The Abdus Salam
International Centre for Theoretical Physics

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2234-3

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Acoustic and electromagnetic waves to the service of modern medicine

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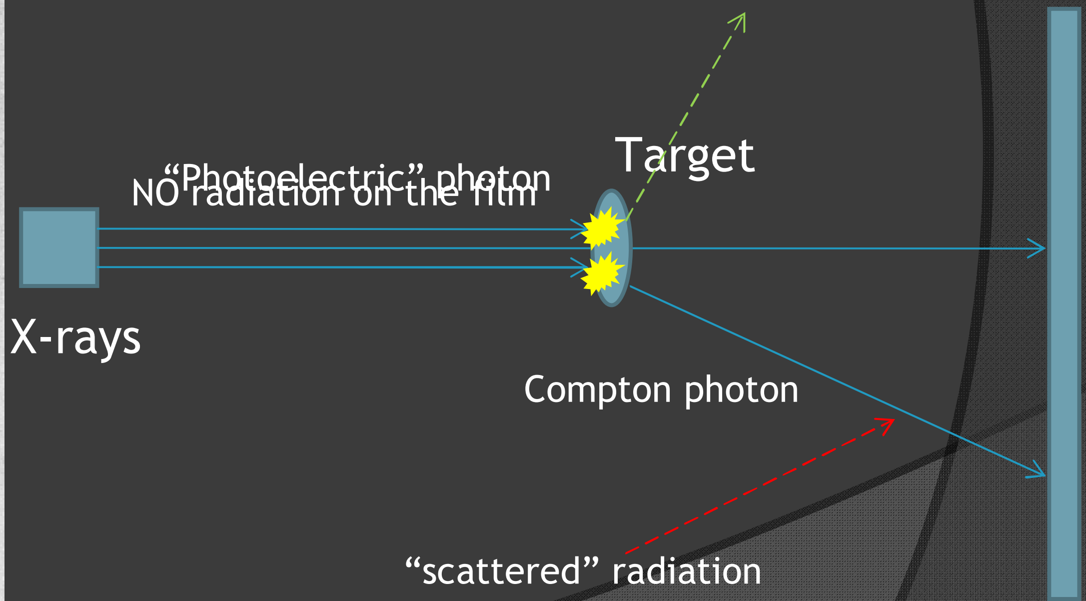
ACOUSTIC AND E.M. WAVES TO THE SERVICE OF MODERN MEDICINE

Outlook

- Ionizing Radiation
  - Transmissive…
    - X-Ray Imaging (keV)
    - C.T. Imaging (keV)
  - Emittive
    - γ-camera (keV-MeV)
    - P.E.T. (MeV)
    - Nucl. Med. Mach.
  - Therapy:
    - Radiotherapy (MeV)
- Non-Ionizing Radiation
  - Ultrasound
    - U.S. Imaging
    - U.S. therapy (HIFU)
  - Microwave
    - M.R. Imaging
    - Magneto-therapy
    - Laser therapy

Ionizing radiation

- Roentgen's wife's hand 1895
  - Not very concerned about "radiation protection"…

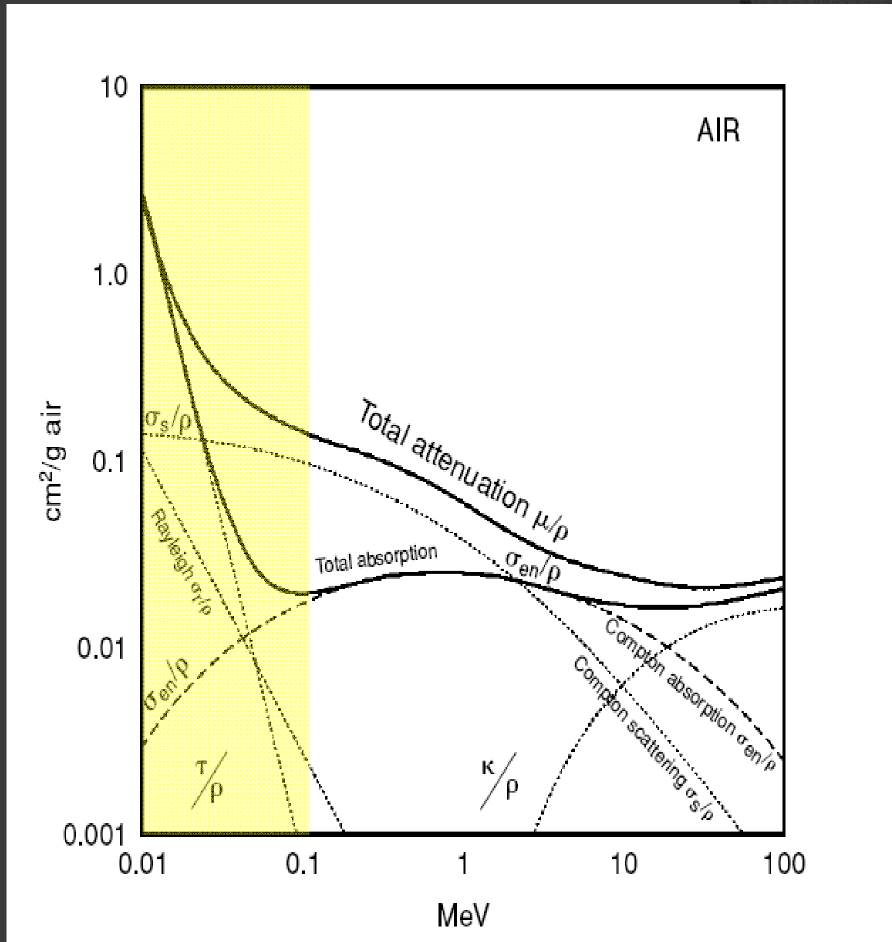


What X-ray do?

- If a photon pass through a tissue, it “blackens” the film (black dot)
- If it produces a photo-electron (photo-electric effect), disappears and do not contribute to the signal (white dot)
- If it is scattered (Compton effect), “blurs” the image because blackens the film in a position not corresponding to its “true” straight trajectory (black dot, *but in the wrong place*)

Three phenomena

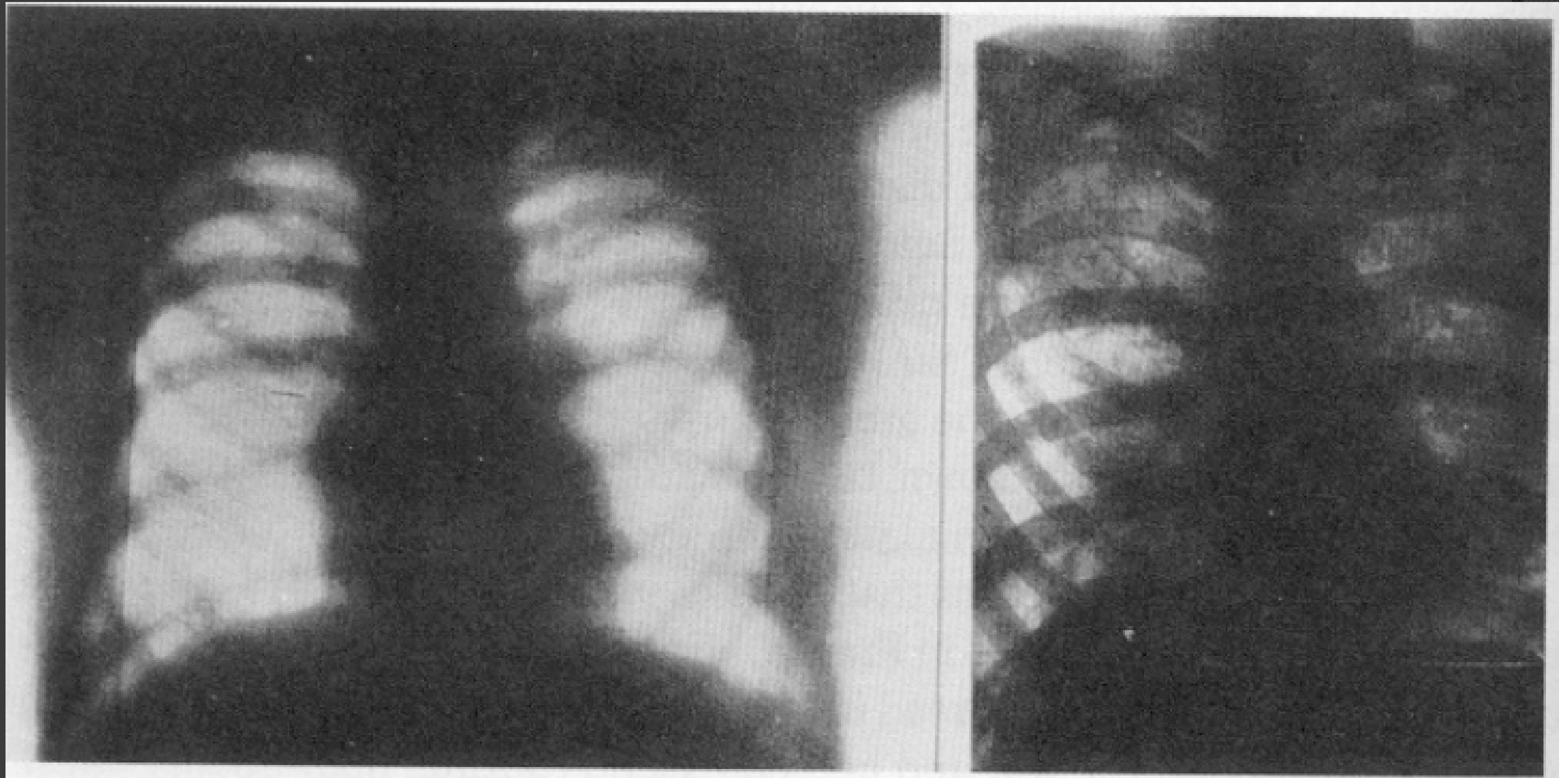
- Photo-electric effect (σ)
  - No radiation on the film (absorption)
  - $\approx(Z/E)^3$
- Compton effect (ρ)
  - Diffusion!
  - $\approx 1/E$
- Pair production (κ)
  - High-energy effect
  - $\approx E$



Evolution?

- Radiation is radiation… Almost no change from 1895
  - higher intensities, collimation ecc. but no qualitative changes
- Detectors are changed! *No more* films but
  - "plates": re-usable solid-state "collectors" of signal (1 per exposure…)
    - Intermediate spatial resolution
    - Digitalized images: possibility of computerized post-processing
    - Slow "frame-rate" (manual switch…)
  - Thin film detectors: solid-state automated detectors
    - Lower resolution ("only" 4096x4096)
    - But 30 exposures per second (a movie!)

Anyway (1902)…

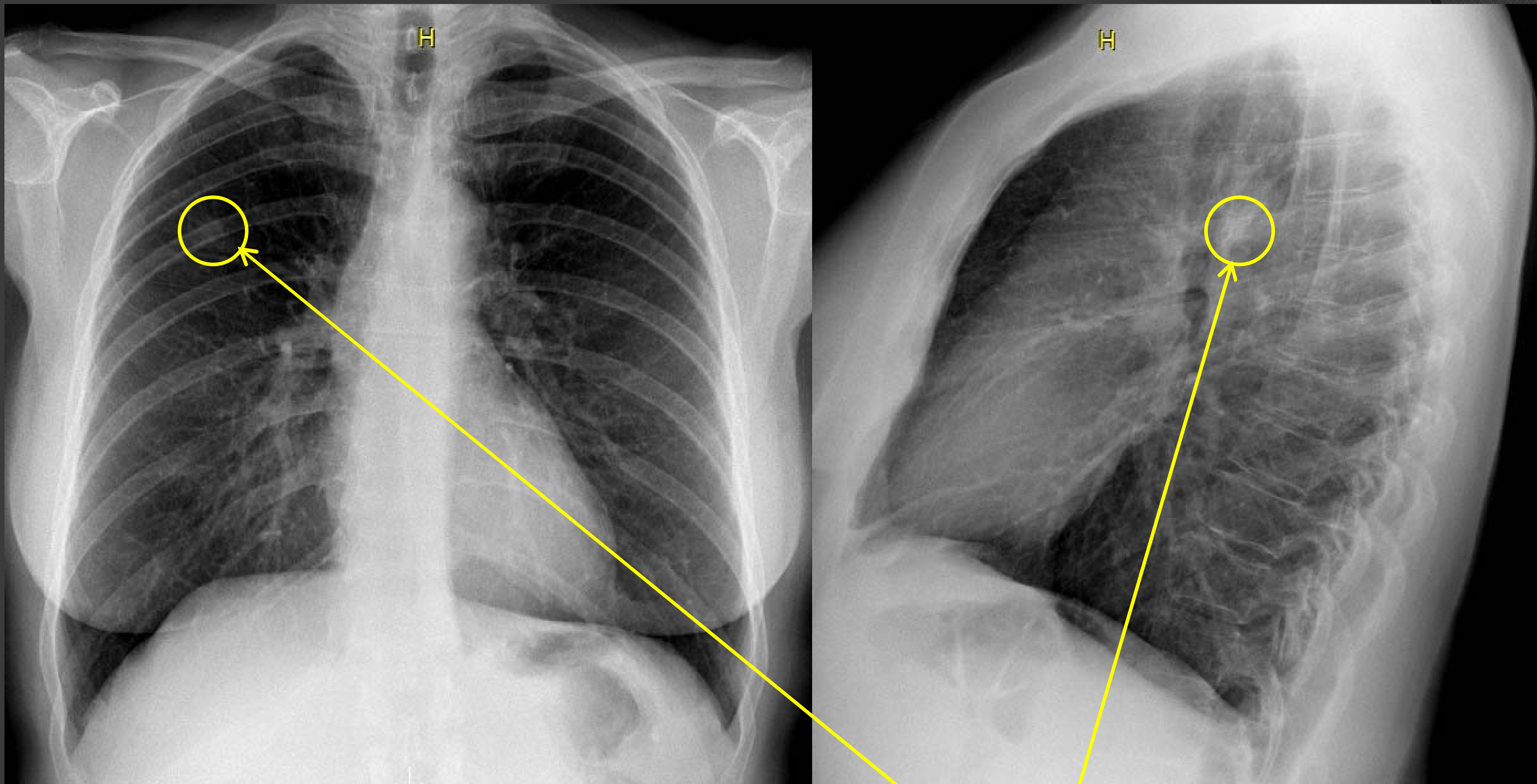


18. Chest X-rays (1902). *Left,* radiograph of normal chest (M. Kassabian, "Instantaneous Skiagraphy of the Thoracic Organs," *Transactions of the ARRS* [1903]: 95–100). *Right,* radiograph of tubercular chest (H. Hulst, "Skiagraphy of the Chest," *Transactions of the ARRS* [1903]: 88–94). Courtesy of the American Roentgen Ray Society.

Today…

2010…

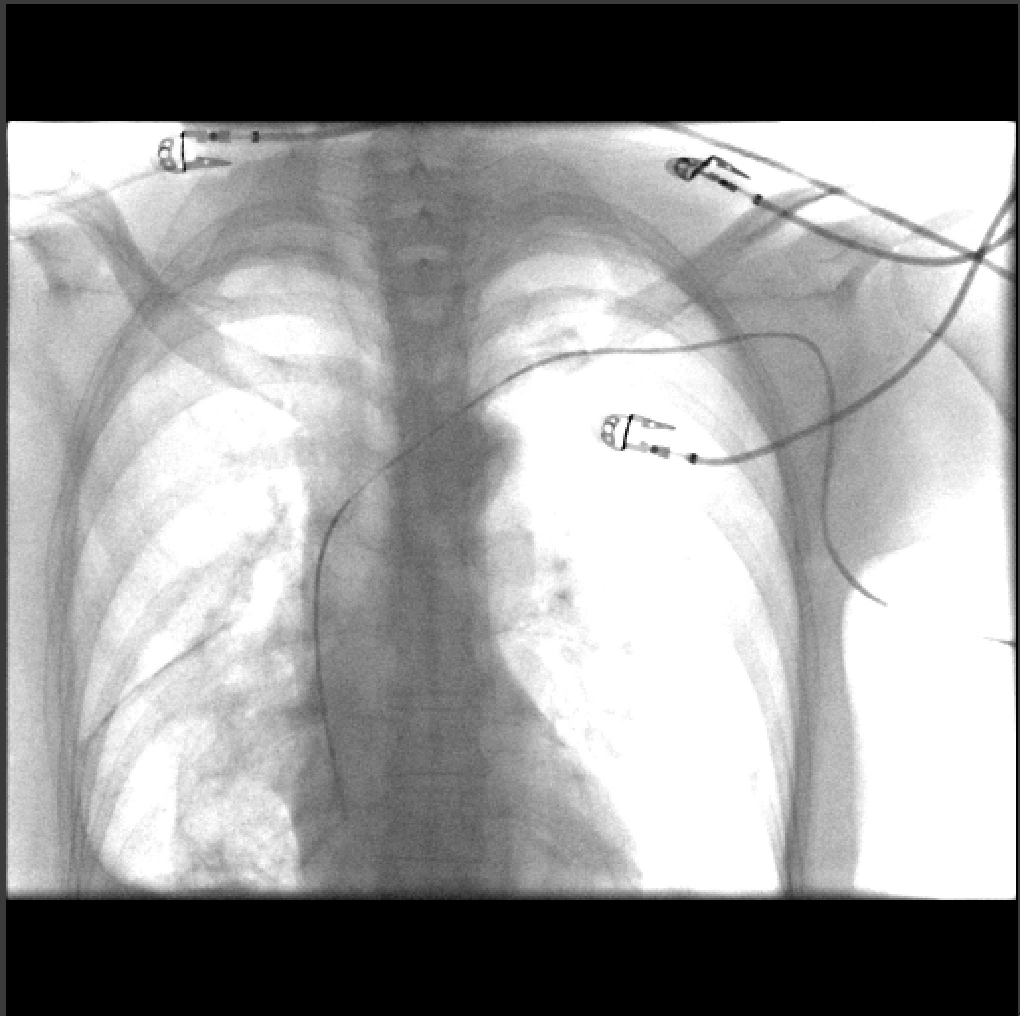
“lateral” view (LL projection)



“frontal” view (PA projection)

focal lesion?

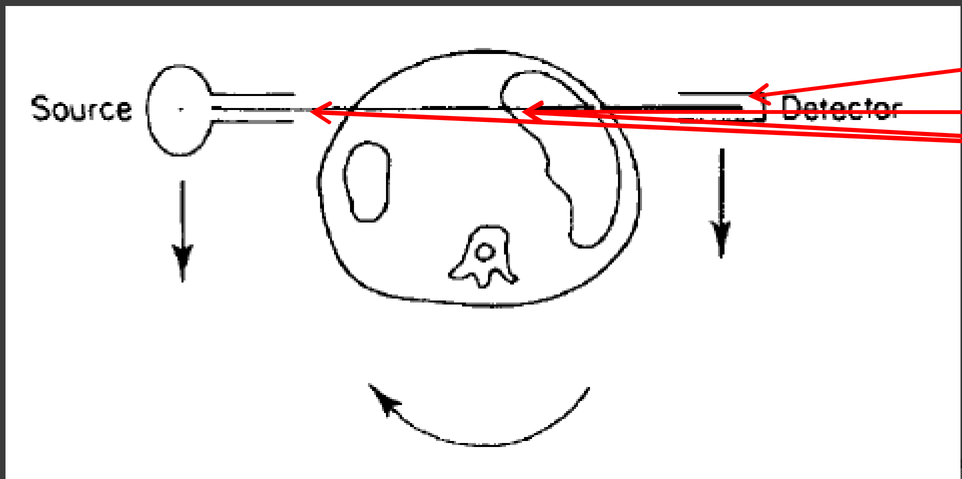
X-rays “movies”



New concepts: *2D* from *1D*

- Q: *Is it possible to determine a 2D density map from an arbitrary number of 1D density profiles?*

- A: “yes, if you know enough profiles” (Cormack ’63,’64)…



$$\frac{I_f}{I_i} = \exp\left\{-\int_{\ell_{if}} \mu(x)\, dx\right\}$$

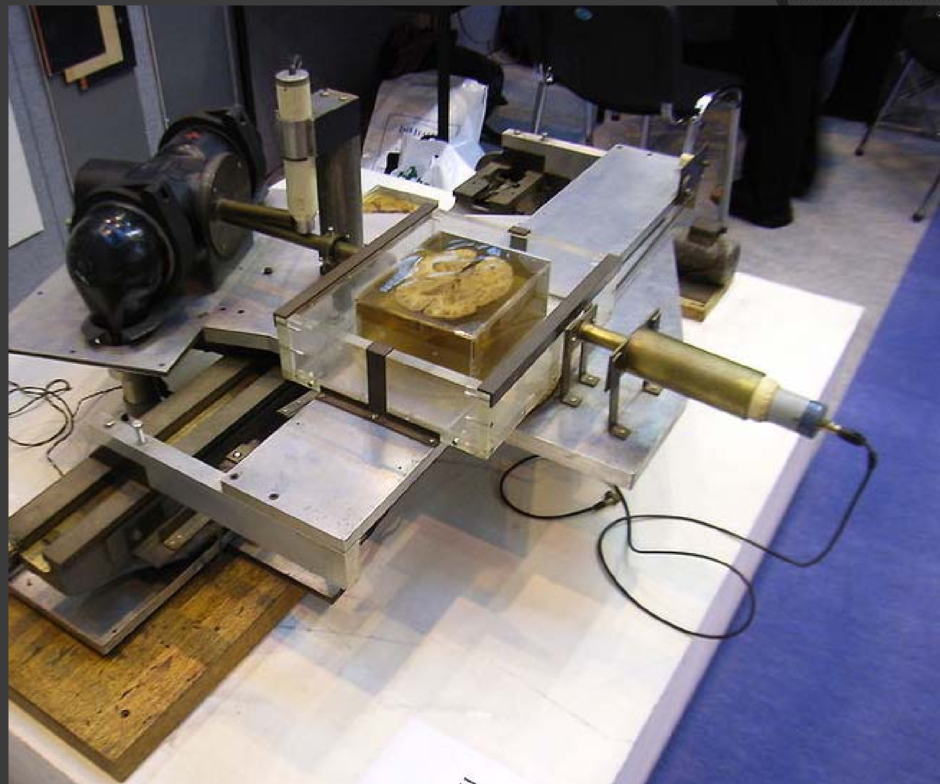
$\mu(x)$ Attenuation coefficient along a direction *x*

2D from *1D*

- The problem to determine the *2D* density map is an inverse problem based on the so-called *2D* "Radon transform"
  - Radon 1917
  - Cormack 1963, 1964 (application to imaging, independently)
- Projection-Slice Theorem: *"For an n-dimensional function f(r), the one-dimensional Fourier transform of the Radon transform of f along a direction p with fixed angle o is identical to the n-dimensional Fourier transform of f(r) evaluated along a line passing through the origin with the same orientation angle in Fourier space"…*
- In effect, nobody calculates Radon transforms…

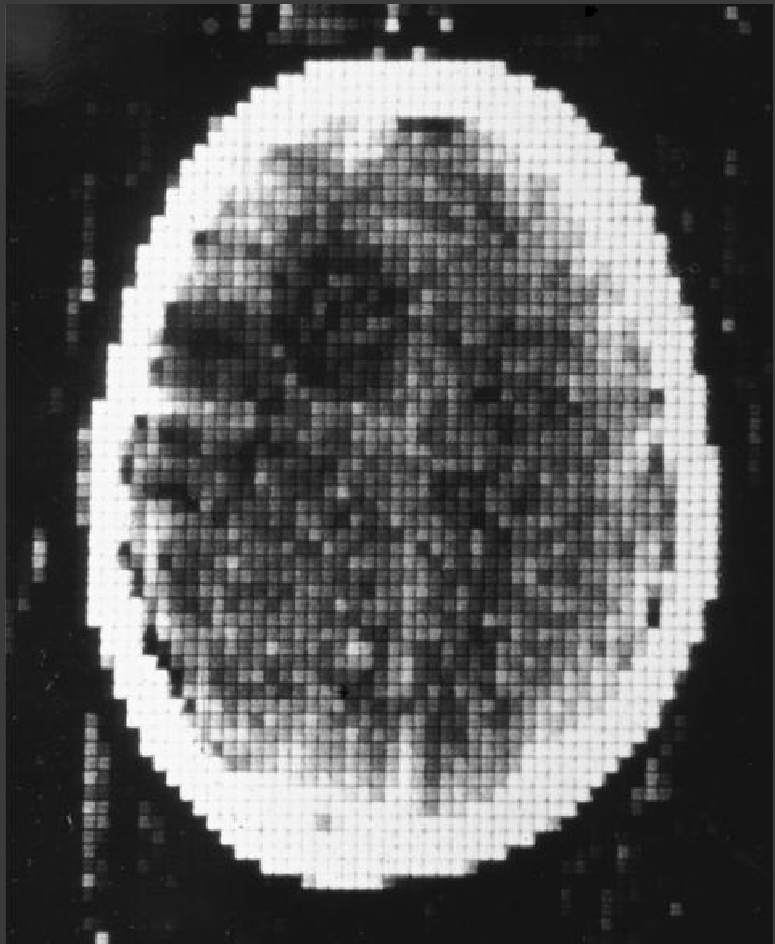
Cormack 1963 → Hounsfield 1973

EMI scanner 1971



Hounsfield prototype

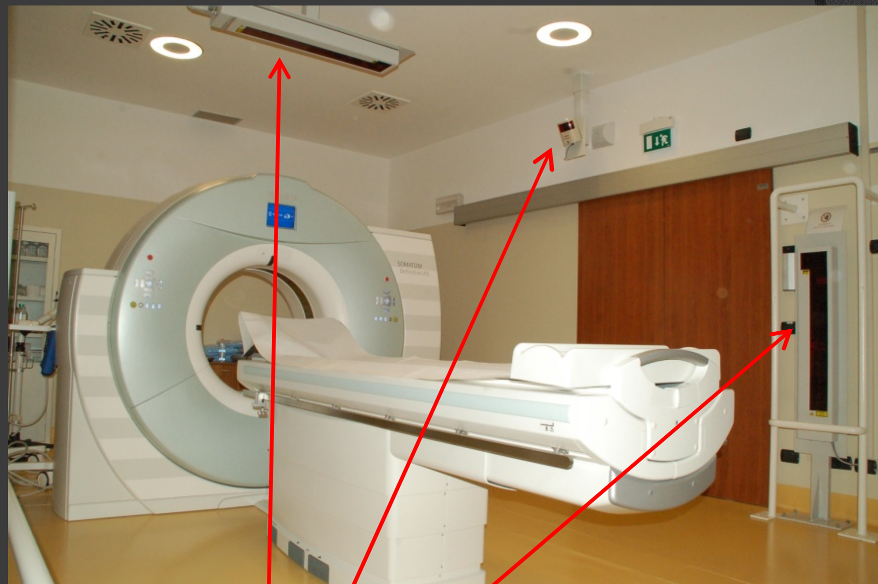
The beginning…



- About 4 minutes to acquire a single slice (8*mm* thick, 64x64 pixels)
- About 7 minutes to reconstruct the image
- 10-15 slices for the brain
- No body applications

The present…

Whole-body scanners with large bore (up to 80*cm*)



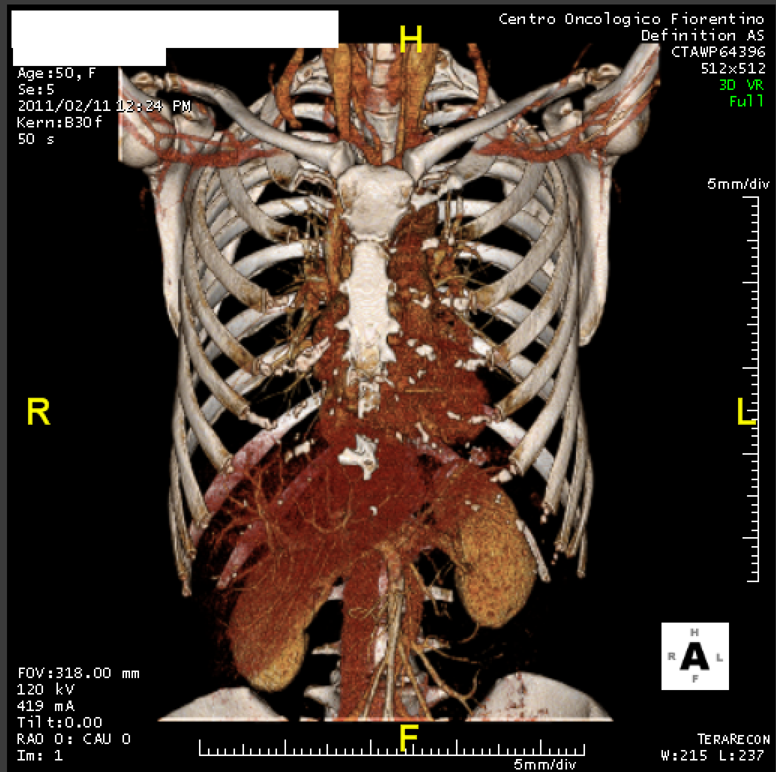
RT table-top

Lasers for RT planning

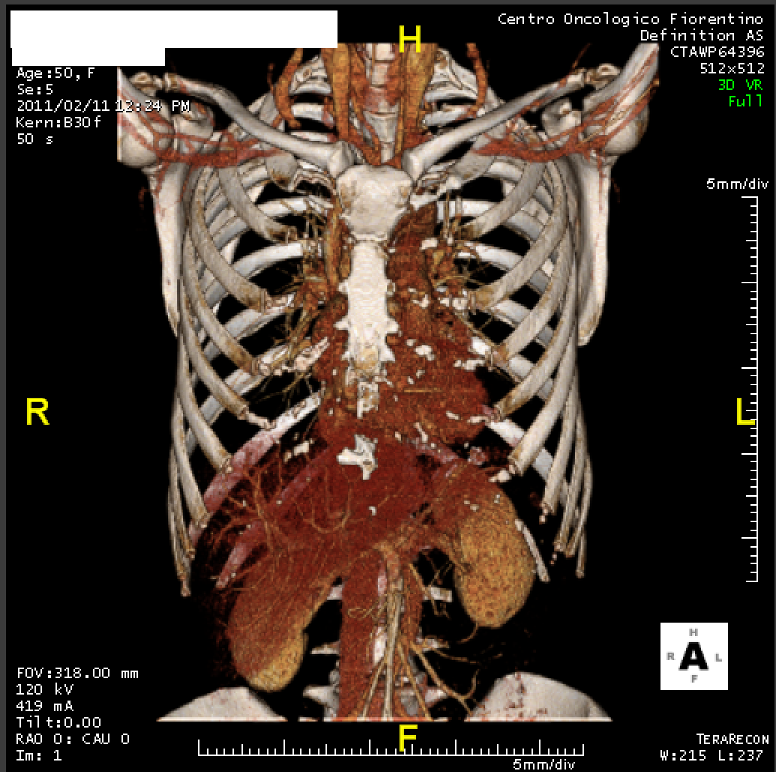
The present…

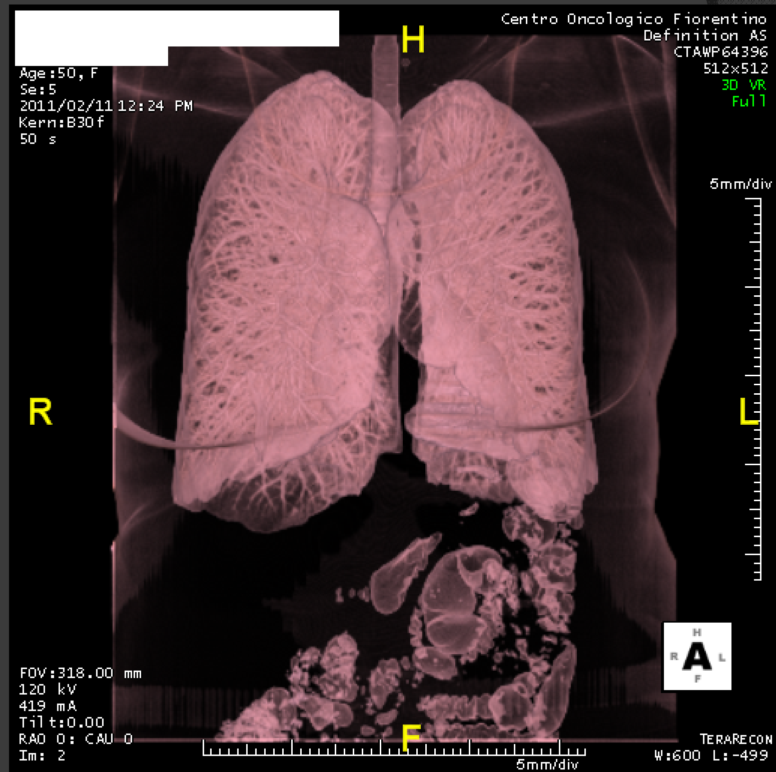
- About *0.33s* to acquire up to 320 images (down to 0.4*mm*, 512x512 pixels)
- About *10s* to reconstruct hundreds of images…
- Many applications: neuro, body, vascular, functional…

And from the same acquisition…

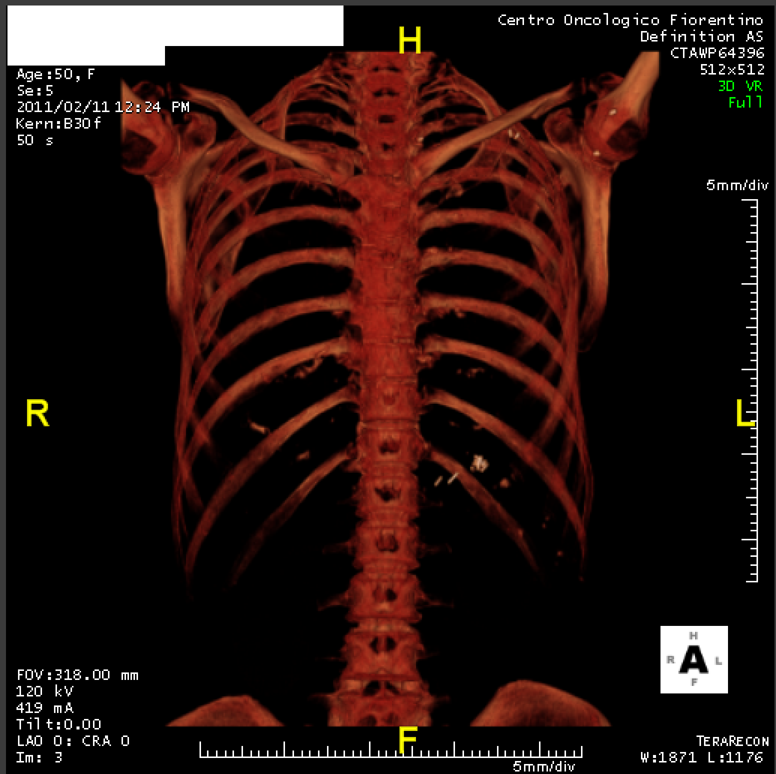


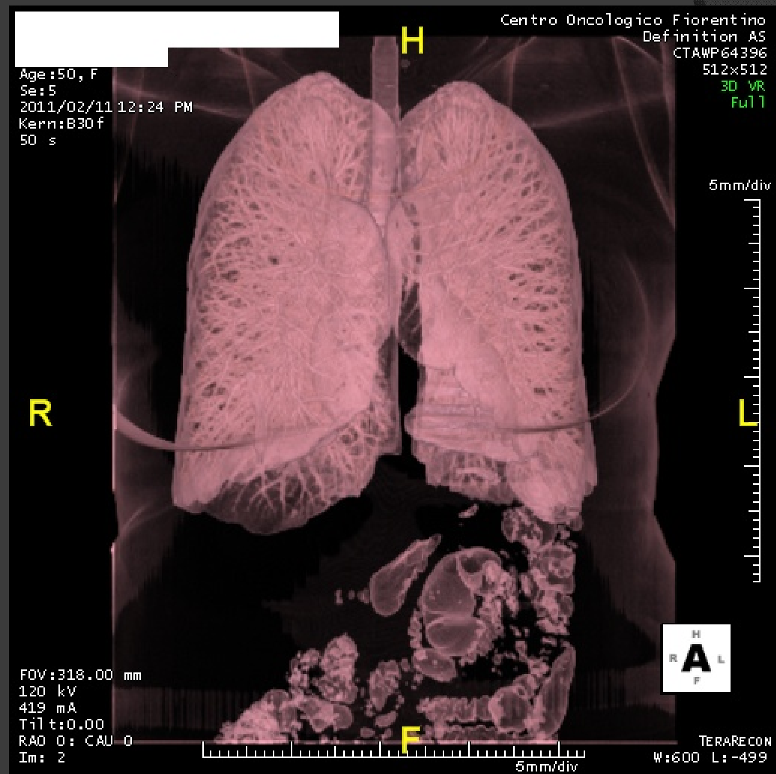
And from the same acquisition…





And from the same acquisition…





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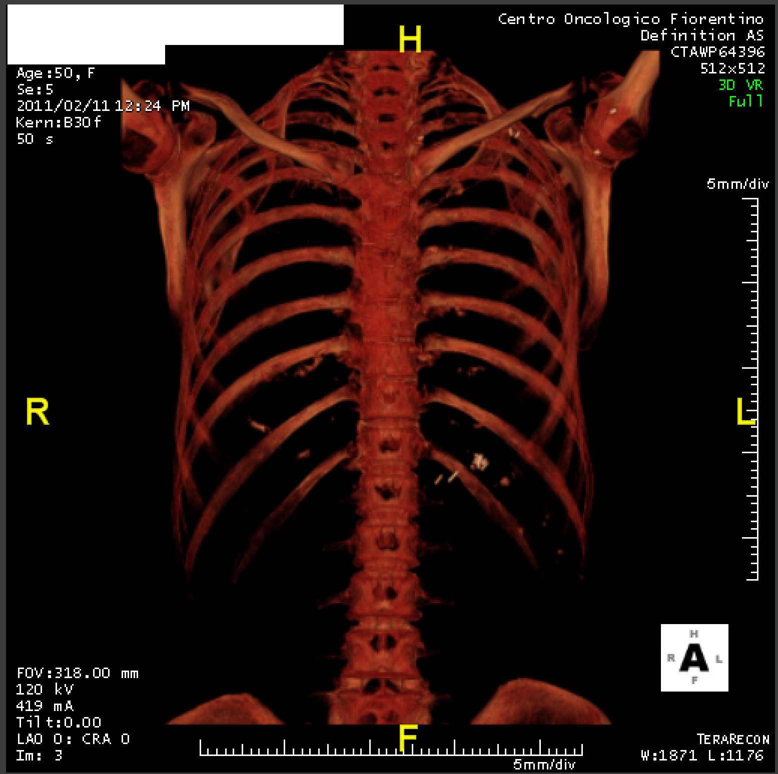

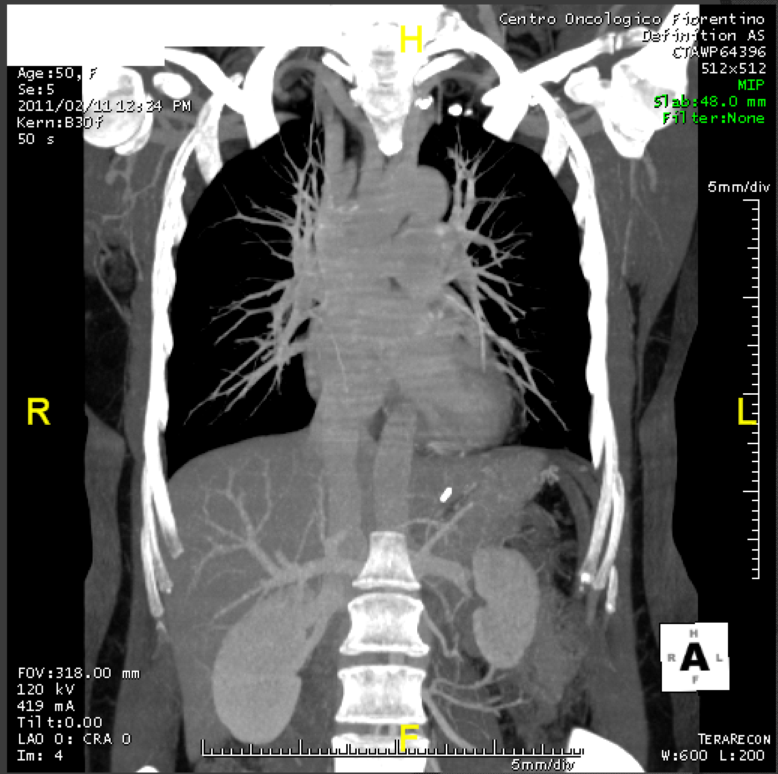

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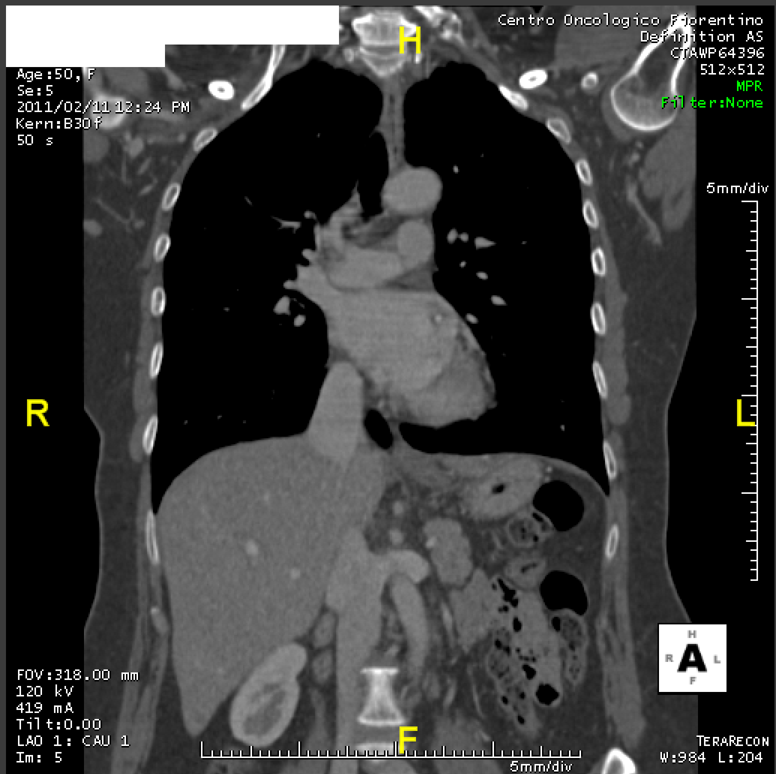

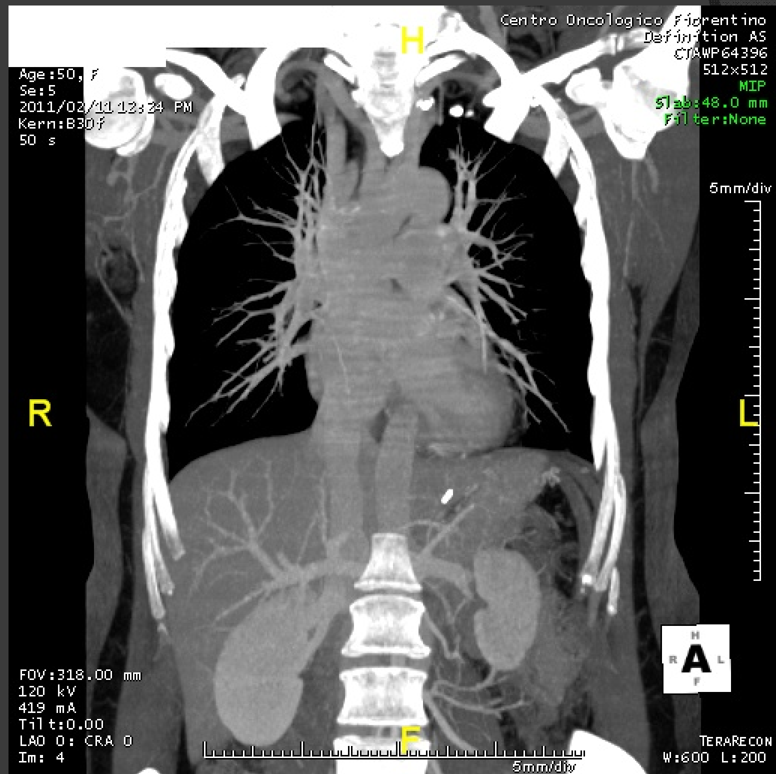

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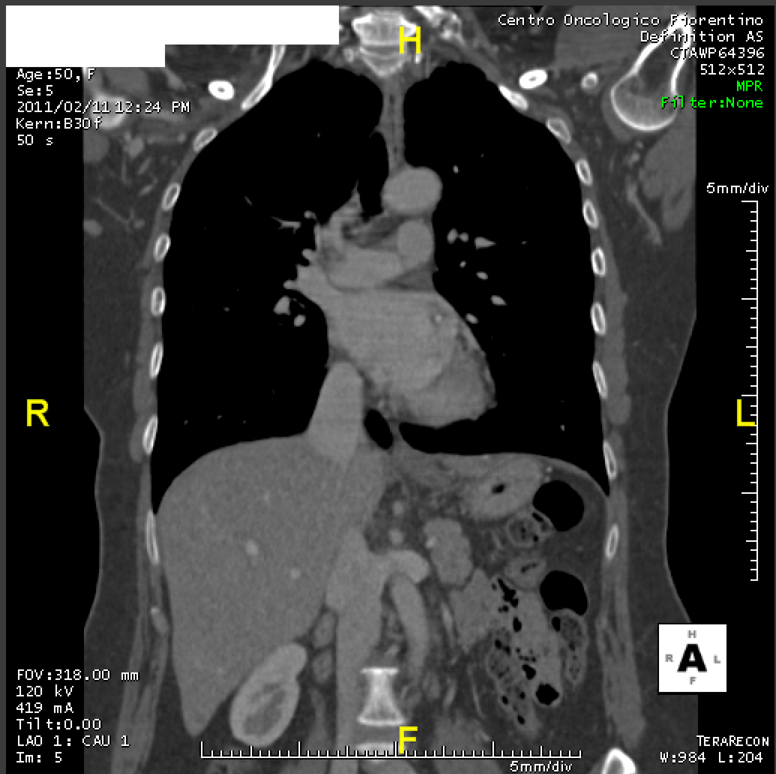

