selected





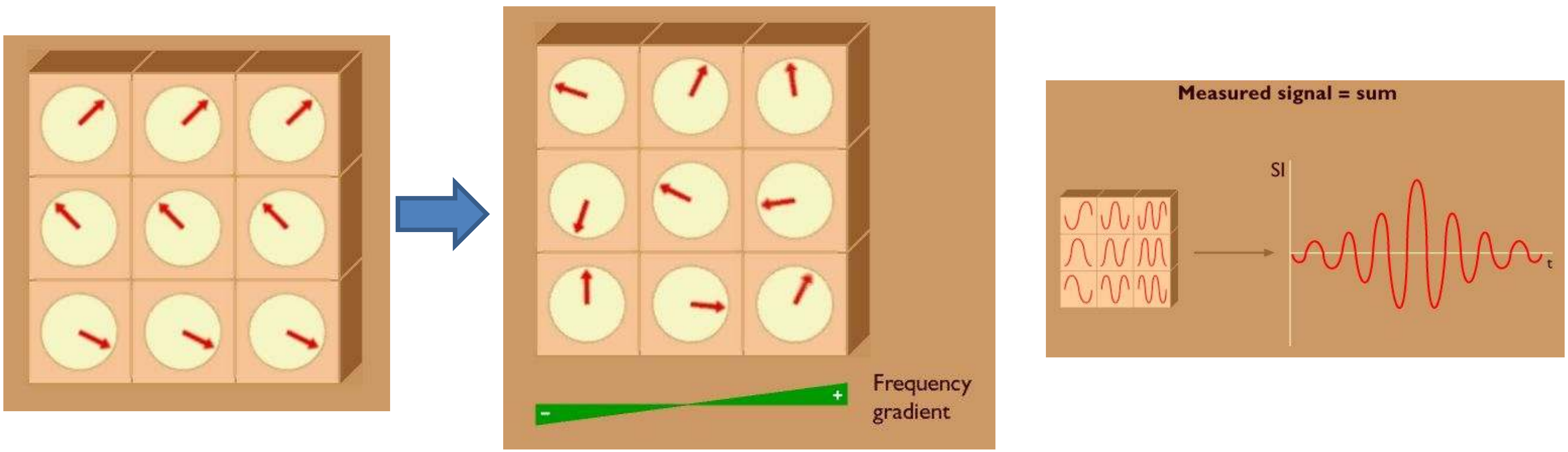
Phase Encoding

- Phase encoding gradient:
  - Orthogonal gradient applied between RF pulse and readout
  - This adjusts the phase along this dimension
  - Analogy: Phase encoding is like time zones. Clocks in different zones will have different phases



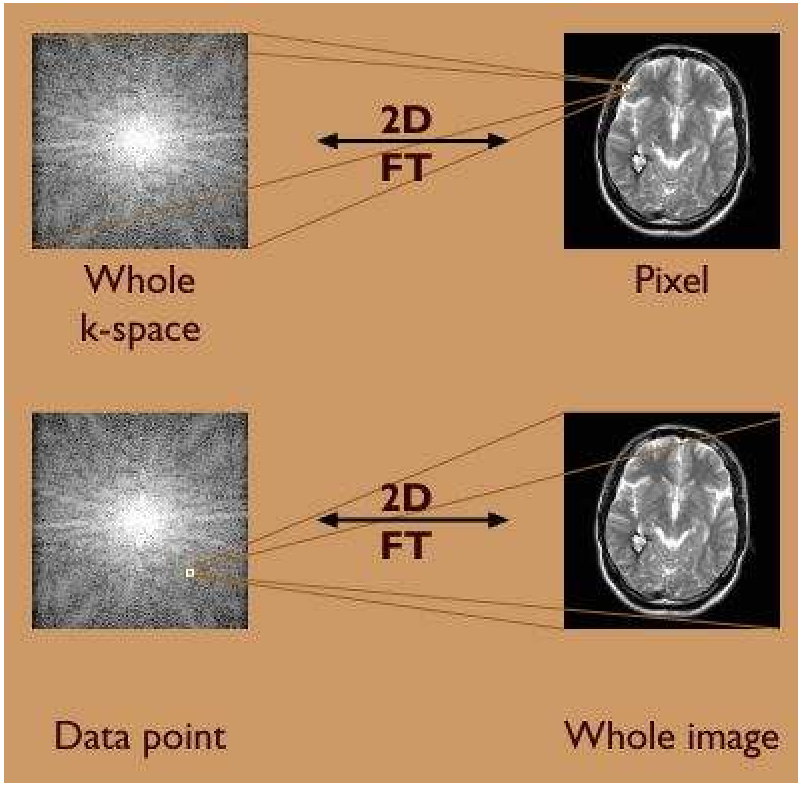
Frequency Encoding

- Frequency encoding gradient:
  - Apply final orthogonal gradient when we wish to acquire image
  - Slice will emit signal at Lamour frequency, e.g. lines at higher fields will have higher frequency signals
  - Aka ‘Readout gradient’



Raw MRI image: k-space (frequency domain)

a k-space domain image is formed using frequency and phase encoding

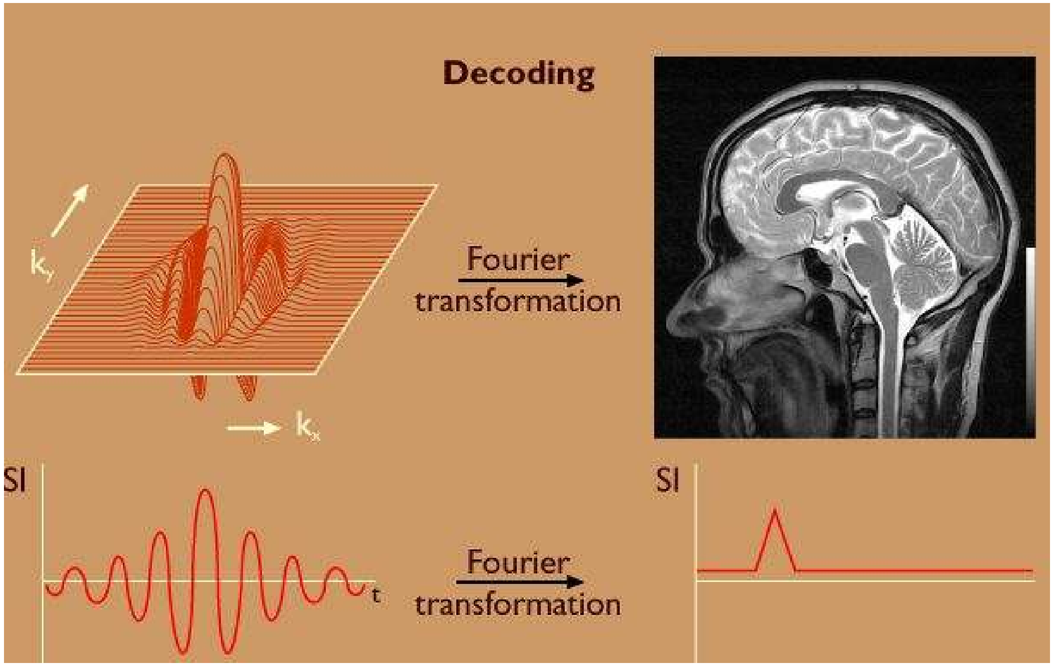


Reconstruction

- Medical scanners automatically reconstruct your data
- You can manually reconstruct data
- Fourier Transforms are slow: 1021-sample data requires >2 million multiplications ($2*N^2$)
- Fast Fourier Transform: 1024-sample data requires 20,000 multiplications (2(N log N))
  - Optimal when data is power of two (64,128,256, 512), reverts to traditional Fourier for prime numbers
  - This is why most image matrices are a power of 2