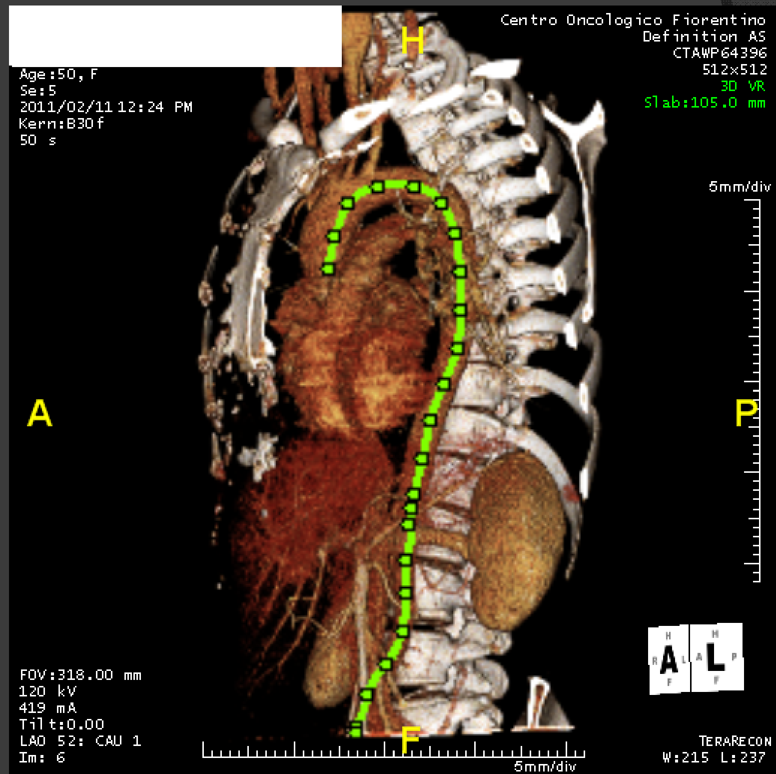

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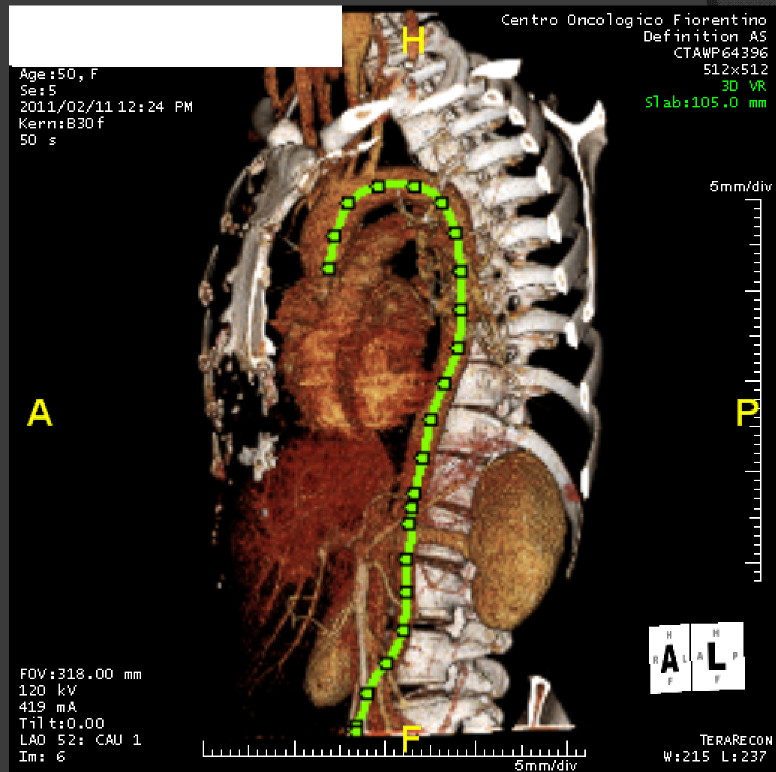
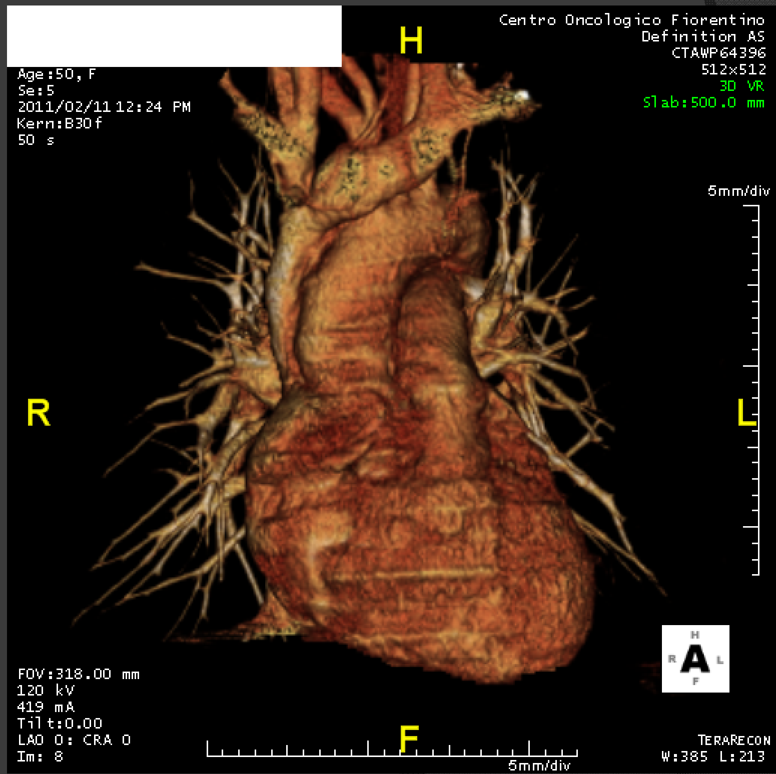


And from the same acquisition…



Positron Emission Tomography (PET)

Radio-tracers

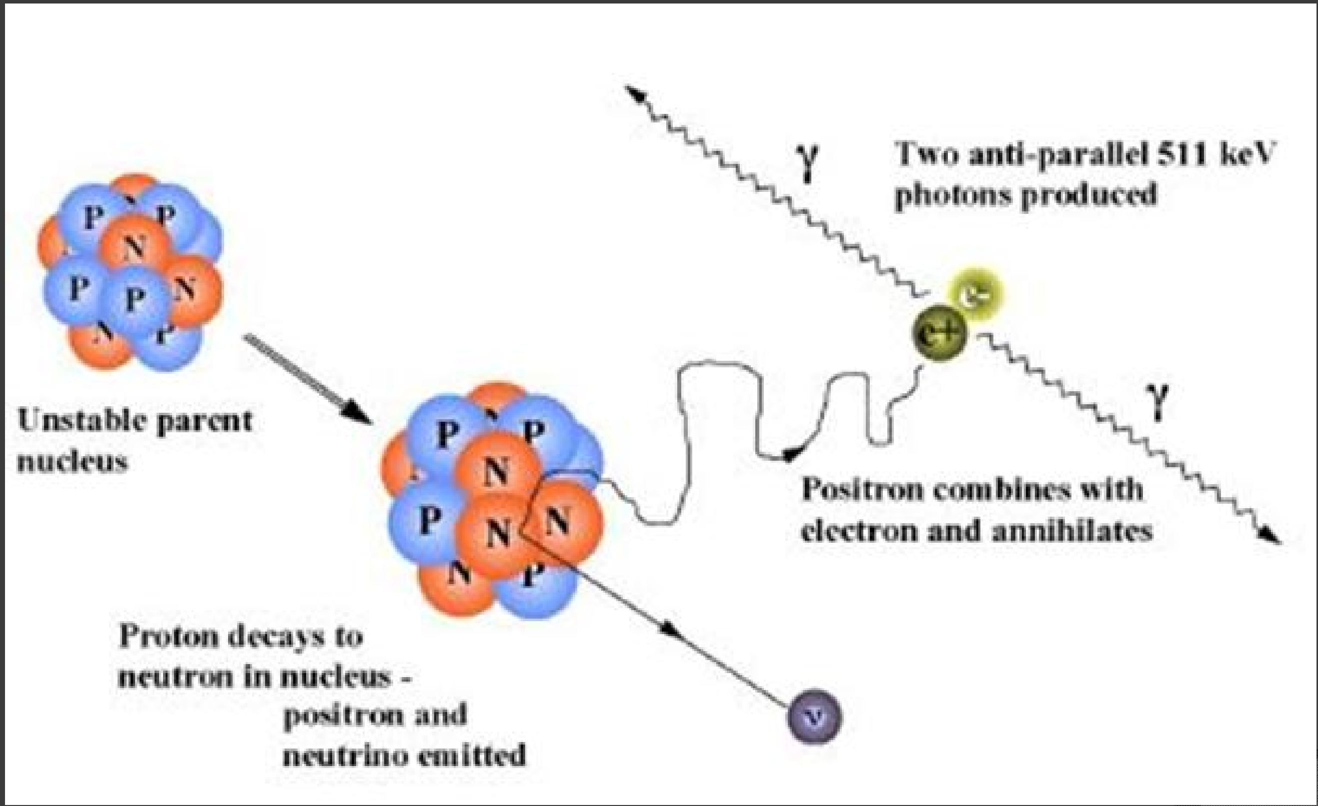
- Choose a radio-nuclide with short lifetime and β^+-decay
  - ex: $^{18}F \rightarrow {}^{18}O^- + \beta^+$, *110'*

- Insert it in a "suitable" biological molecule
  - ex: *2-deoxy-2-(¹⁸F)fluoro-D-glucose* substitution for the normal hydroxyl group at the **2'** position in the glucose molecule (^{18}FDG)
    - ^{18}FDG initially follows the metabolic path of glucose and in about an hour enters a cell
    - Inside the cell, undergoes a metabolic change and remains trapped for three to six hours
    - Enough time to decay and scan the concentration…

Radio-tracers: ^{18}FDG

- A cancer cell is usually hypoxic (very high grow rate: not enough oxygen!)
- No Krebs cycle: only cytosol respiration (glycolysis), very high glucose consumption ("hungry" cells)
- High concentration of ^{18}FDG: "high" radioactivity
- High PET signal!

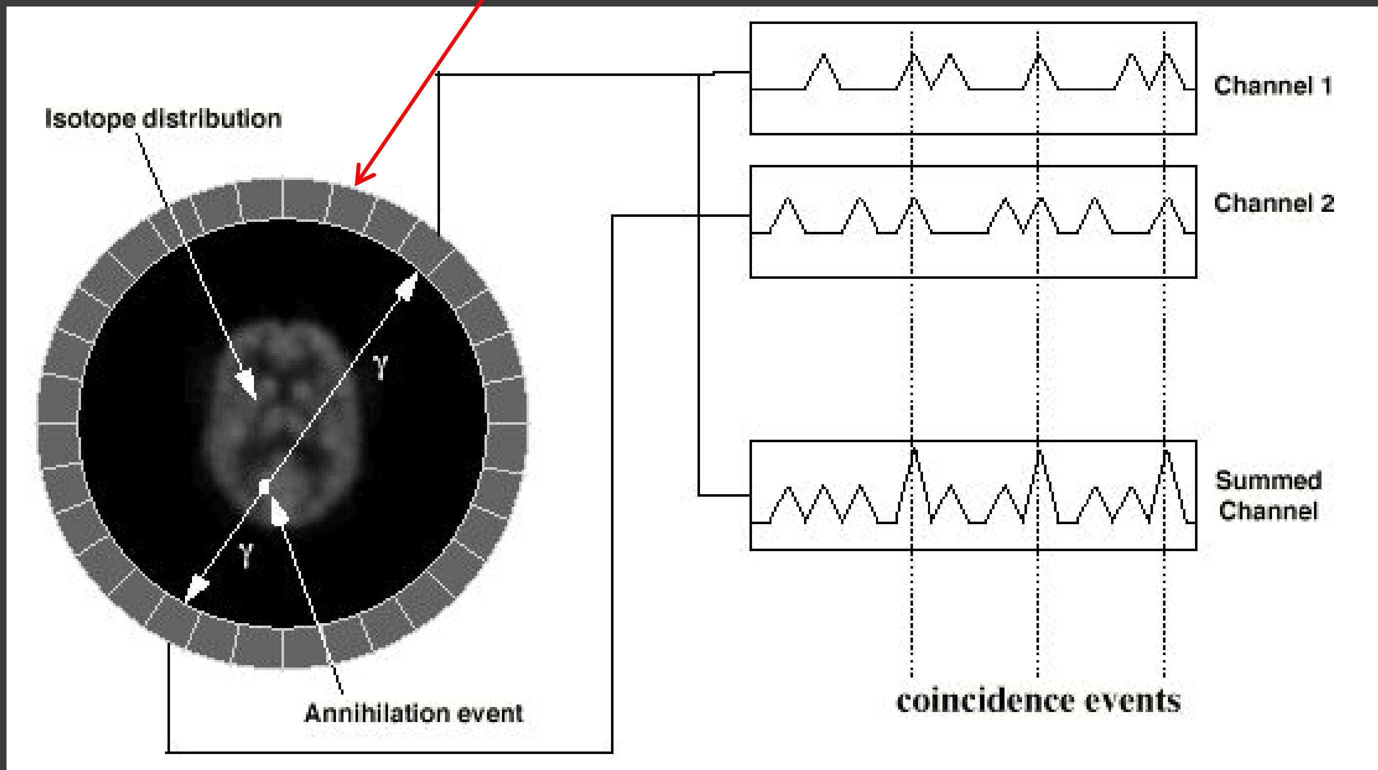
“PET” signal?



Two anti-parallel 511 keV photons produced
γ
γ
e-
e+
Unstable parent nucleus
Positron combines with electron and annihilates
Proton decays to neutron in nucleus - positron and neutrino emitted
ν

“PET” signal?

Single-crystal detectors

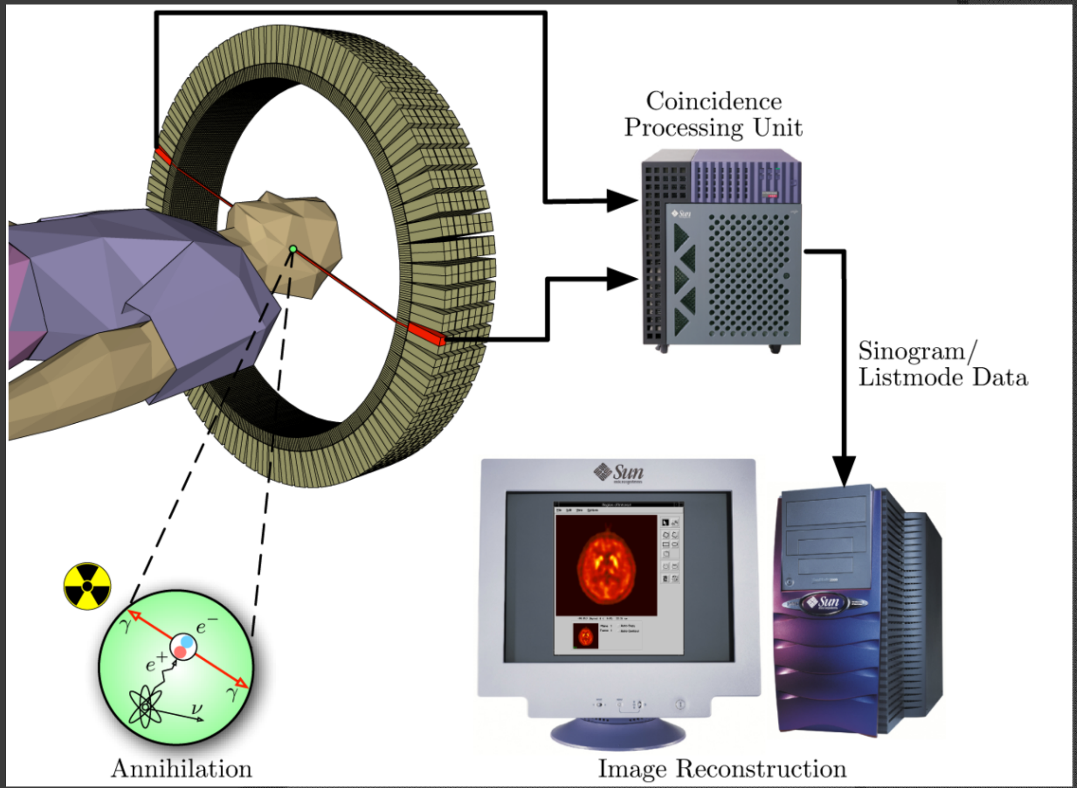


PET Signal – 2

- Intrinsically low spatial risolution (about *1cm*)
- High sensibility
- Very high specificity

Q: How to *localize* a lesion?

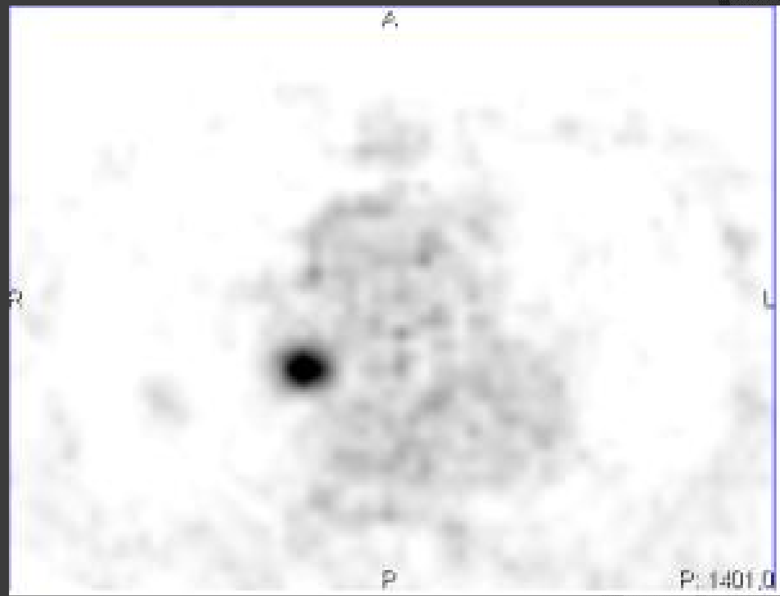
A: CT *co-registration*



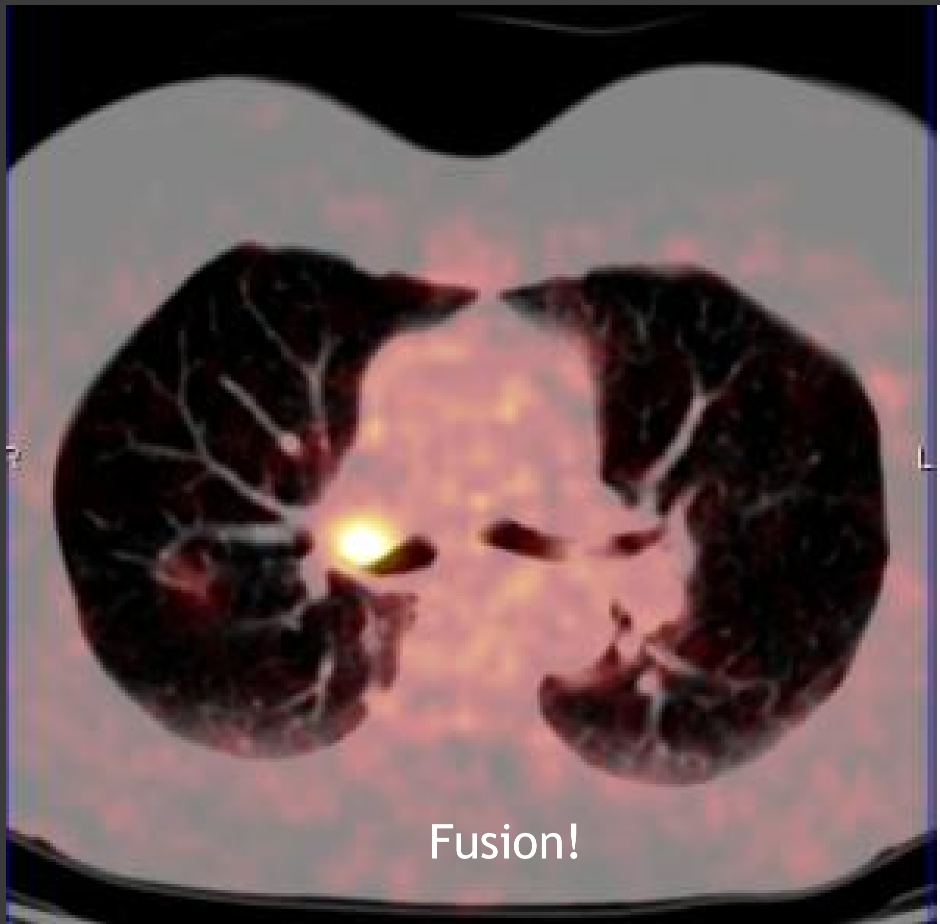
Coregistration?

1. obtain a CT image

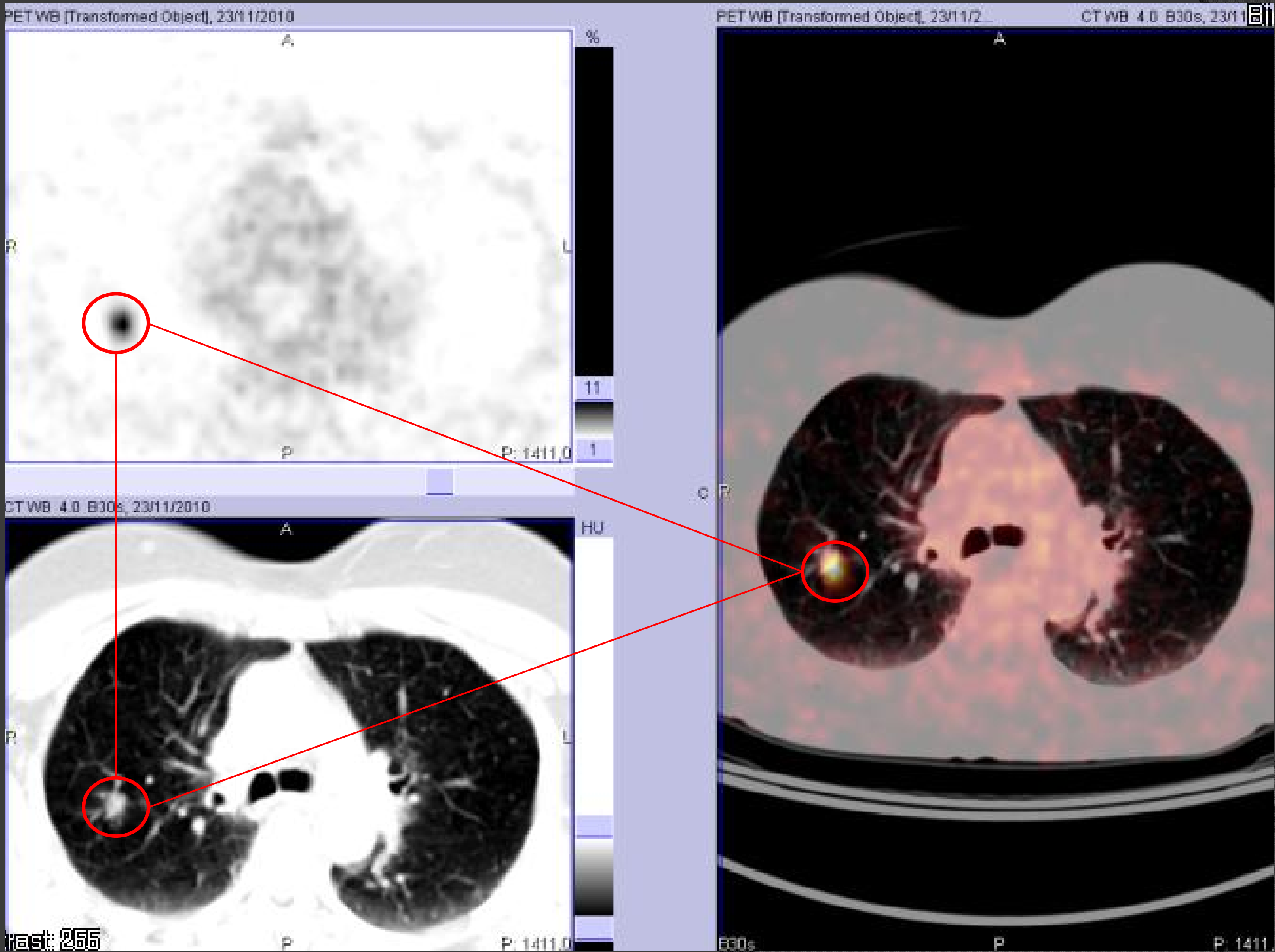
2. obtain a PET image
(without moving the patient)



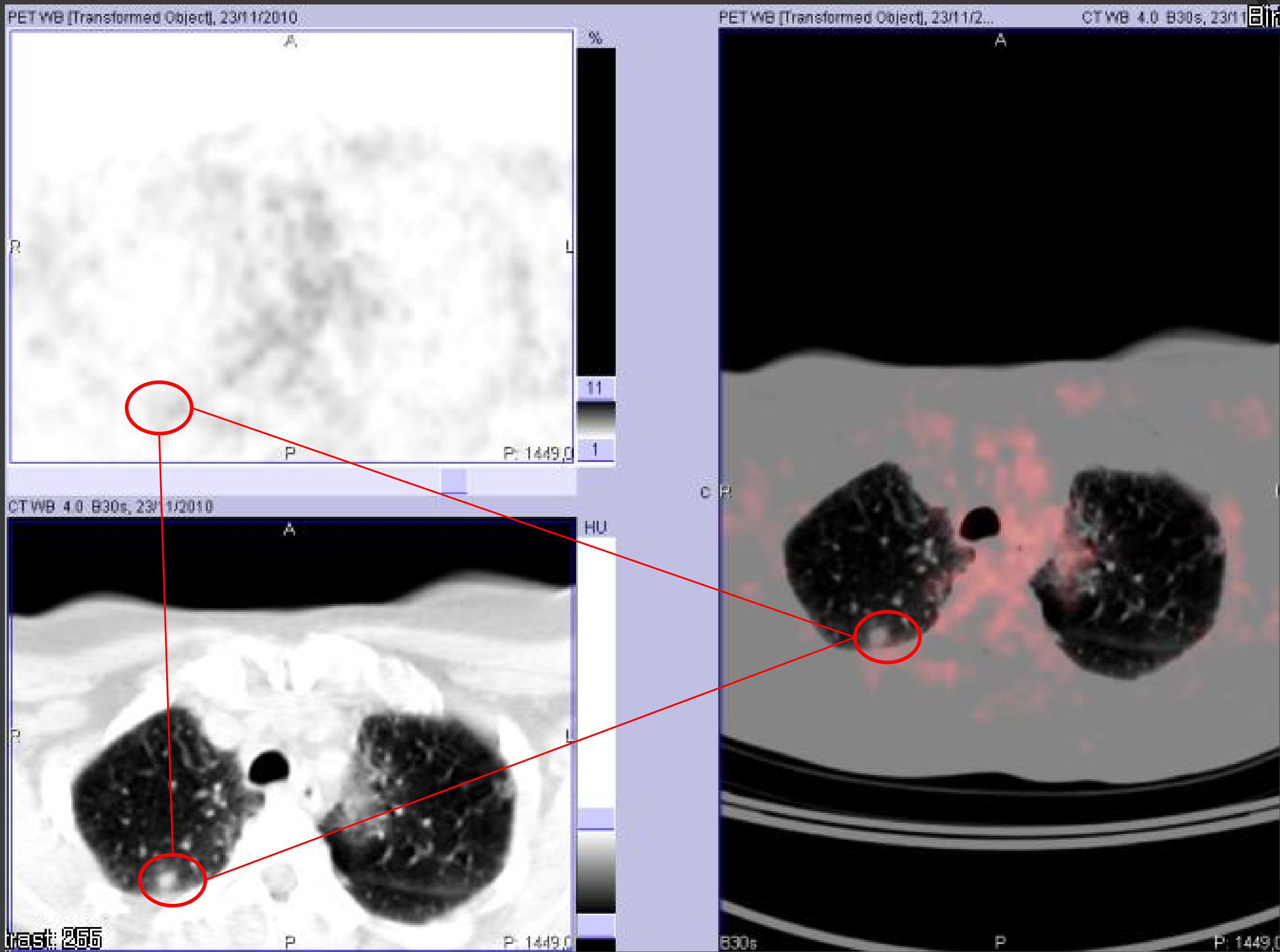
Coregistration?



PET-CT: the positive strength



PET-CT: the *negative* strength



PET-CT

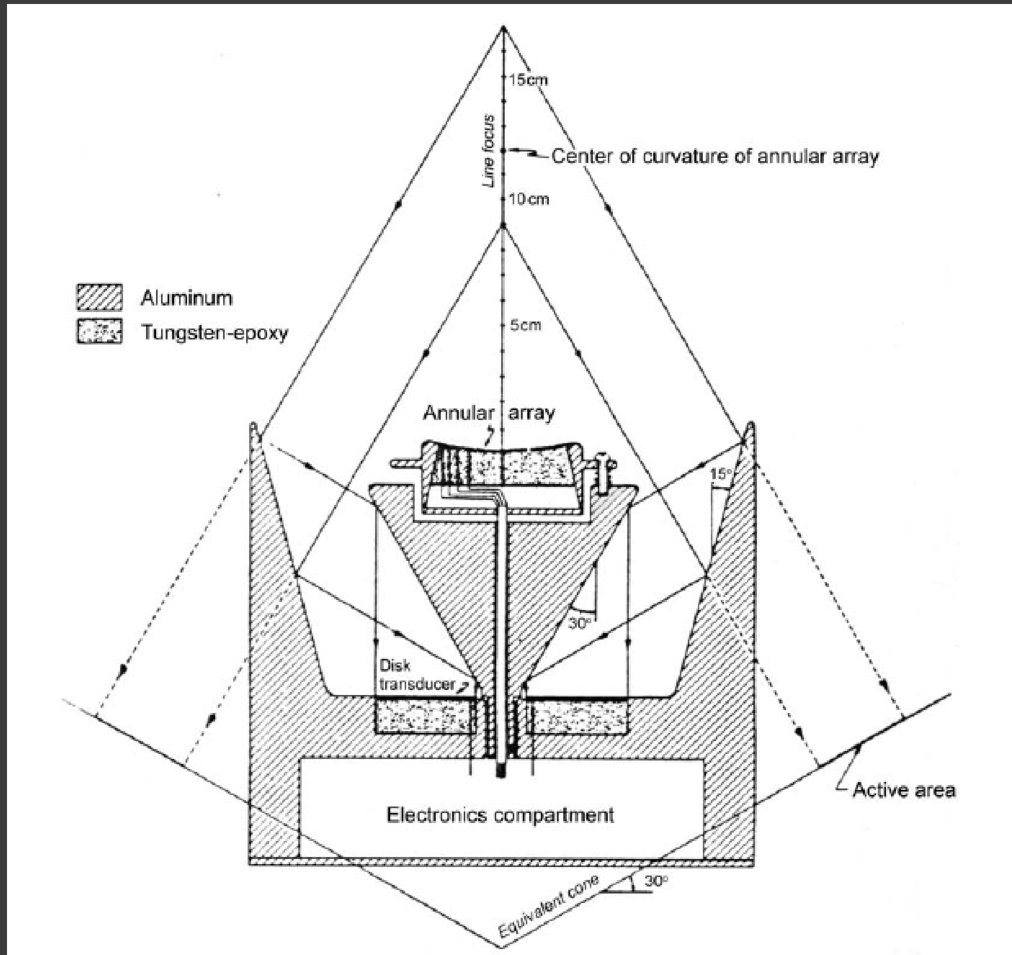
- “Functional” Imaging
- Morphologic Imaging
- low radiation dose
- Intermediate-to-high radiation dose
- Quantitative informations (“SUV”)
- Qualitative informations

Together: Whole-Body imaging with
sensitivity close to 90%, specificity higher than 90%

Acoustic waves

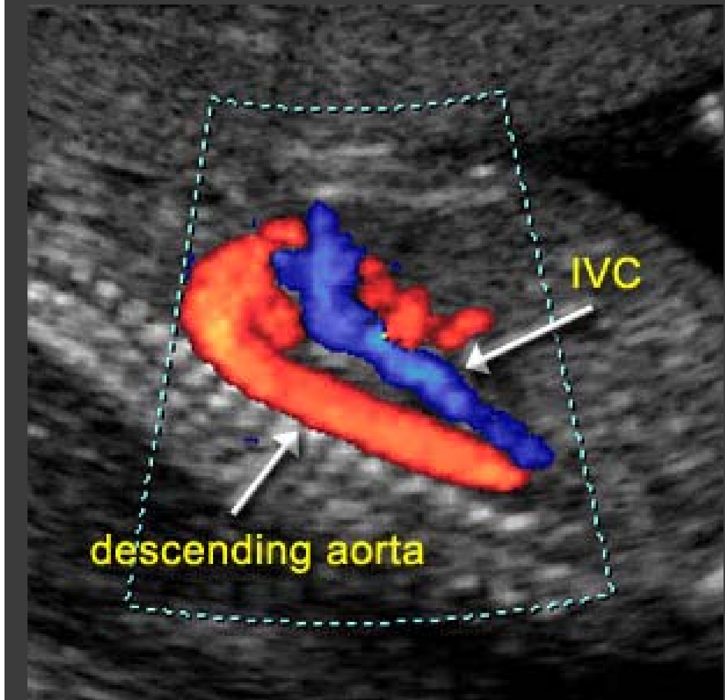
- “Sonar” principle:
  - US emitted by a transducer of suitable geometry
  - Echo received by the same transducer
    - Time of the detection
    - Intensity “ “ “ “
- Image formation by juxtaposing pixel-by-pixel the signal received along a longitudinal plane

US Scanner

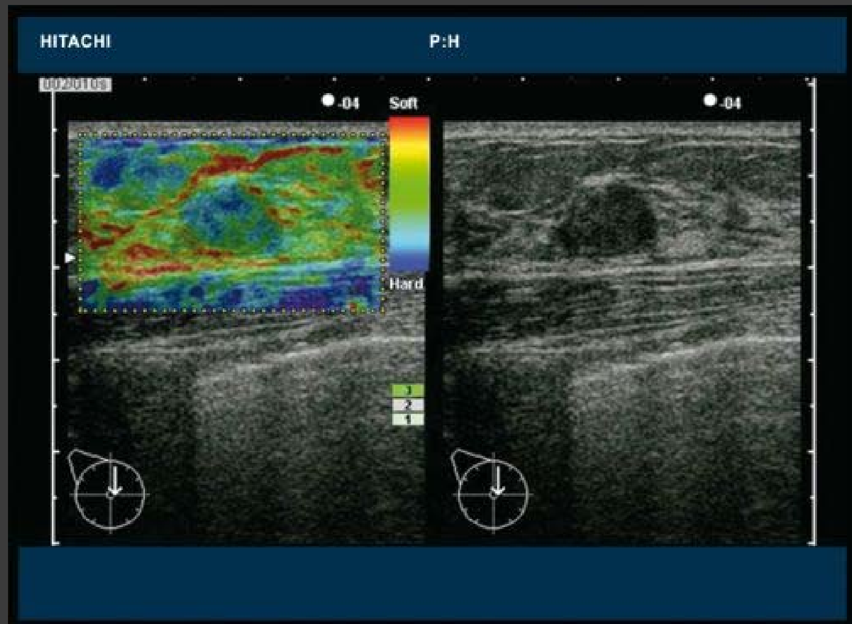

15cm
Line focus
Center of curvature of annular array
10cm
Aluminum
Tungsten-epoxy
5cm
Annular array
15°
30°
Disk transducer
Active area
Electronics compartment
Equivalent cone
30°

… and images

“standard” US image

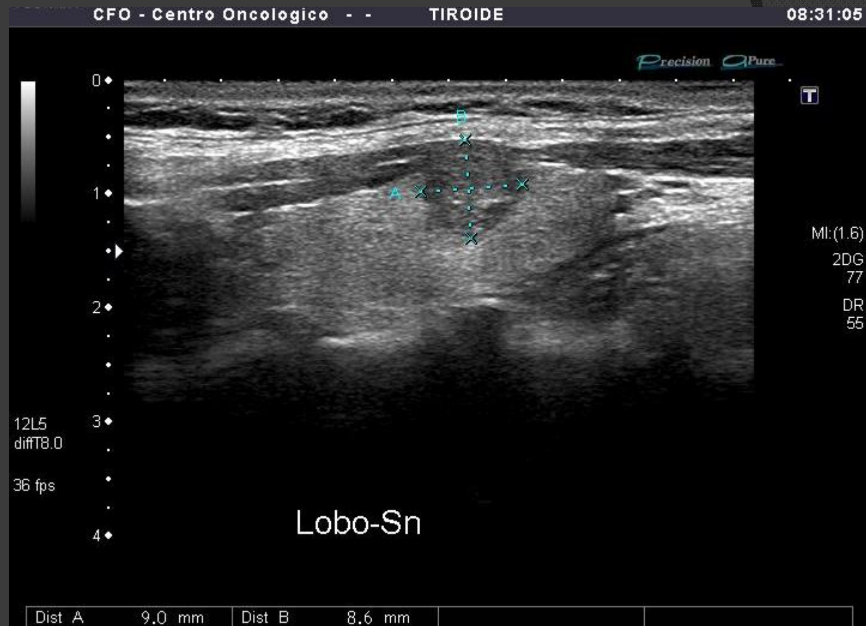


“Doppler” image



Elastography

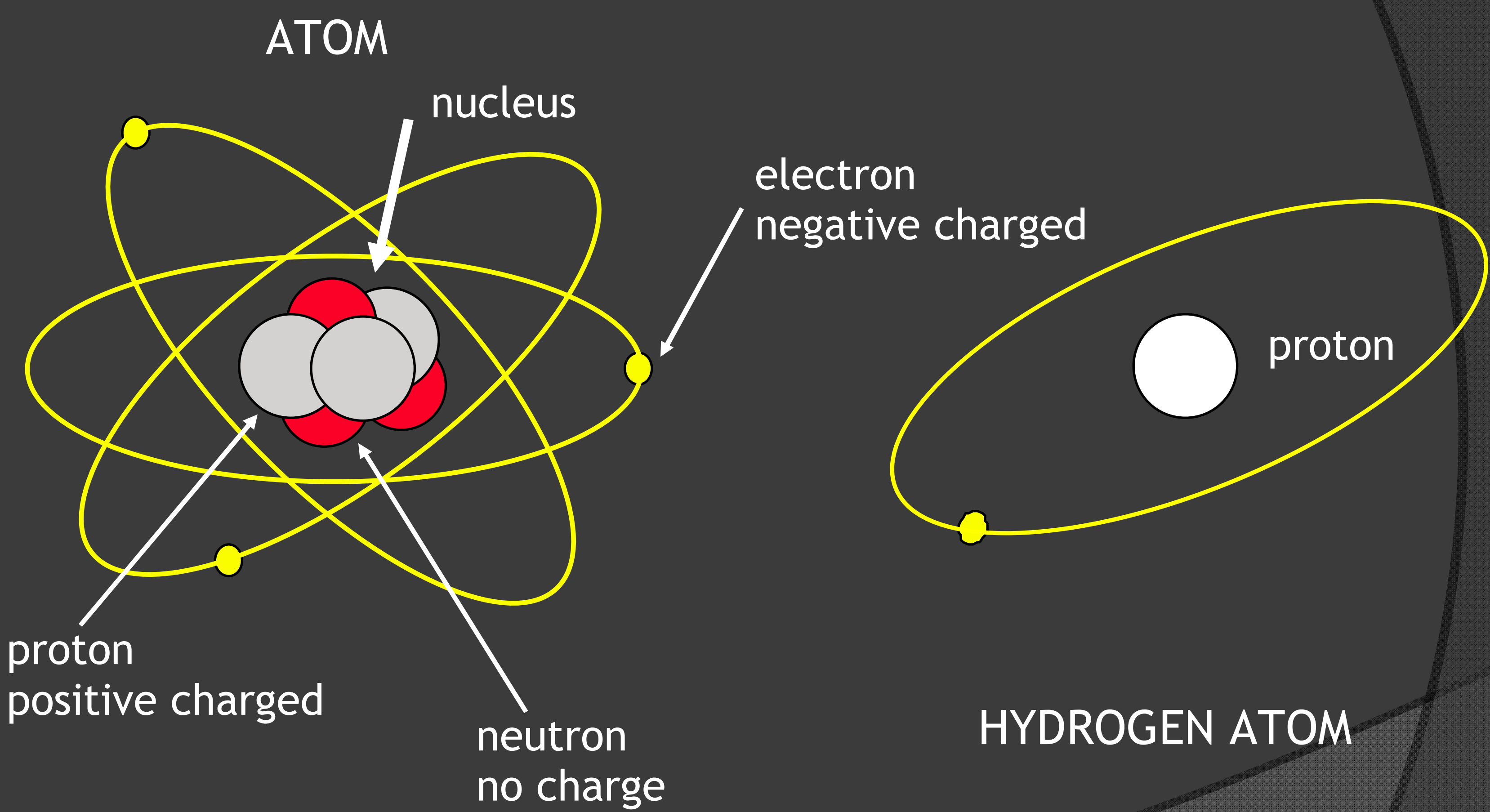
Example: Thyroid



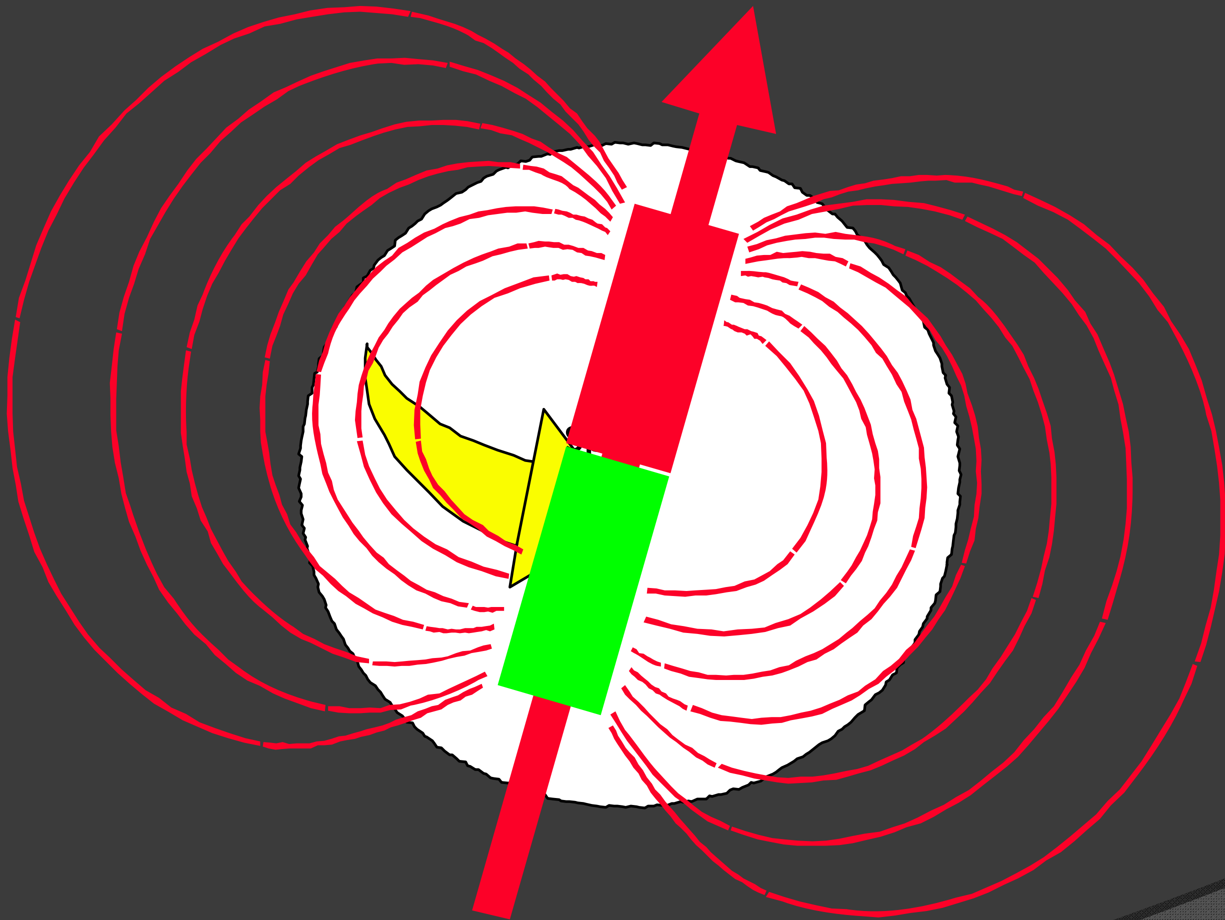
Non-Ionizing Radiation

- Optical radiation
  - Laser
  - Optic fibers for communication
  - Trans-luminescence
- Microwaves
  - Magnetic properties:
    - Magnetic Resonance Imaging
    - Magnetic Resonance Spectroscopy (and Spectroscopic Imaging)

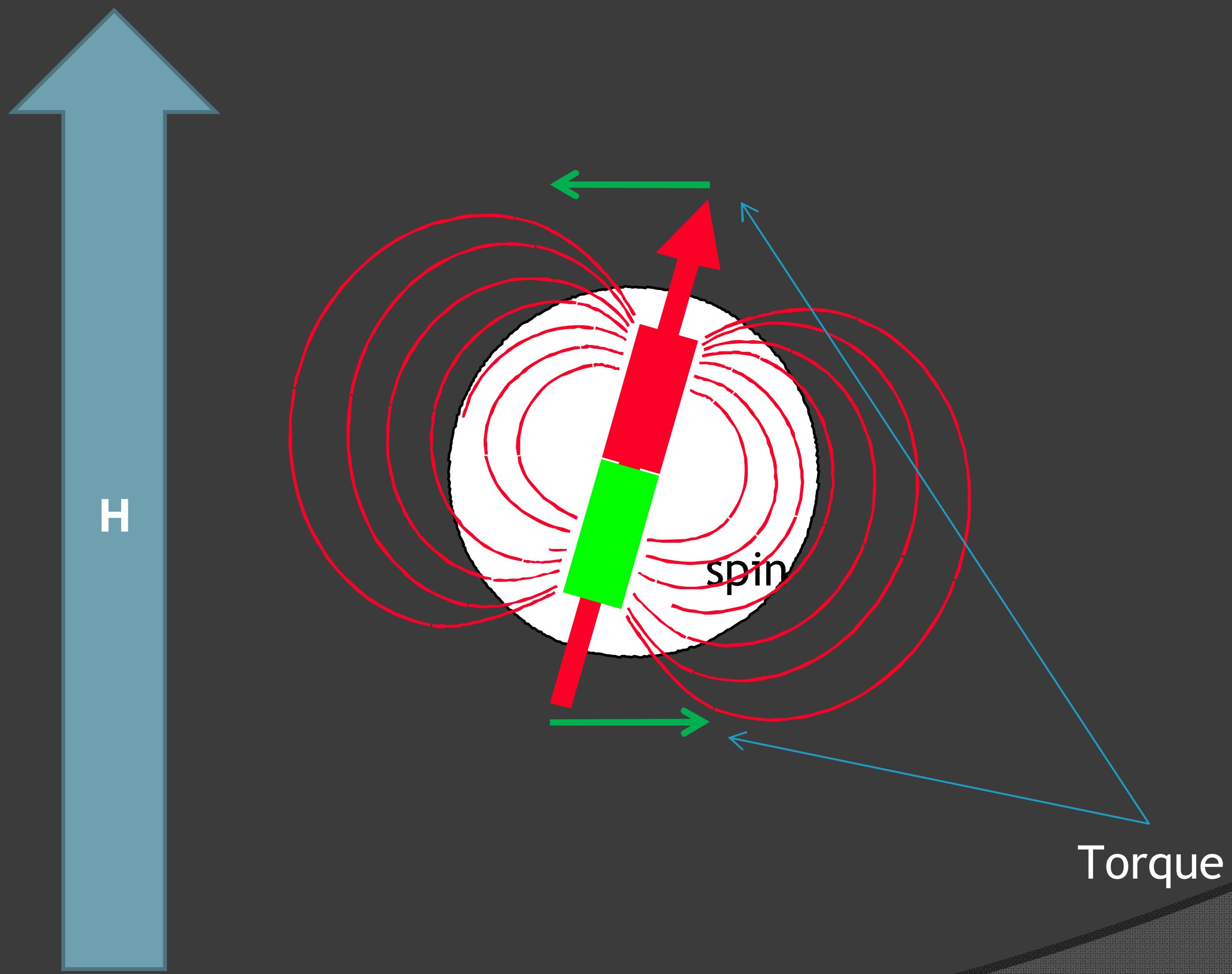
Magnetic properties of matter

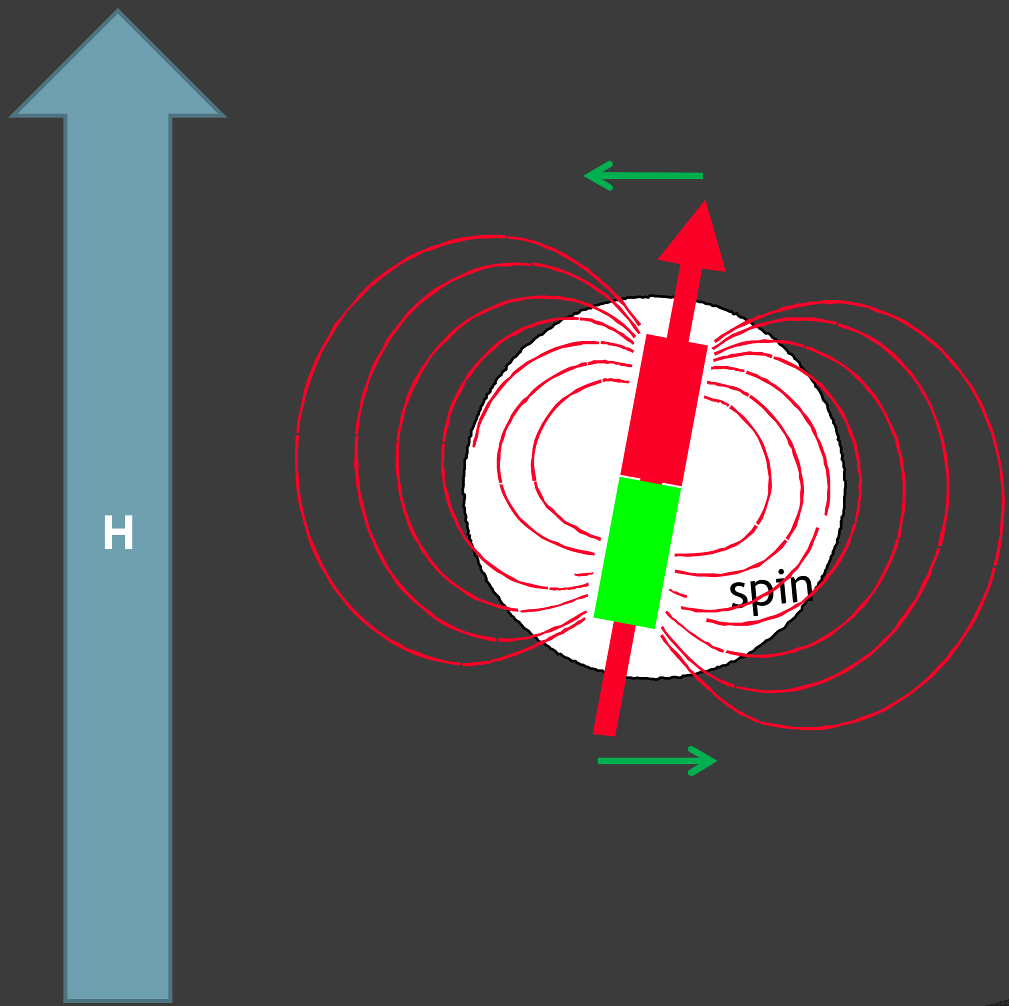


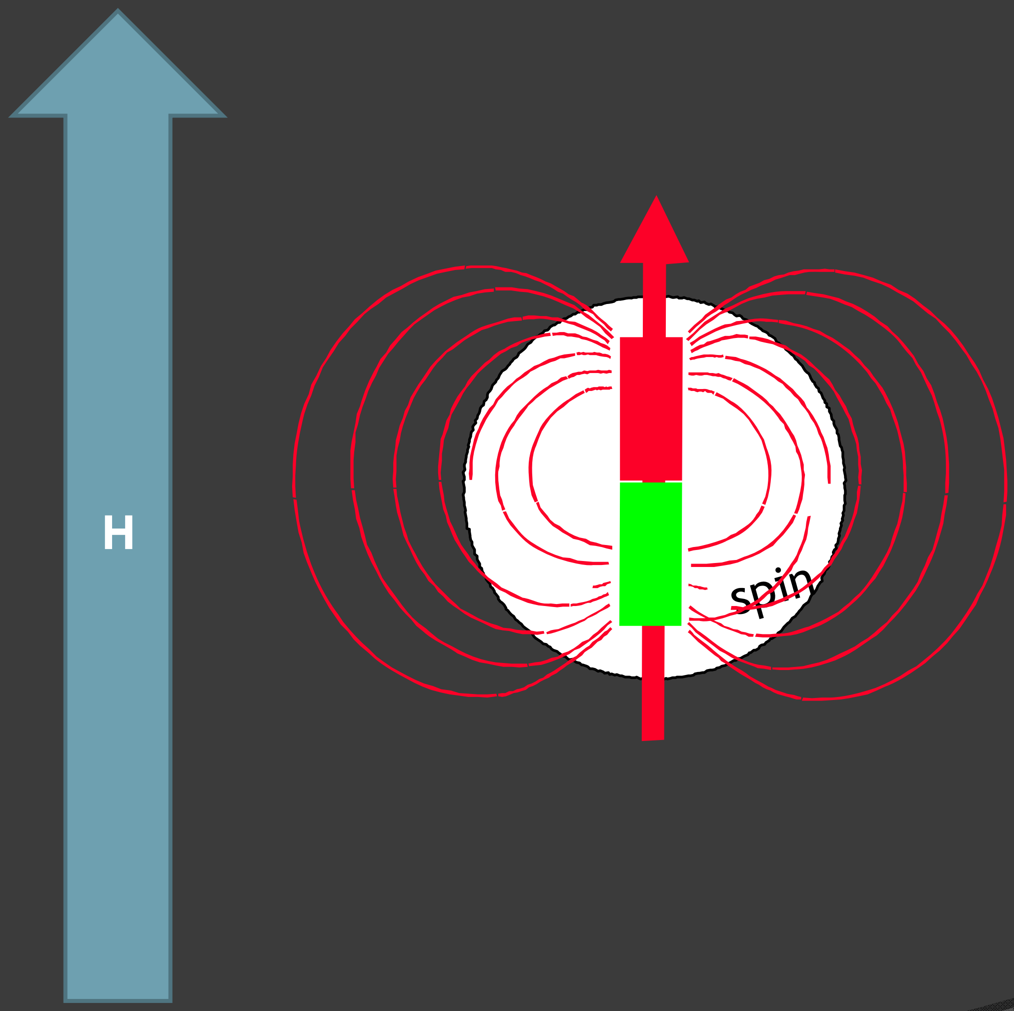
Spin and magnetism



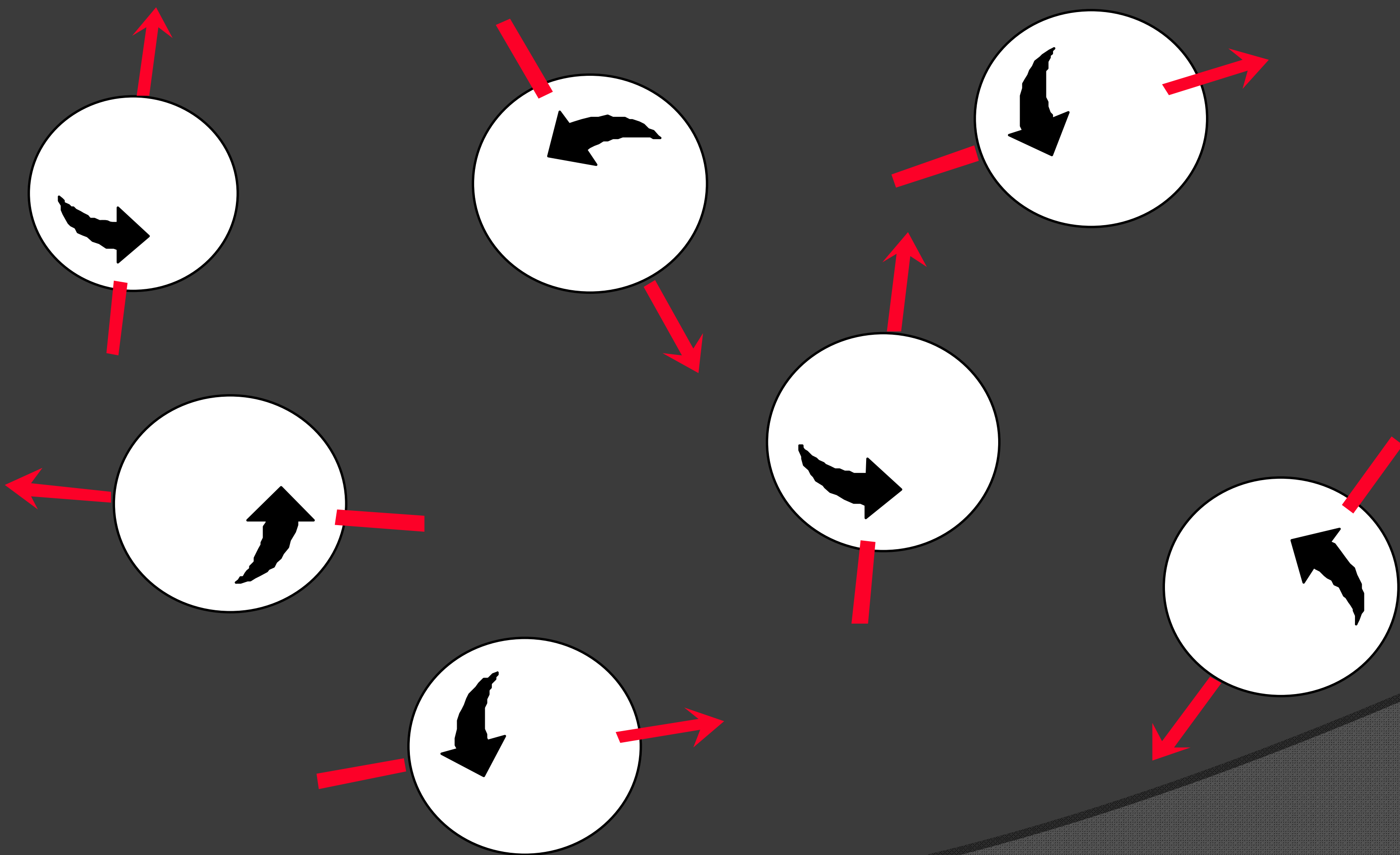
In an external magnetic field

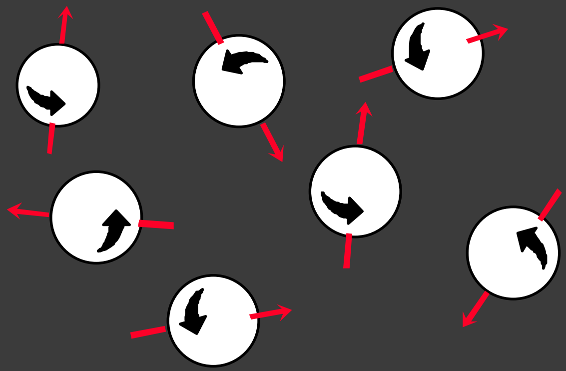



H
spin

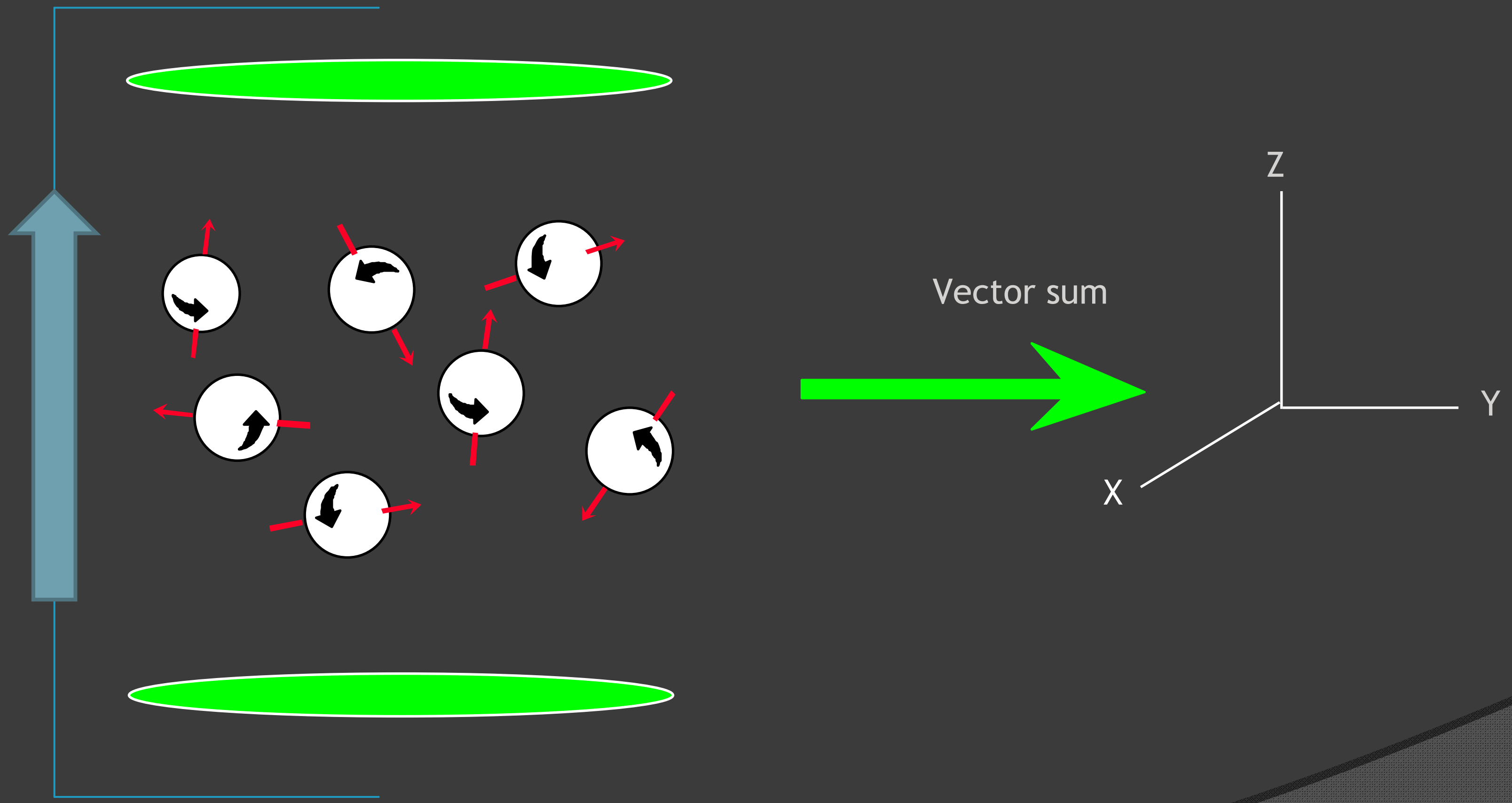

H
spin

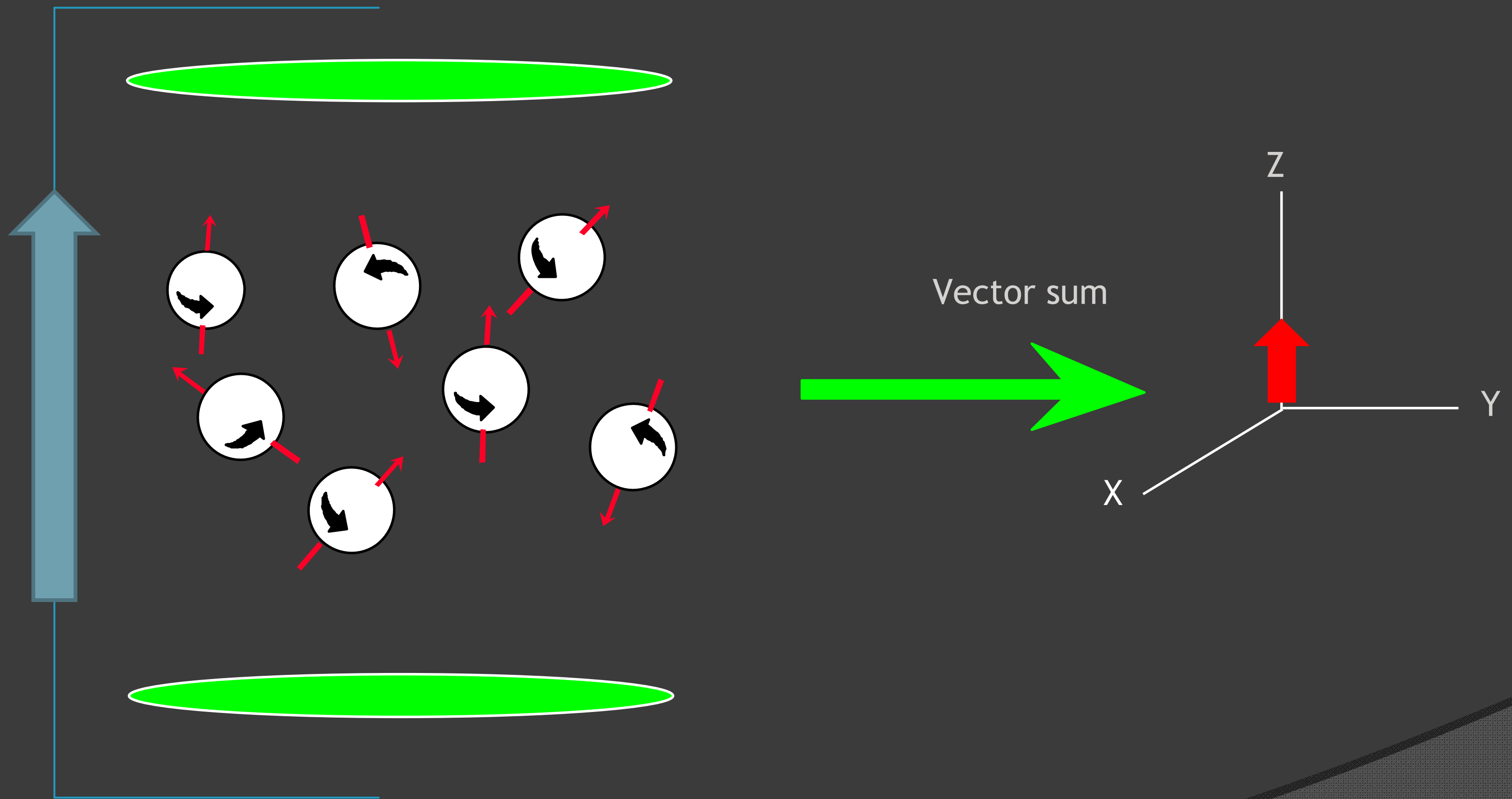
Many spins…



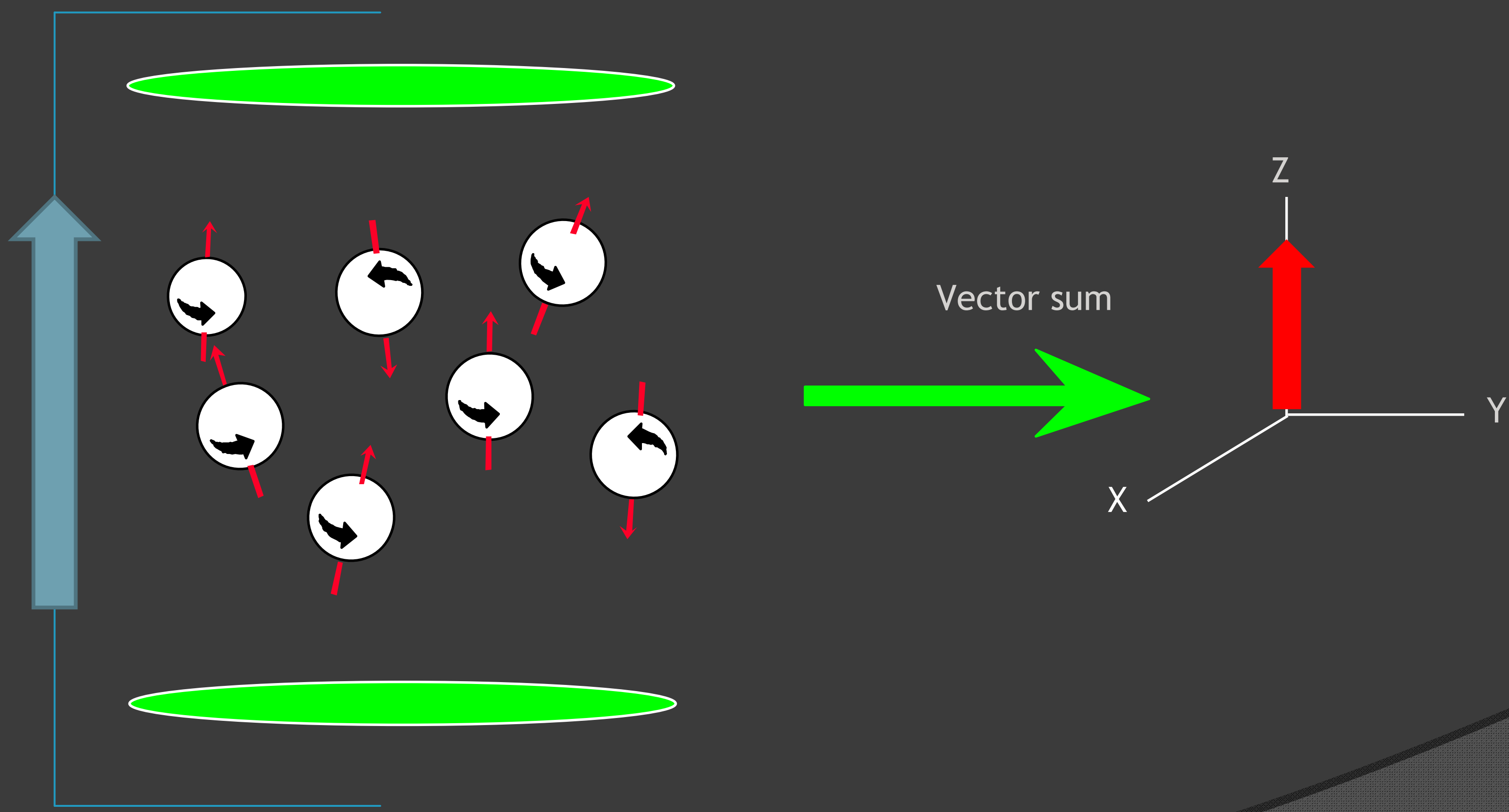


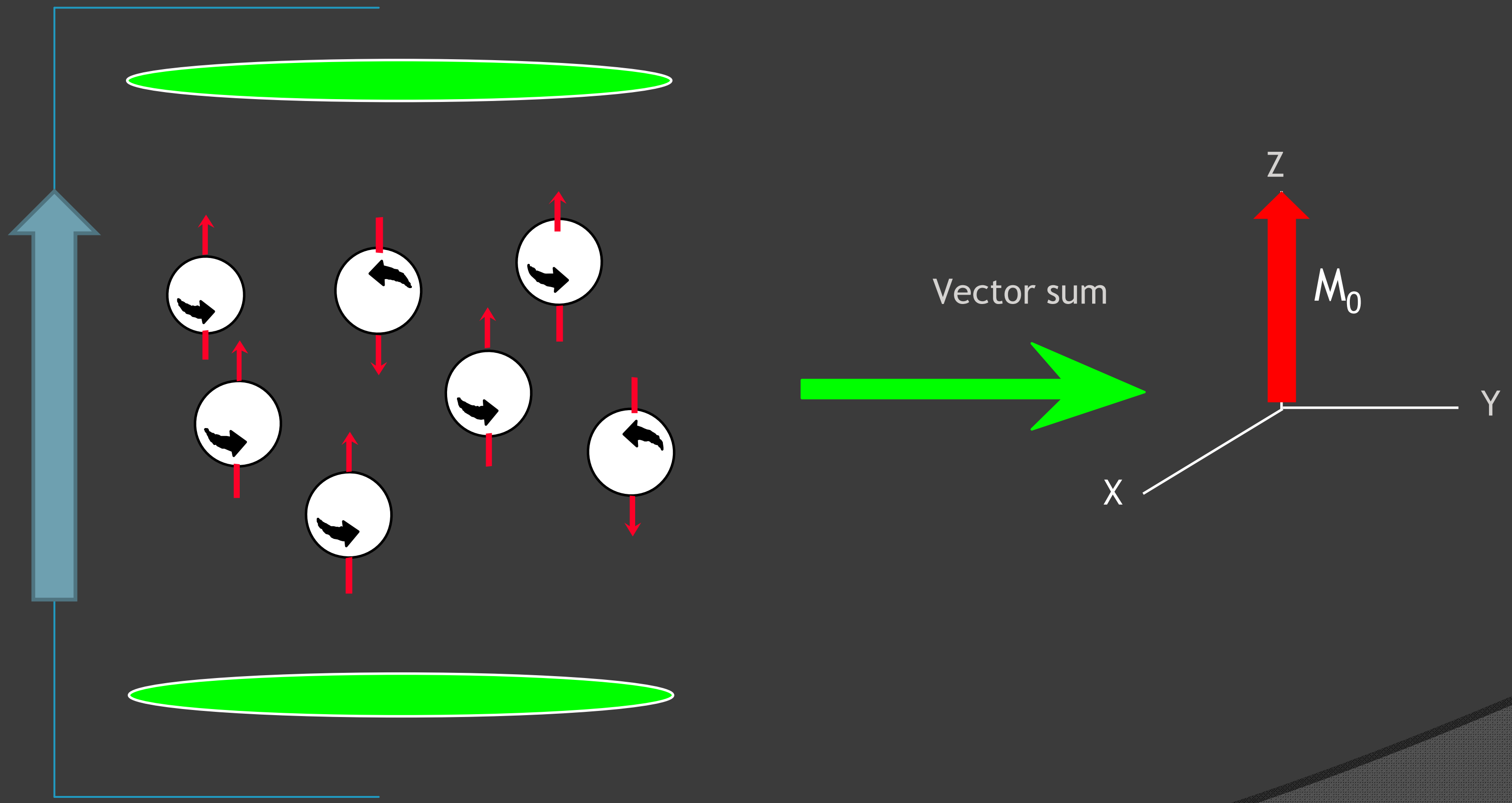
In a magnetic field…



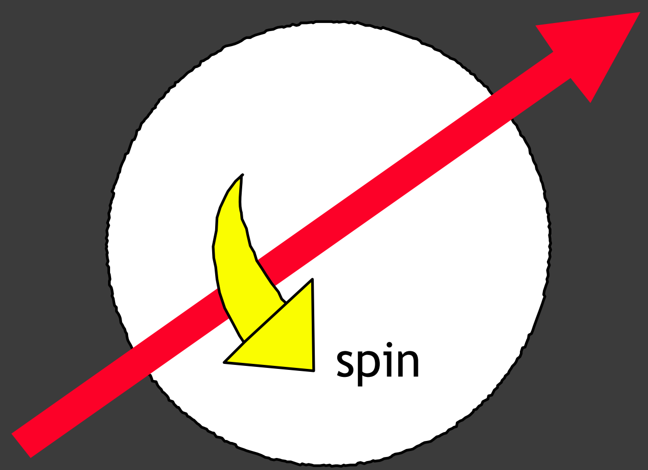


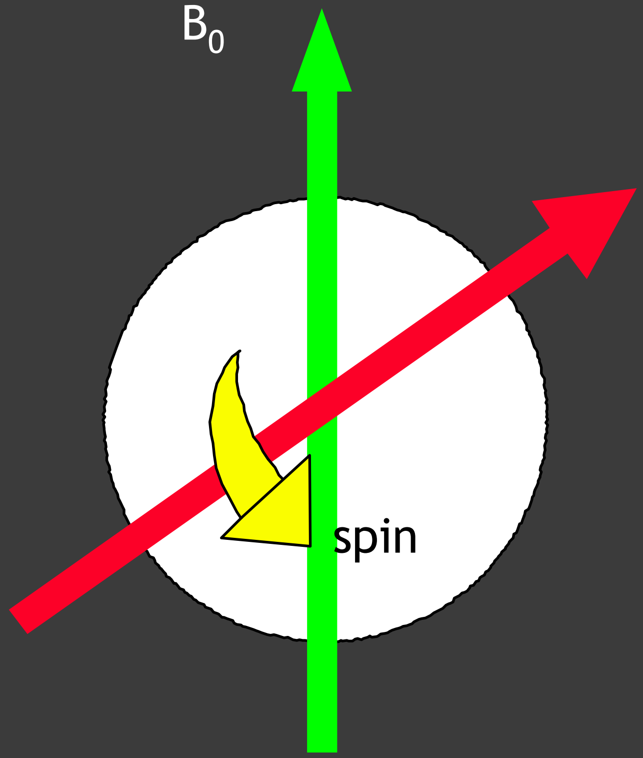
Vector sum
Z
Y
X


Vector sum
Z
Y
X


Vector sum
Z
M_0
Y
X

Is it really so simple?...





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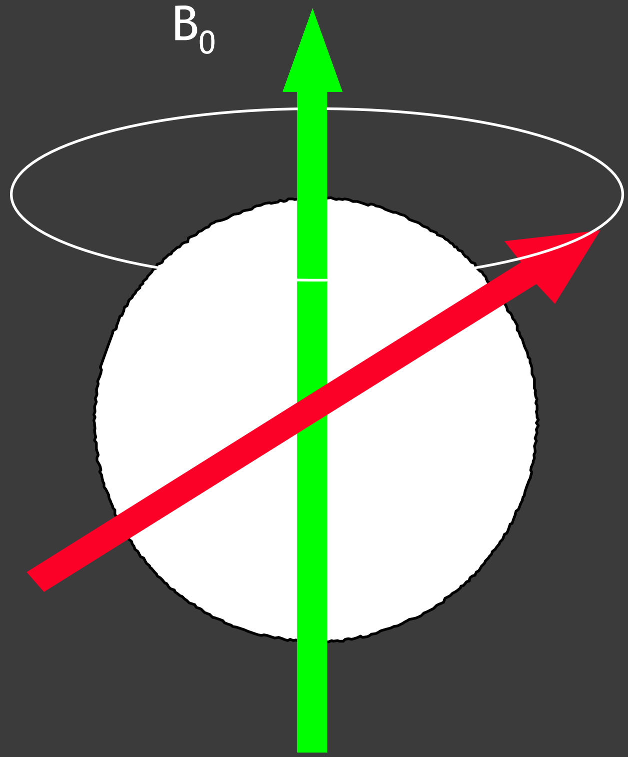
spin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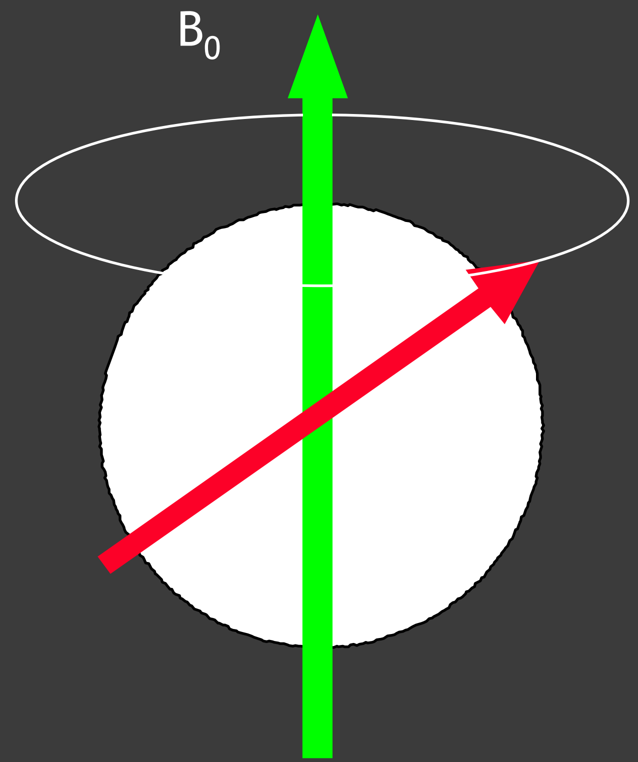
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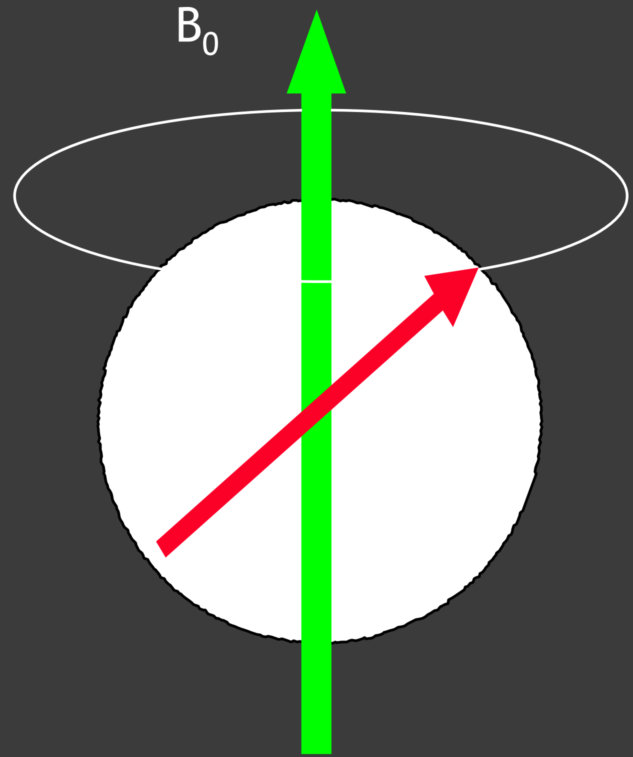
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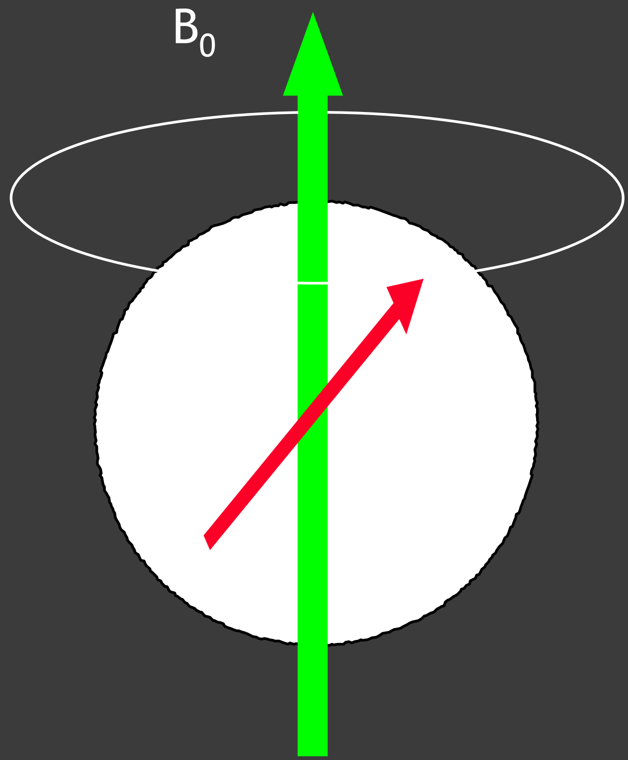

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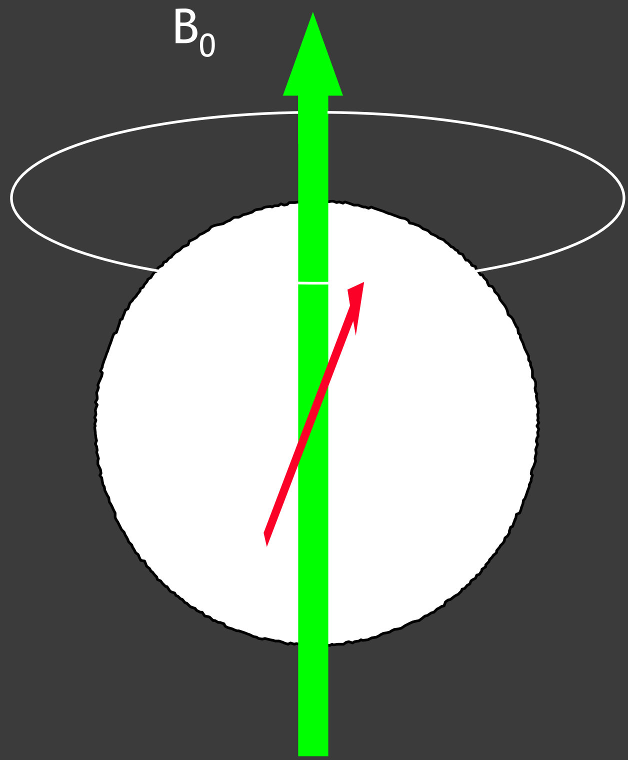
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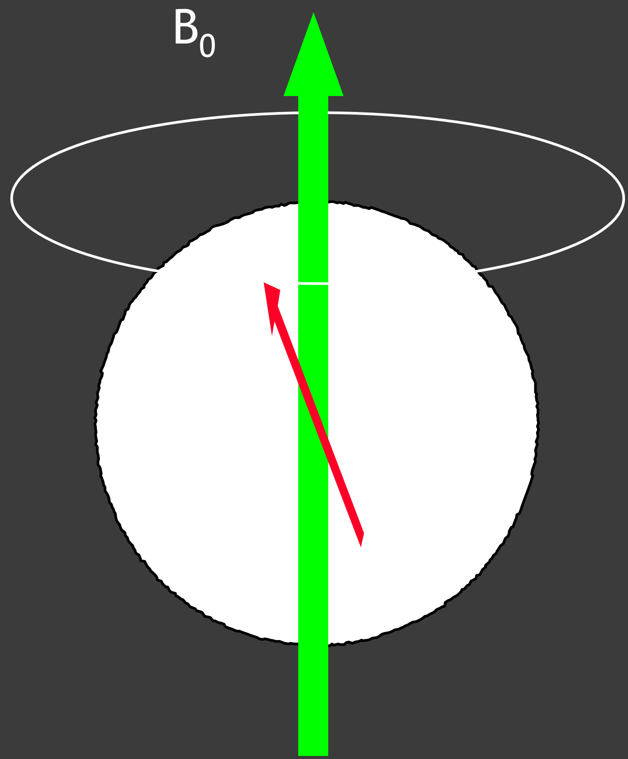
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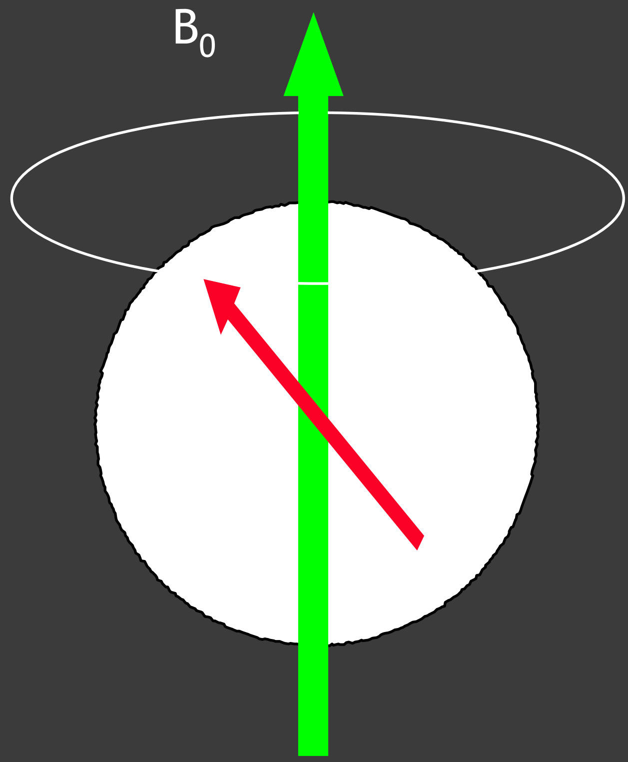
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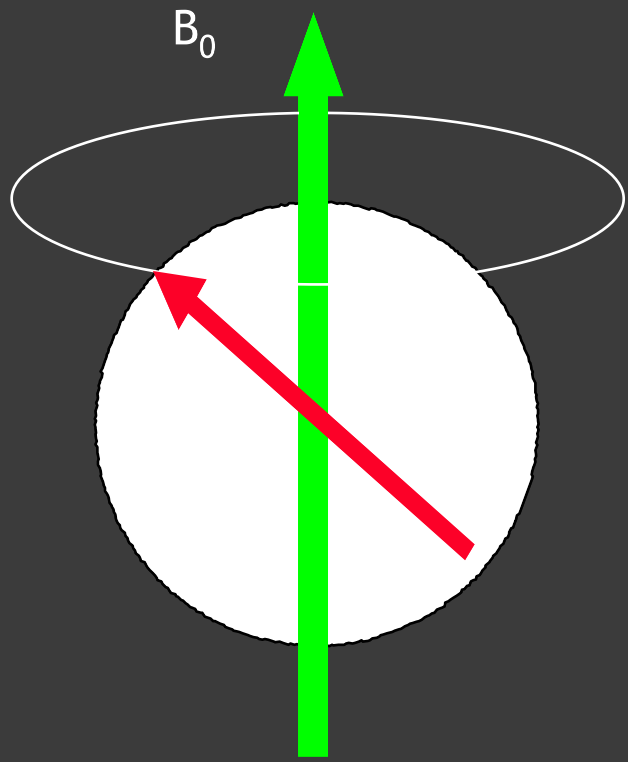
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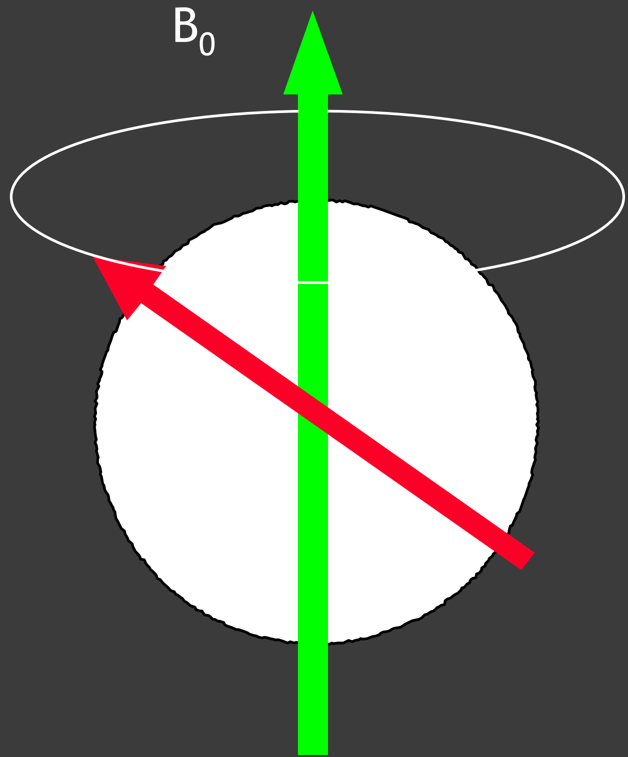
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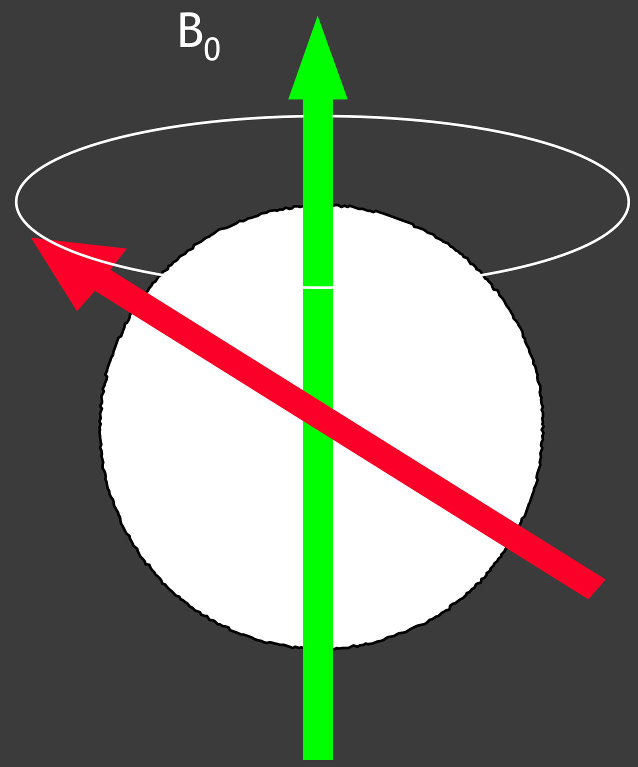
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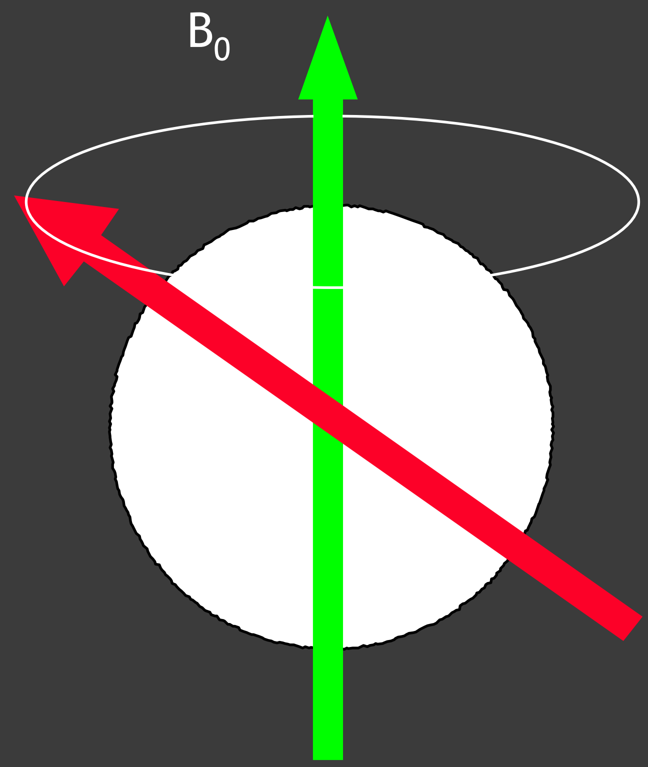
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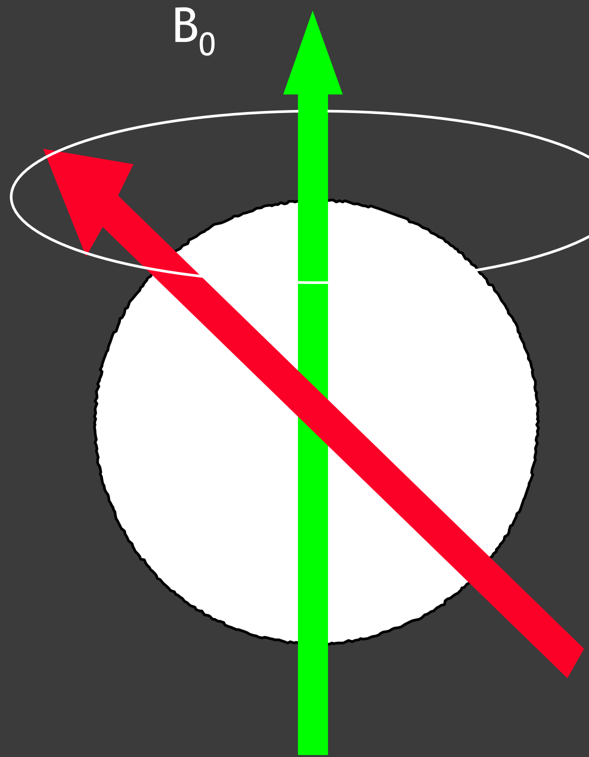
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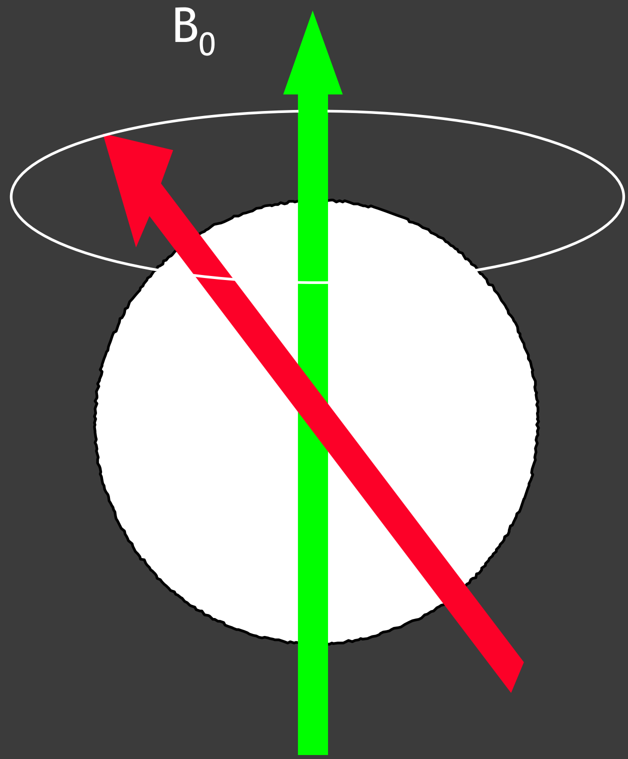
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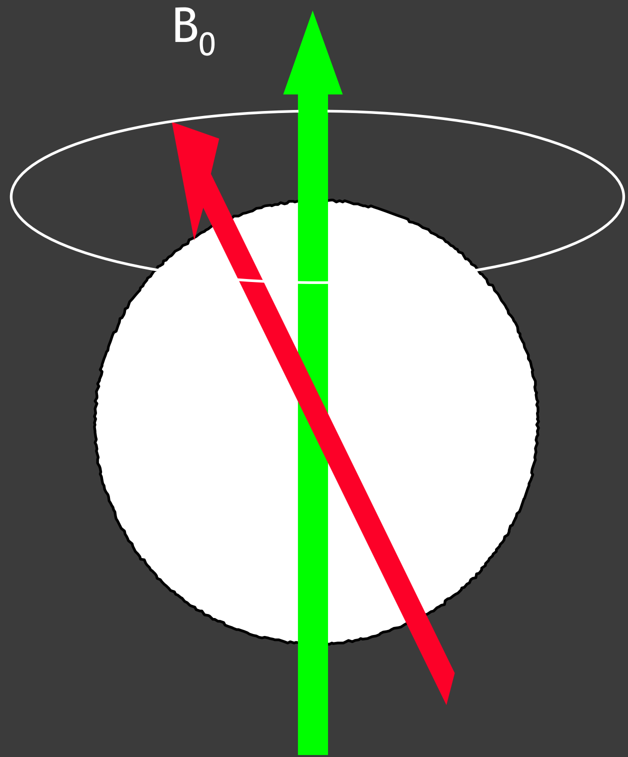
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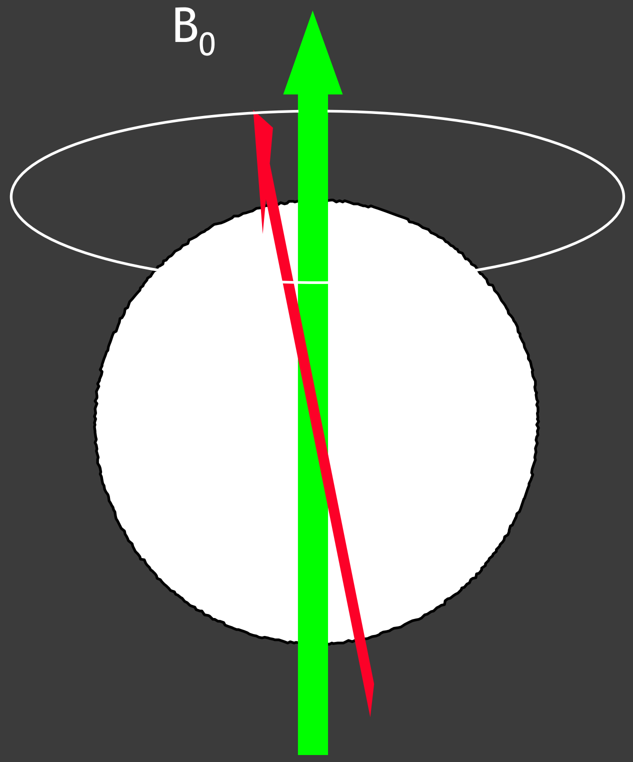
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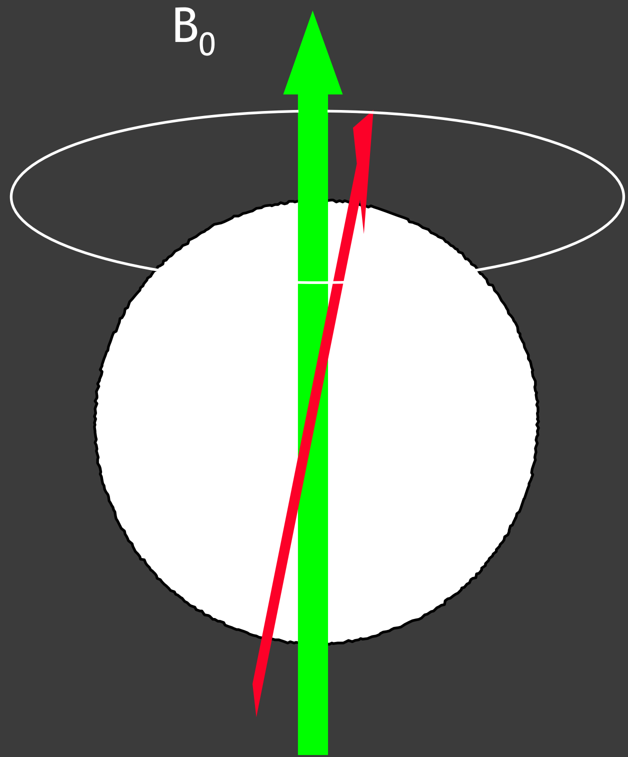
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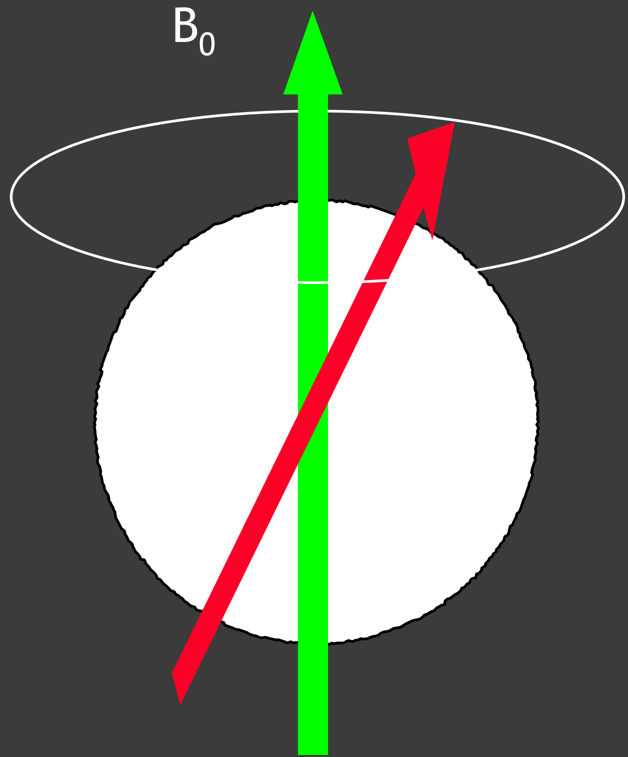
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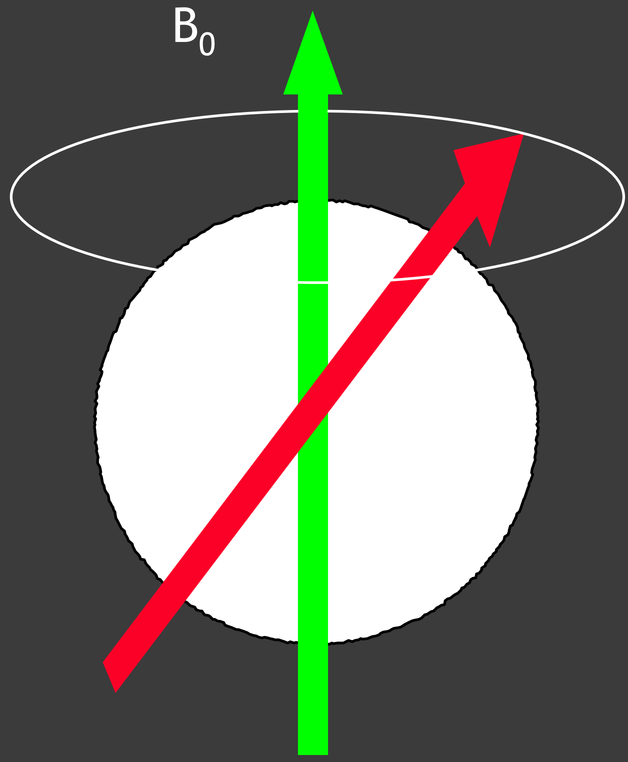
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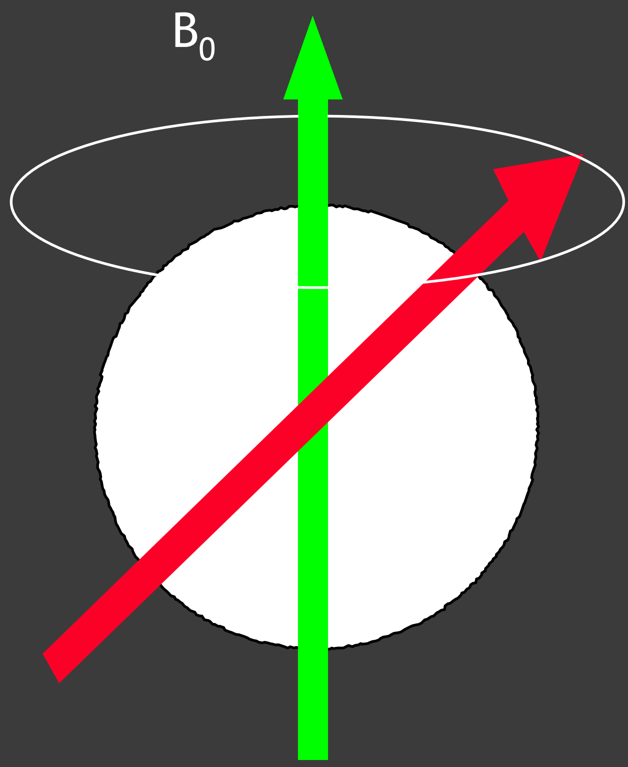