MRI task is to acquire k-space image then transform to a spatial-domain image. k_x is sampled (read out) in real time to give N samples. k_y is adjusted before each readout

MR image is the magnitude of the Fourier transform of the k-space image



The k-space Trajectory

- Equations that govern 2D k-space trajectory

$$k_x = \int_0^t G_x(t)dt$$

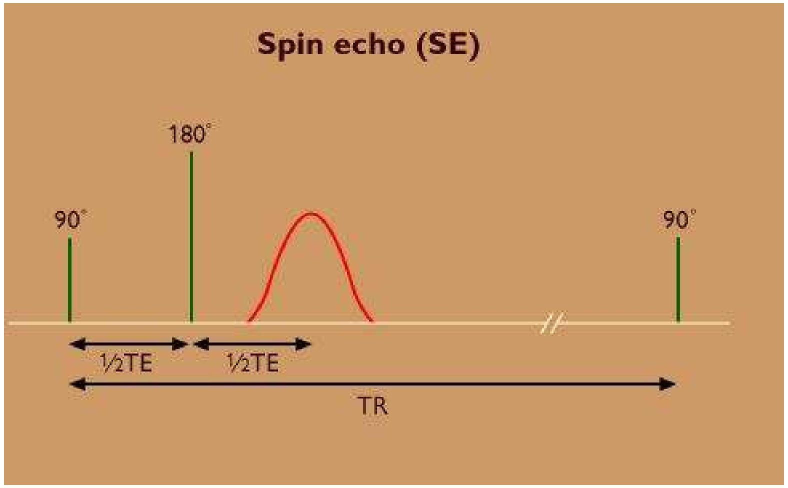
if G_x is constant $\quad k_x = gG_x t$

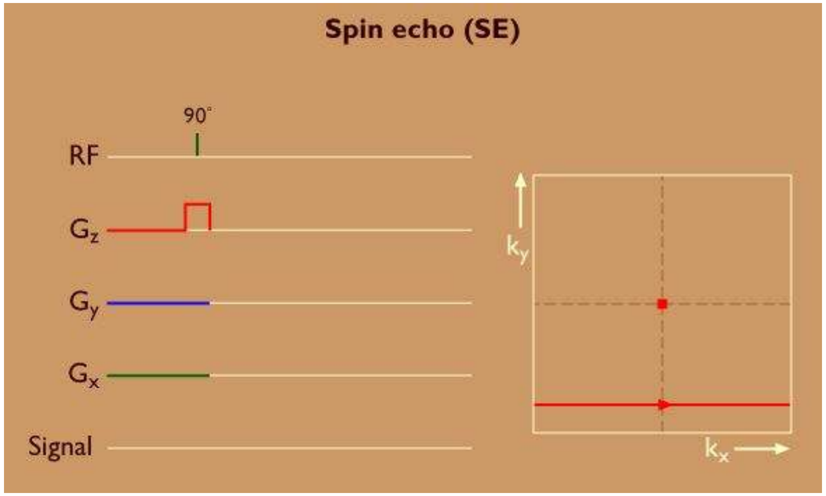
$$k_y = \int_0^{t'} G_y(t)dt$$

The k_x, k_y frequency coordinates are established by <u>durations</u> (t) and <u>strength</u> of gradients (G)

Primary types of Pulse sequences

- Spin Echo (SE):
  - The most commonly used pulse sequence
  - Uses 90° radio frequency pulses to excite the magnetization and one or more 180° pulses to refocus the spins to generate signal echoes: SE
  - The two variables of interest in spin echo sequences is TR and TE