$$\omega = \gamma B_0$$

The Larmor frequency is a peculiar characterics of any NUCLEAR (not atomic) species

Nucleus	ω (0.5 T)	ω (1.0 T)	ω (1.5 T)
^{1}H	21.3 MHz	42.6 MHz	63.8 MHz
^{19}F	20.0 MHz	40.1 MHz	60.2 MHz
^{31}P	8.6 MHz	17.2 MHz	25.7 MHz
^{23}Na	5.7 MHz	11.3 MHz	17.1 MHz
^{13}C	5.4 MHz	10.7 MHz	16.1 MHz

Nuclear

- It uses a peculiarity of a single nuclear species
- The nucleus involved in MRI is the simplest one: ^1H

Selection of the Hydrogen nucleus due to abundance and transparency

Magnetic

- Each element has peculiar magnetic characteristics
- These properties can be observed in strong external magnetic fields

Interaction between static magnetic field, e.m. field (RF) and spins

$$\omega_L = \gamma B_0$$

Frequency of the precession of the spin and/or of the external e.m. field

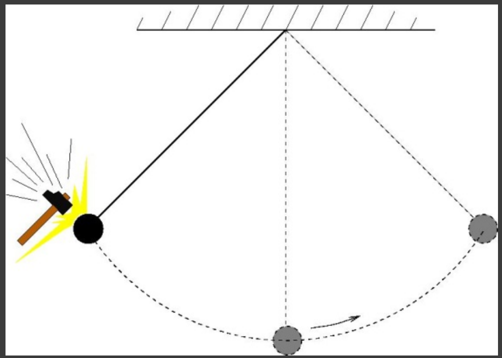
Magneto-gyric factor and static magnetic field

Resonance

- Optimal ("resonant") energy transfer

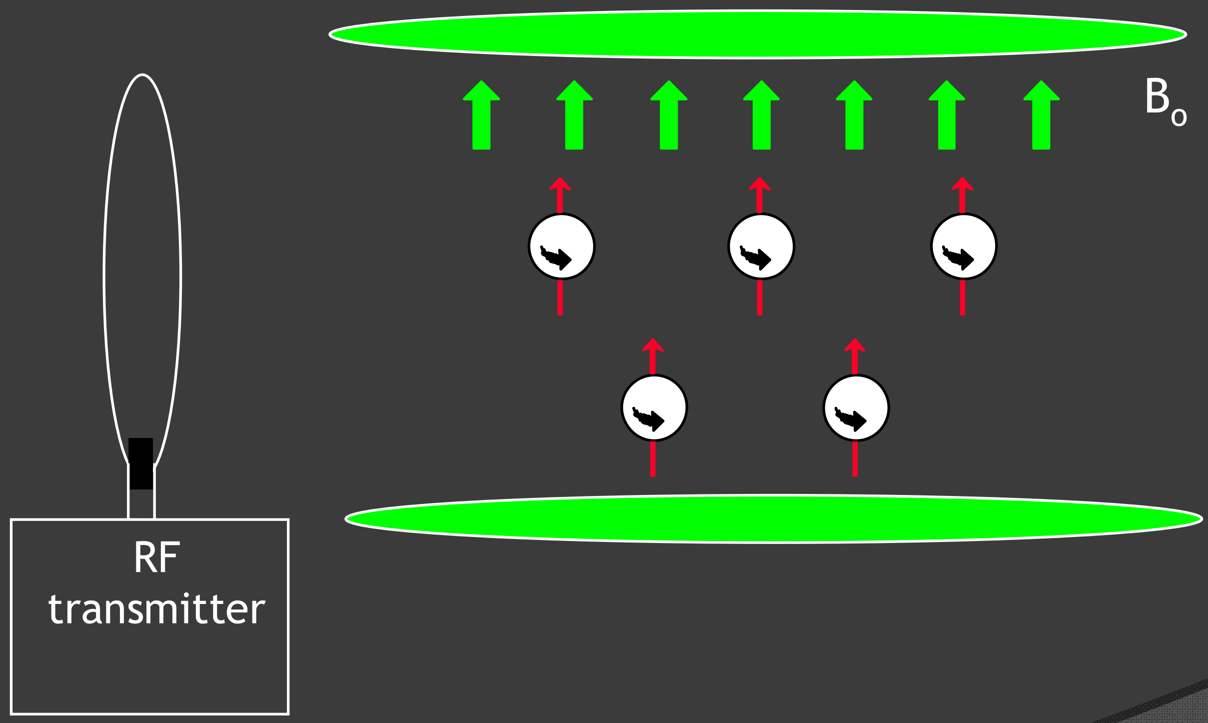
- Matching between typical frequency scales (pendulum, Larmor…)

- Optimal energy transfer between "engine" and "wheels"

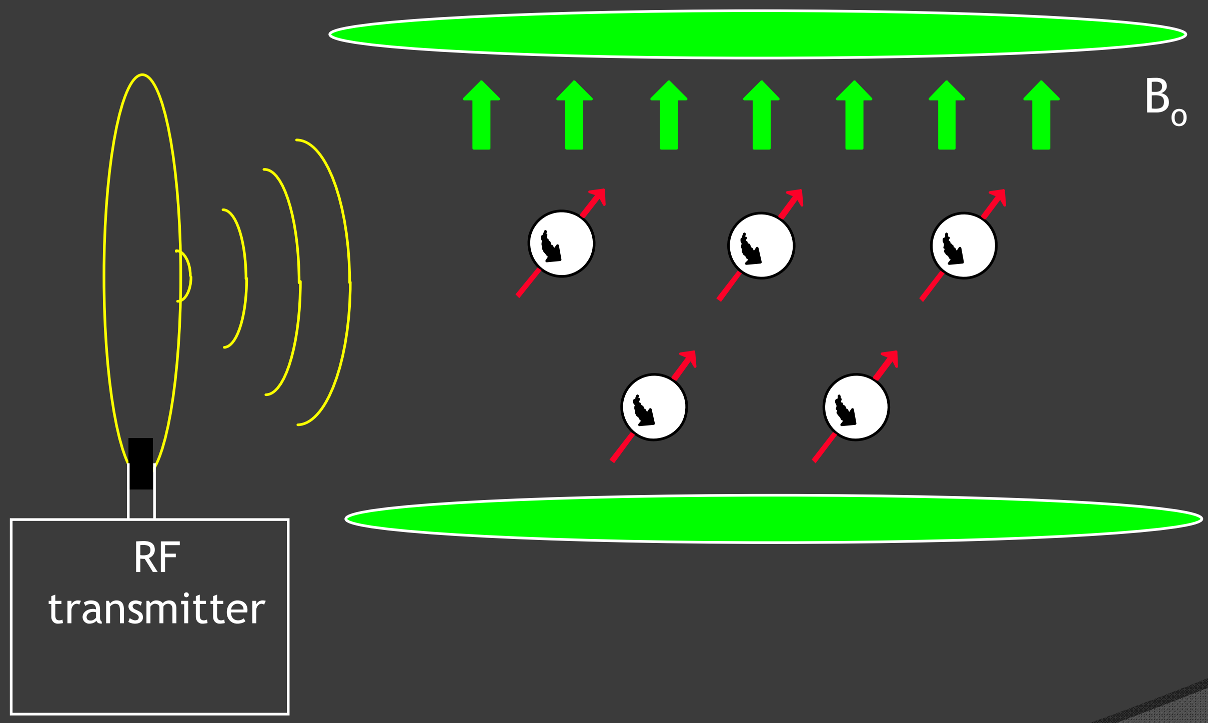


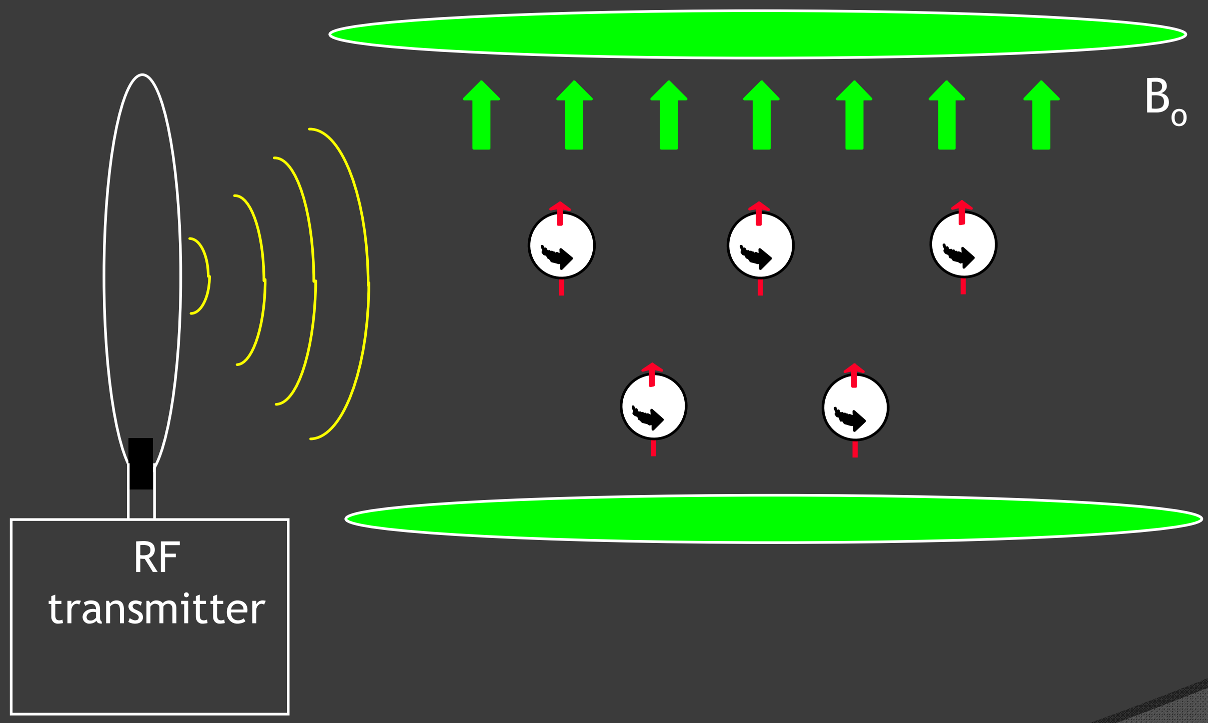
Resonance frequency:
$\omega_0 = 2\pi / T_{pendulum}$

Signal production: excitation

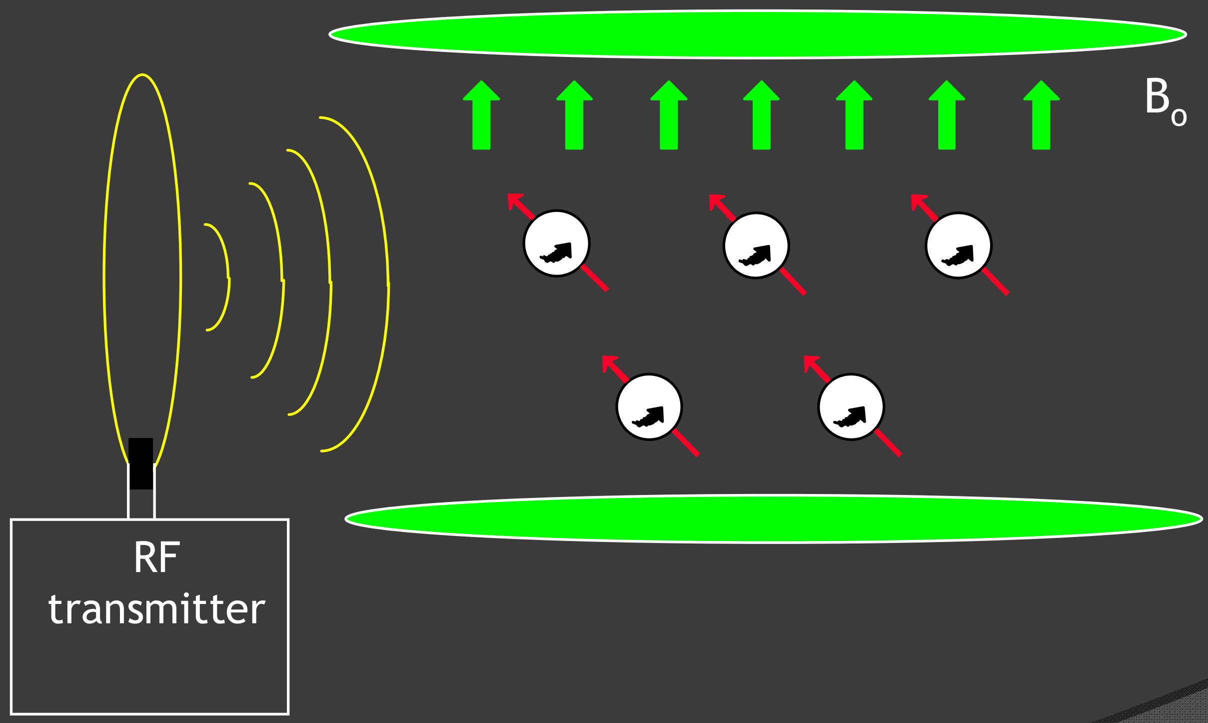


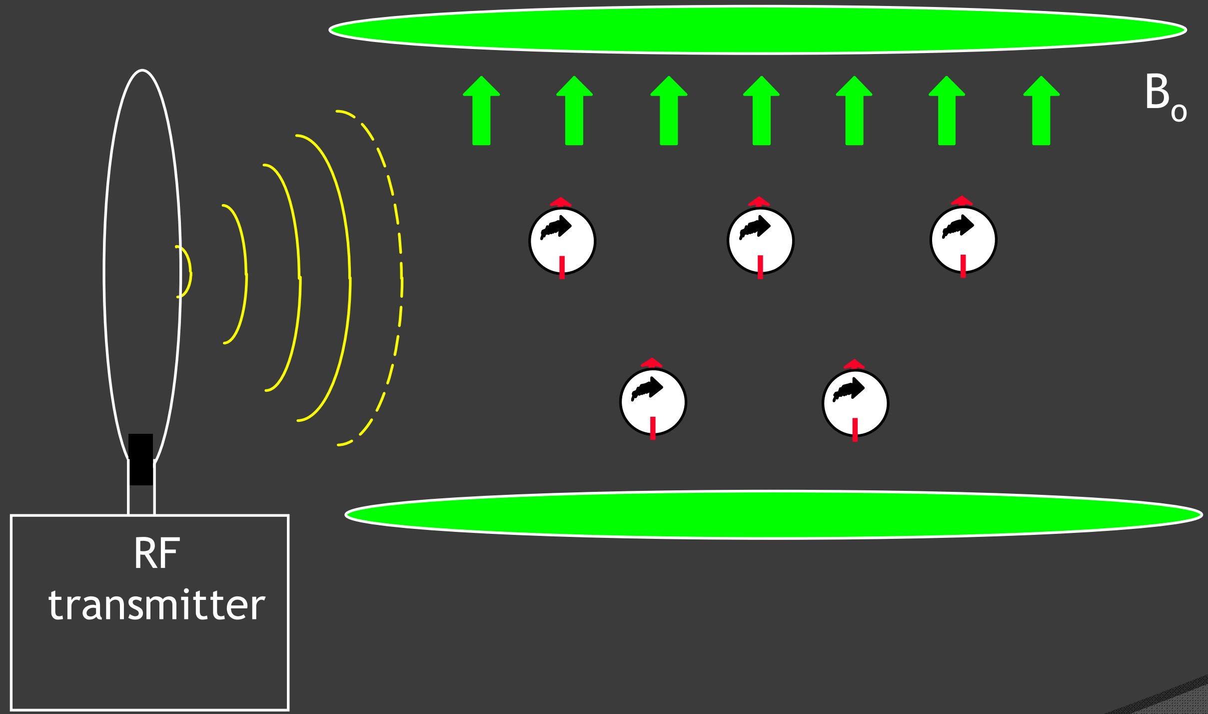
Transmission coil


B_o
RF transmitter



B_o
RF transmitter


B$_o$
RF transmitter



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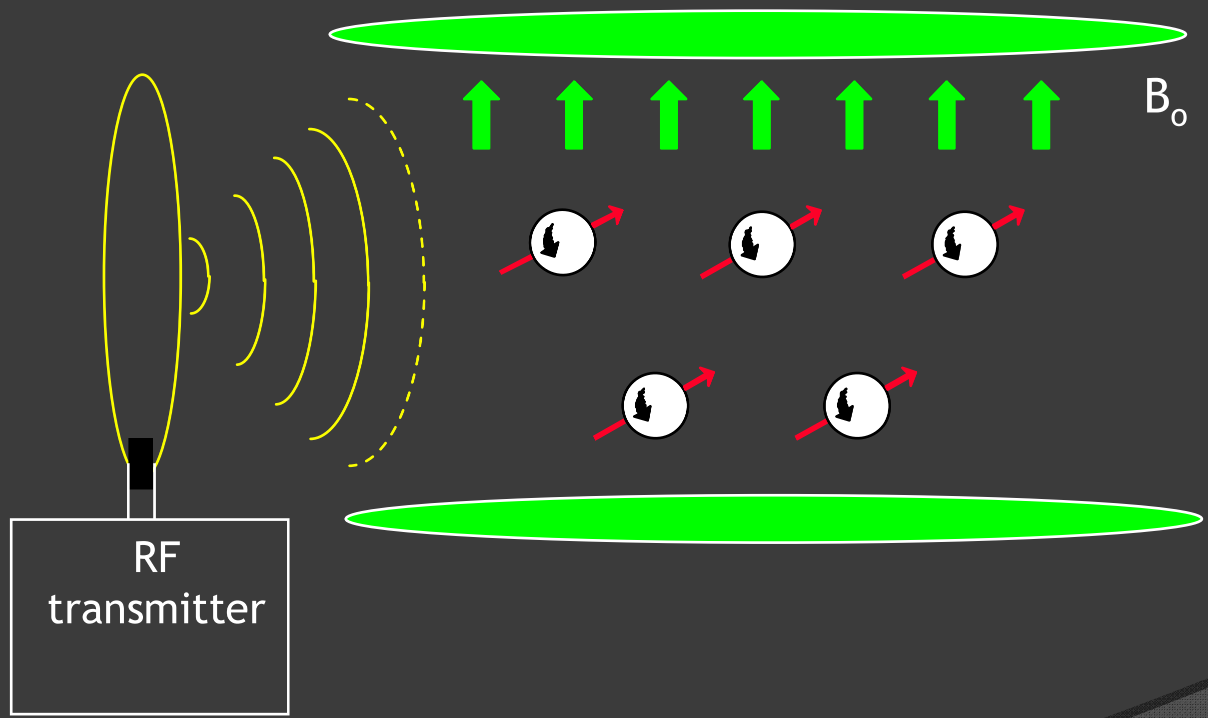
RF transmitter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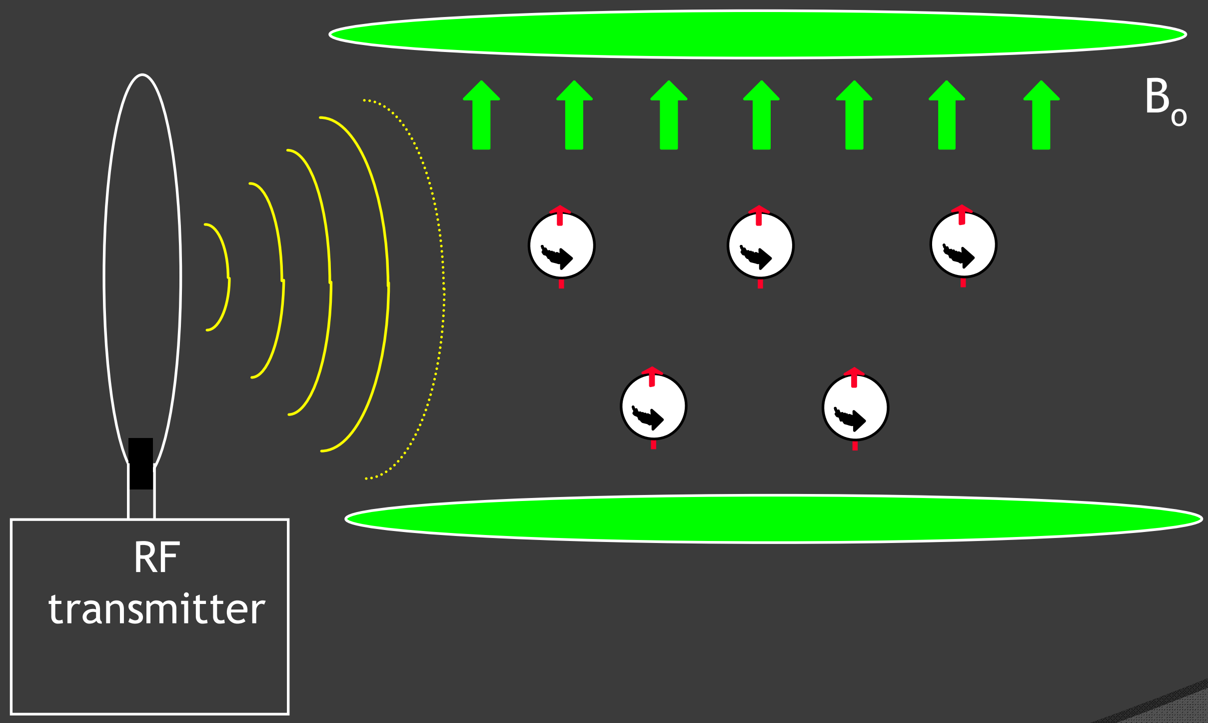
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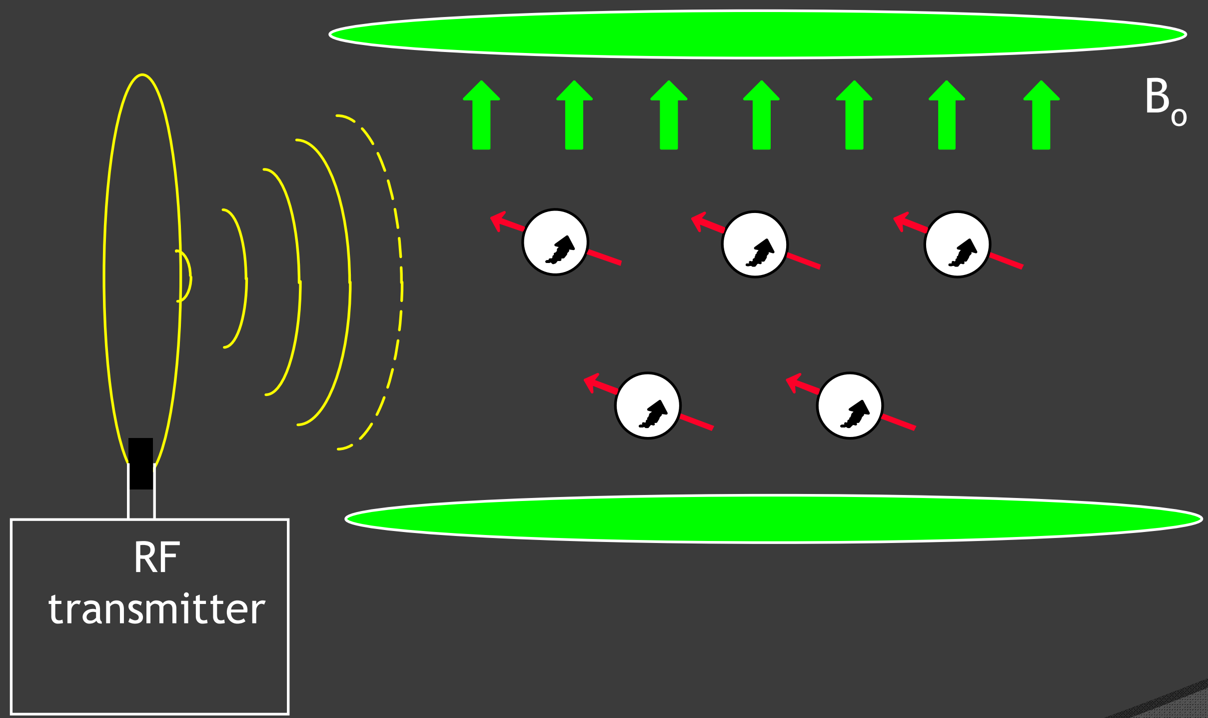
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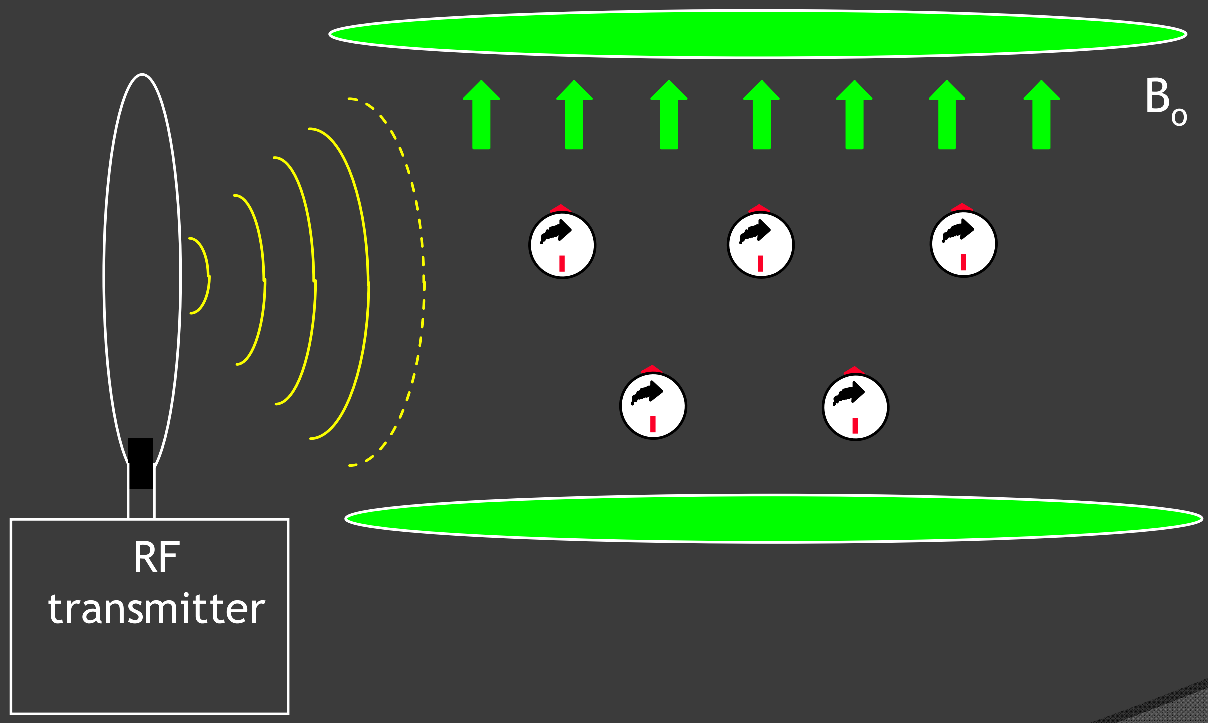
RF transmitter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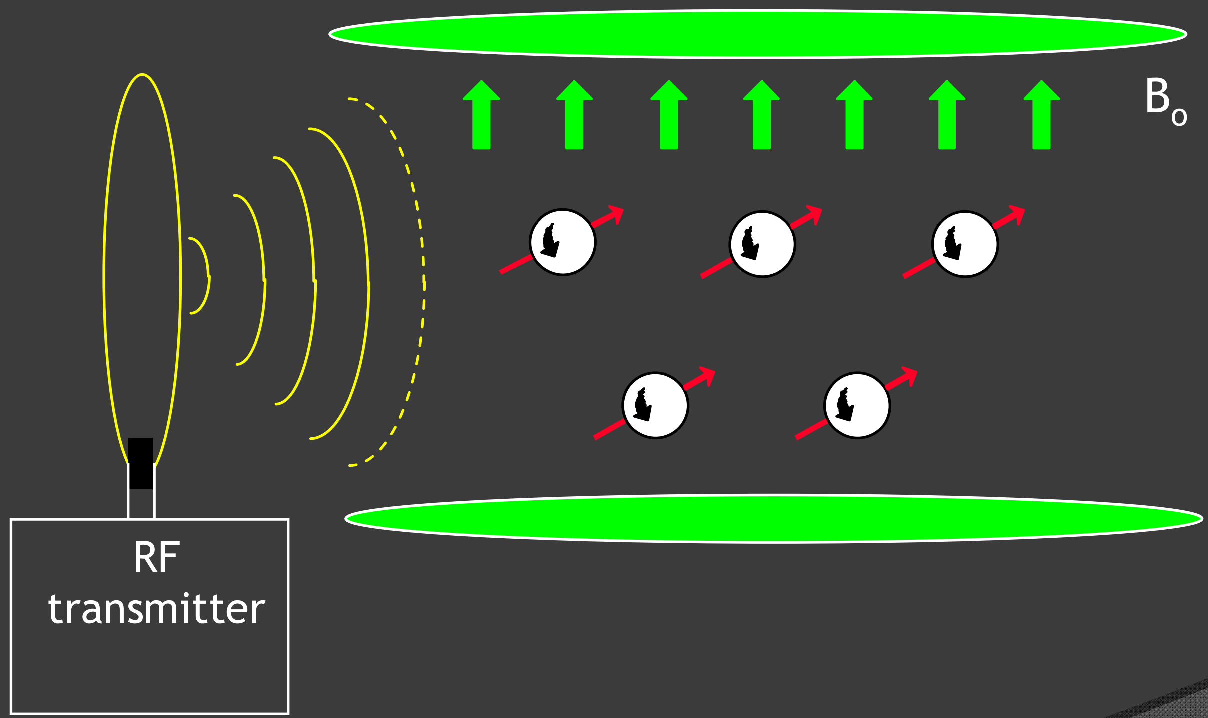
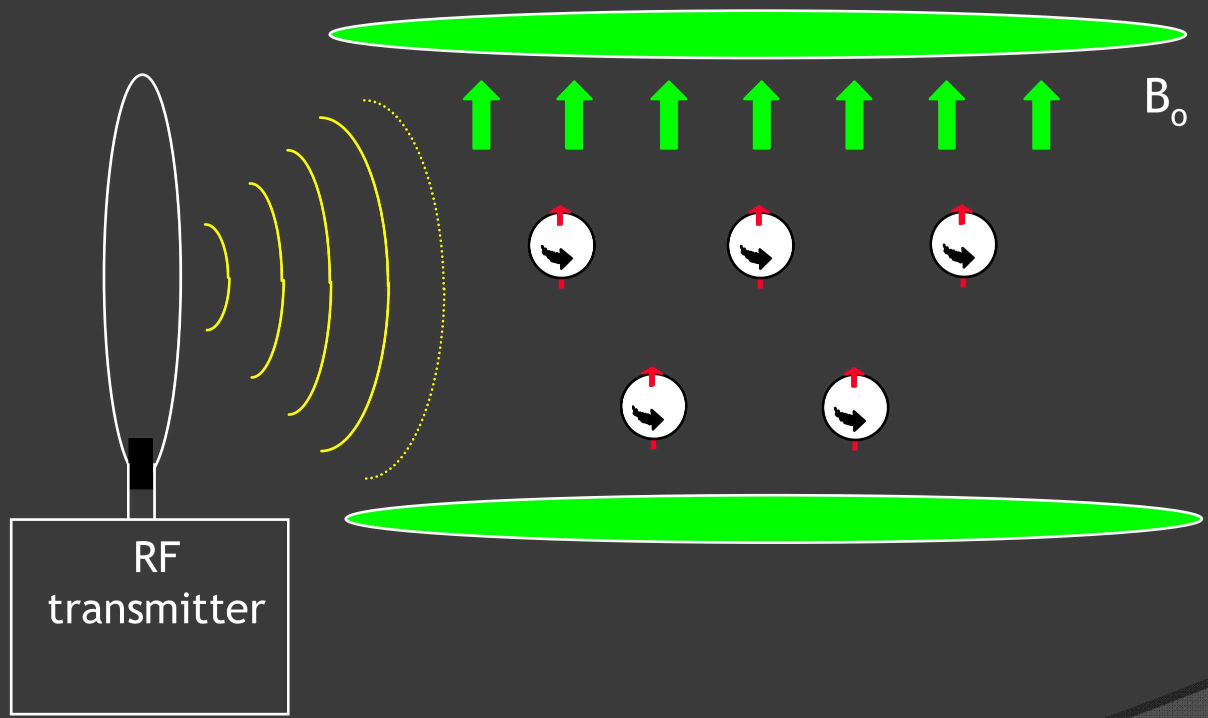
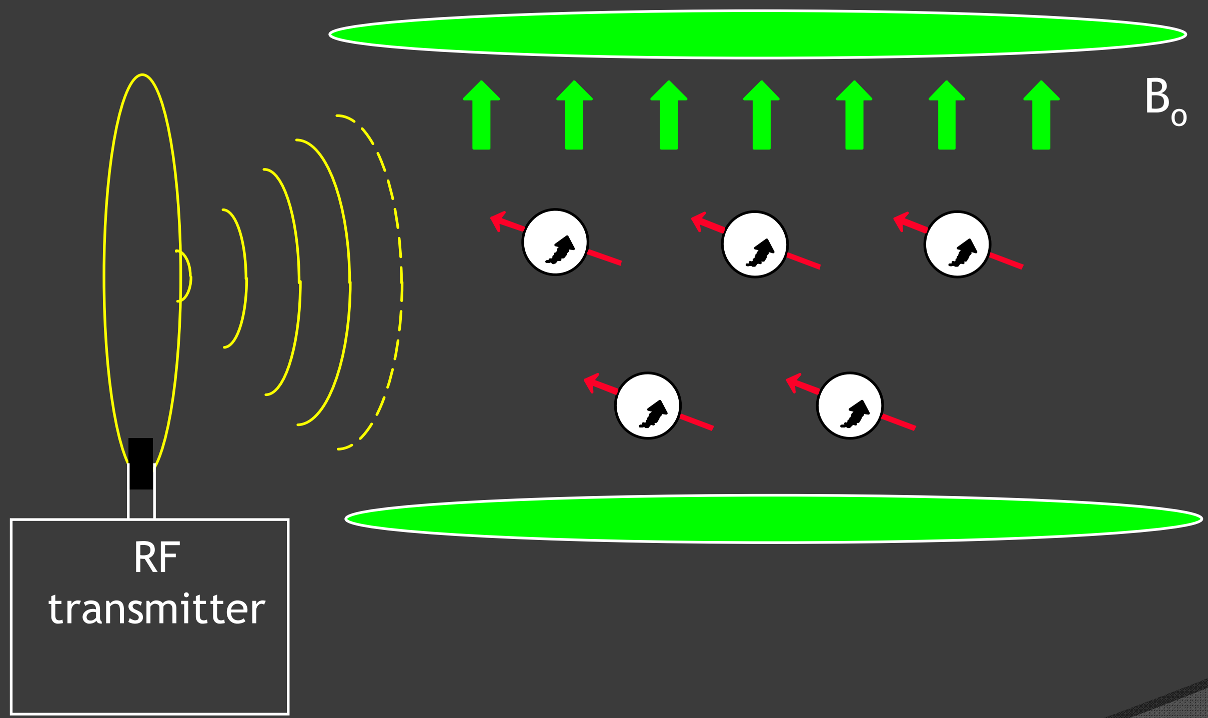


B_o
RF transmitter


B$_o$
RF
transmitter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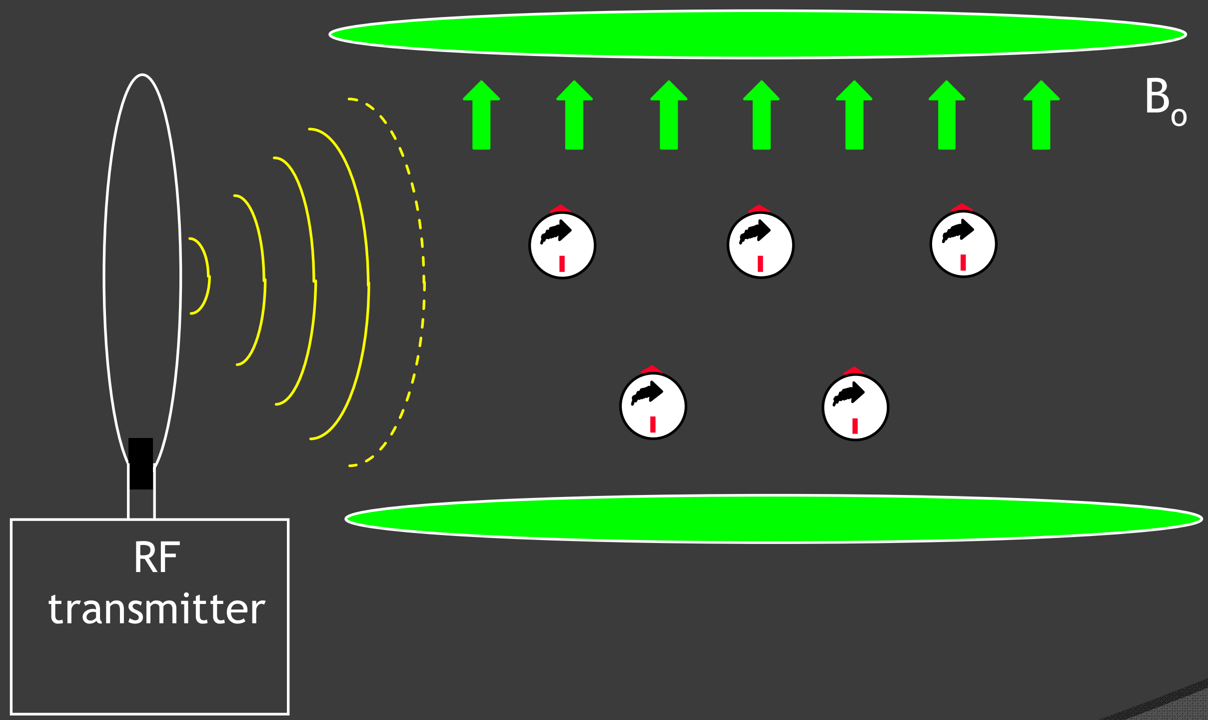
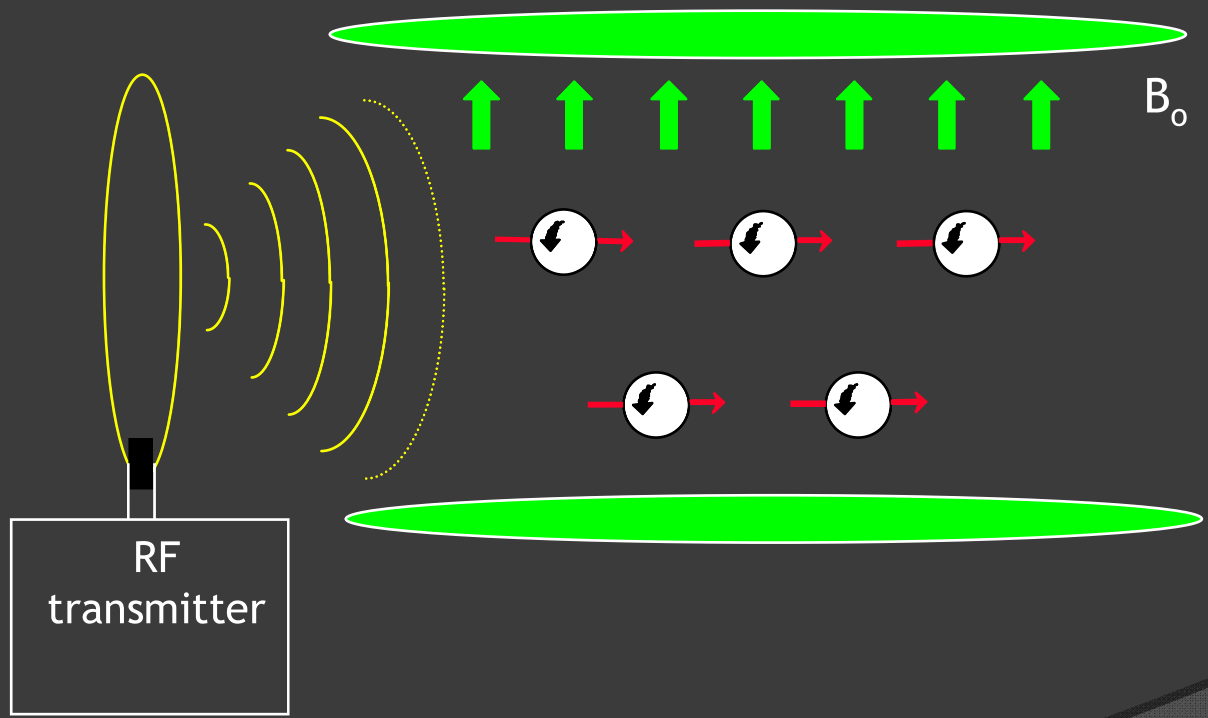
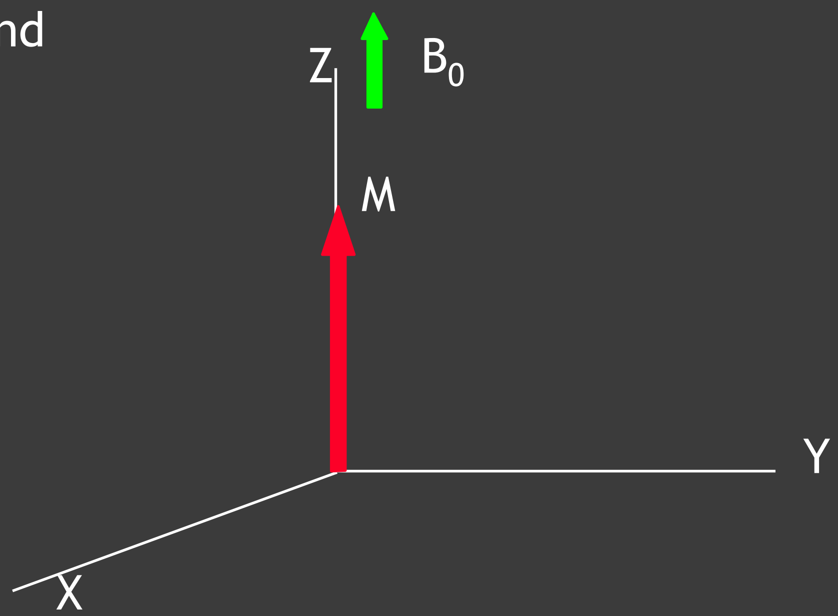
RF transmitter