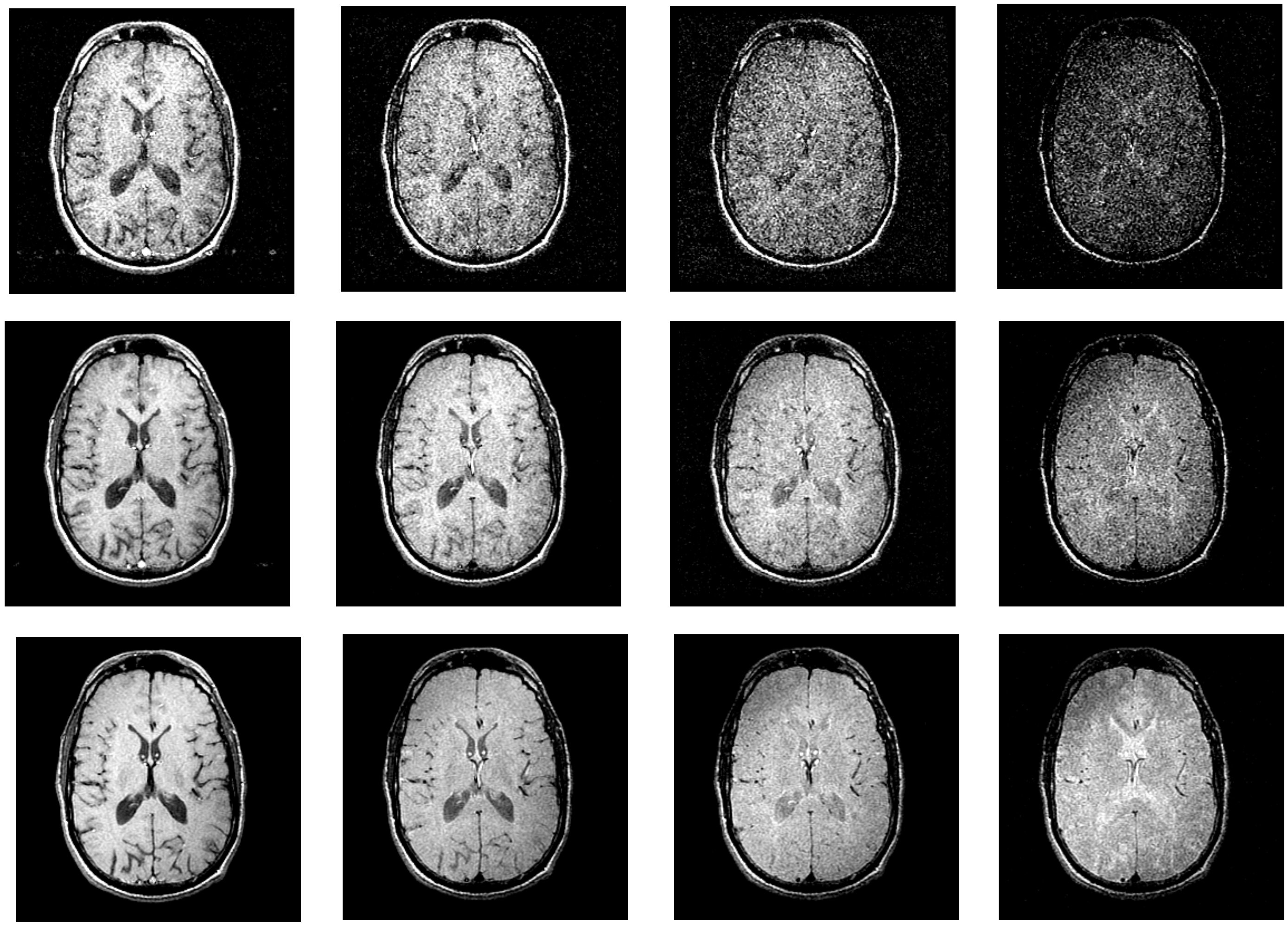
Spin-Echo Image

TE = 20 ms | TE = 50 ms | TE = 75 ms | TE = 100 ms

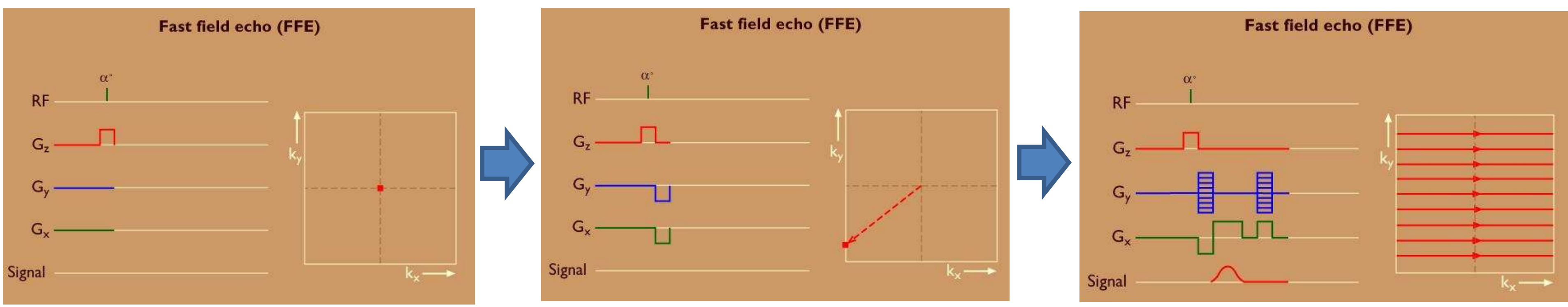
TR = 250 ms

TR = 500 ms

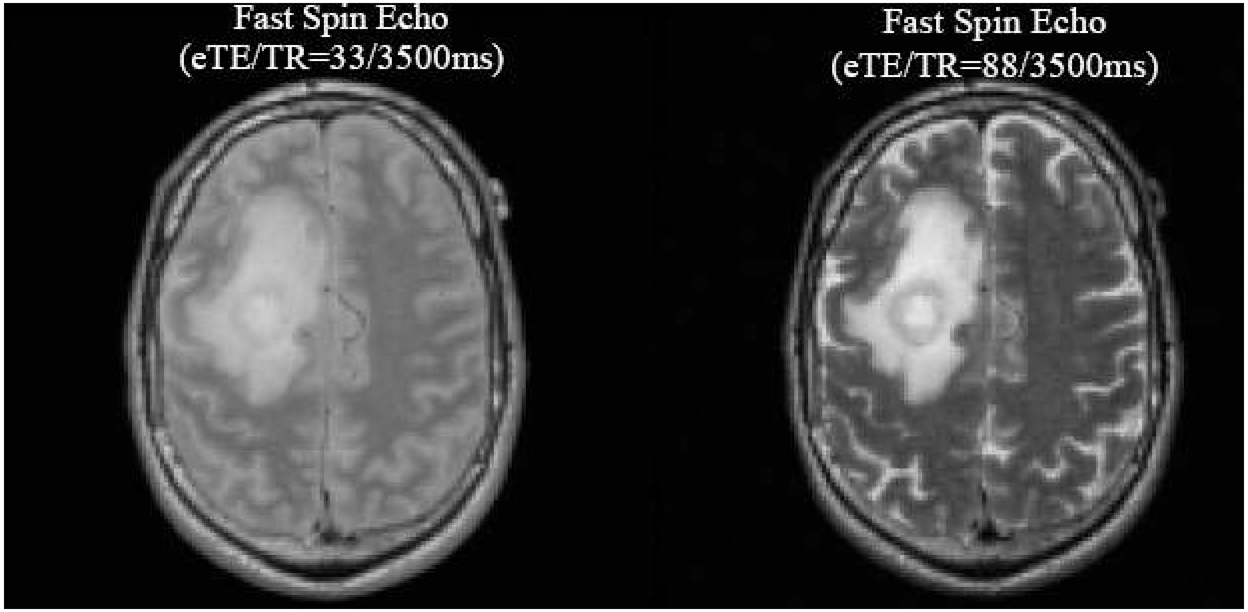
TR = 1000 ms



- Fast Spin Echo (FSE):
  - Characterized by a series of rapidly applied 180° rephasing pulses and multiple echoes, changing the phase encoding gradient for each echo
  - TE may vary from echo to echo in the echo train
  - T2 weighted imaging profits most from this technique
  - T2 weighted FSE images, both water and fat are hyperintense

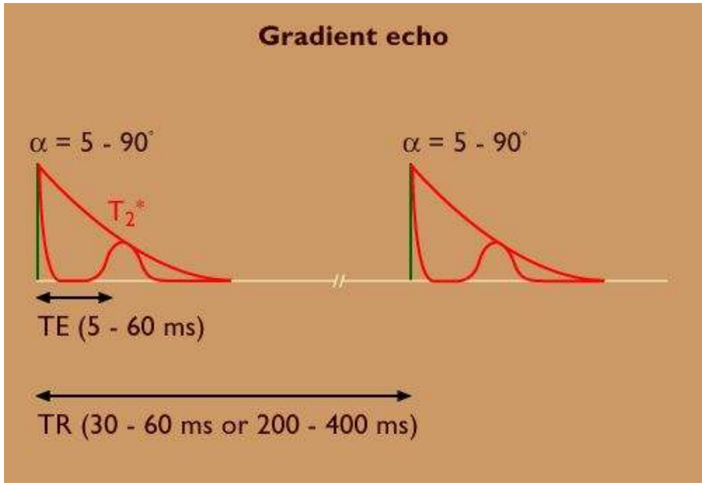


Fast Spin Echo (FSE)



- Gradient Echo (GRE):

  - generated by using a pair of bipolar gradient pulses
  - no refocusing 180° pulse and the data are sampled during a gradient echo, which is achieved by dephasing the spins with a negatively pulsed gradient before they are rephased by an opposite gradient with opposite polarity to generate the echo
  - short repetition time

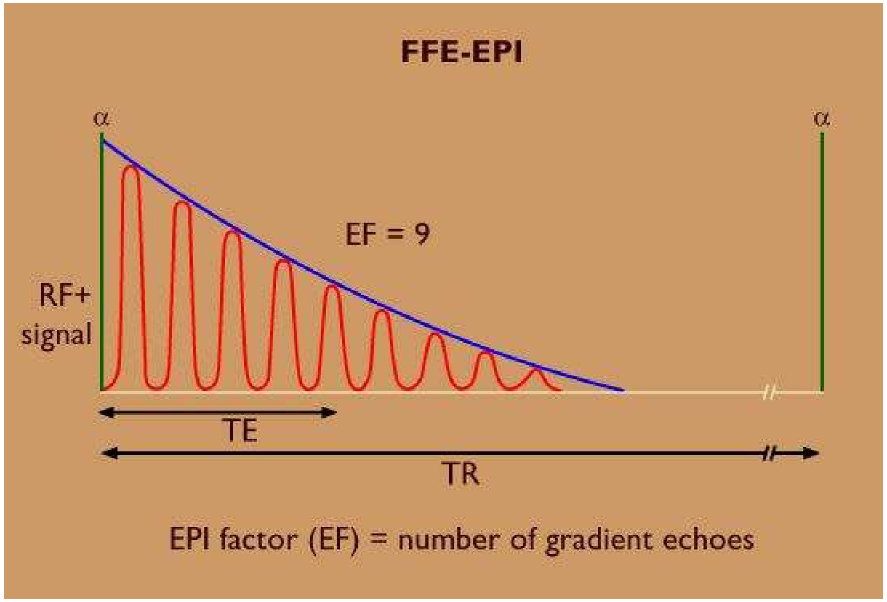


- Fast Low Angle Shot (FLASH):

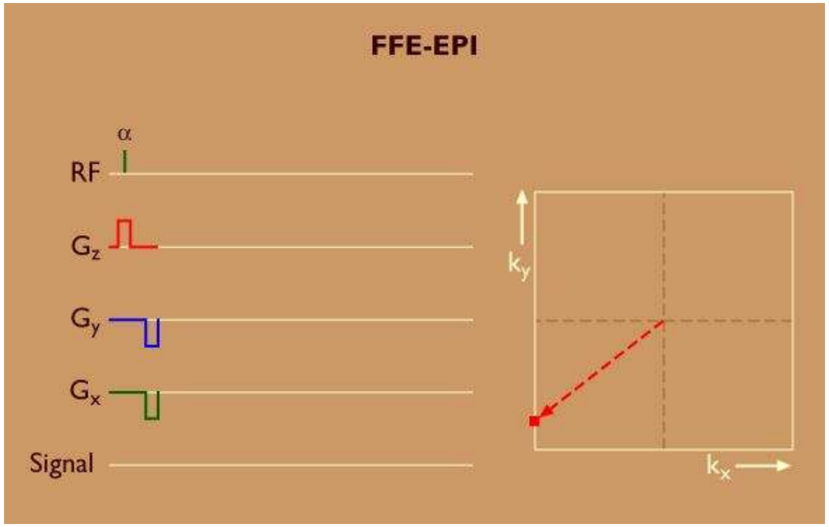
  - a fast sequence producing signals called gradient echo with low flip angles
  - uses a semi-random spoiler gradient after each echo to spoil the steady state by causing a spatially dependent phase shift
  - extremely short TR times are possible, as a result the sequence provides a mechanism for gaining extremely high T1 contrast

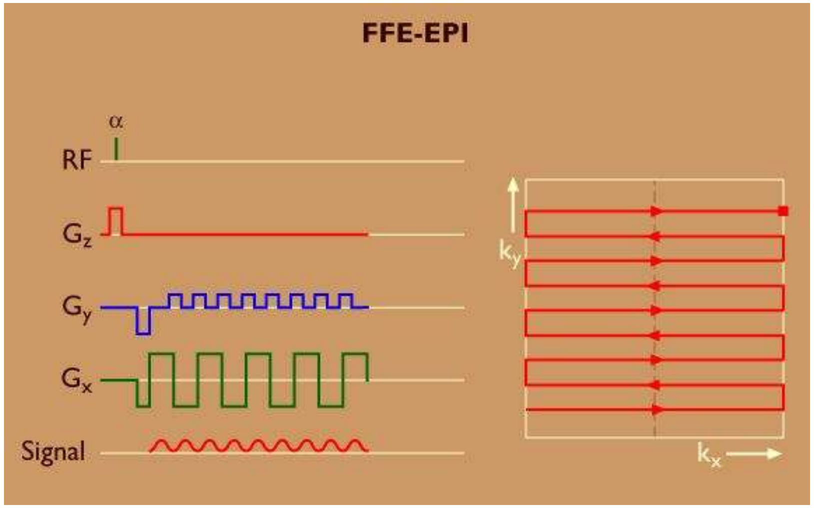
- Echo Planar Imaging (EPI):

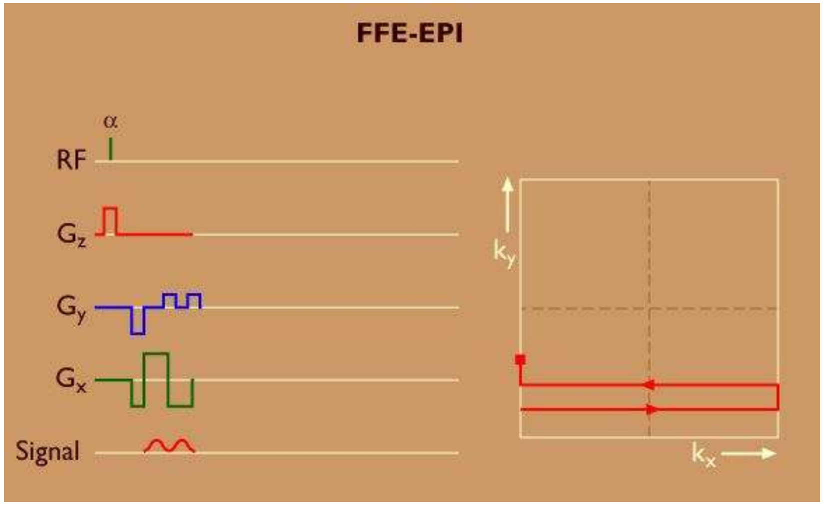
  - used in applications like diffusion, perfusion, and functional magnetic resonance imaging
  - complete image is formed from a single data sample (all k-space lines are measured in one repetition time) of a gradient echo or spin echo sequence with an acquisition time of about 20 to 100 ms