B$_o$
RF transmitter

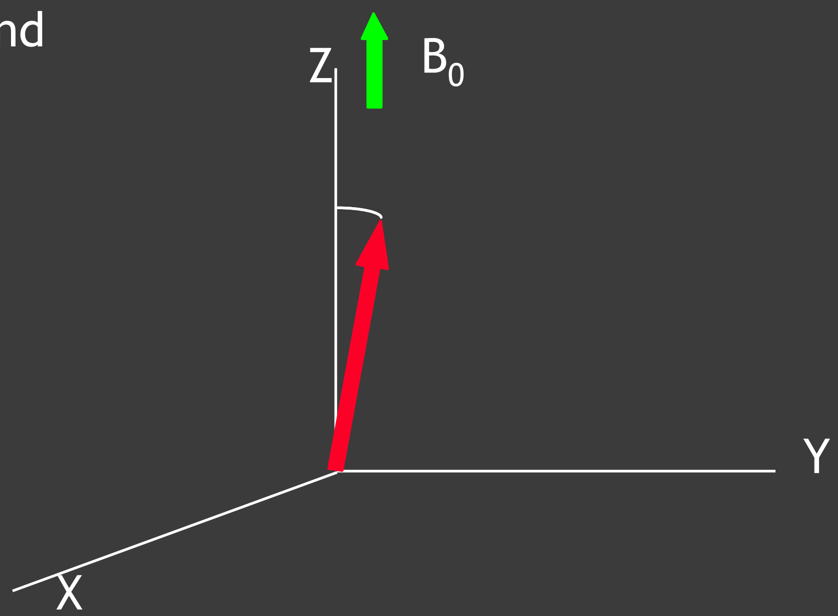

B_o
RF transmitter

Magnetization: excitation “path”

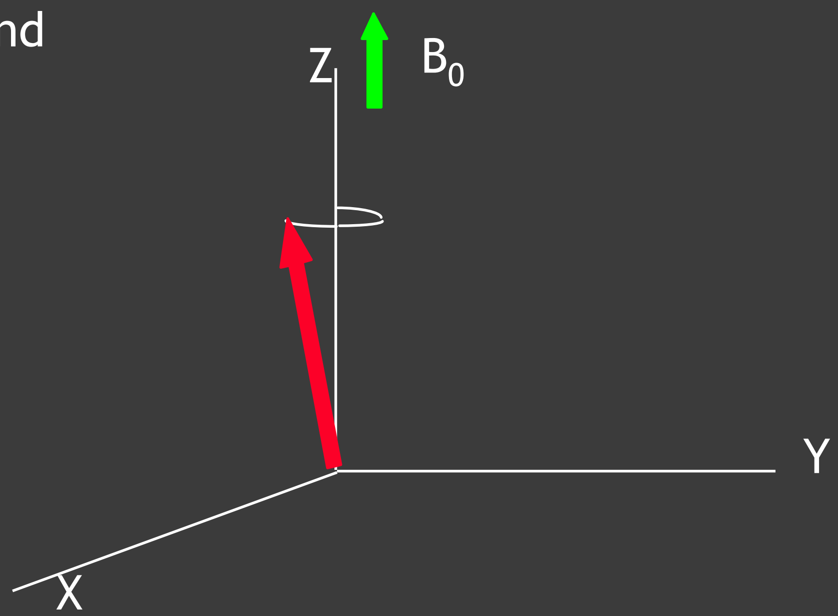
net magnetisation and
90° pulse



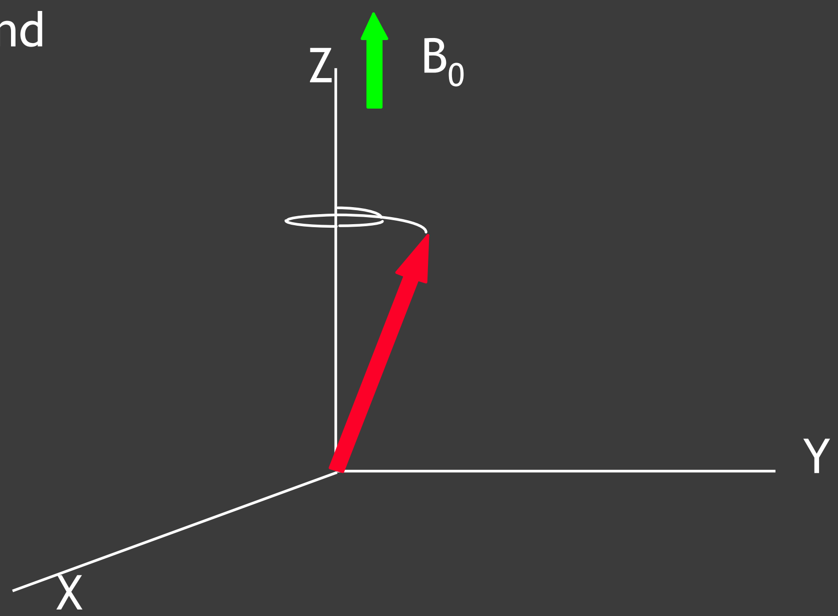
net magnetisation and
90° pulse



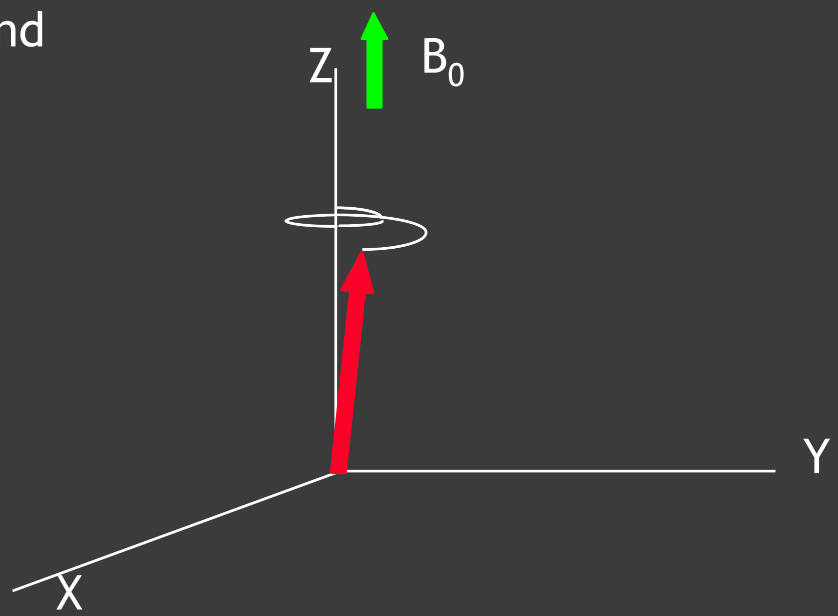
net magnetisation and
90° pulse



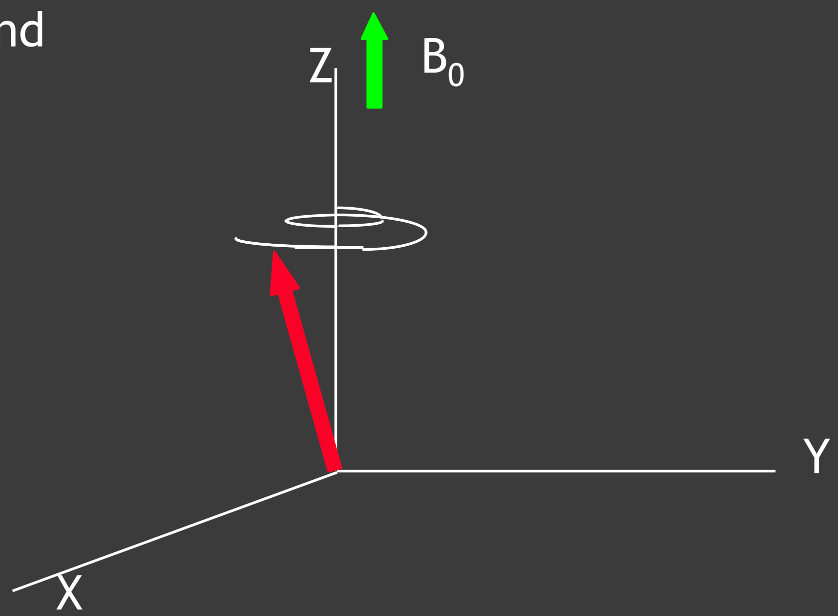
net magnetisation and
90° pulse



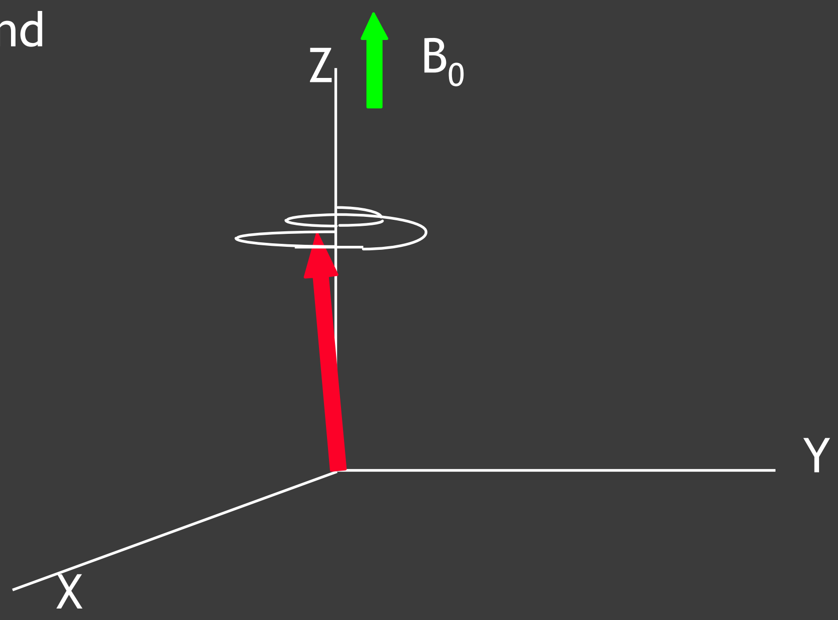
net magnetisation and
90° pulse



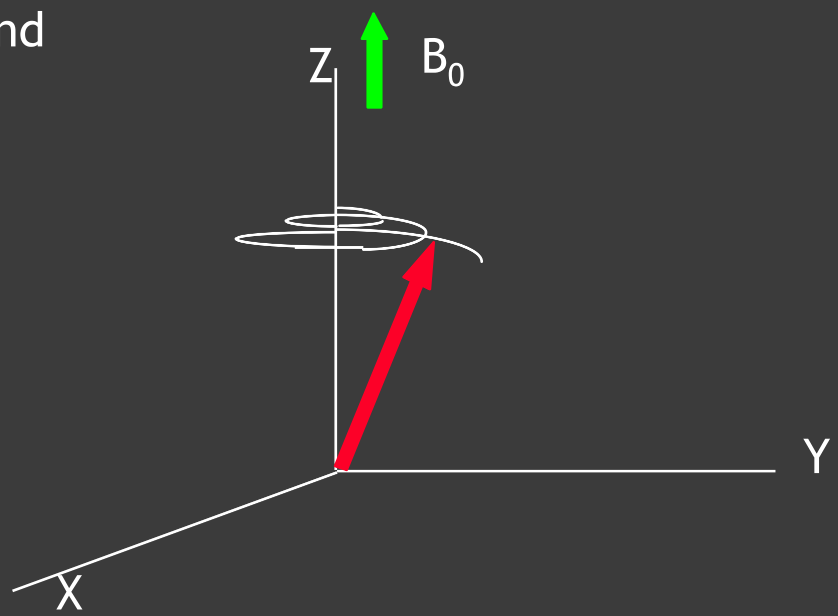
net magnetisation and
90° pulse



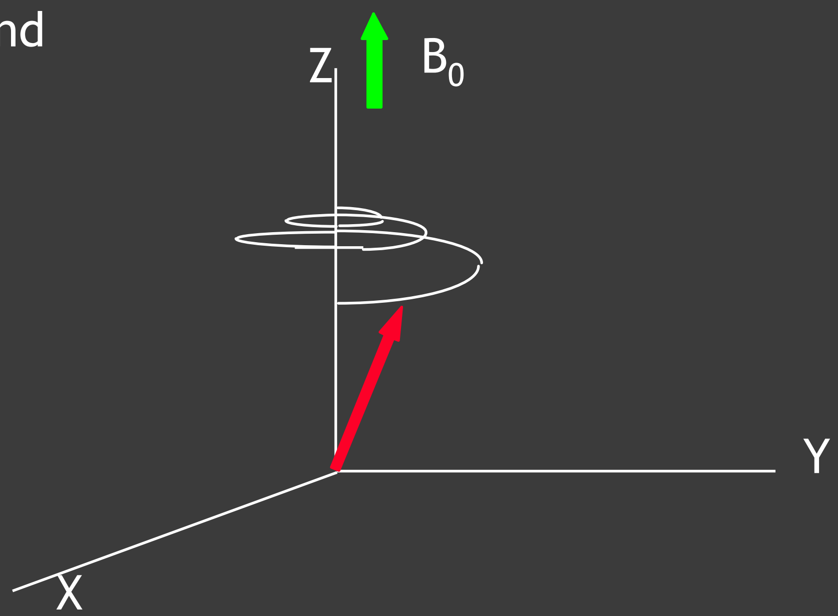
net magnetisation and
90° pulse



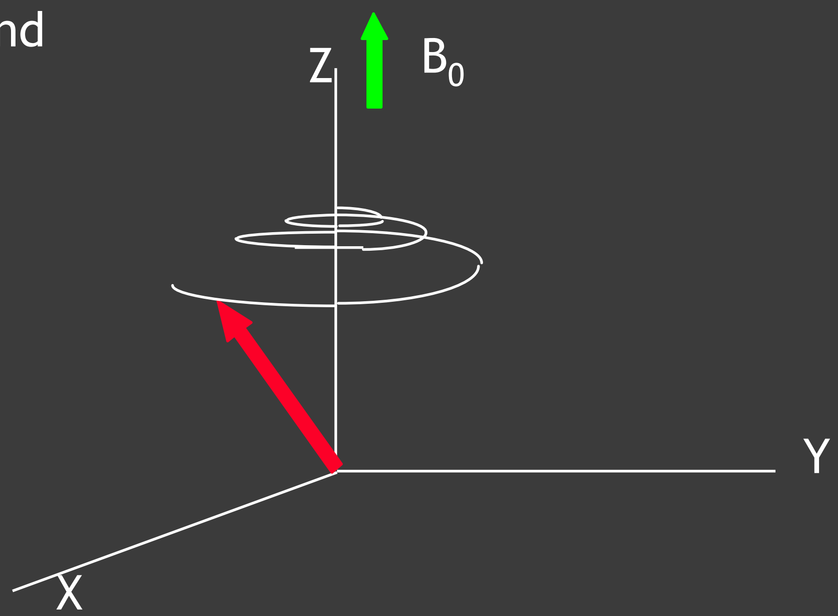
net magnetisation and
90° pulse



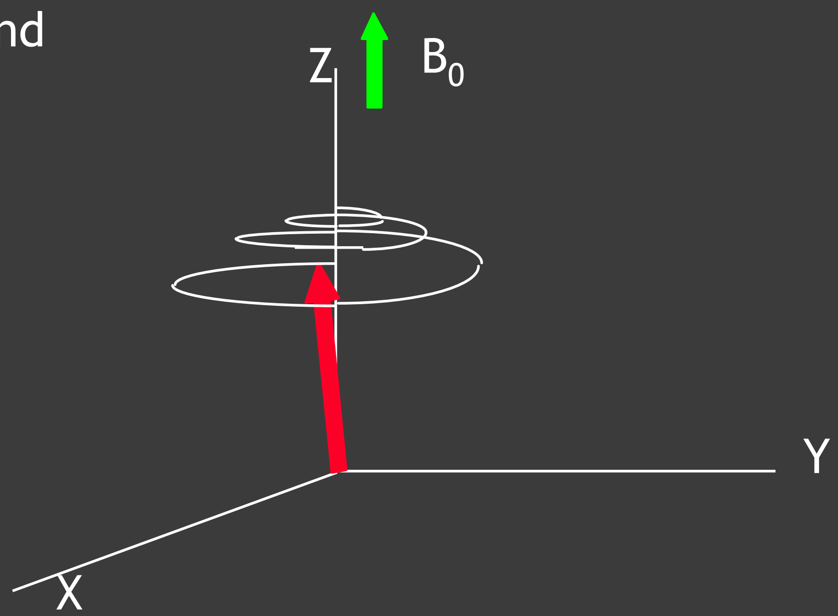
net magnetisation and
90° pulse



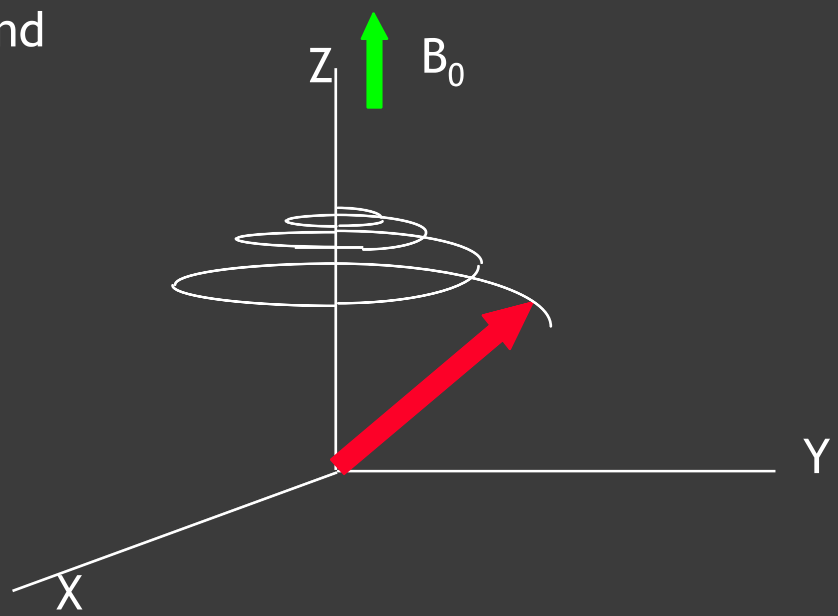
net magnetisation and
90° pulse



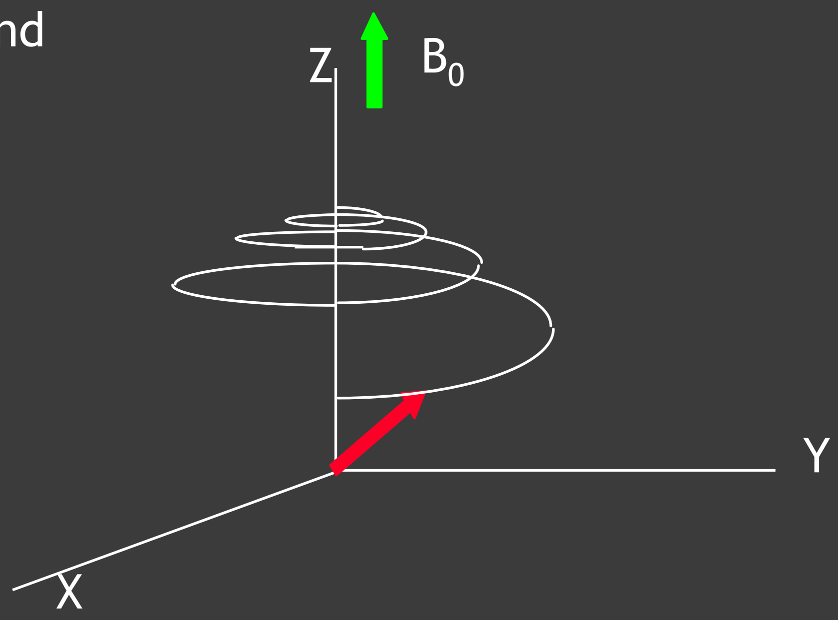
net magnetisation and
90° pulse



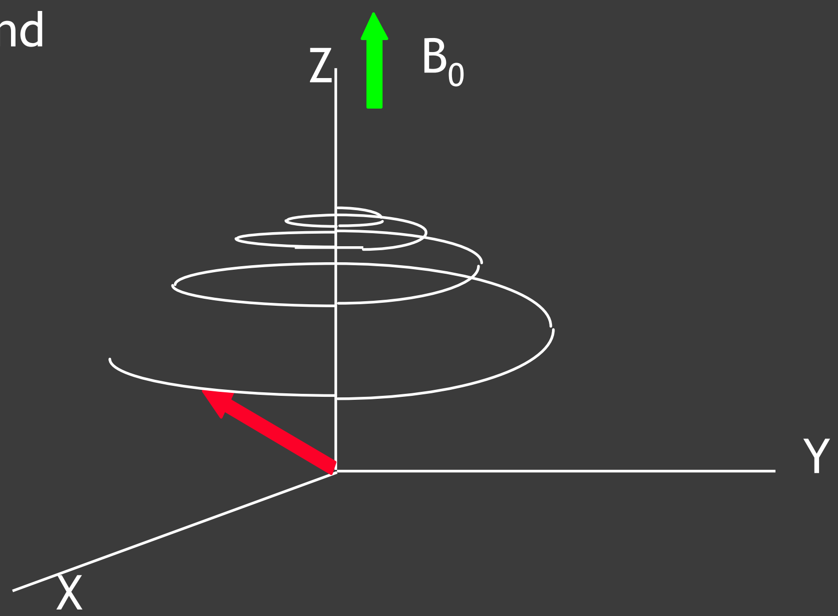
net magnetisation and
90° pulse



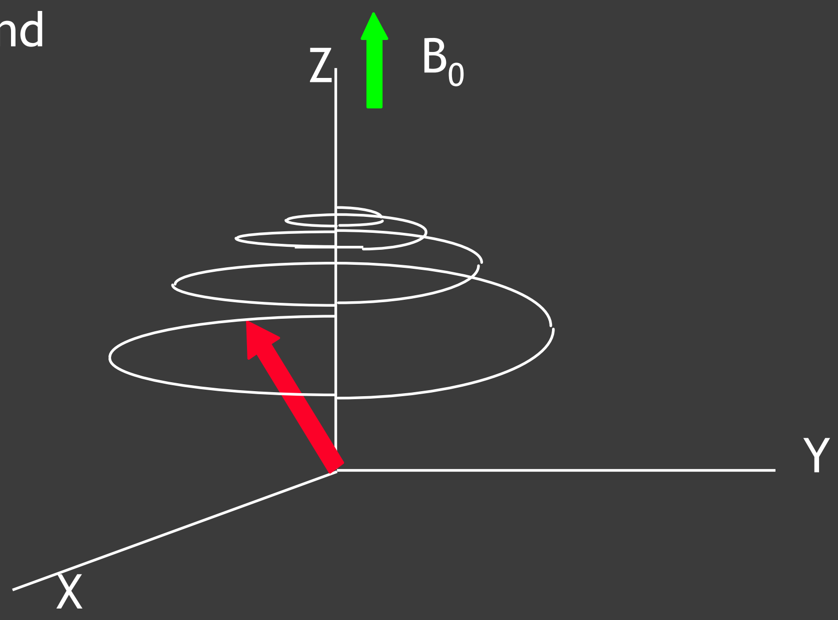
net magnetisation and
90° pulse



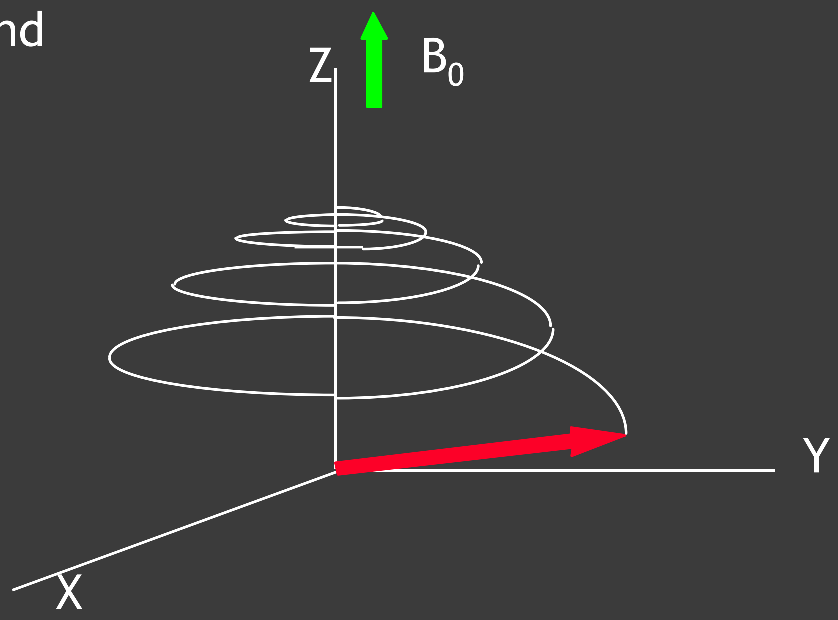
net magnetisation and
90° pulse



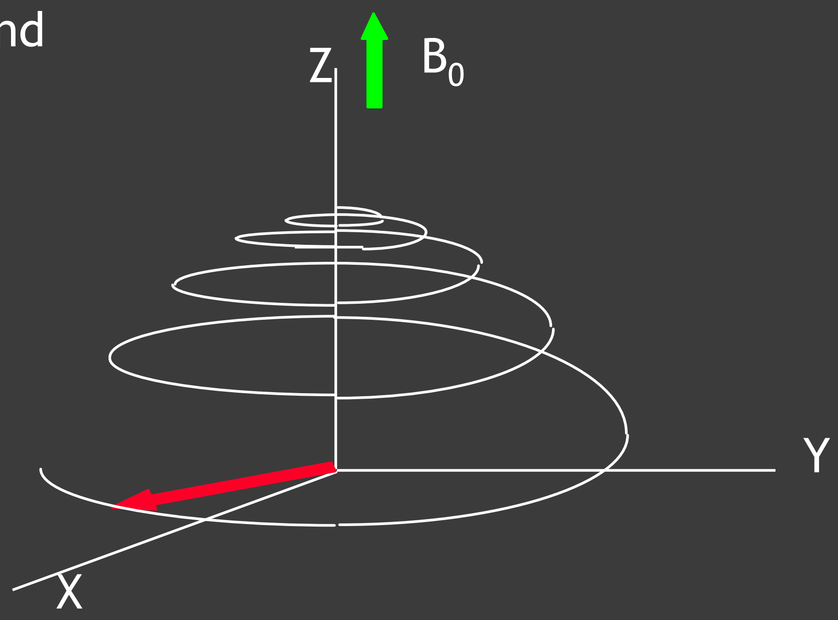
net magnetisation and
90° pulse



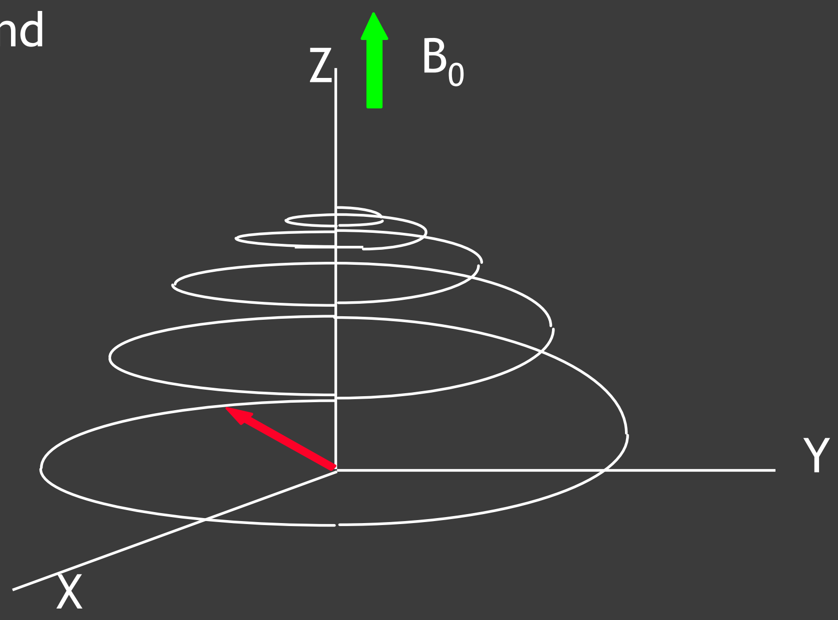
net magnetisation and
90° pulse



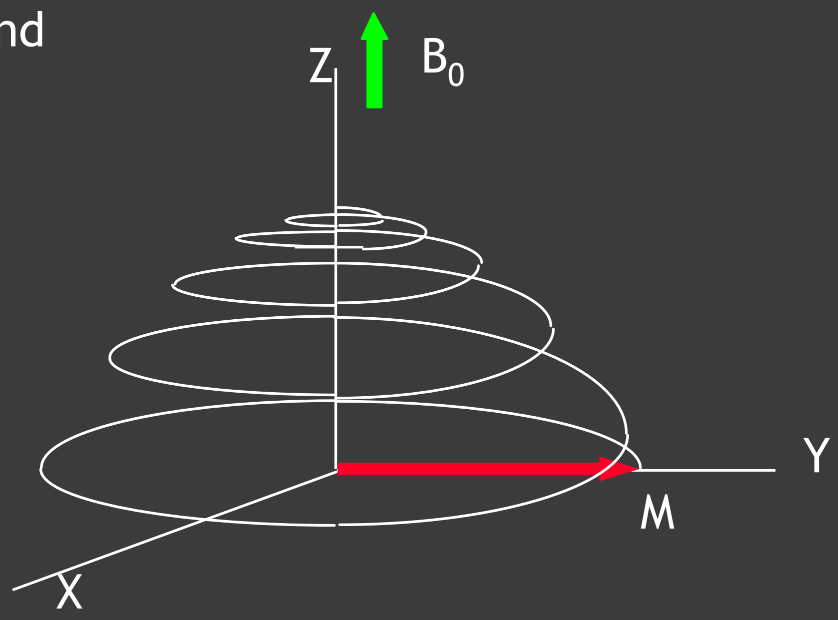
net magnetisation and
90° pulse



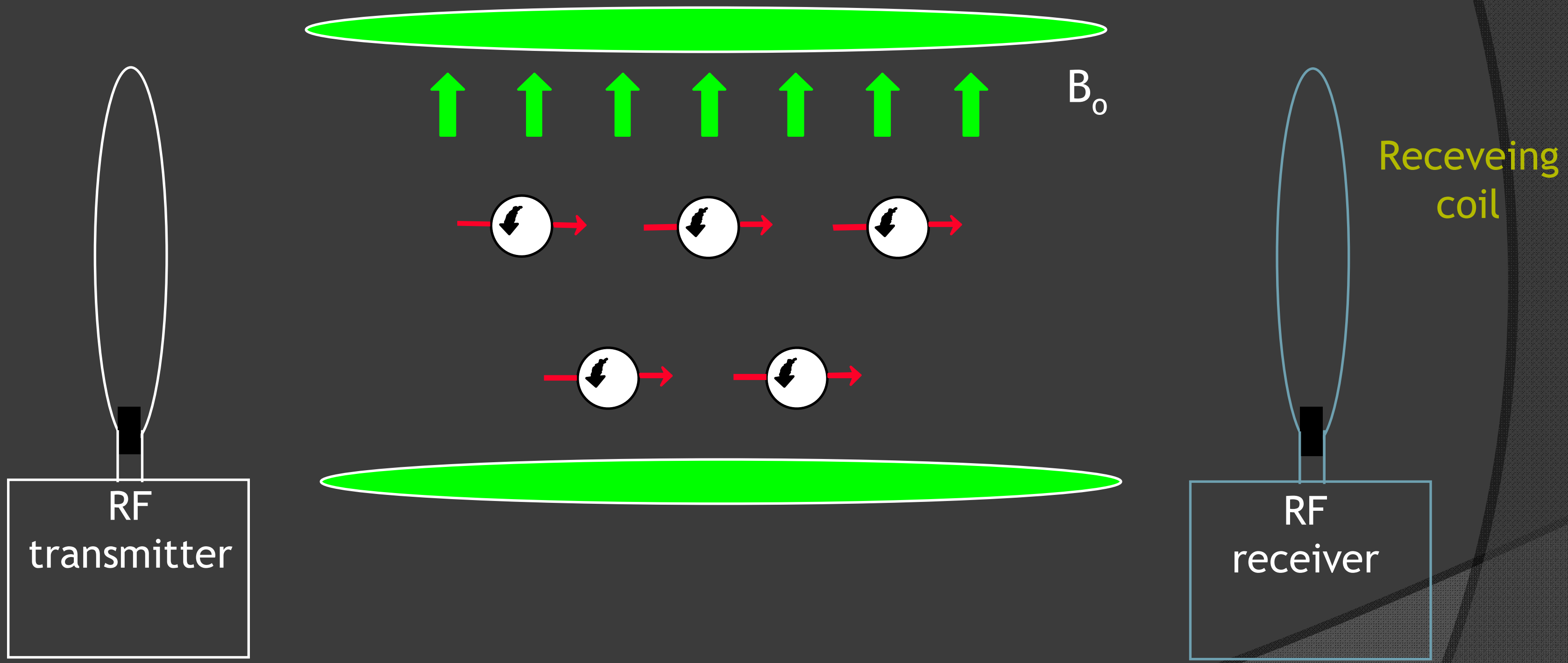
net magnetisation and
90° pulse

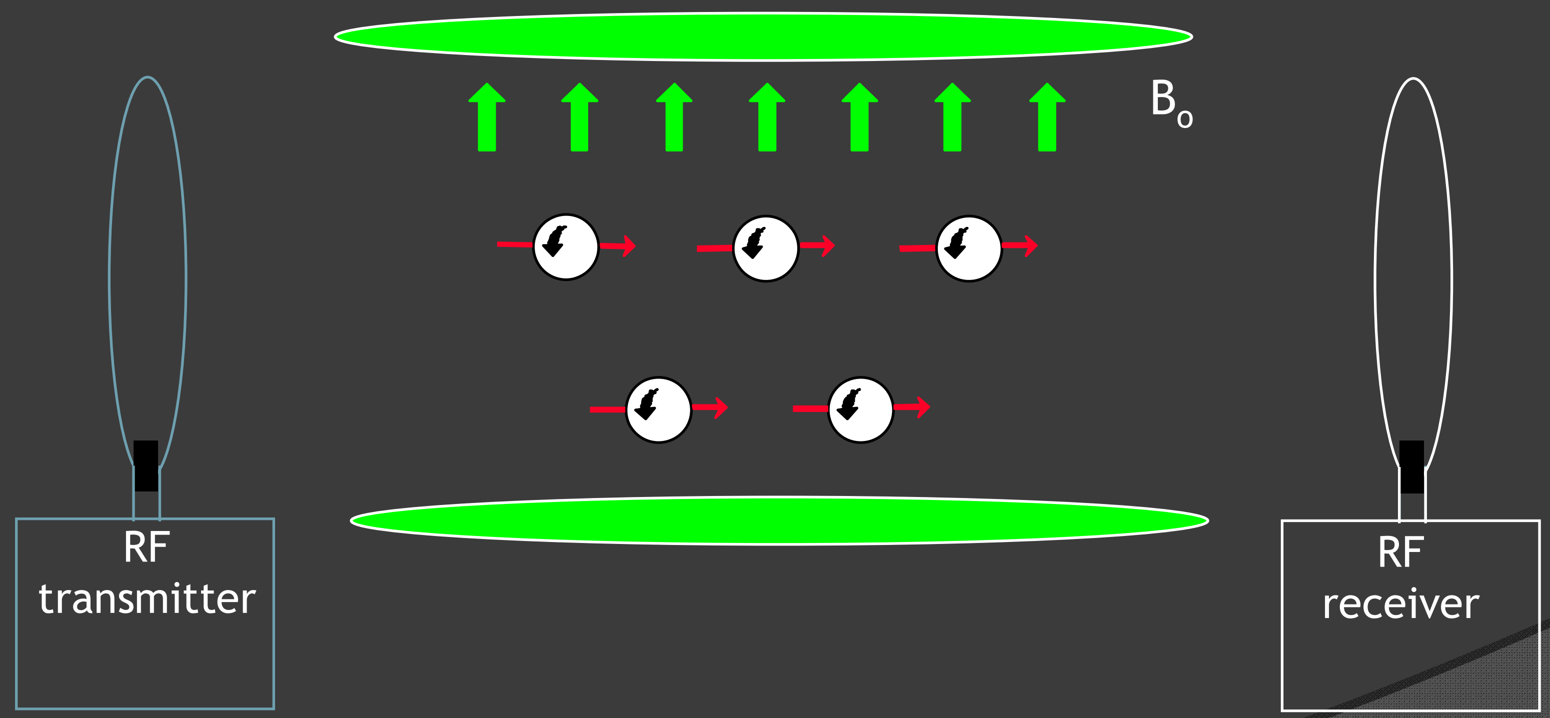


net magnetisation and
90° pulse

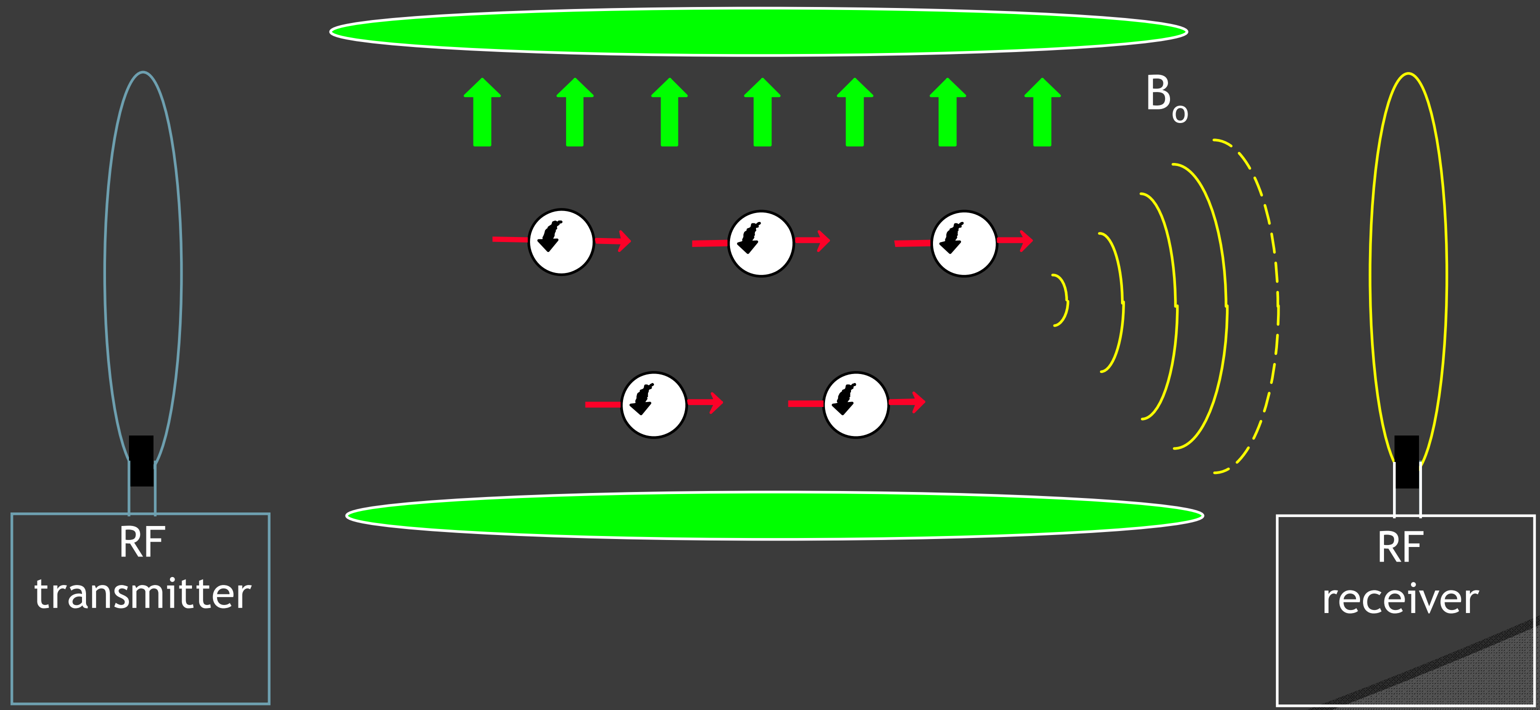


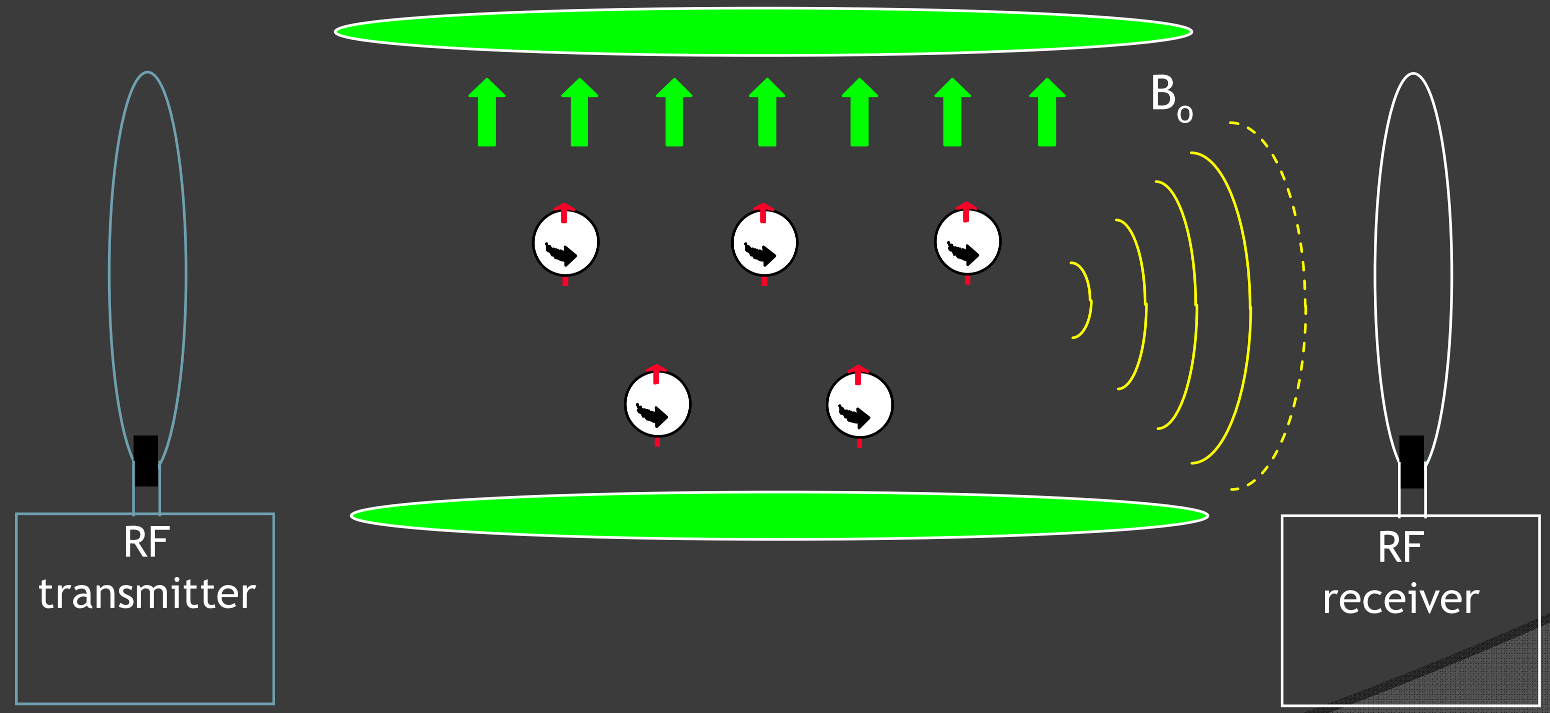
Signal detection: induced e.m.f.