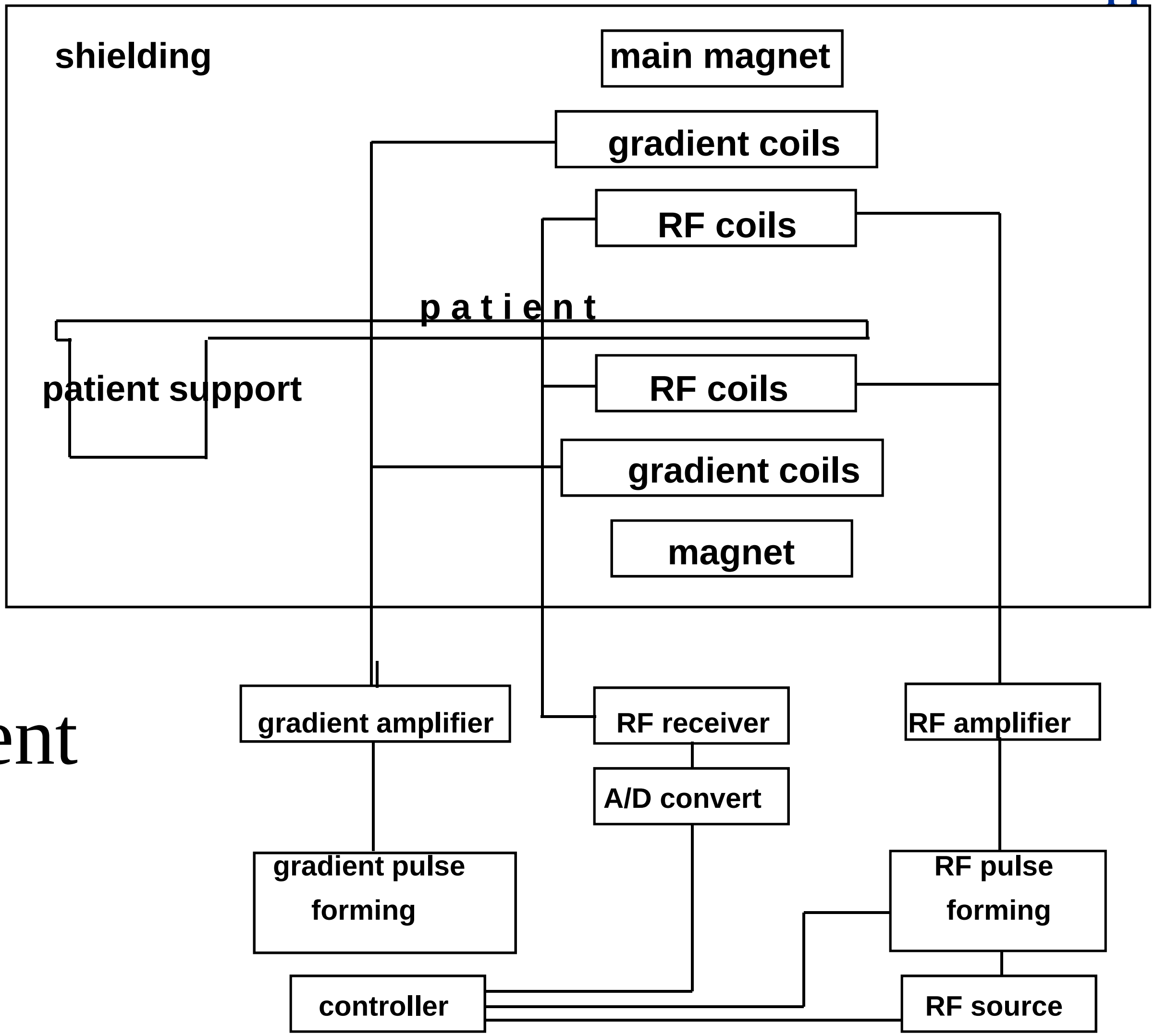
EPI


FFE-EPI
α
RF
G_z
G_y
G_x
Signal
k_y
k_x

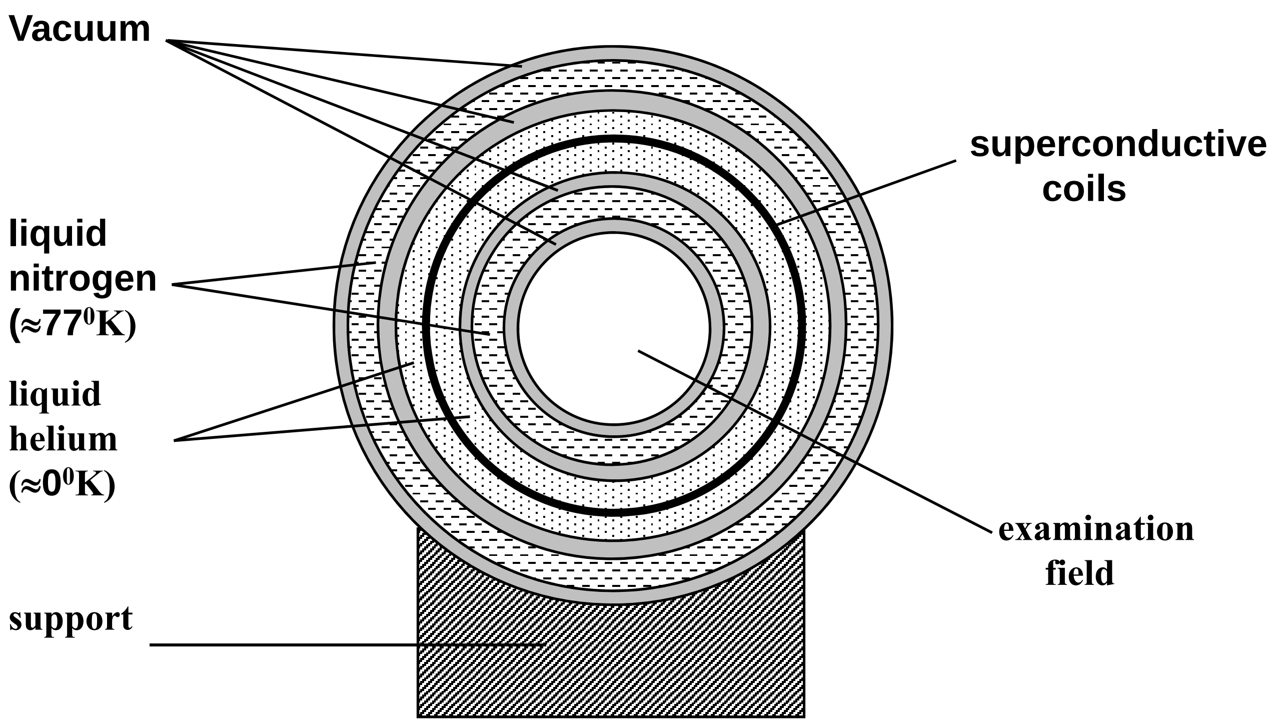

FFE-EPI
α
RF
G_z
G_y
G_x
Signal
k_y
k_x

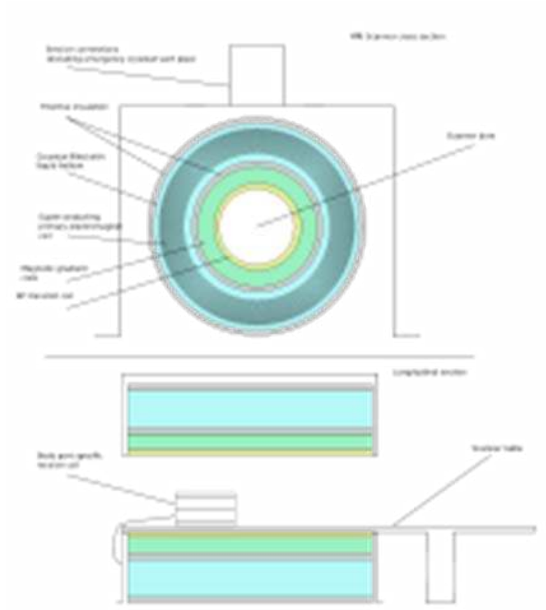