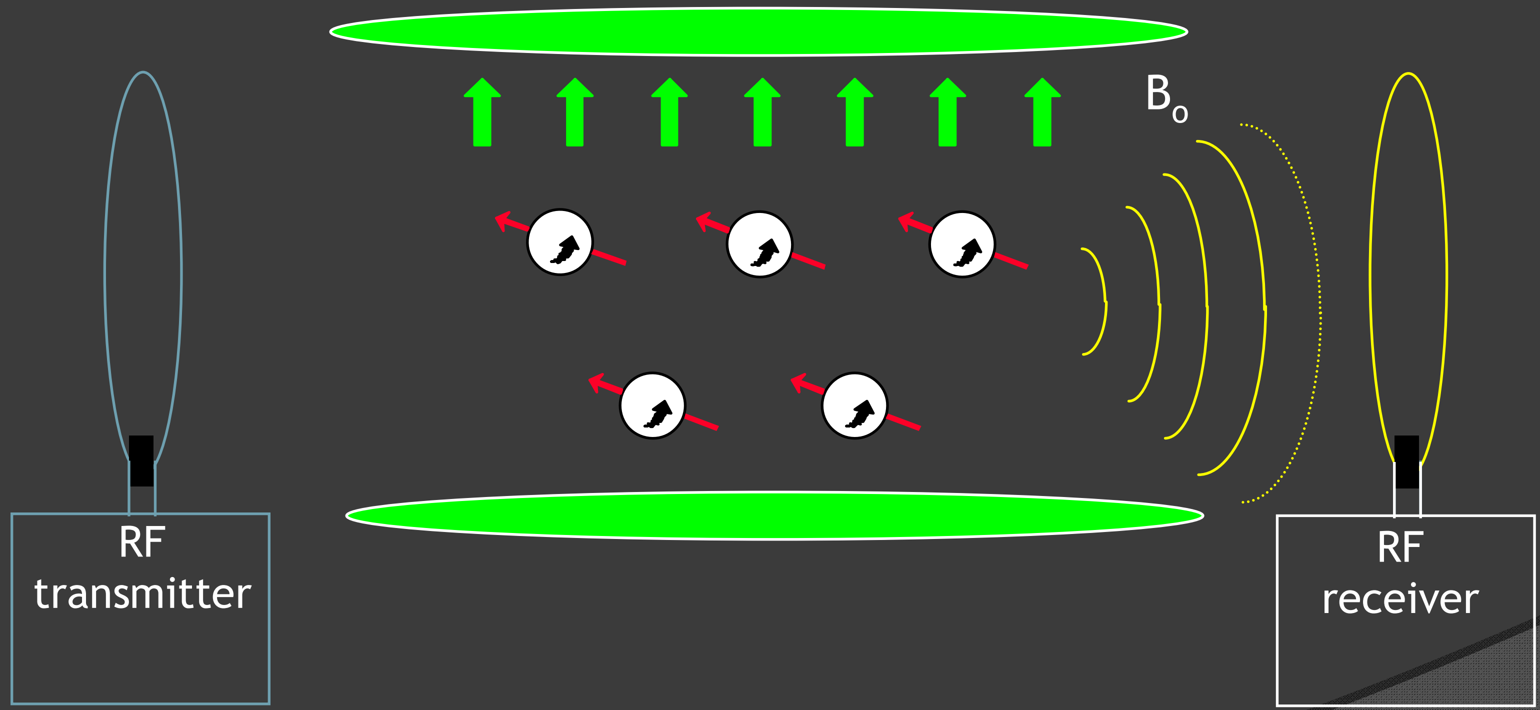


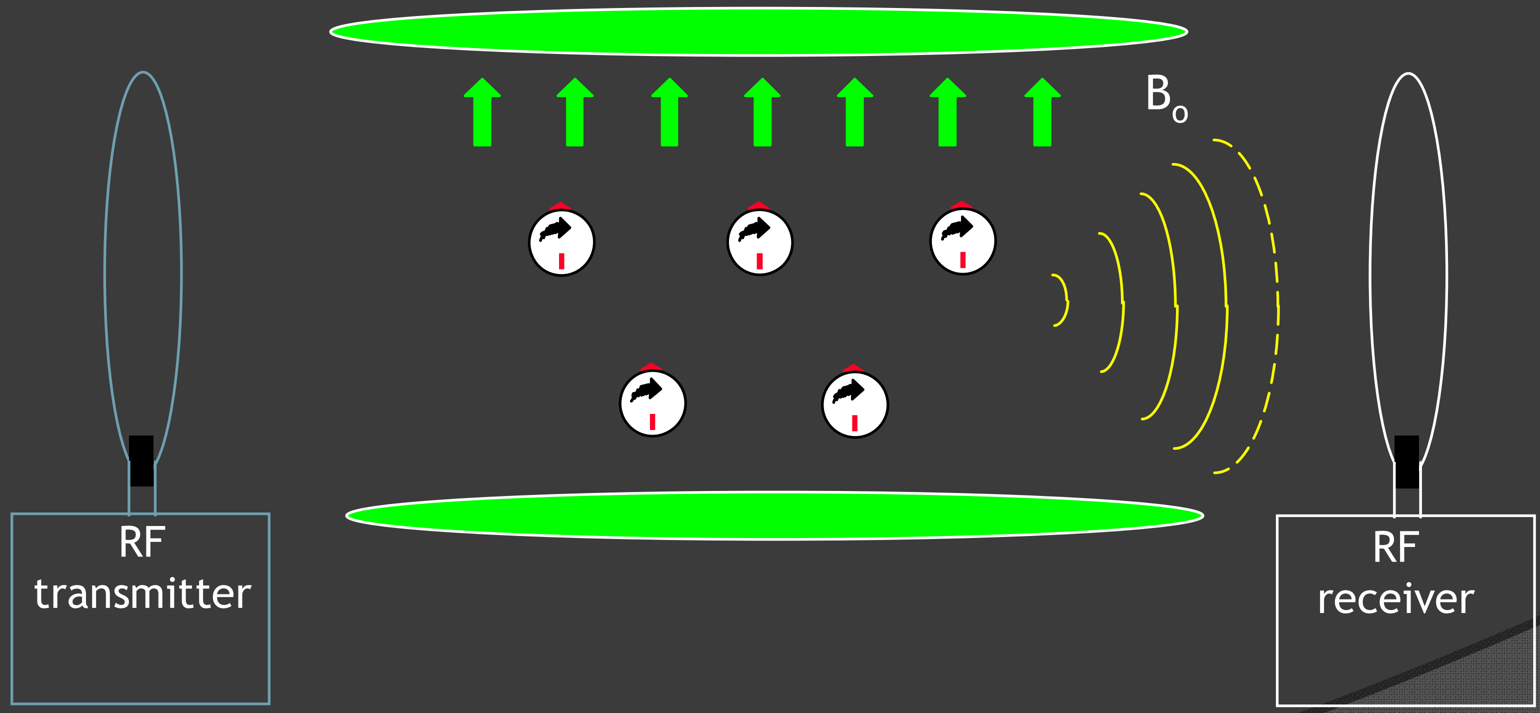


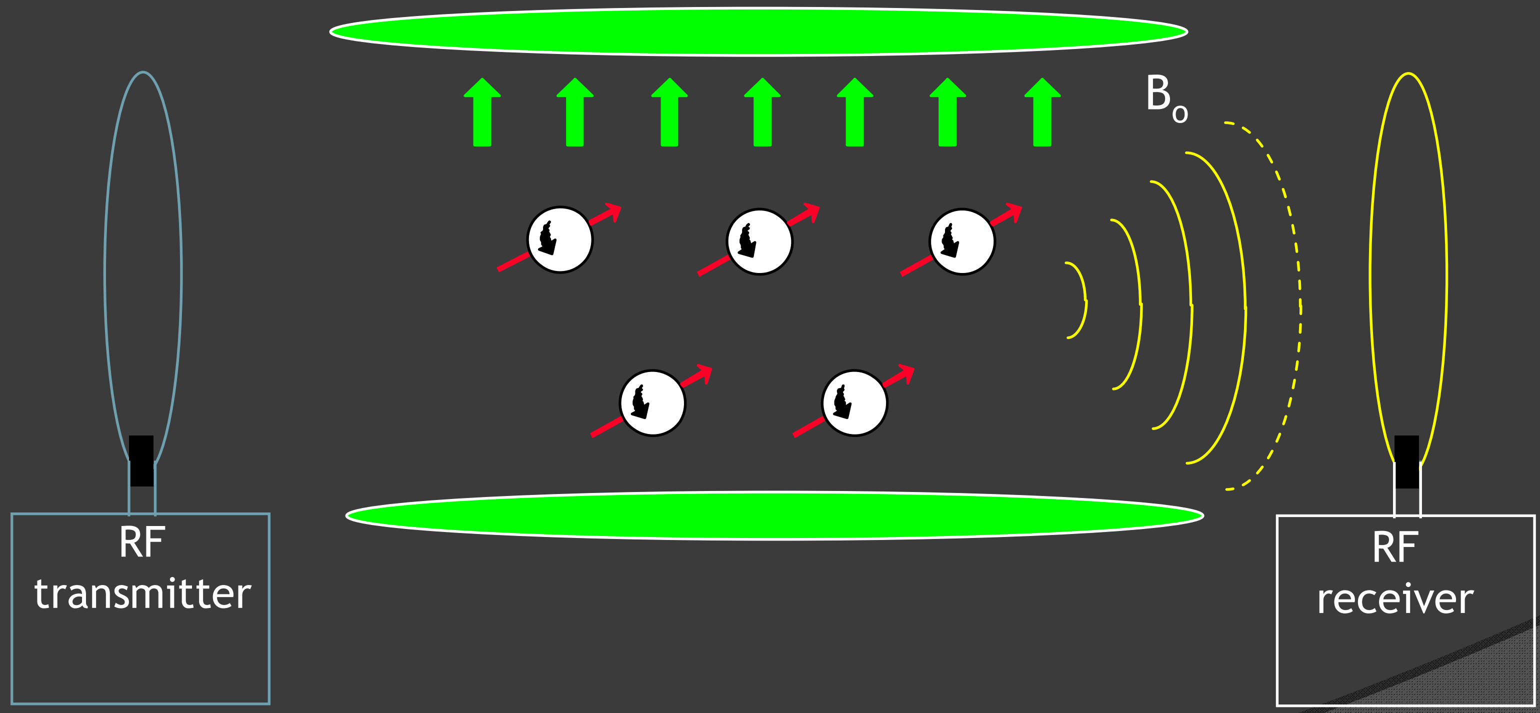
B_o
RF transmitter
RF receiver

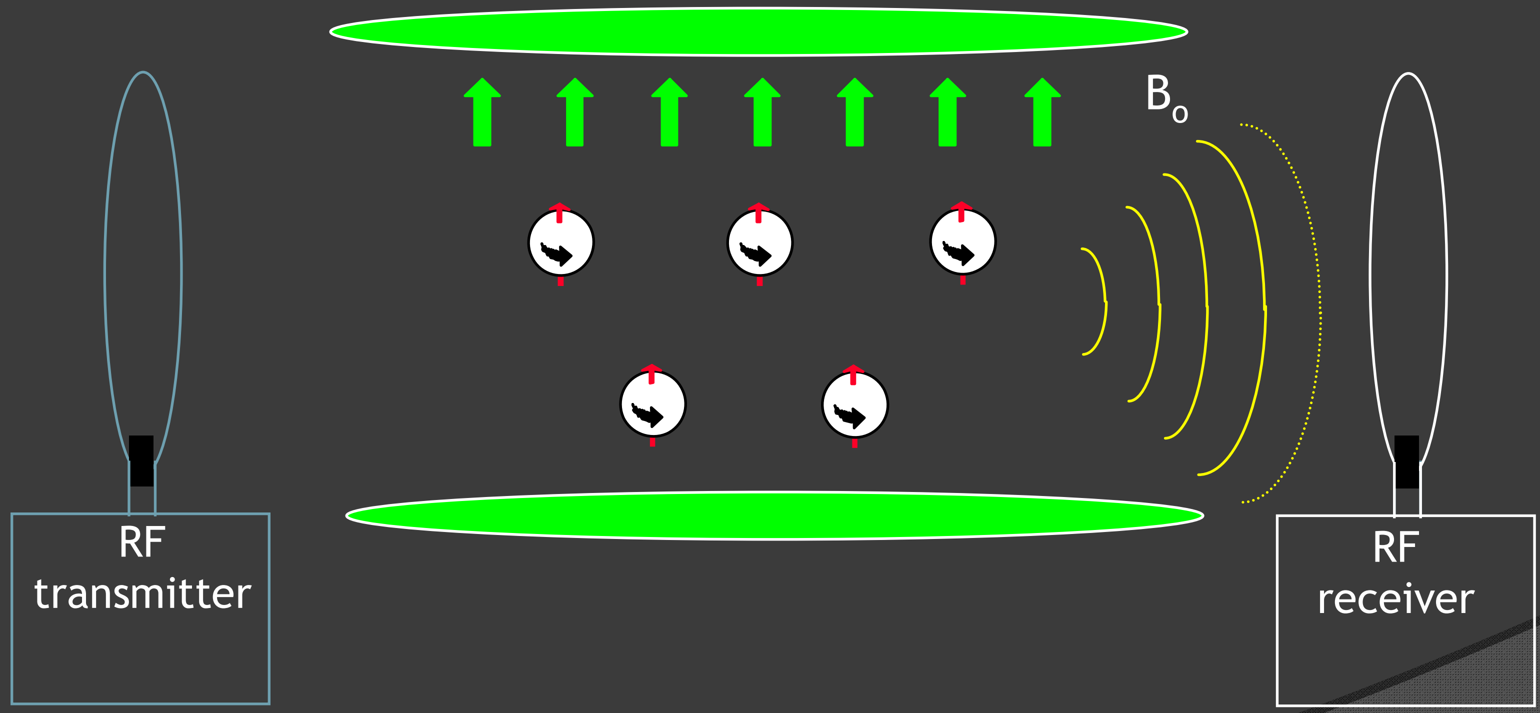

RF
transmitter
B_o
RF
receiver

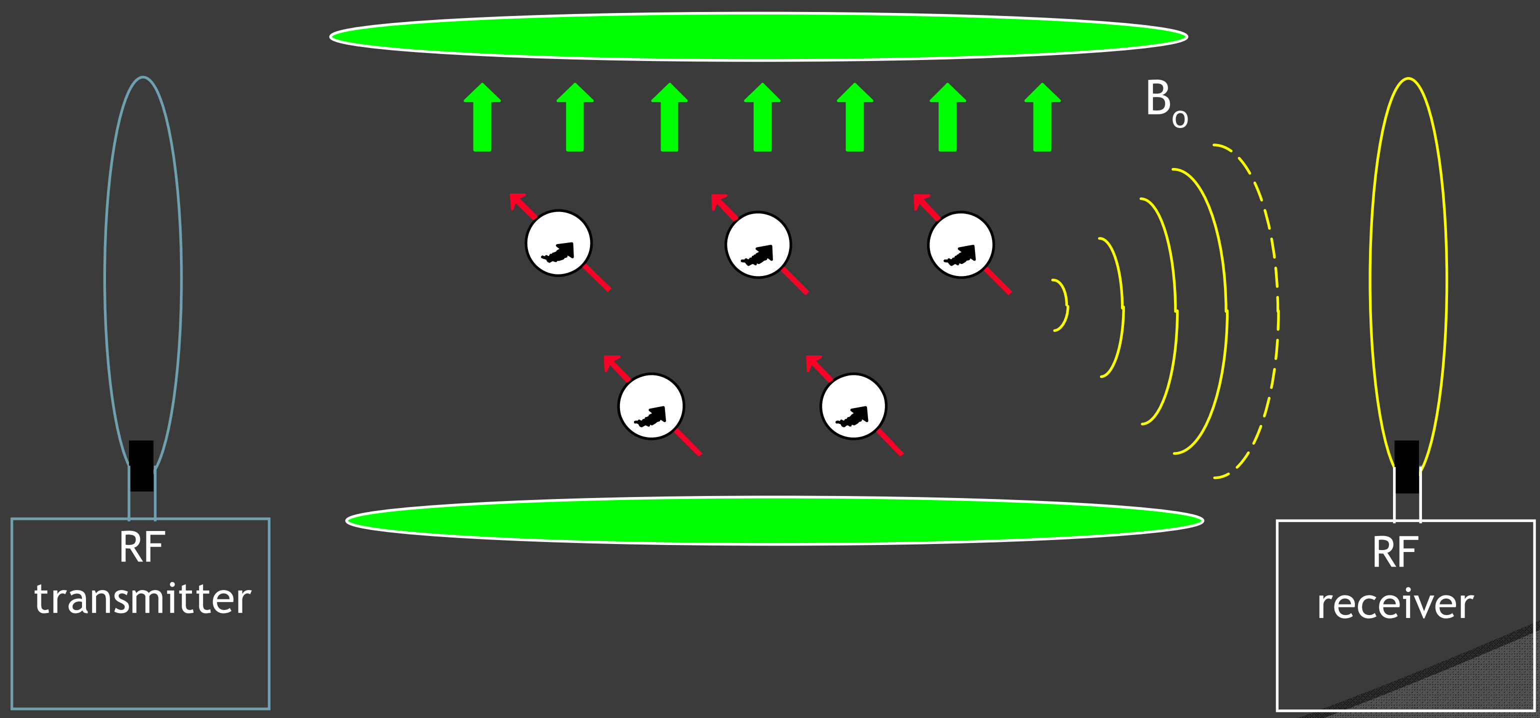

B$_o$
RF
transmitter
RF
receiver


B$_o$
RF
transmitter
RF
receiver


B o
RF
transmitter
RF
receiver


B$_o$
RF
transmitter
RF
receiver


RF
transmitter
B$_o$
RF
receiver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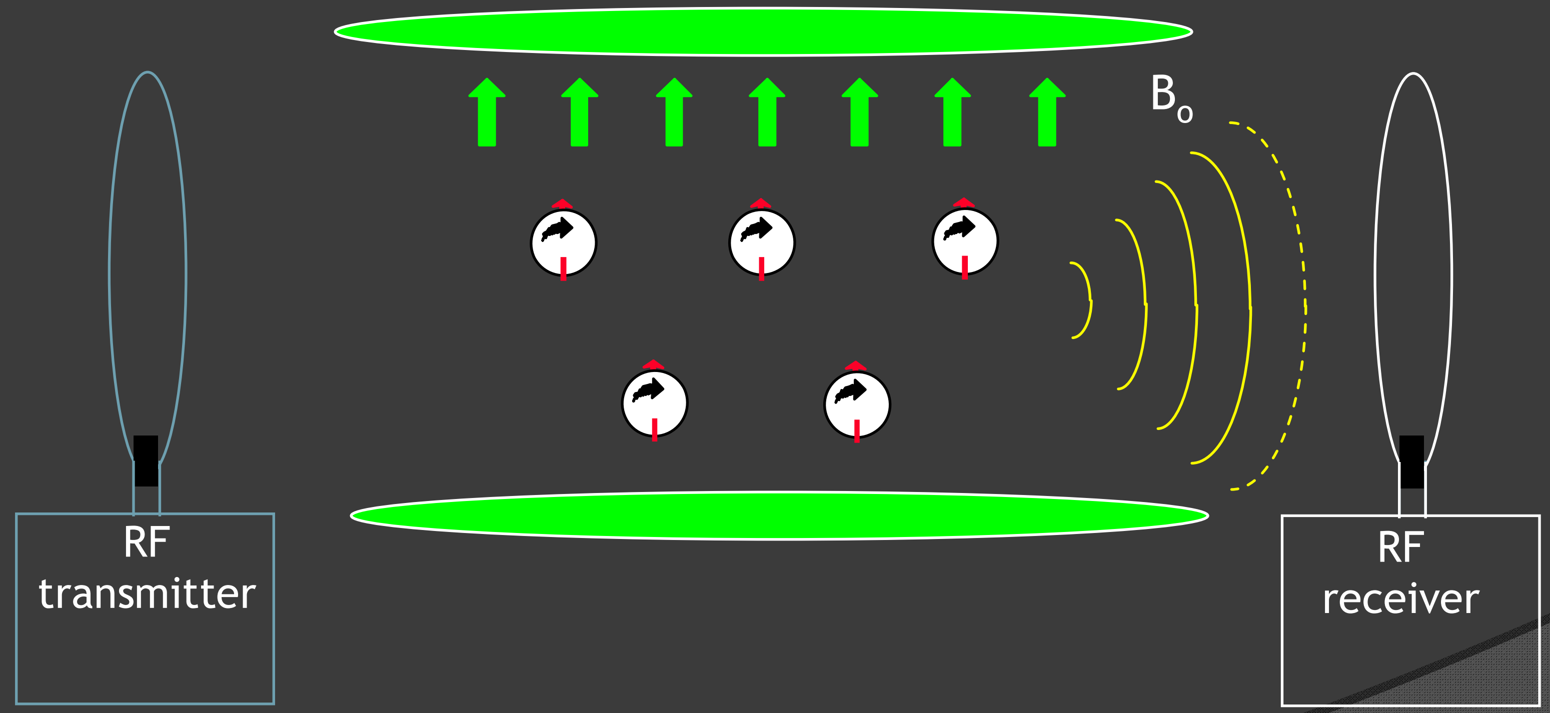
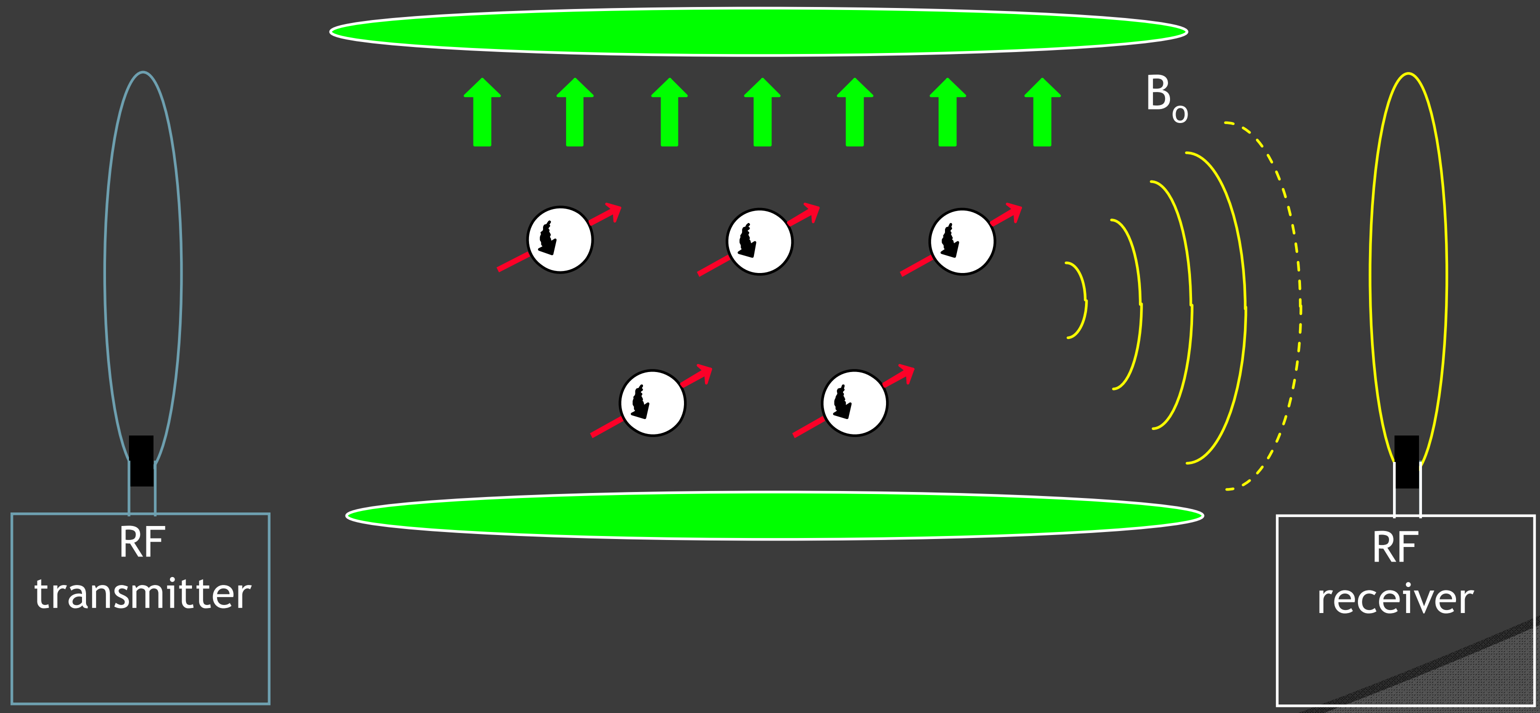
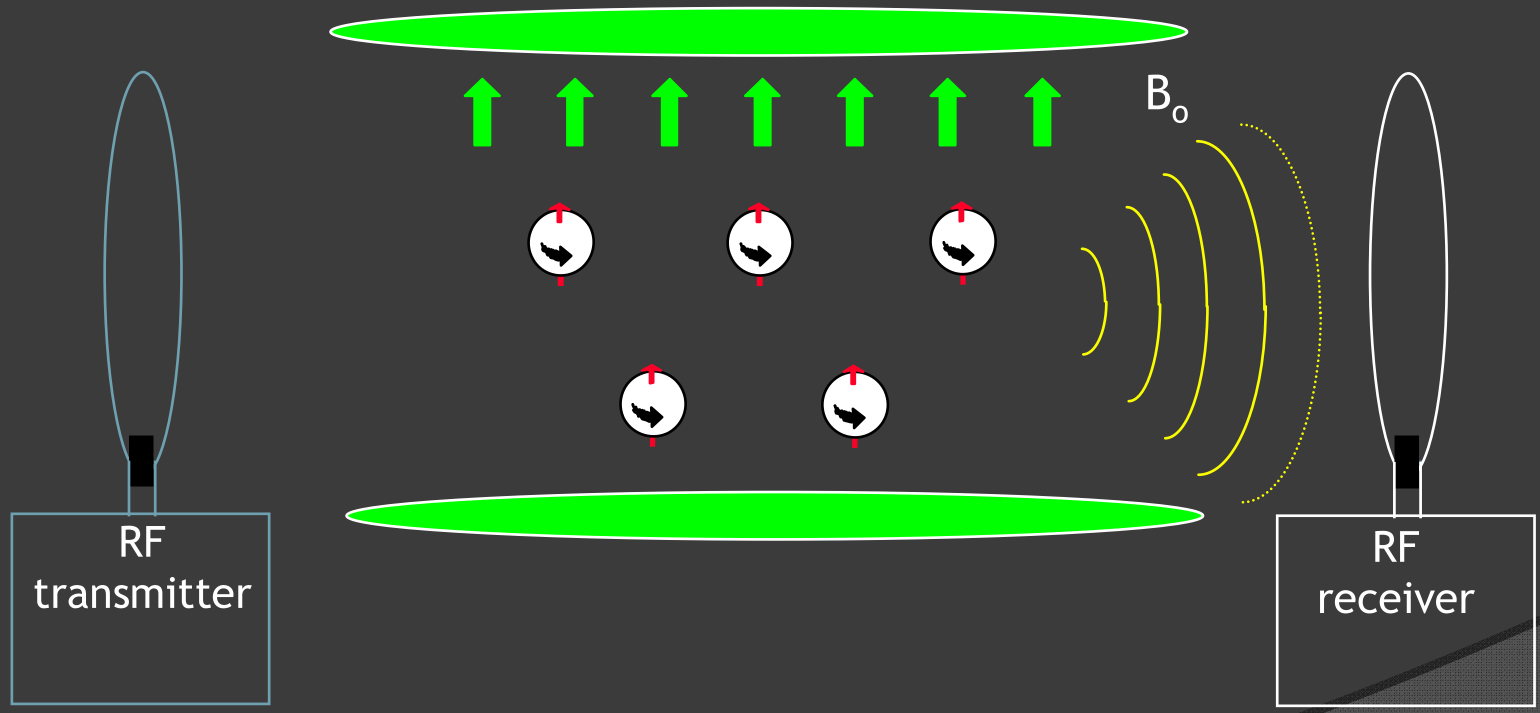
transmitter
B_o
RF
receiver


B0
RF transmitter
RF receiver


B$_o$
RF
transmitter
RF
receiver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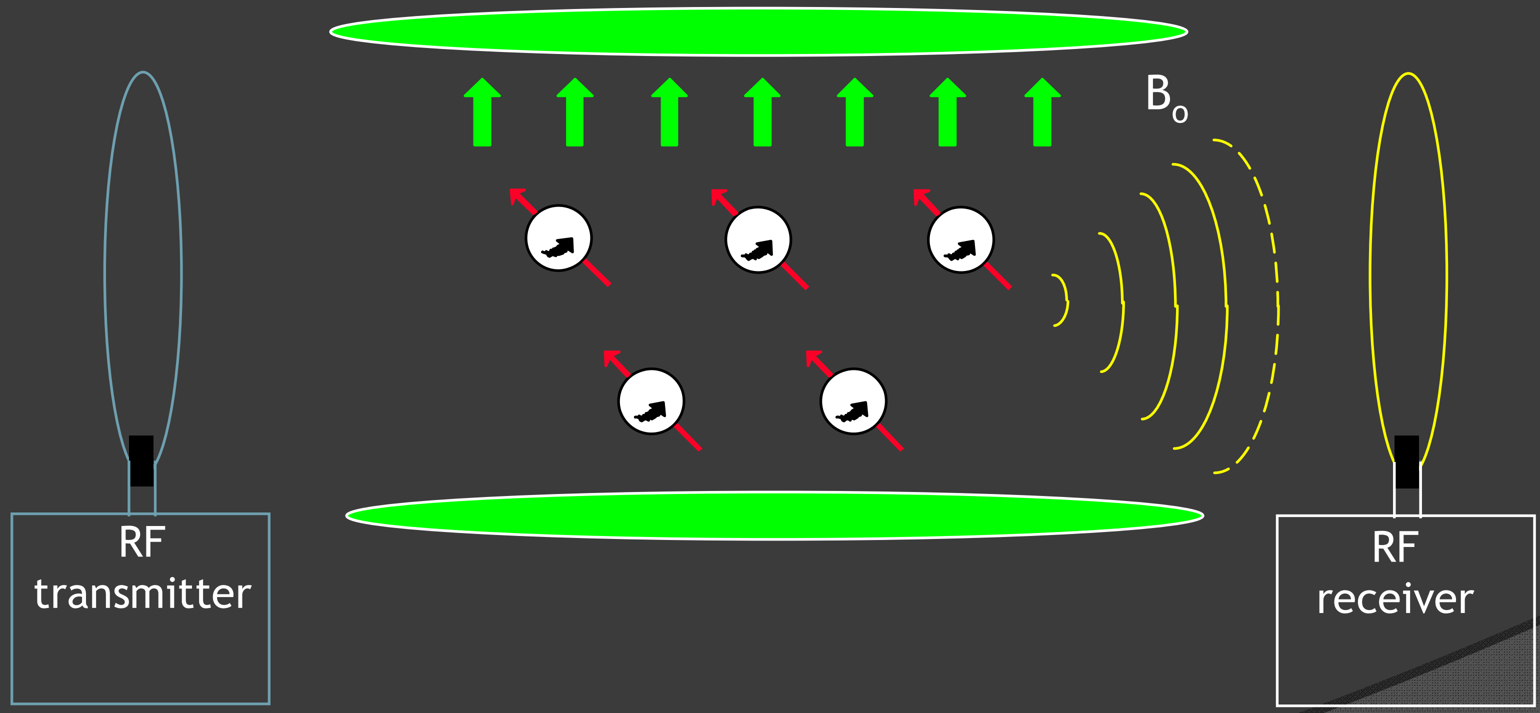
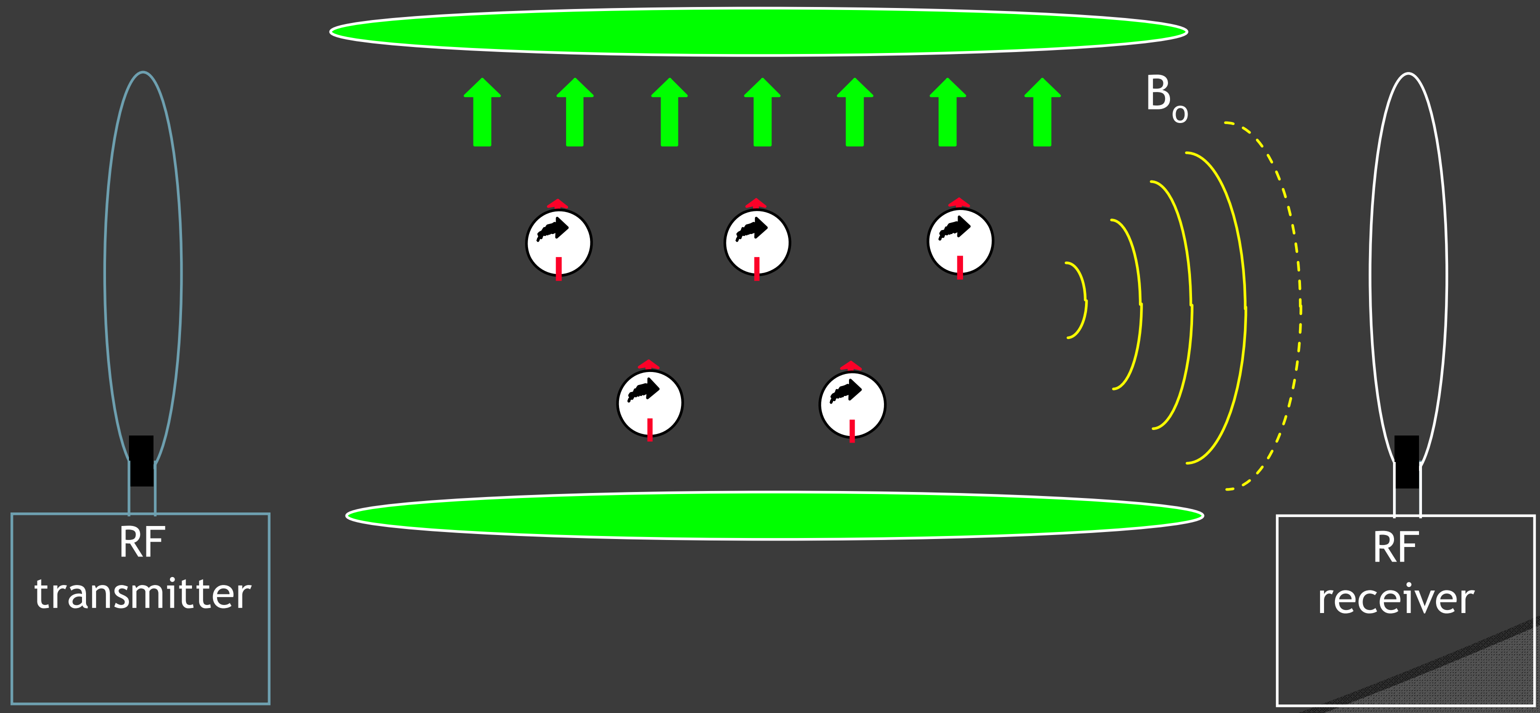
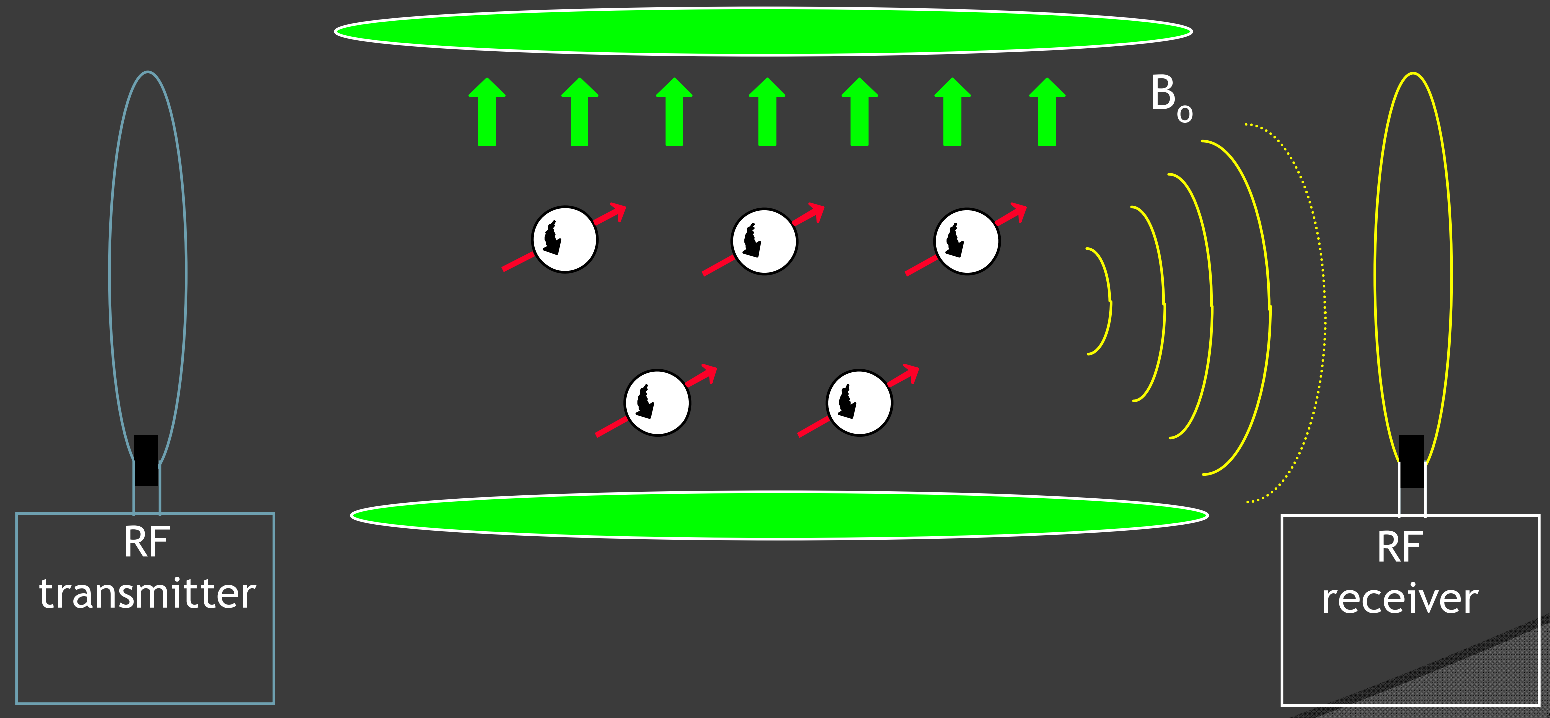
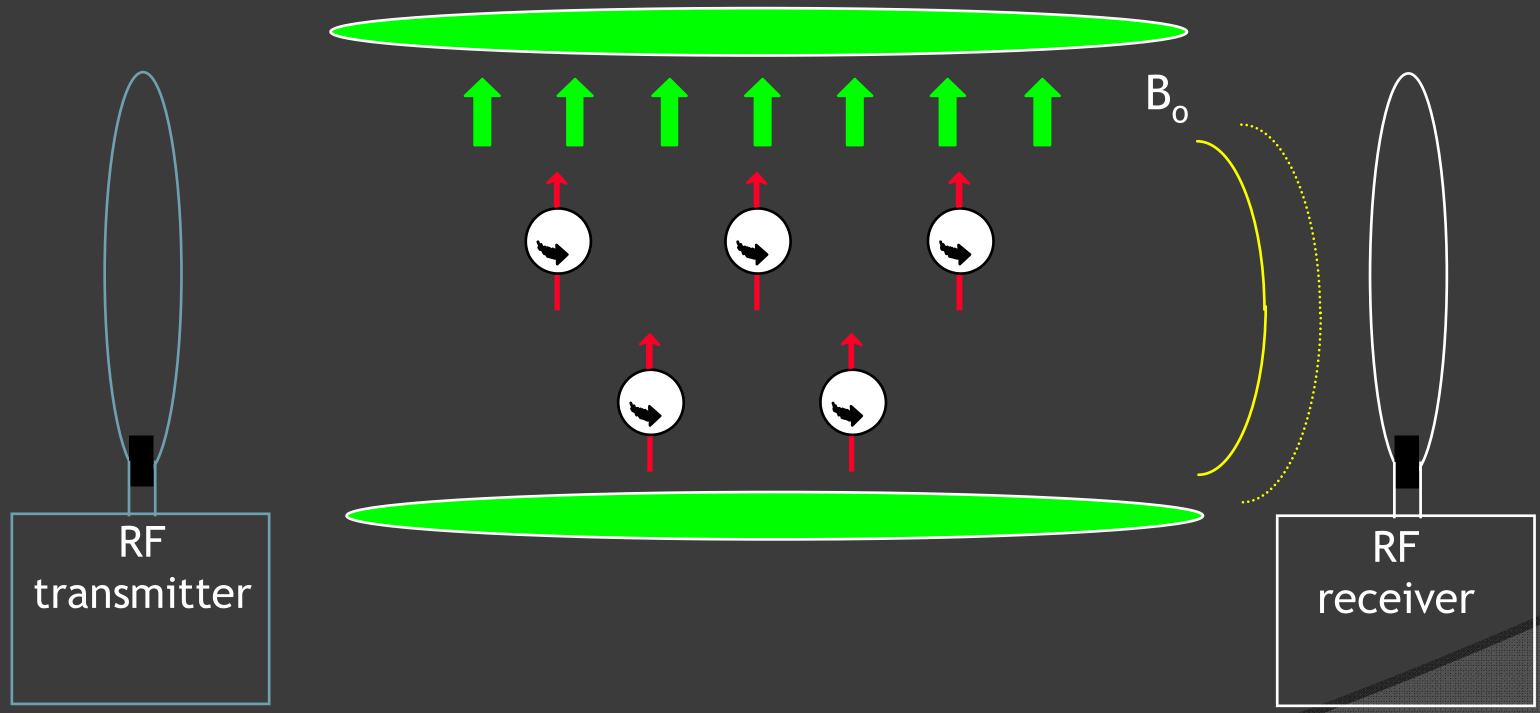
RF
transmitter
RF
receiver


RF
transmitter
B_o
RF
receiver

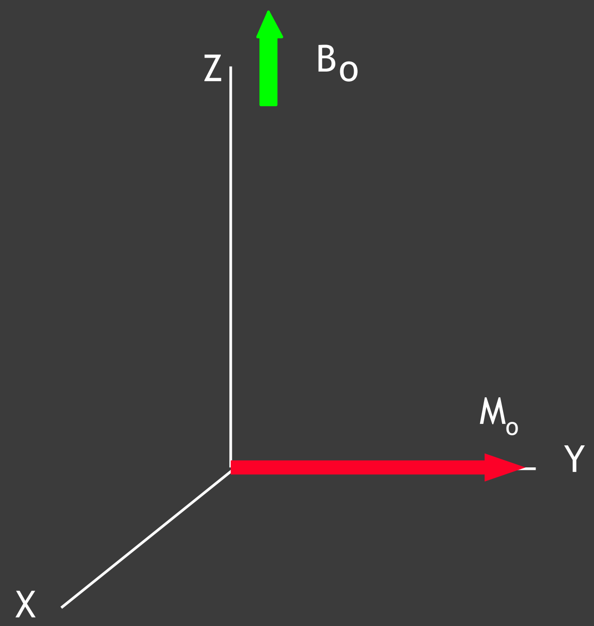

B$_o$
RF
transmitter
RF
receiver

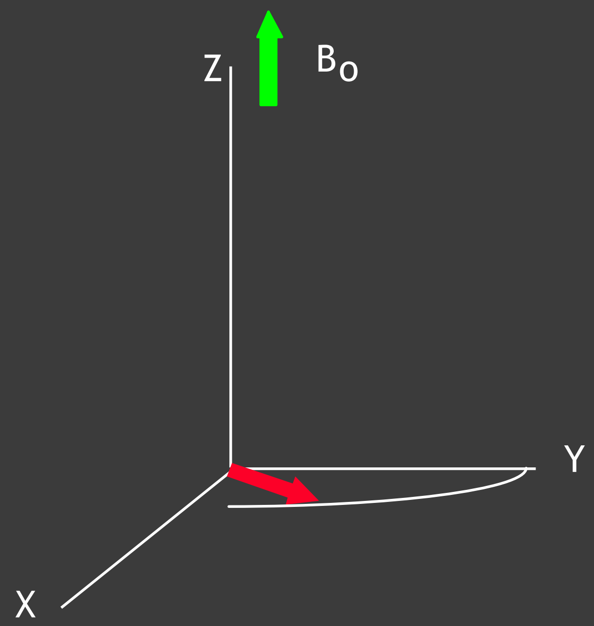

RF
transmitter
B_o
RF
receiver

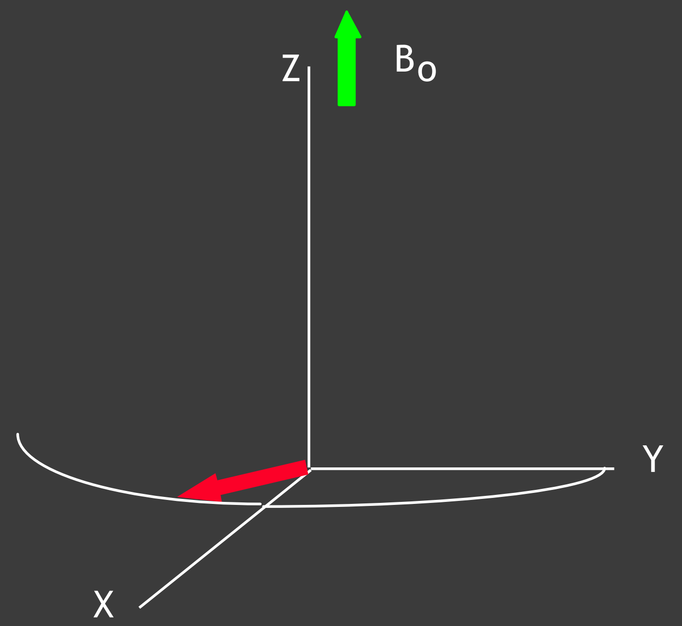


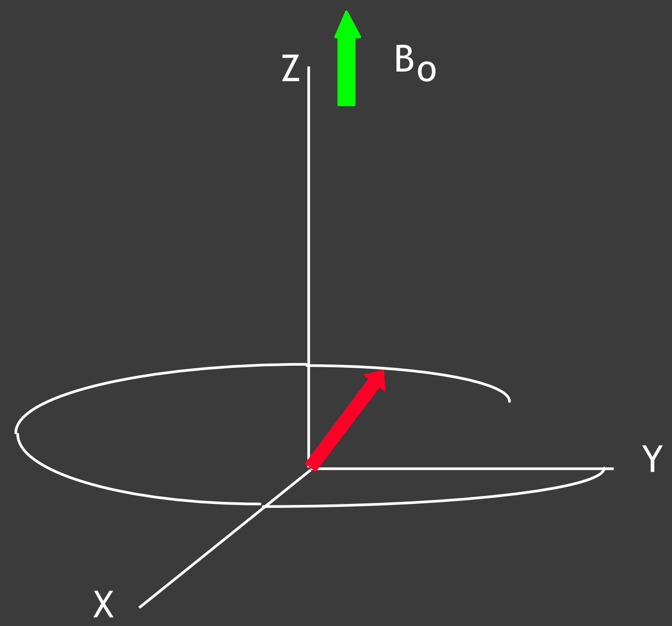
B_o
RF
transmitter
RF
receiver

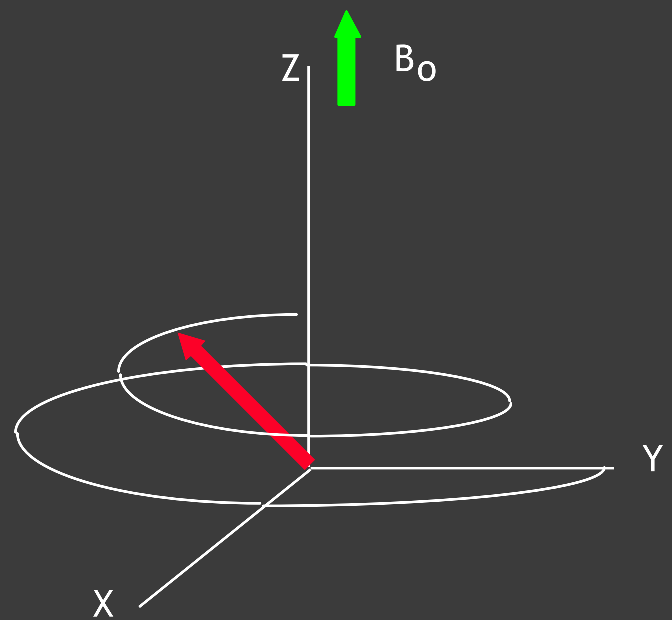
Relaxation: magnetization “path”



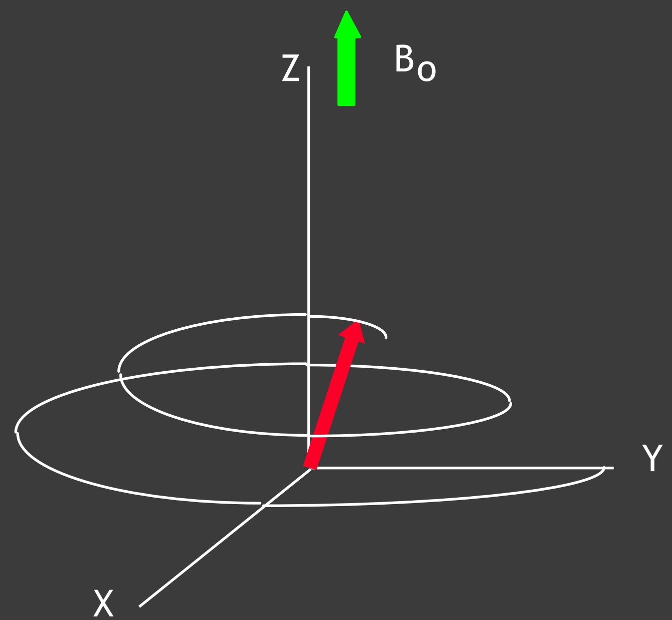

Z
B_0
Y
X


Z
B_o
Y
X


Z
Bo
Y
X



Z
B_o
Y
X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Y
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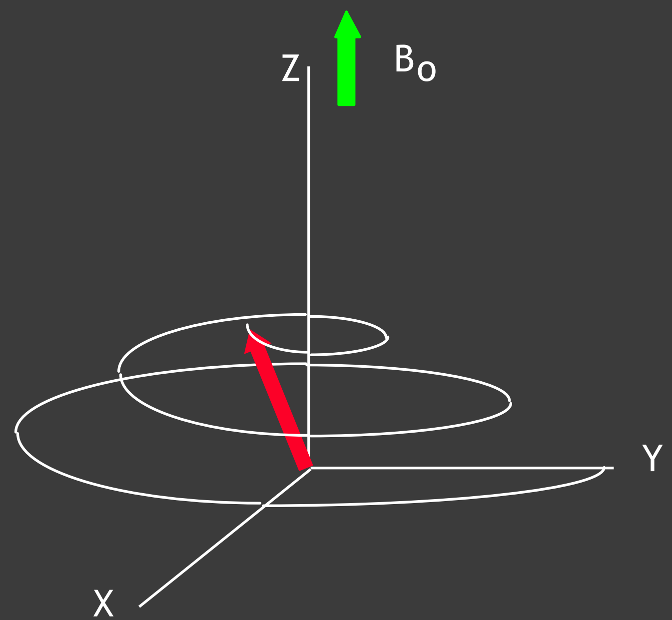
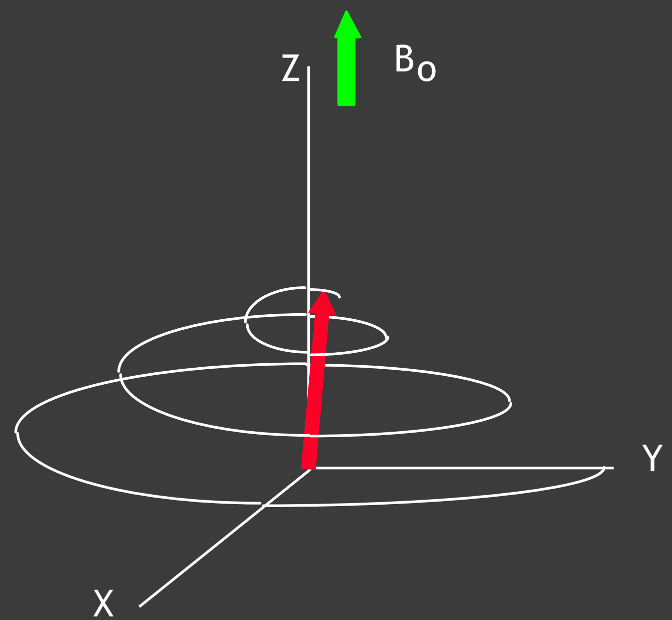
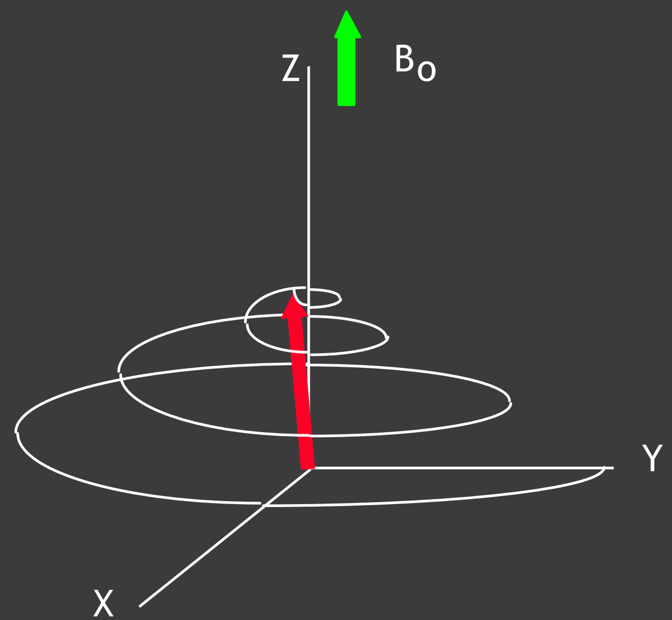

Z
B_o
Y
X


Z
B_O
Y
X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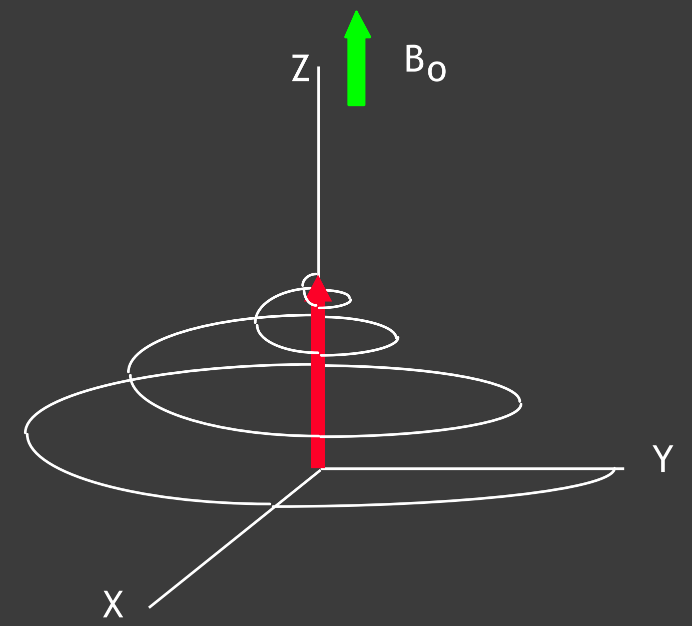
B_0
Y
X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B0
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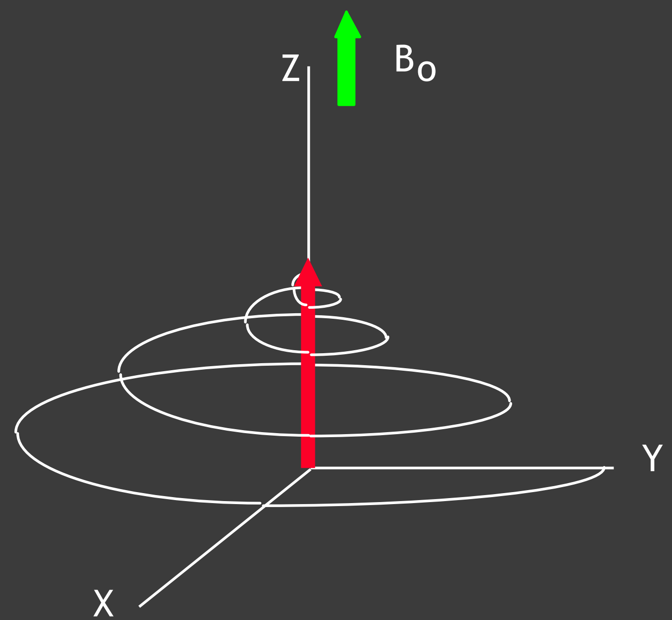
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B_o
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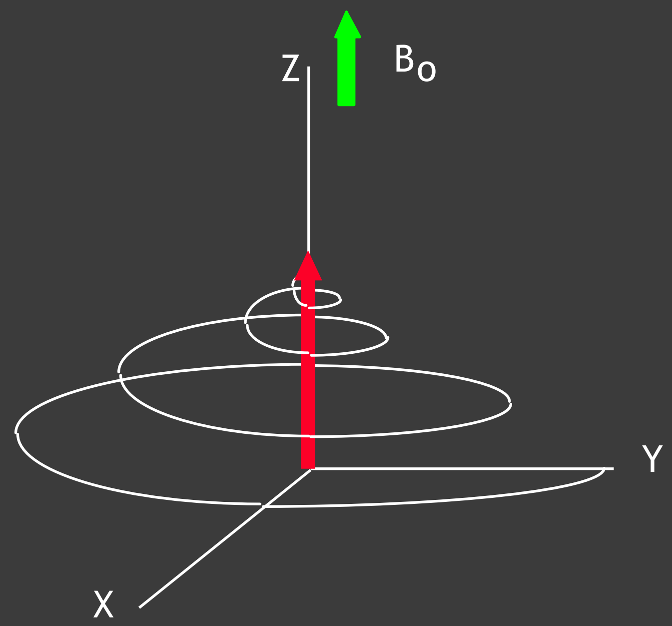
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B_O
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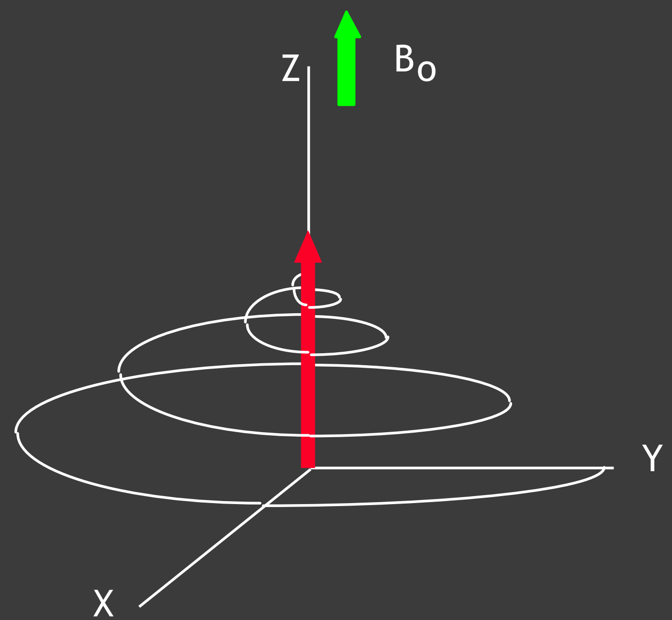
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B_O
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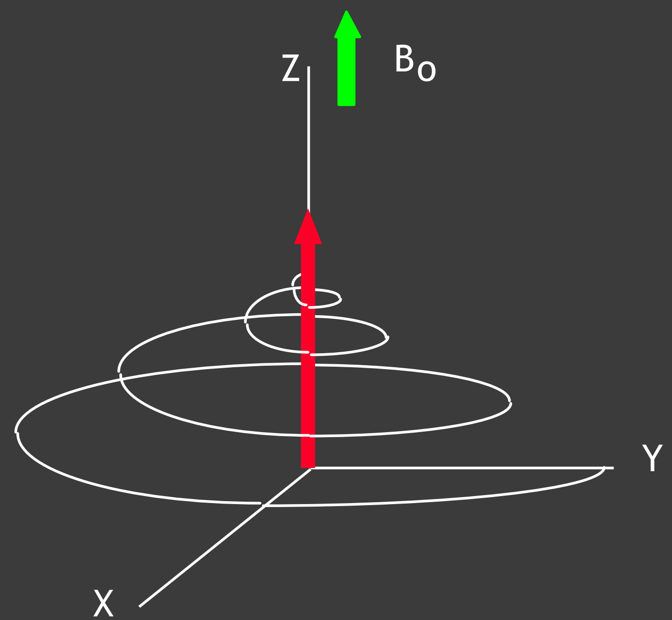
X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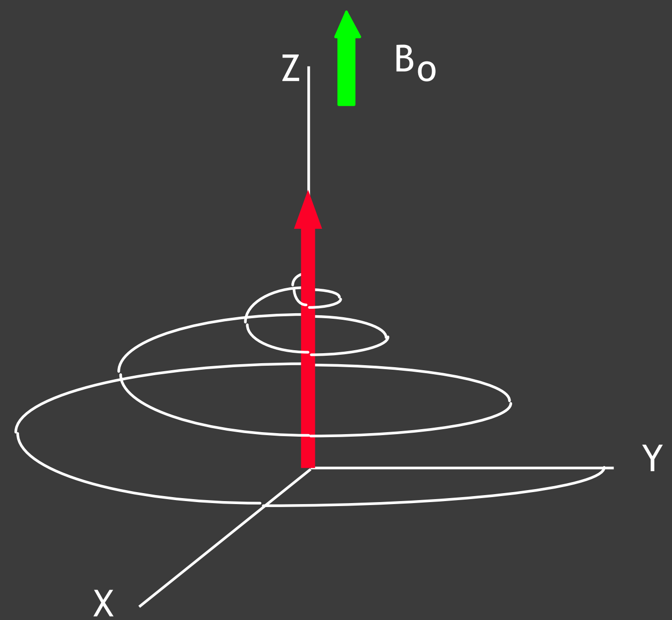
X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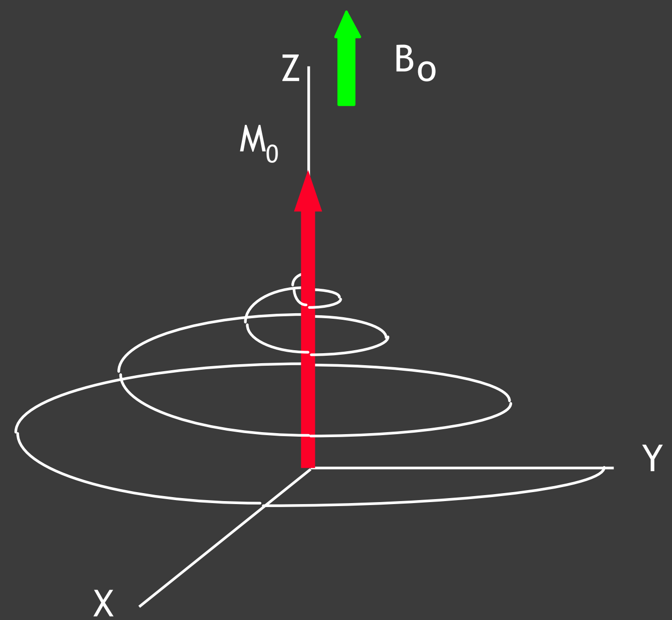
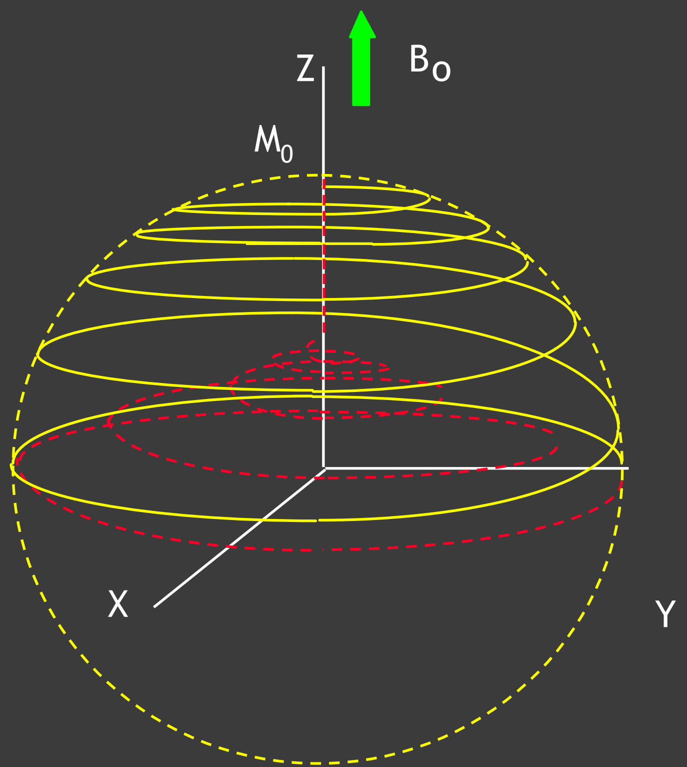
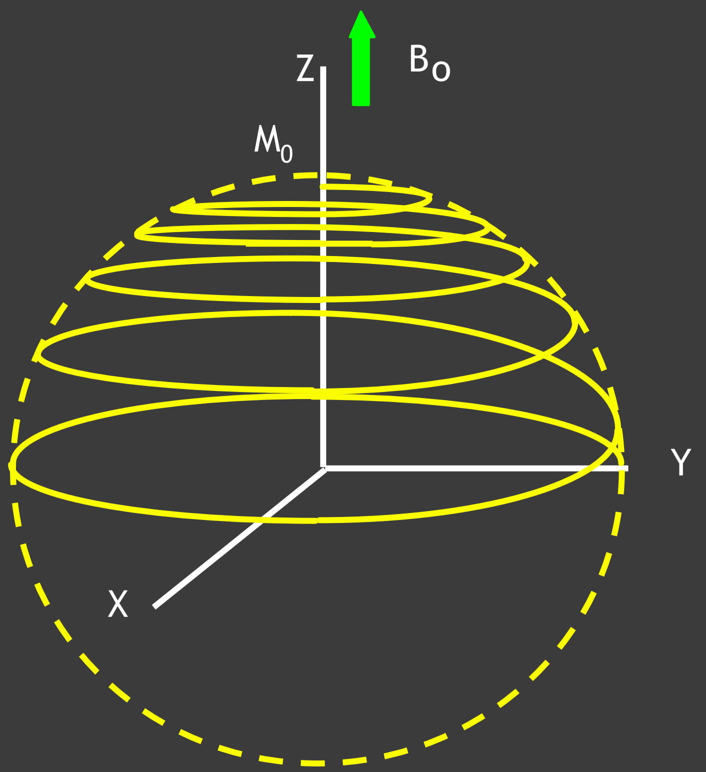
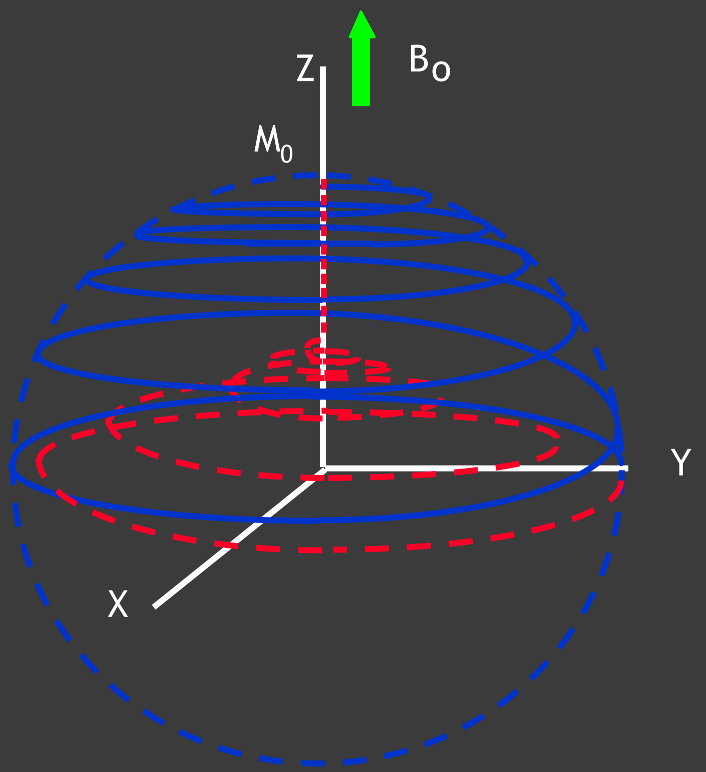

Z
B_0
M_0
Y
X

Excitation-relaxation path



Excitation



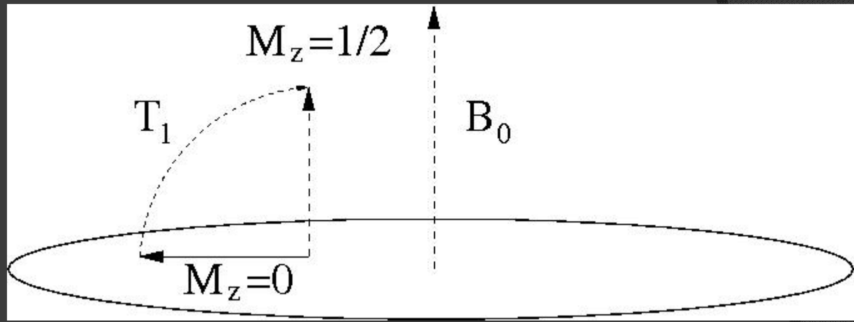


Excitation

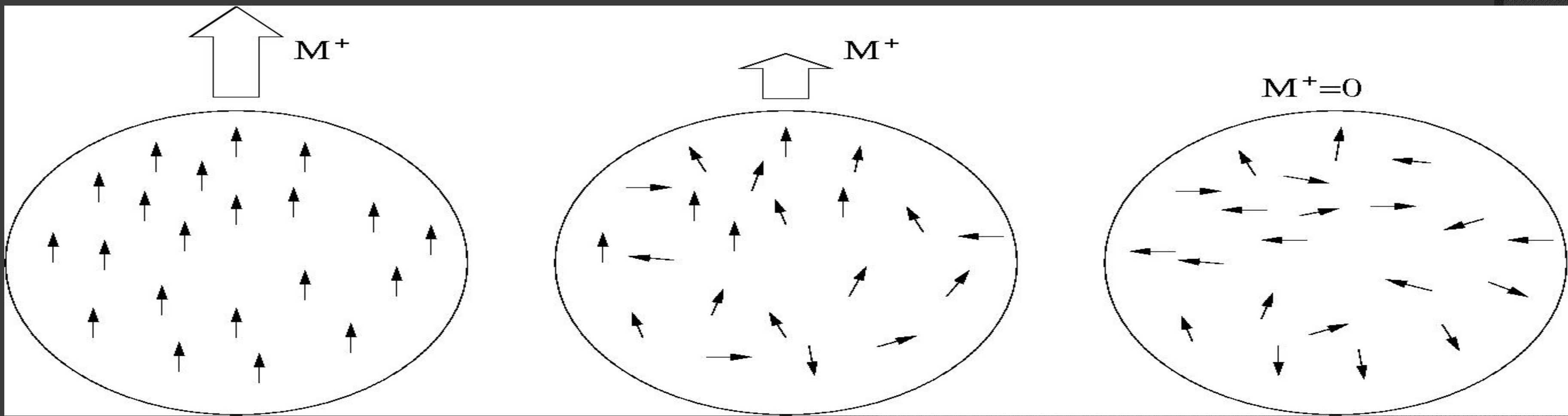
Relaxation

T_1 and T_2

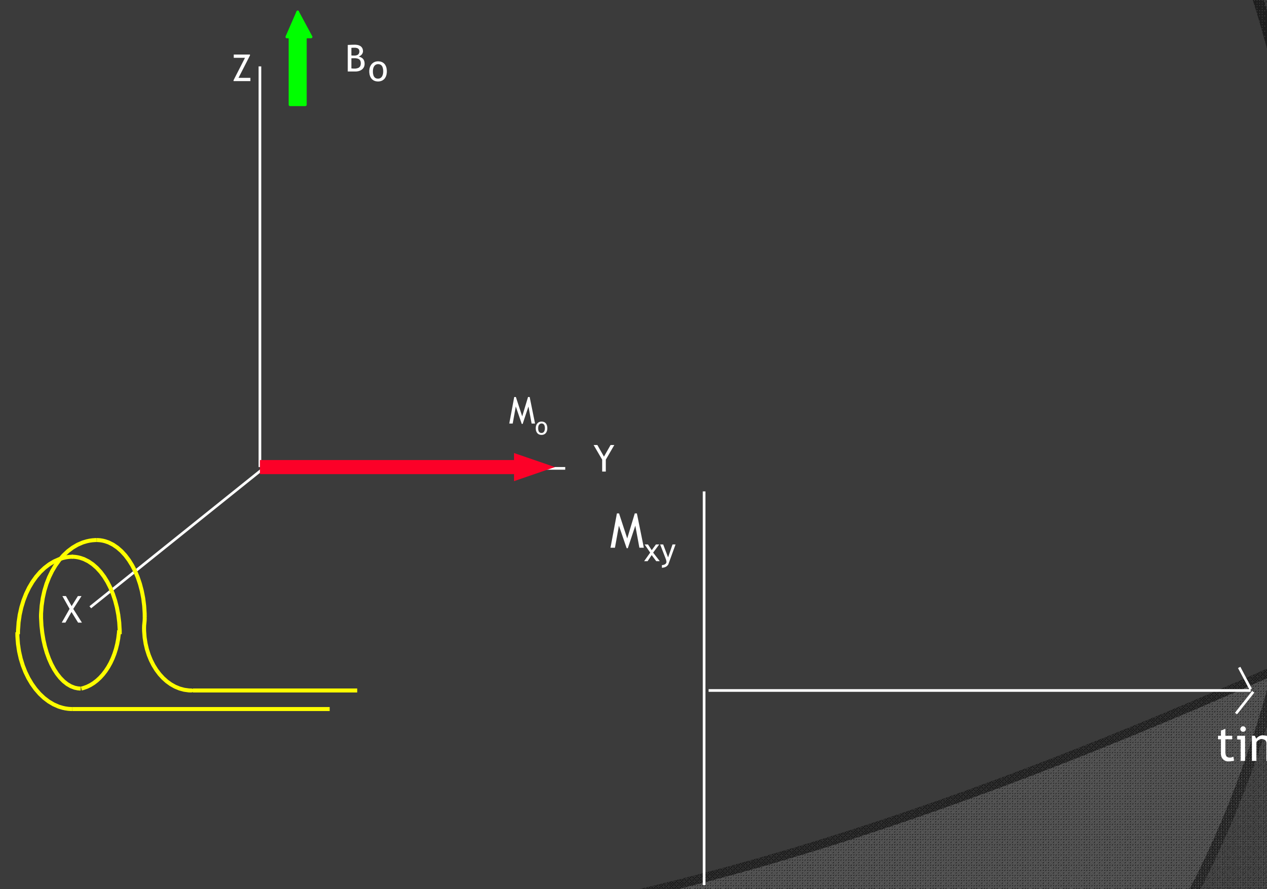
- T_1 : timescale for M_z "recovery" – process with energy exchange

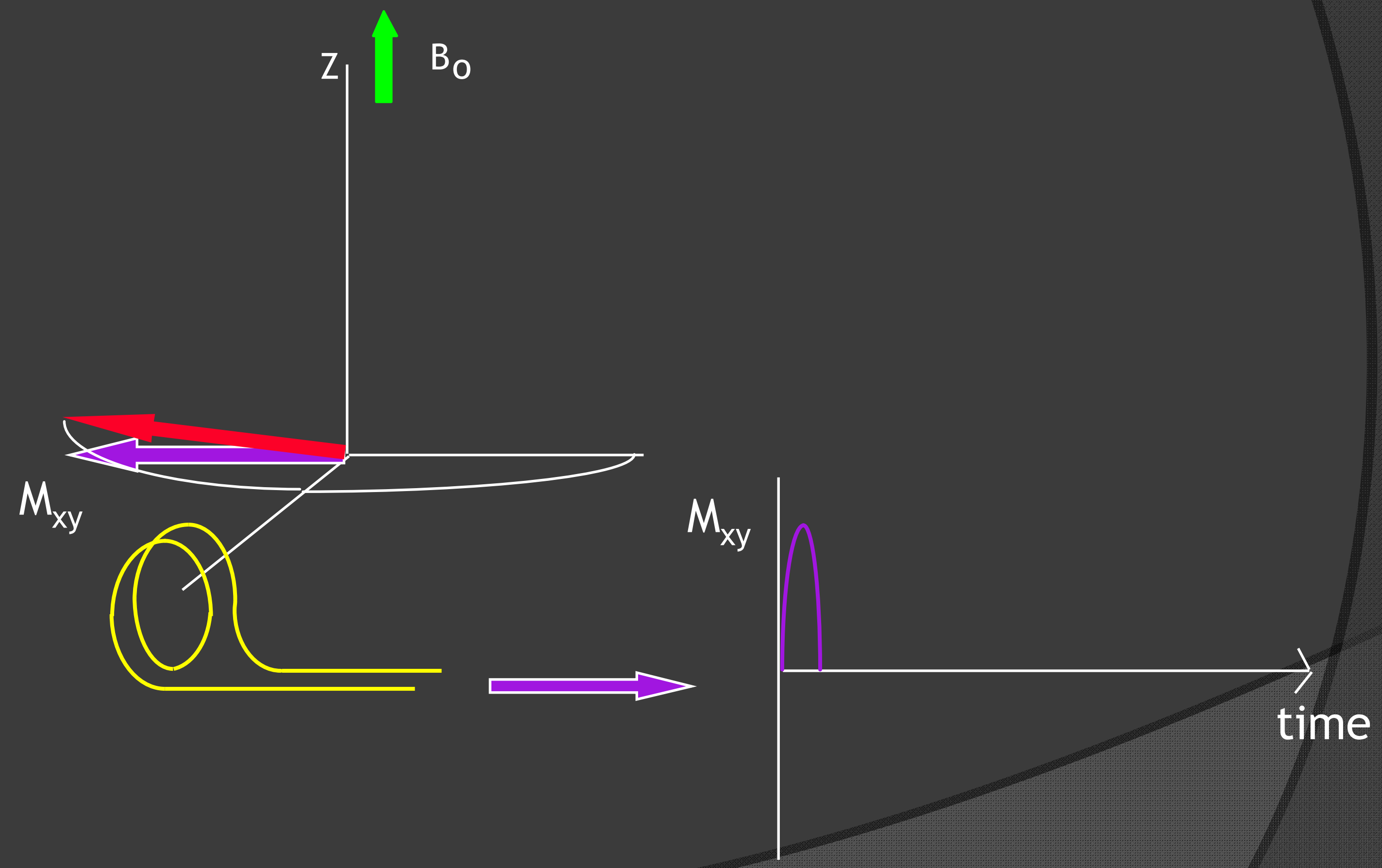


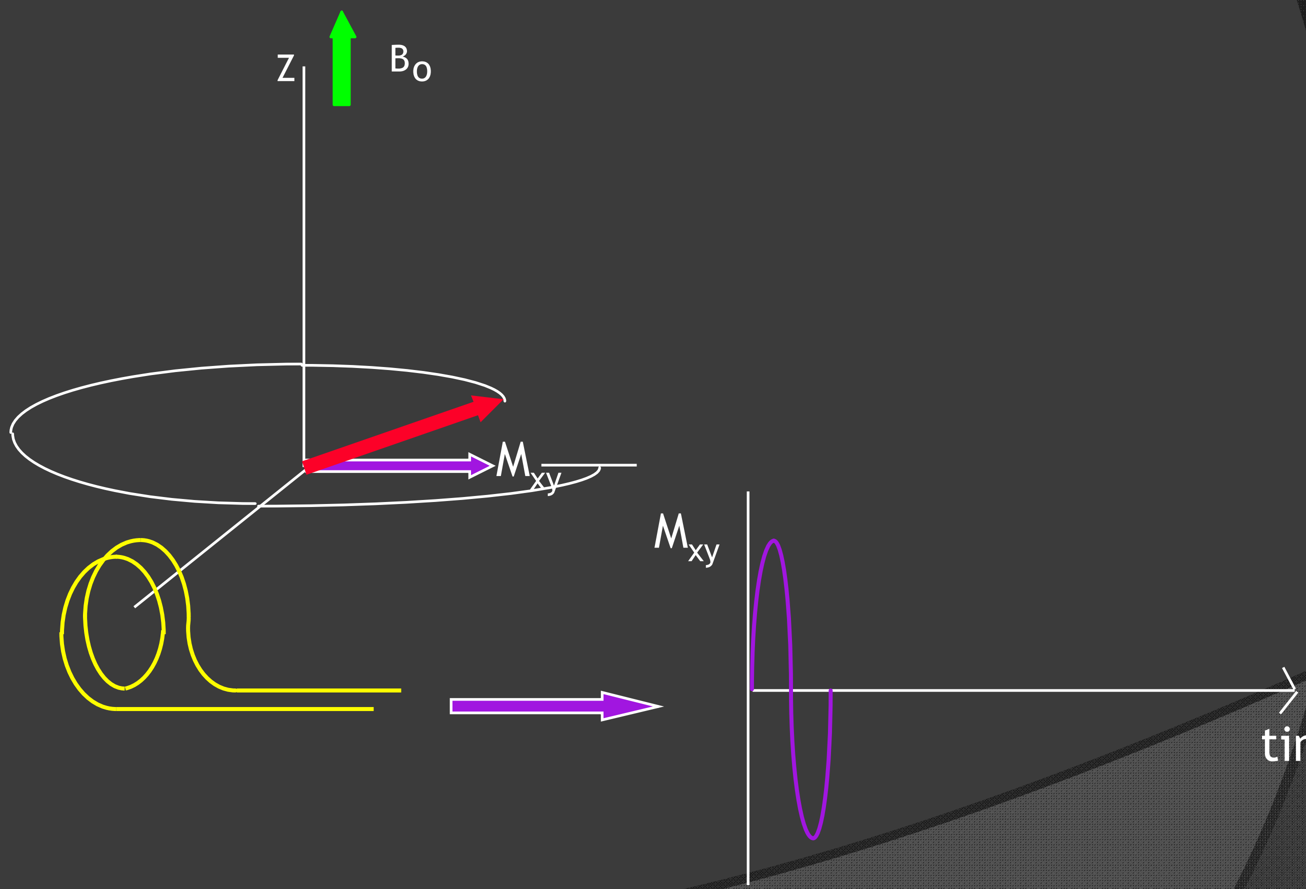
- $T_2 \ll T_1$: timescale of decay of $M_+ = M_x + iM_y$; no energy exchange

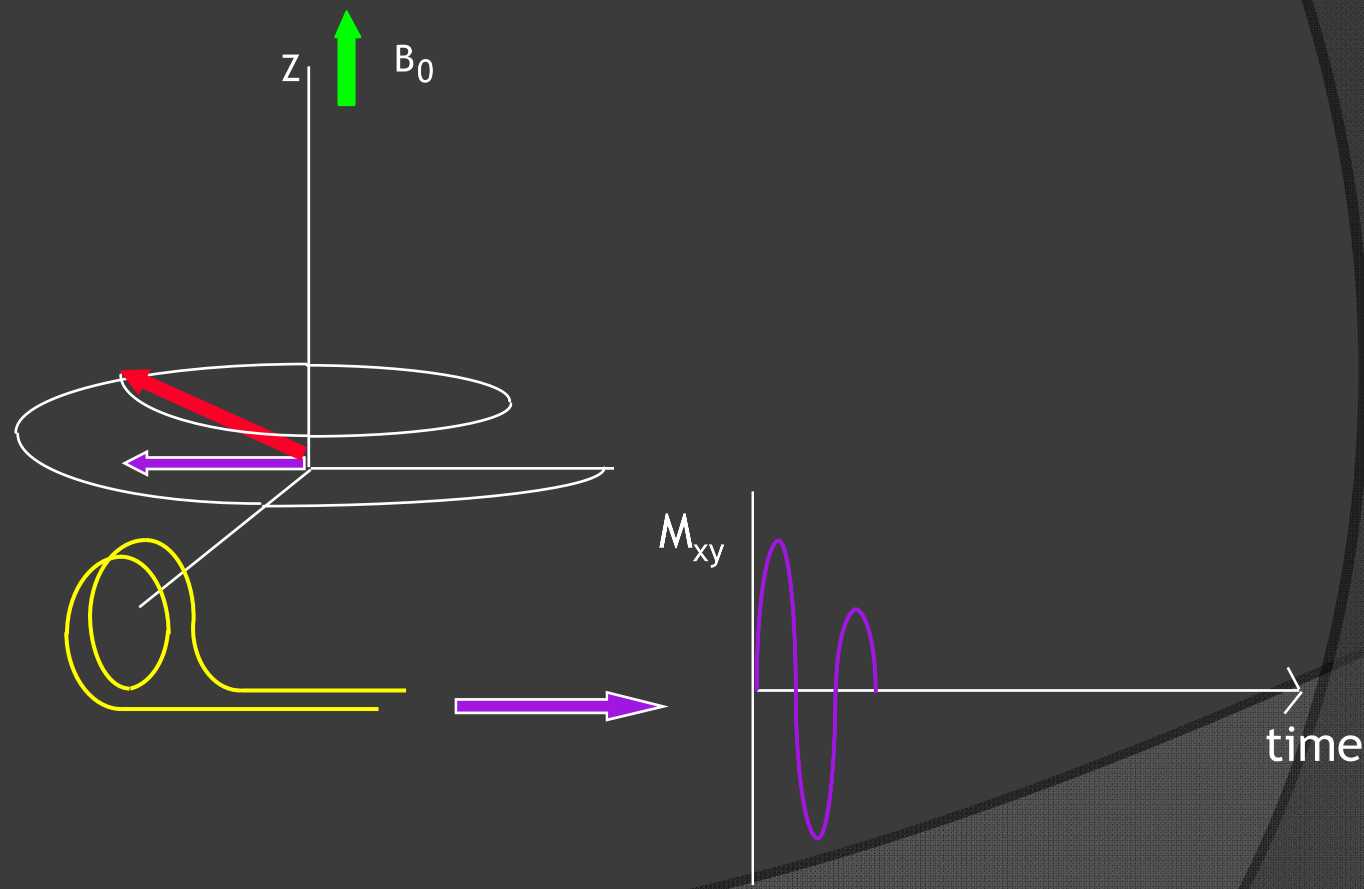


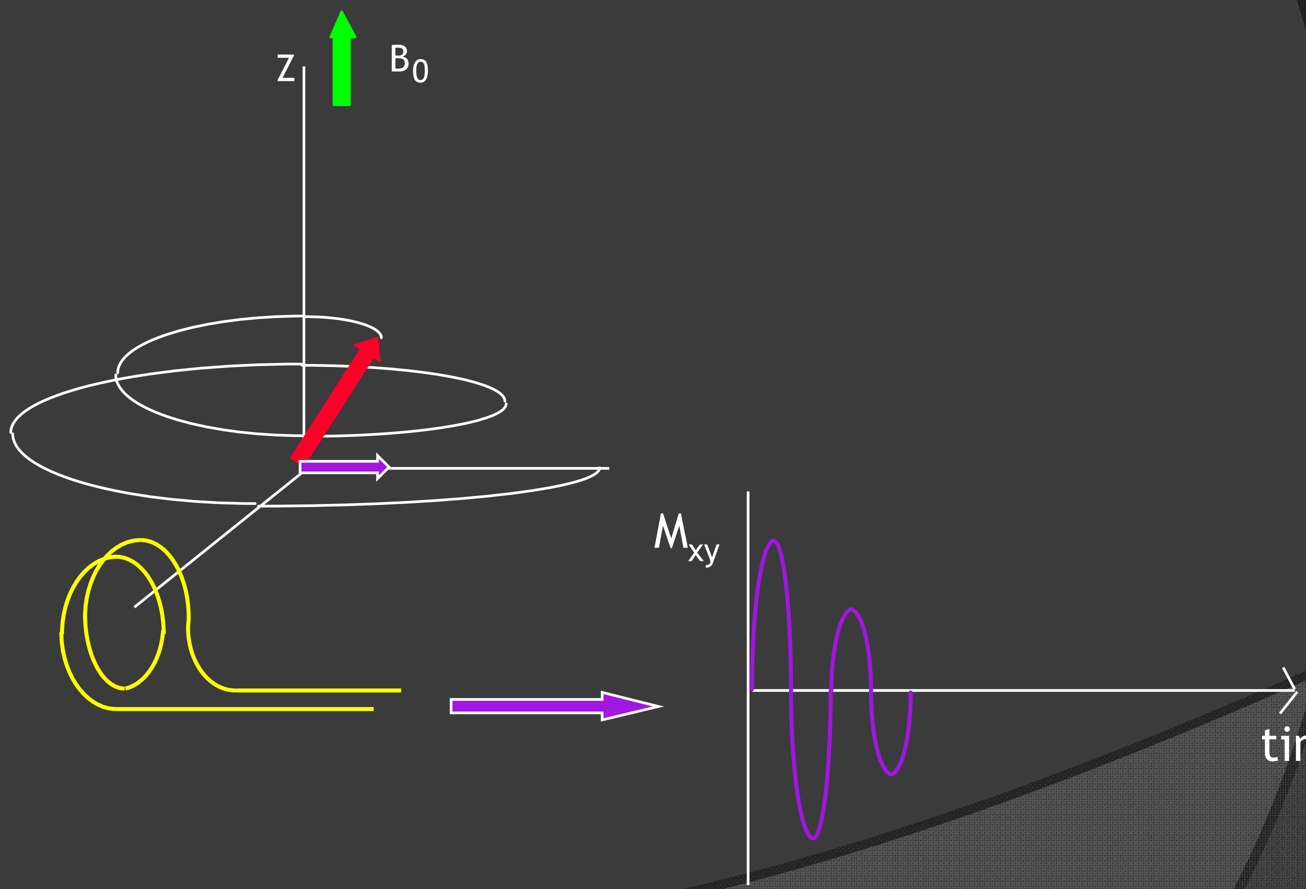
M_+ relaxation "path"