FFE-EPI
α
RF
G_z
G_y
G_x
Signal
k_y
k_x

MRI equipment schematics

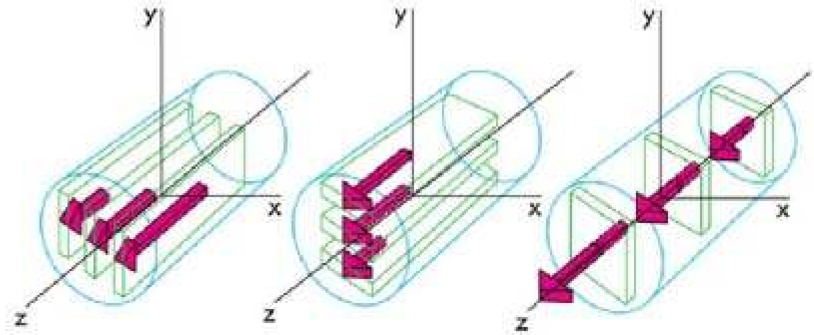


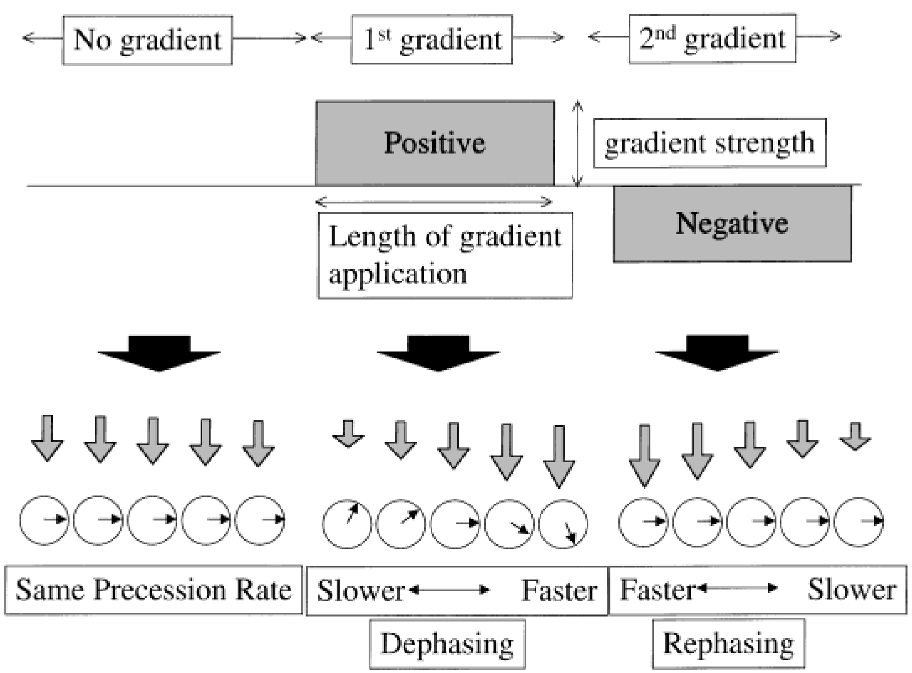
Typical structure of an MR superconductive magnet bore

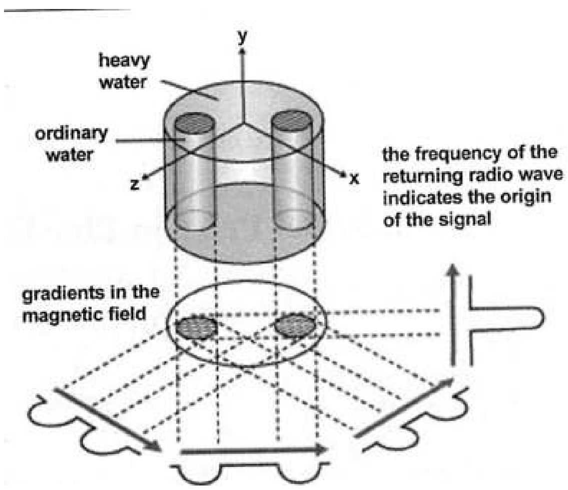




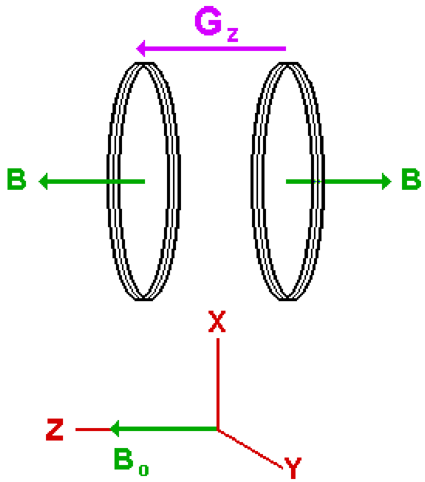
Gradient coils



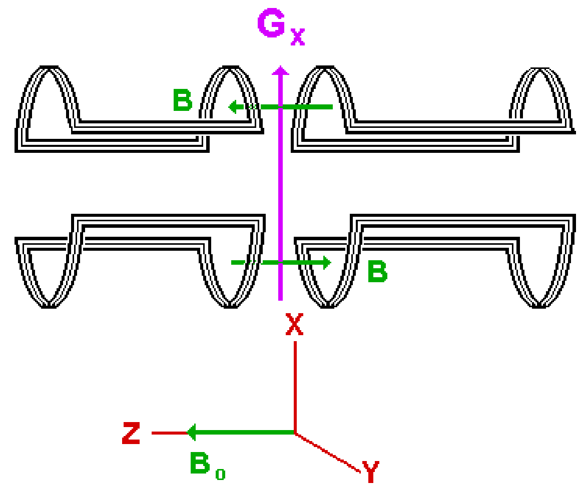




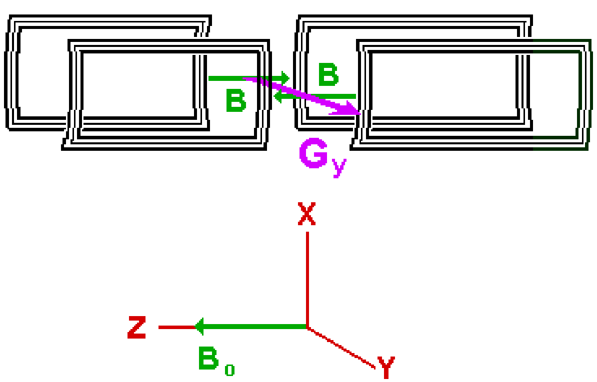
Z Gradient Coil



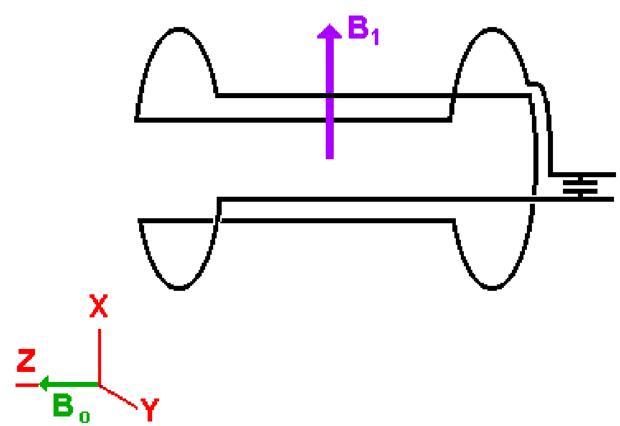
X Gradient Coil

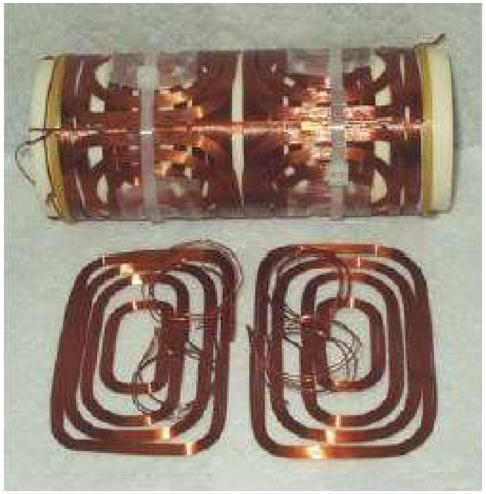


Y Gradient Coil



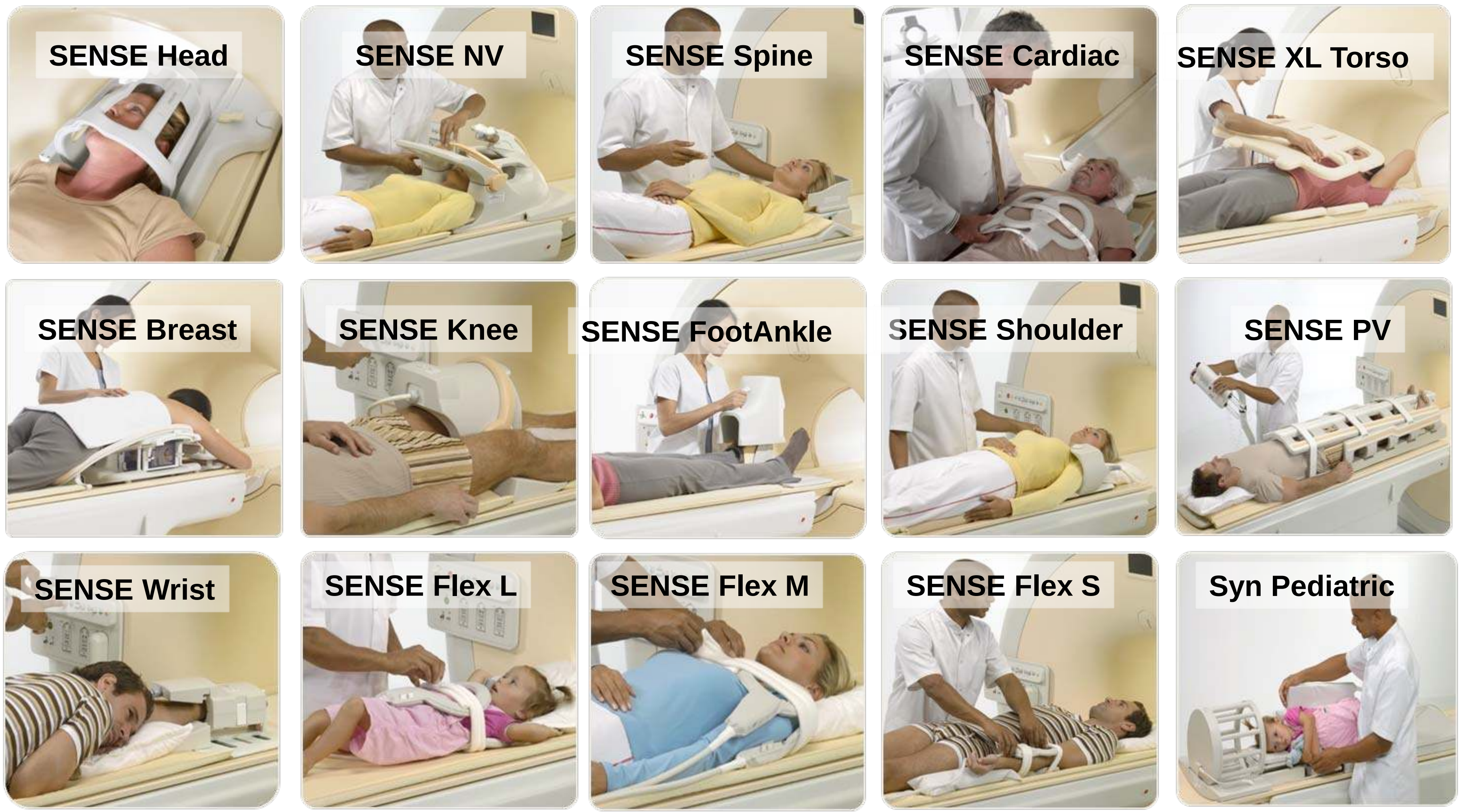
Saddle Coil



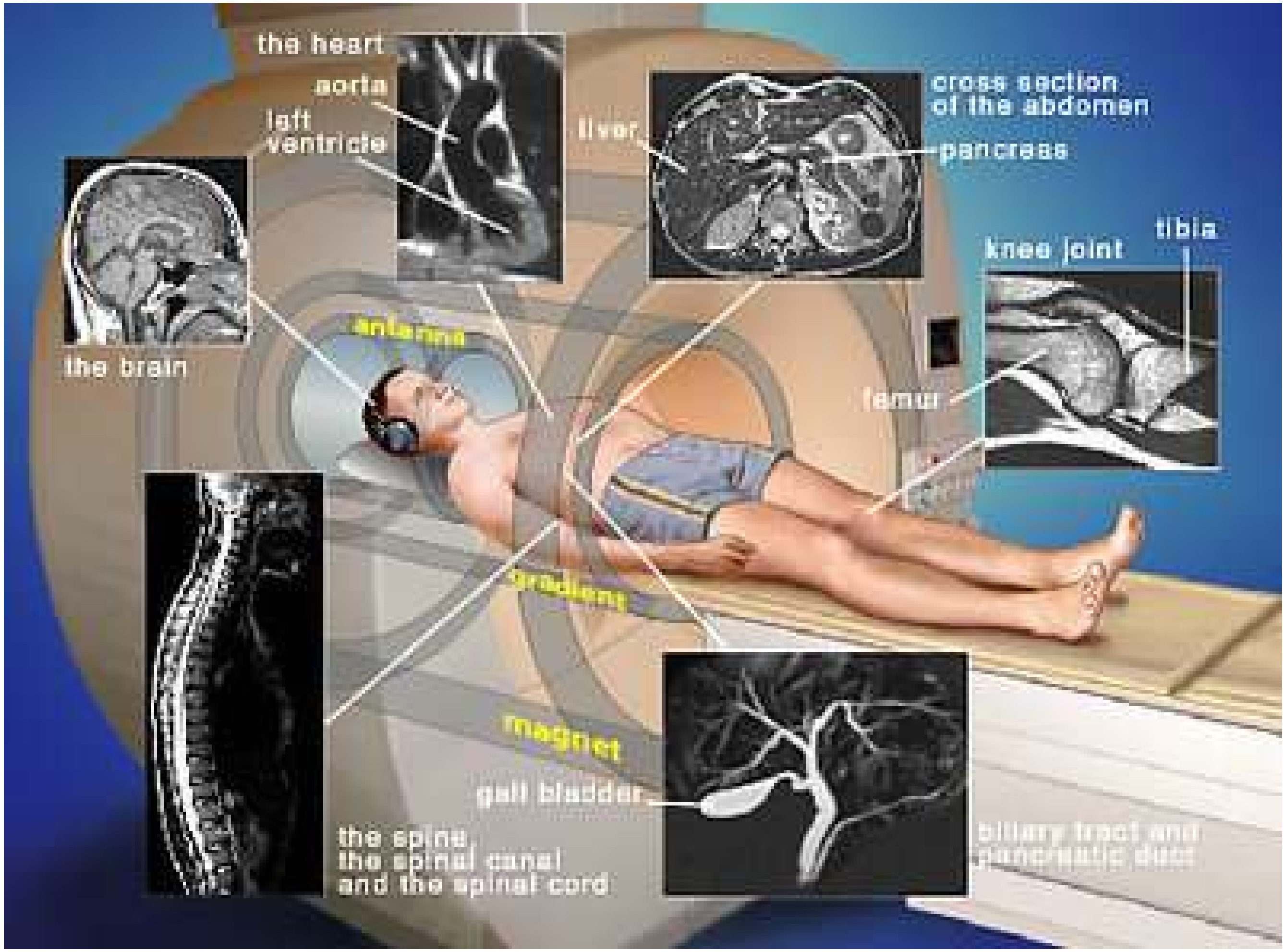


Gradient coil system

„naked” receiver coils without cover


SENSE Head
SENSE NV
SENSE Spine
SENSE Cardiac
SENSE XL Torso
SENSE Breast
SENSE Knee
SENSE FootAnkle
SENSE Shoulder
SENSE PV
SENSE Wrist
SENSE Flex L
SENSE Flex M
SENSE Flex S
Syn Pediatric

Biomedical Imaging: Magnetic Resonance Imaging - Basics



MR safety:

- Projectile Effects: External
- Projectile Effects: Internal
- Acoustic Noise
- Radiofrequency Energy
- Gradient field changes
- Claustrophobia

Scanner visit

- Anyone with implanted metal should see a doctor before going to the scanner
  - Pacemaker, cochlear implant, shunt, clip, etc.
  - Dental work and piercings are fine

Projectile Effects: Internal

- Motion of implanted medical devices
  - Clips, shunts, valves, etc.
- Motion or rotation of debris, shrapnel, filings
  - Primary risk: Metal fragments in eyes
- Swelling/irritation of skin due to motion of iron oxides in tattoo and makeup pigments

Acoustic noise:

- Potential problem with all scans
  - Short-term and long-term effects
- Sound level

- OSHA maximum exposure guidelines
  - 2-4 hours per day
- Earplugs reduce these values by 14-29 dB, depending upon fit

Radiofrequency Energy

Tissue Heating

- Specific Absorption Rate (SAR; W/kg)
  - Pulse sequences are limited to cause less than a one-degree rise in core body temperature
  - Scanners can be operated at up to 4 W/kg (with large safety margin) for normal subjects, 1.5 W/kg for compromised patients (infants, fetuses, cardiac)
- Weight of subject critical for SAR calculations

Burns

- Looped wires can act as RF antennas and focus energy in a small area
  - Most common problem: ECG leads
  - Necklaces, earrings, piercings, pulse oximeters, any other cabling

Gradient field changes:

Peripheral nerve stimulation

- May range from distracting to painful
- Risk greatly increased by conductive loops
  - Arms clasped
  - Legs crossed

Theoretical risk of cardiac stimulation

- No evidence for effects at gradient strengths used in MRI

Claustrofobia:

Most common subject problem

- About 10% of patients

Ameliorated with comfort measures

- Talking with subject
- Air flow through scanner
- Panic button
- Slow entry into scanner

FDA MRI Guidelines		
B_o	Adults, Children, and Infants age > 1 month	8 T
	neonates (infants age < 1 month)	4 T
dB/dt	No discomfort, pain, or nerve stimulation	
SAR Specific Absorption Rate	whole body, average, over ≥15 min	4 W/Kg
	head, average, over ≥10 min	3 W/Kg
	head or torso, per g of tissue, in ≥5 min	8 W/Kg
	extremities, per g of tissue, in ≥5 min	12 W/Kg
Acoustic Level	Peak unweighted	140 dB
	A-weighted rms with hearing protection	99 dBA