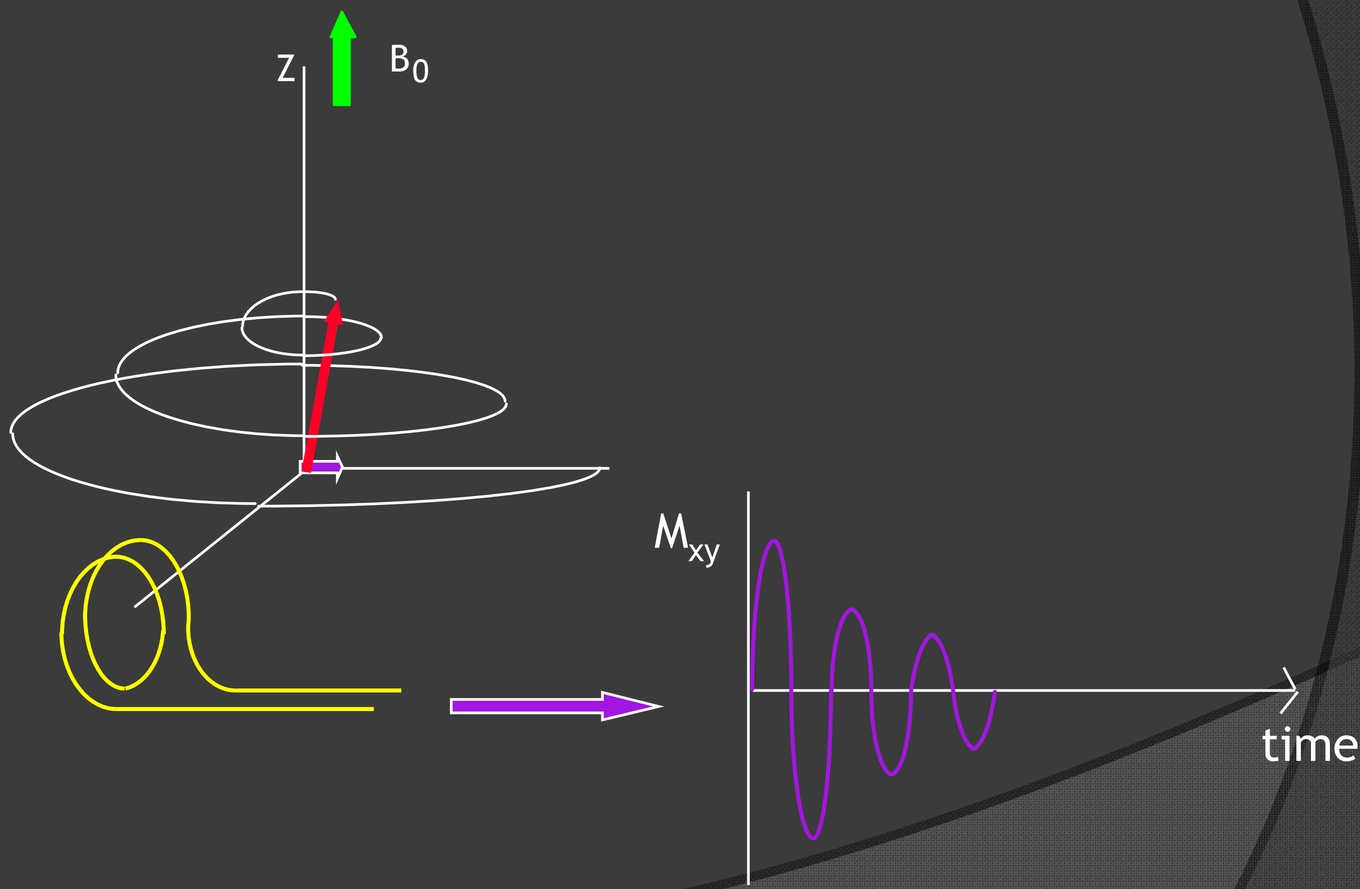


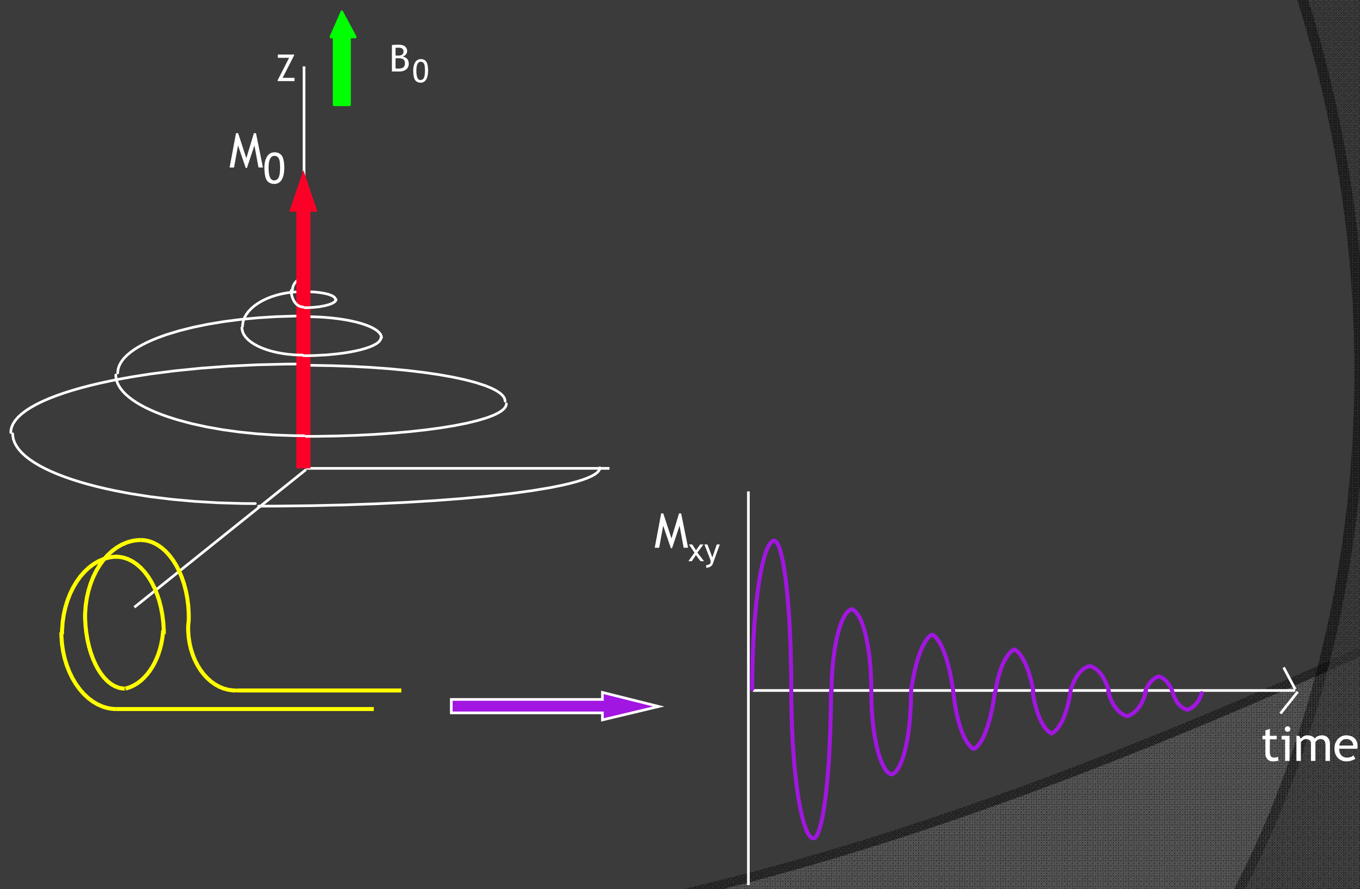

Z
B_o
M_{xy}
M_{xy}
time


Z
B_o
M_{xy}
M_{xy}
time

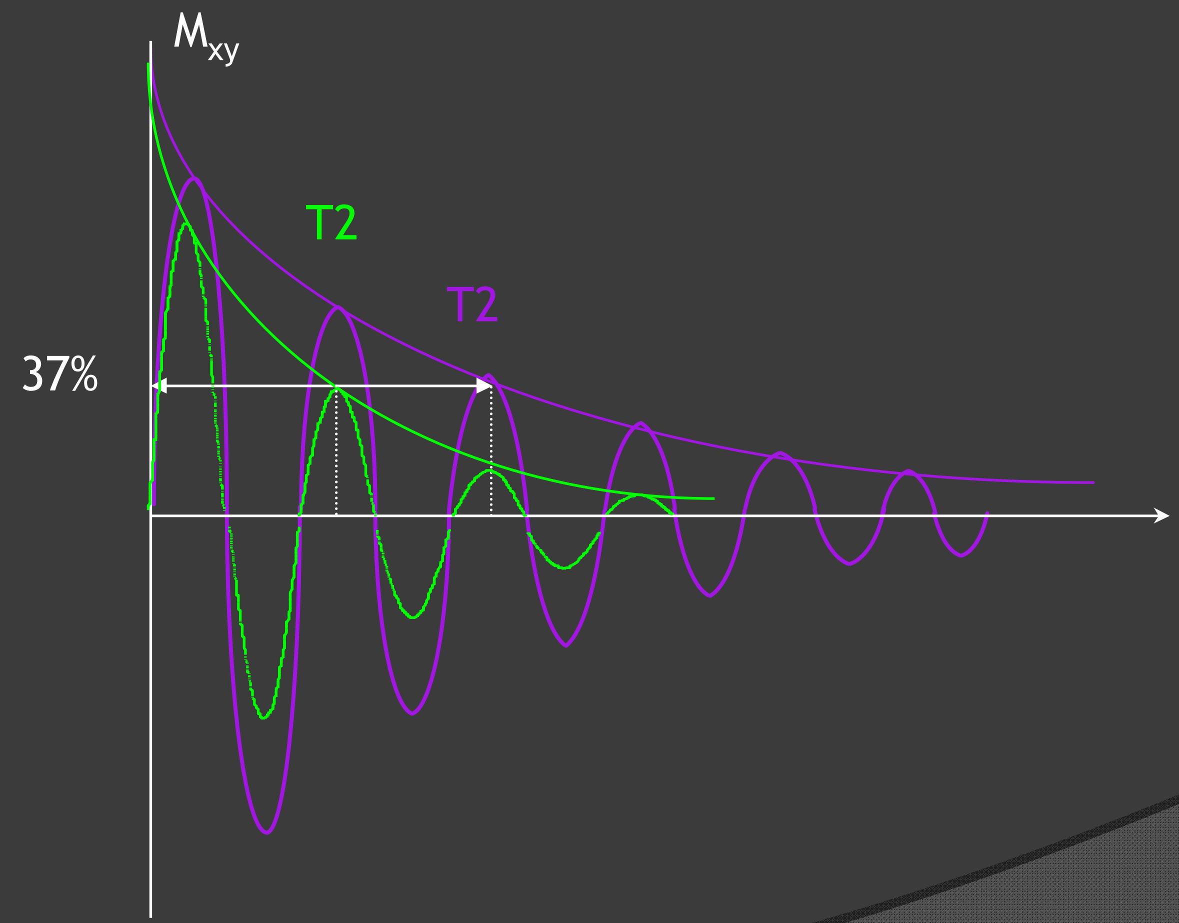

Z
B0
Mxy
time


Z
B_0
M_{xy}
time

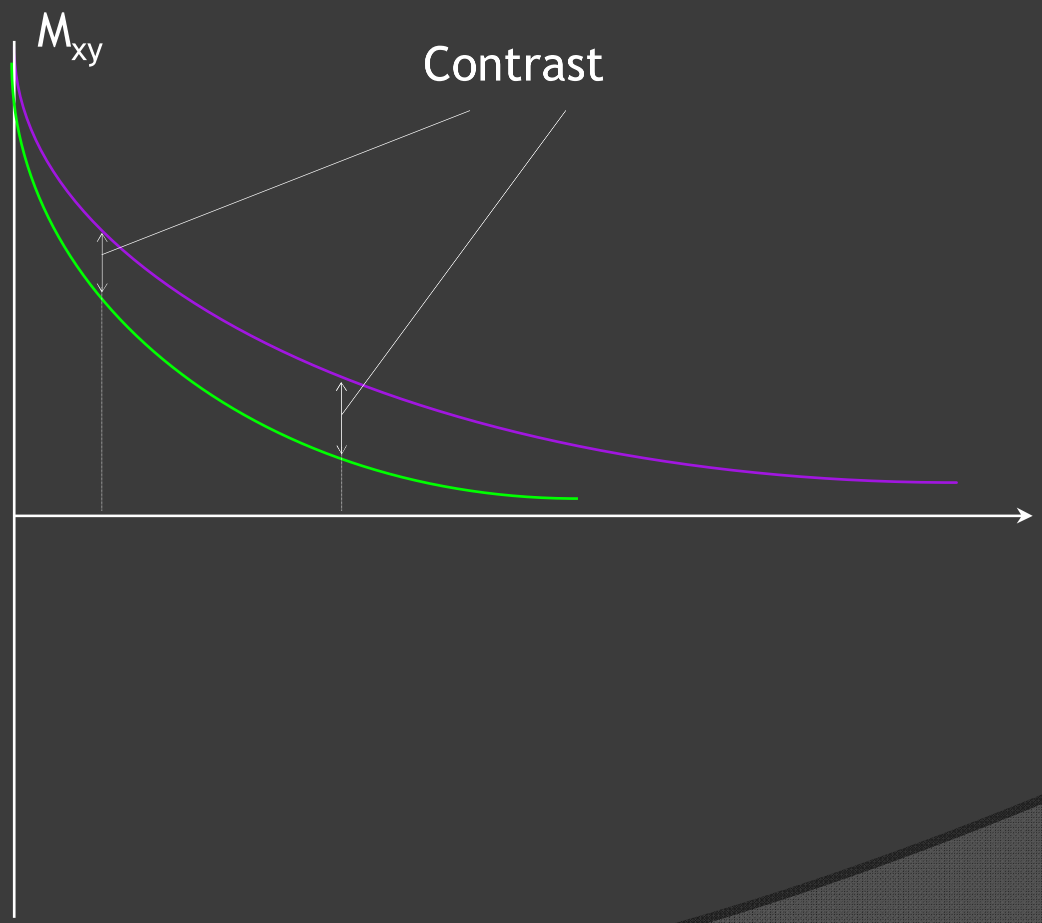

Z
B_0
M_{xy}
time


Z
B_0
M_0
M_{xy}
time

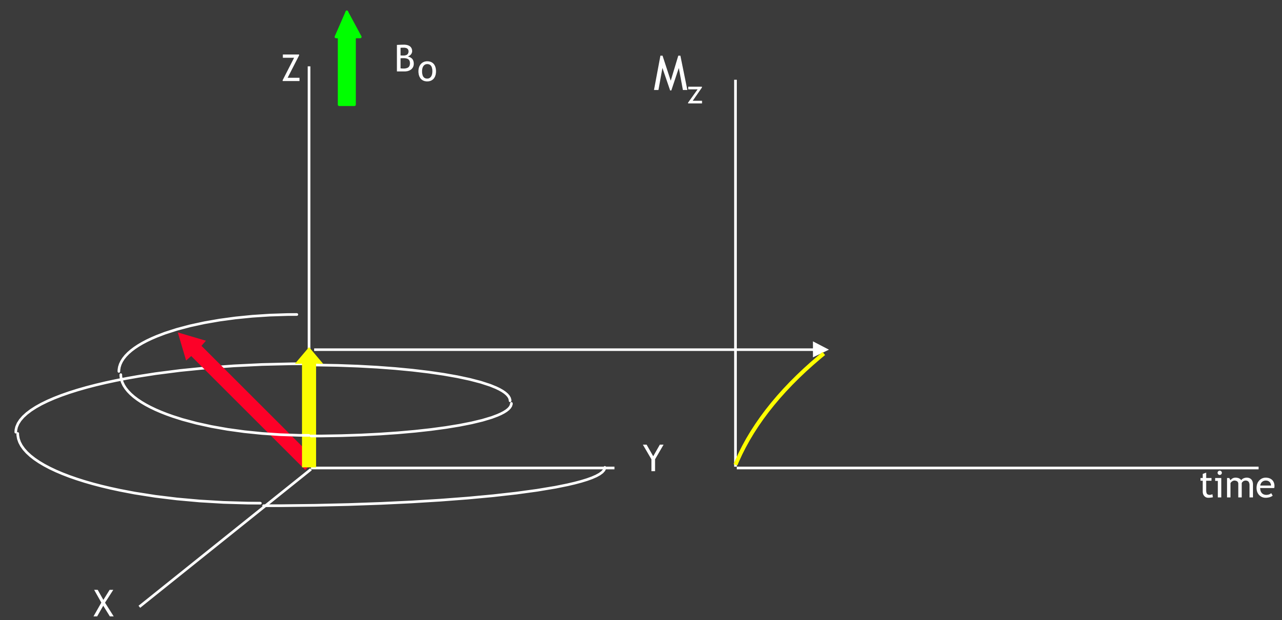
T_2!



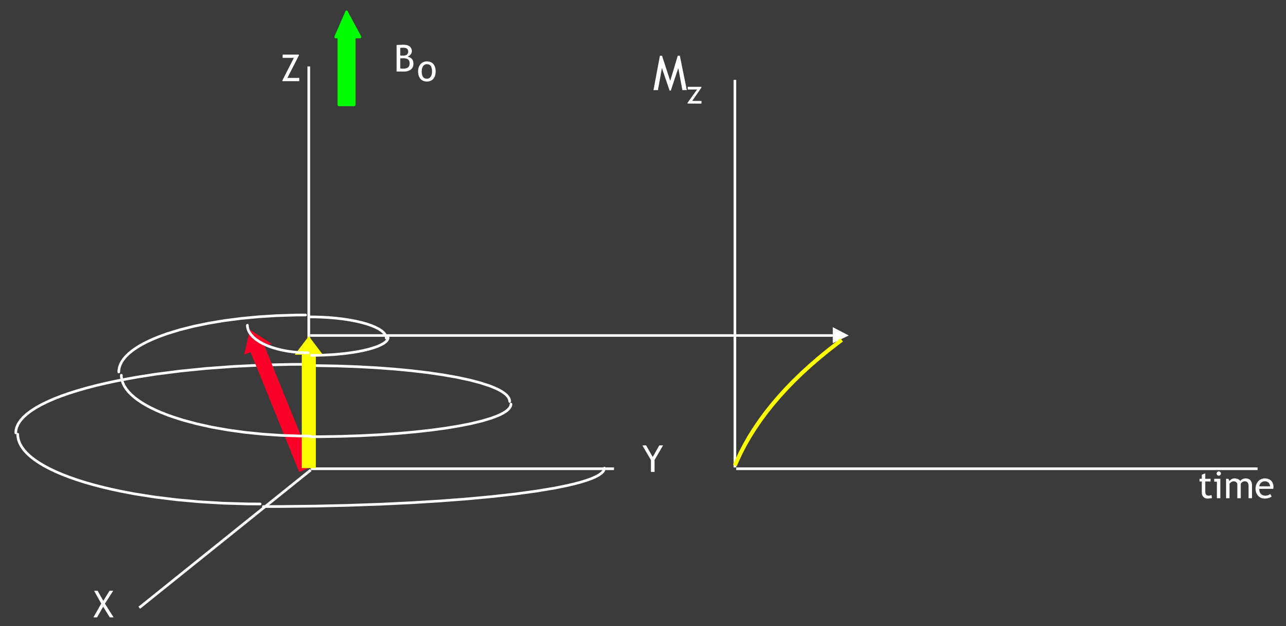
T_2!



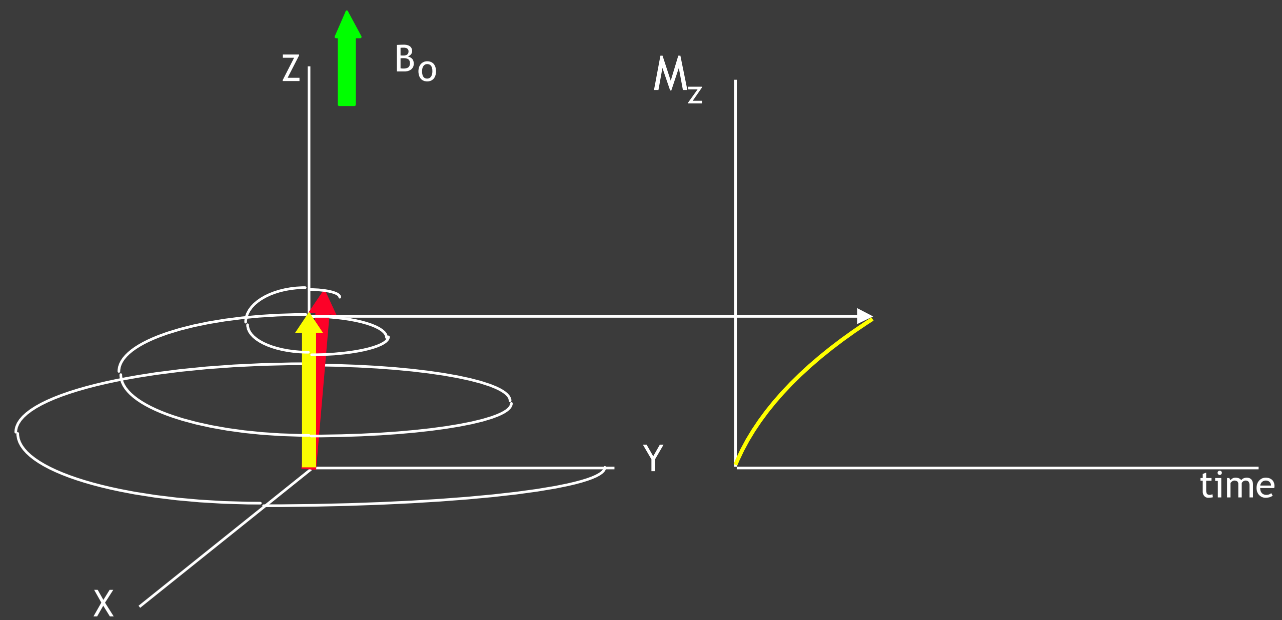
T_1…



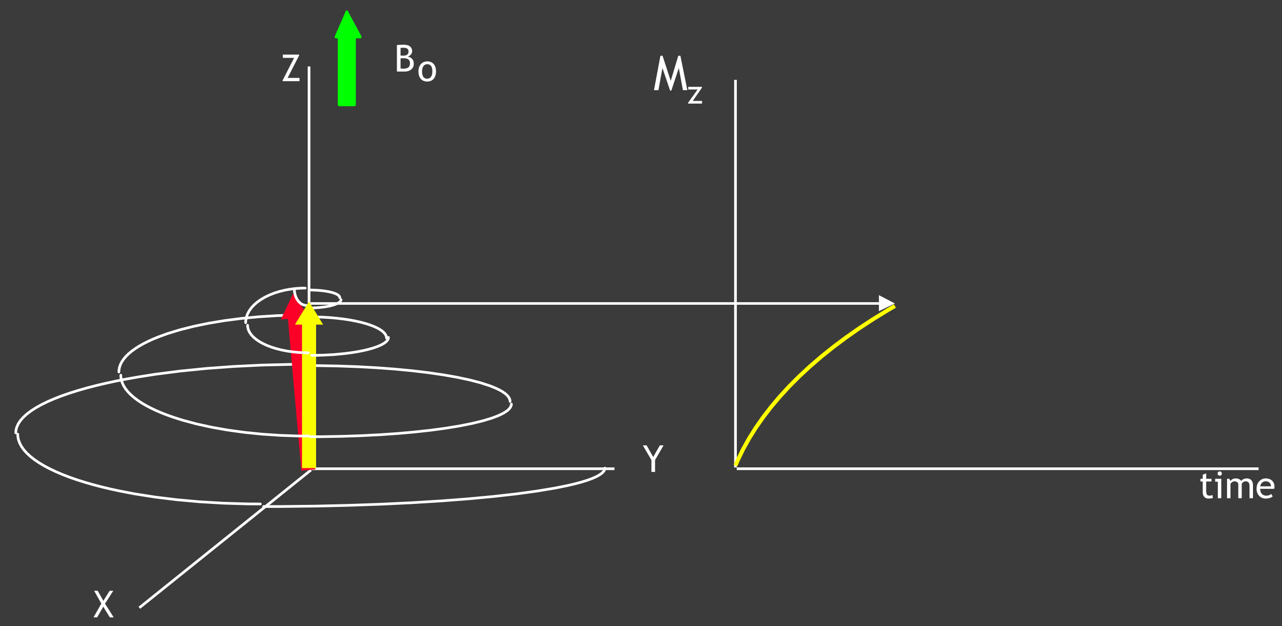
T_1…



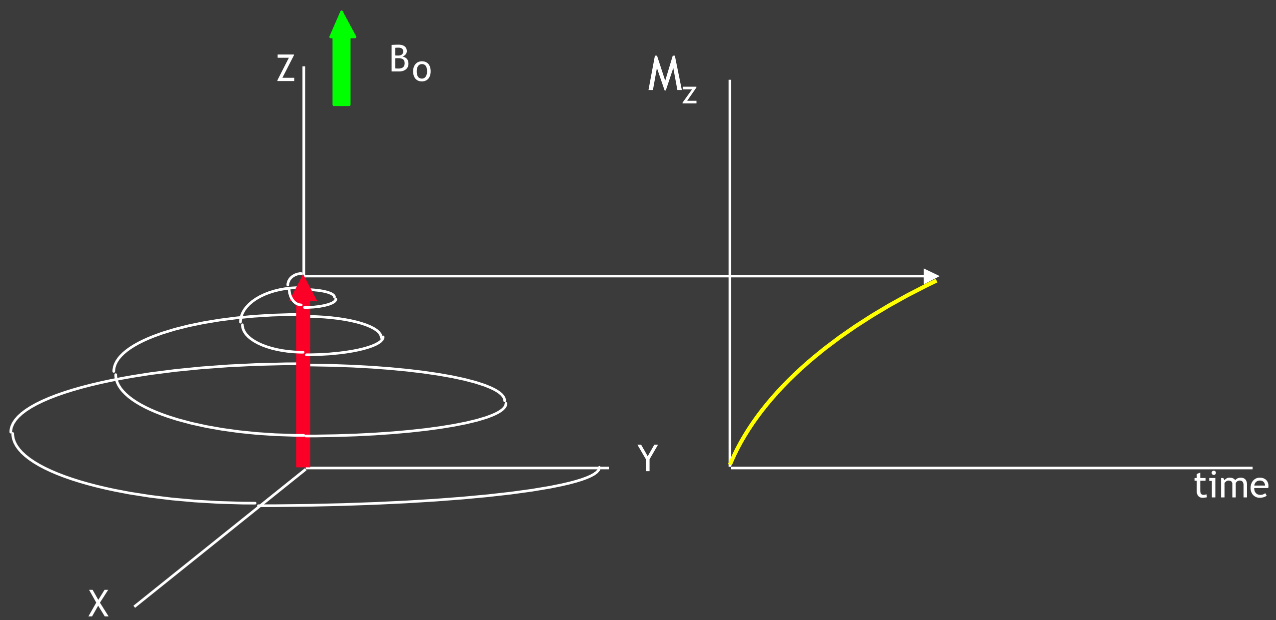
T_1…



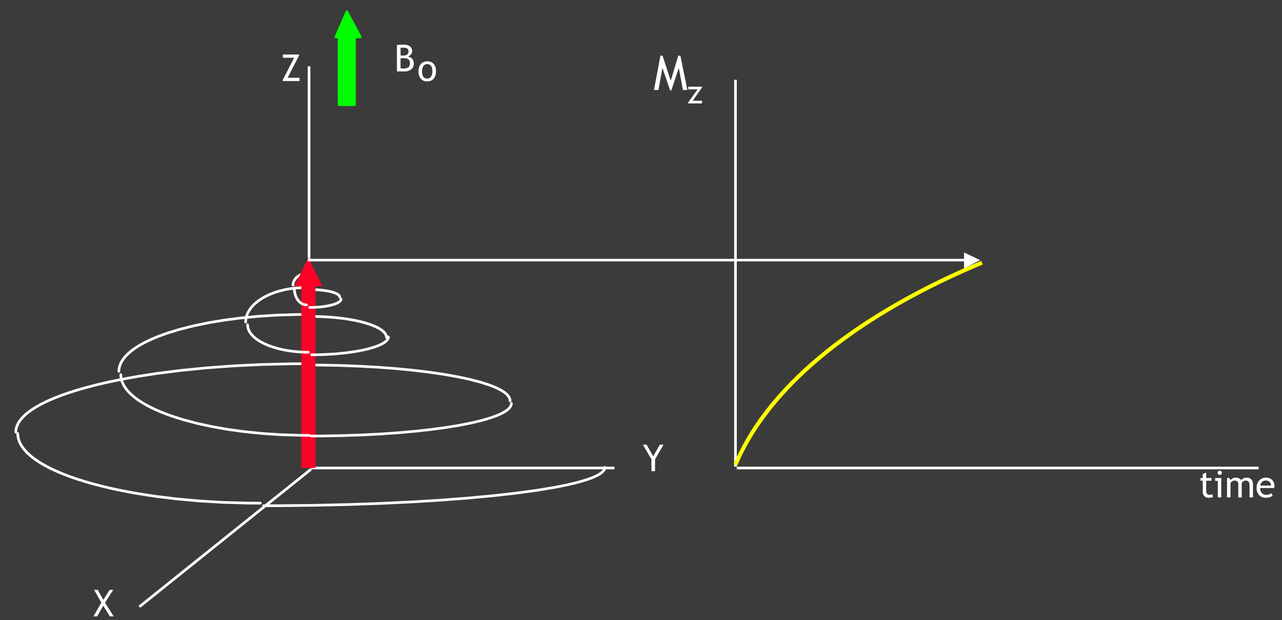
T_1…



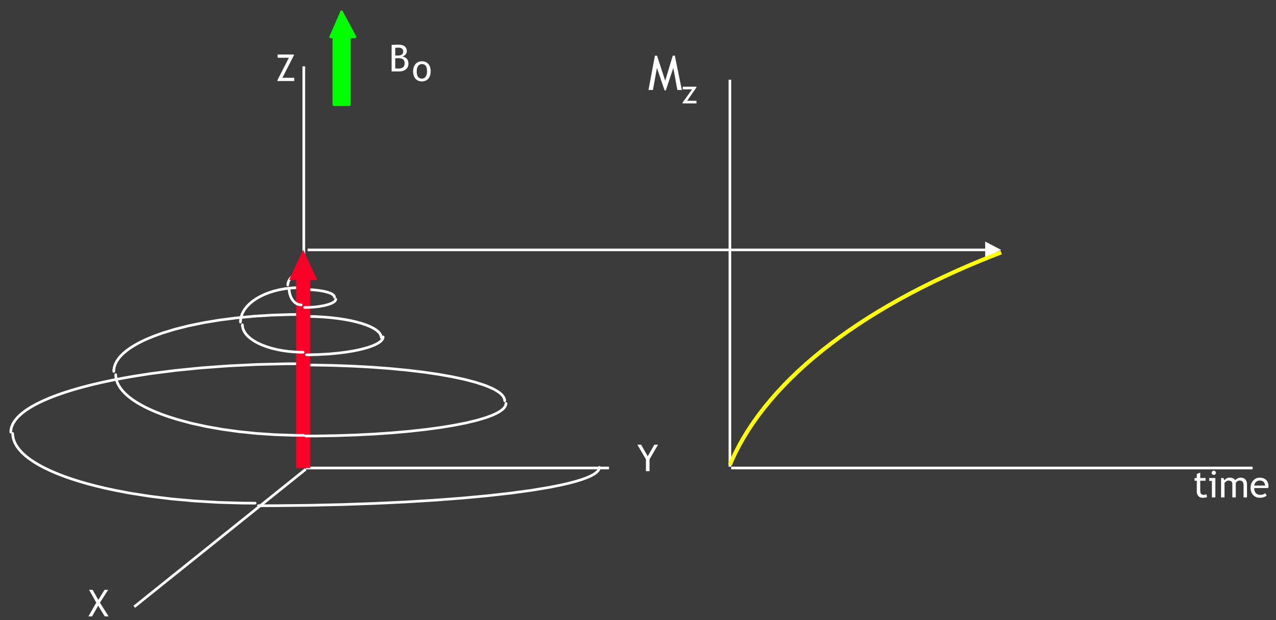
T_1…



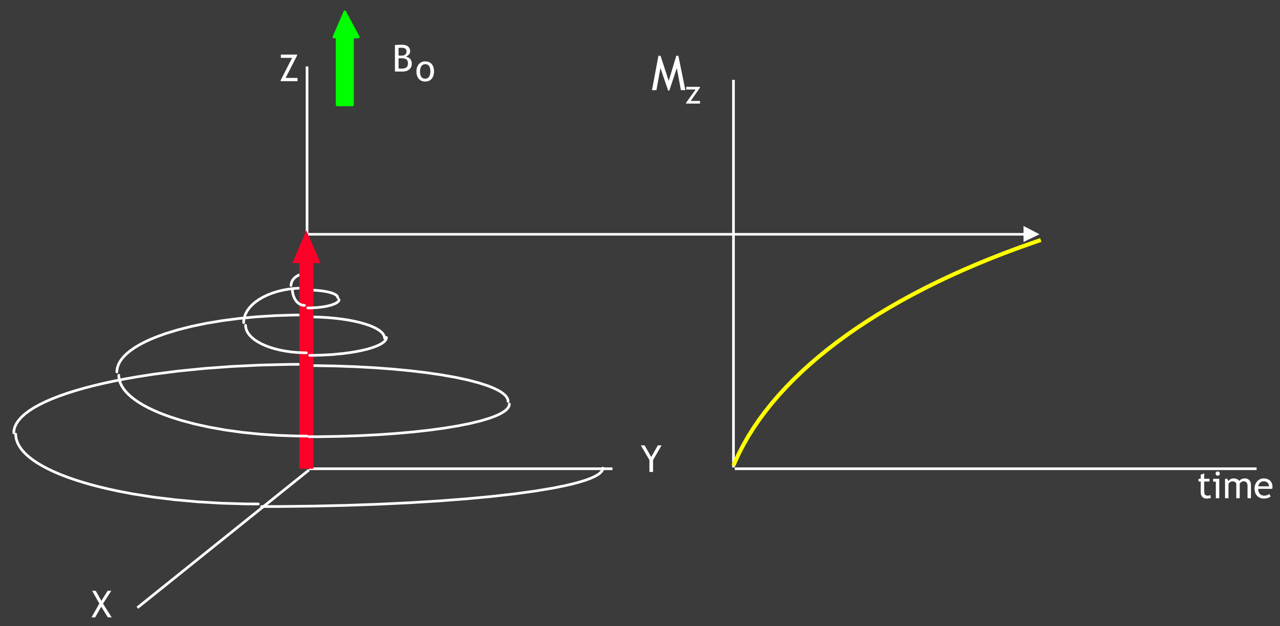
T_1…



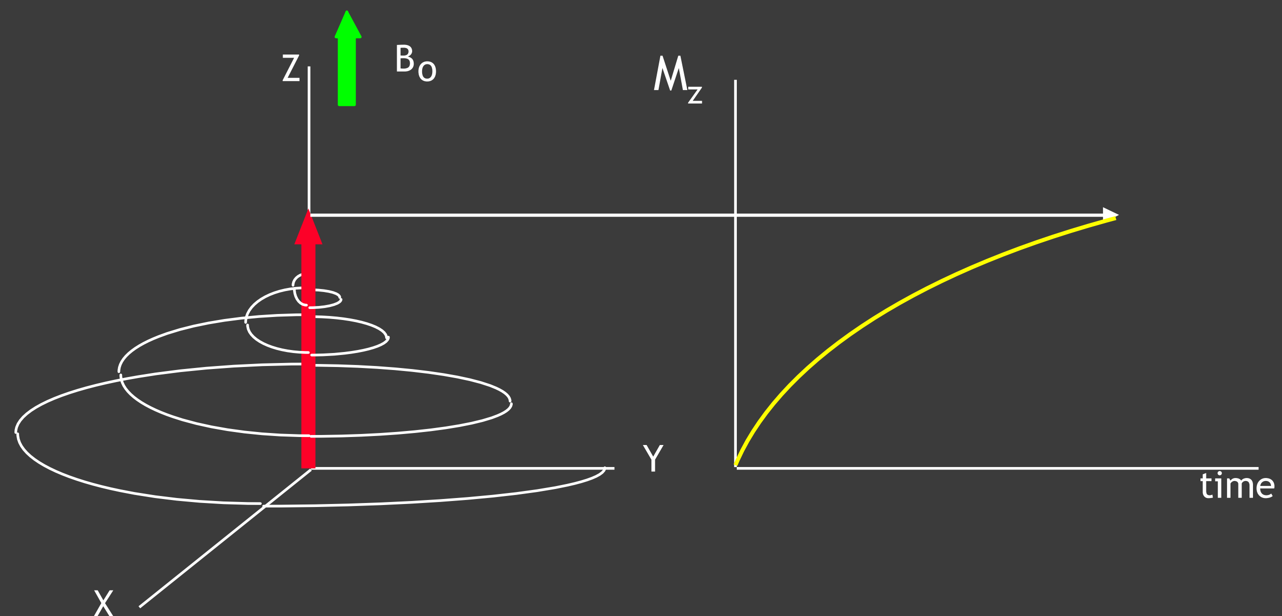
T_1…



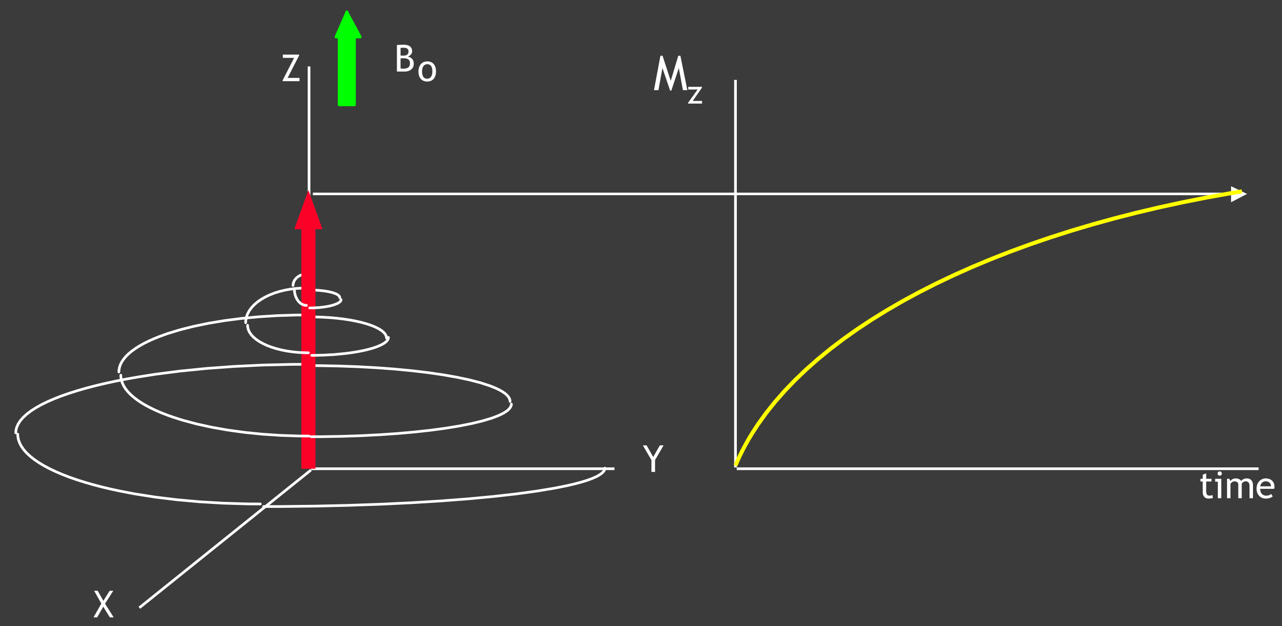
T_1…



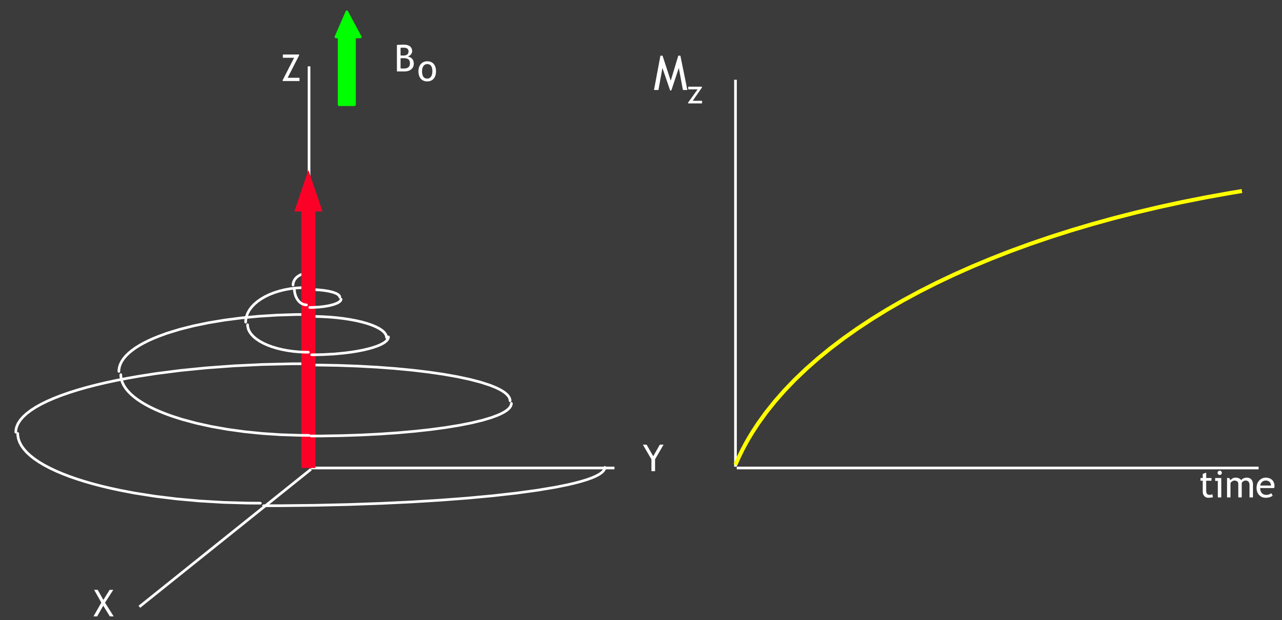
T_1…



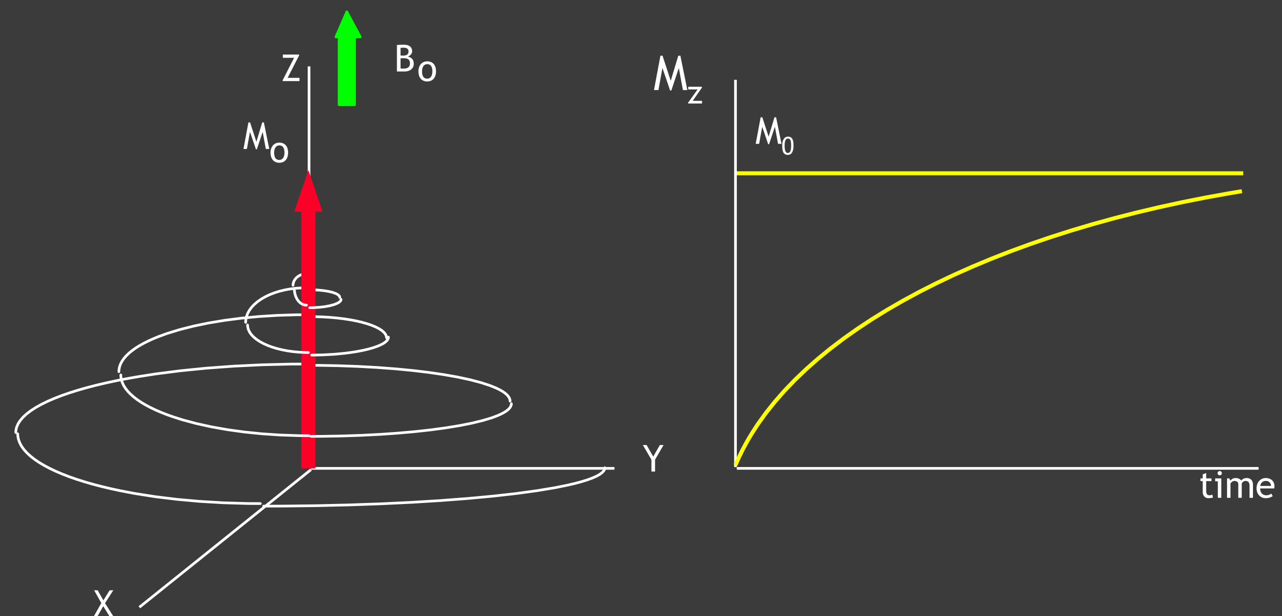
T_1…



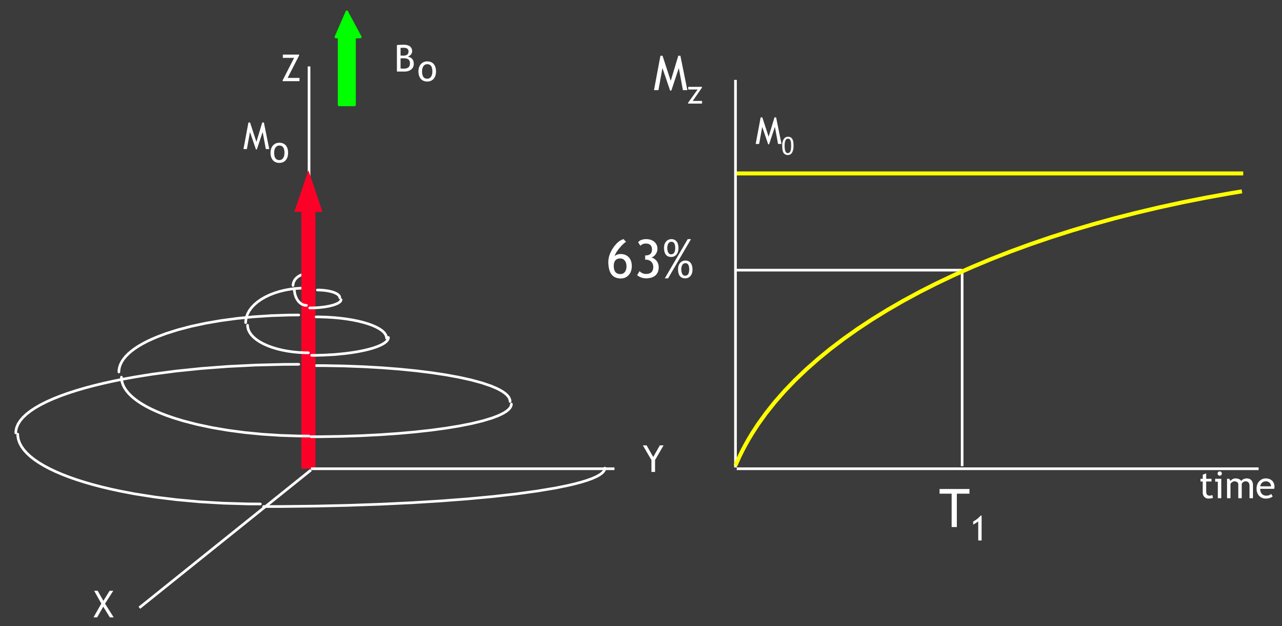
T_1…



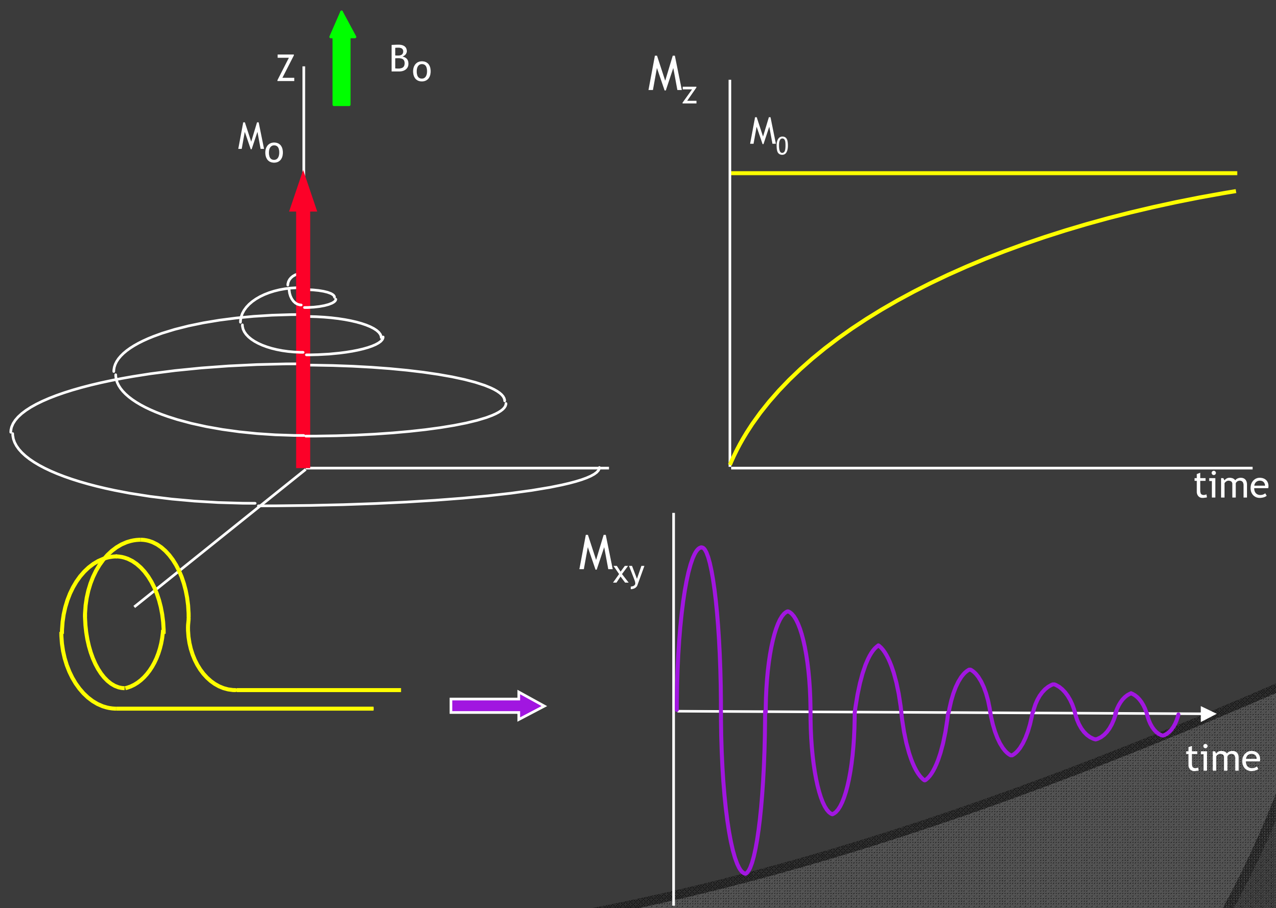
T_1…



T_1!



“transversal” e “longitudinal” relaxation



NMR characteristics of some tissue (at 1.5 *Tesla* and room temperature)

Tissue	Relative proton density	T_1 (ms)	T_2 (ms)
Lipids	1	260	80
Bone marrow	0.4	400	60
White matter	0.85	790	90
Gray matter	0.8	920	100
Blood	0.95	1200	100
CSF	1	>4000	>2000
Cortical bone	<0.1		
Air	<0.01		

Image construction

- The NMR image is not a picture

- Complex map of proton density and relaxation properties…

This is a MRI acquisition

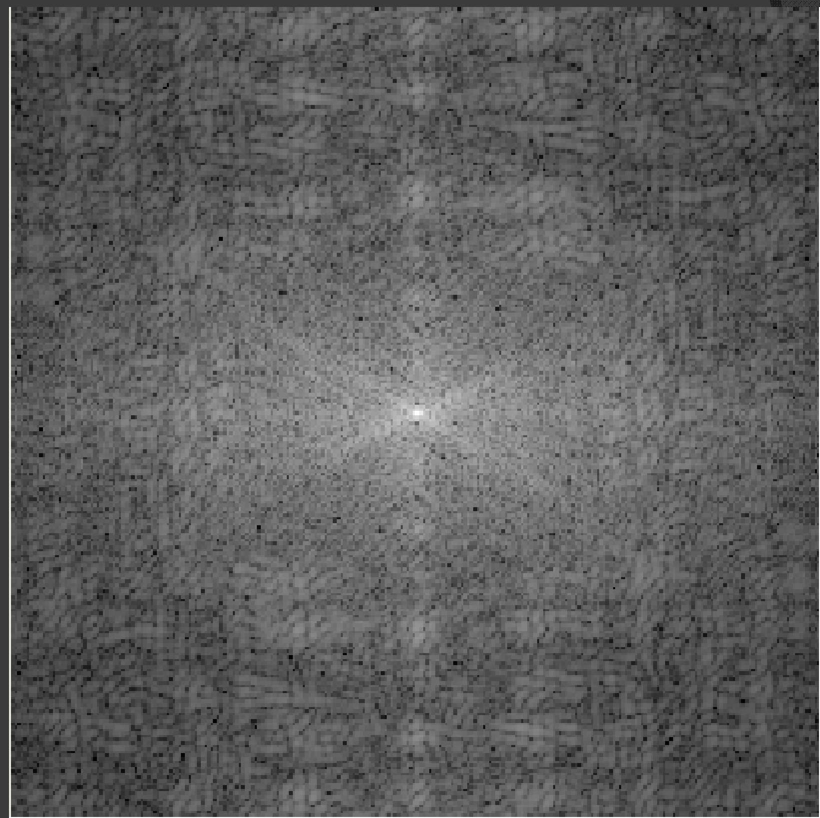
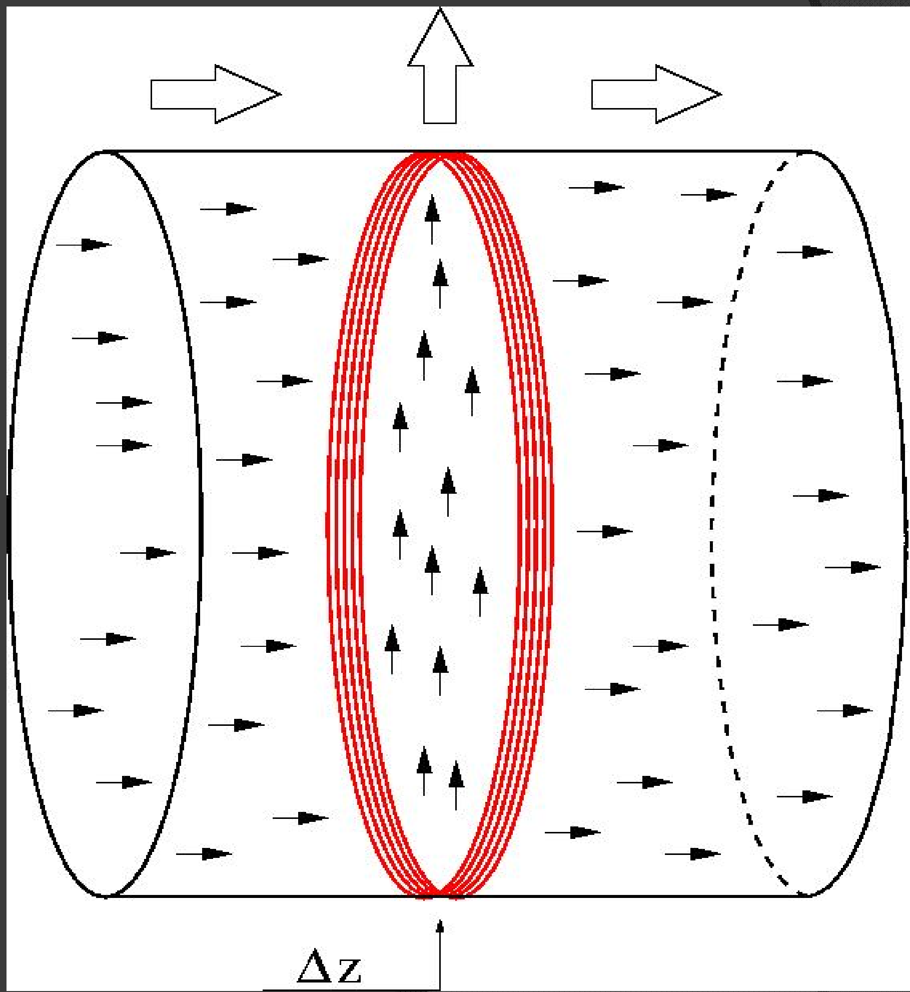


Image construction – 2

- “slice” gradient
- 90° RF-pulse

Selective excitation of a single slice with thickness selected by the *waveform* of the gradient pulse: a magnetization vector M_+ is generated in the plane orthogonal to the static field; M_+ rotates around the static field at the Larmor frequency



“Slice” selection

1. Choice of a slice with center in z_0 (sagittal, axial, coronal, *oblique*)

2. Choice of the thickness (Δz)

3. *Slice-selective RF pulse*: RF-pulse associated with a field gradient to excite the spins *only* in slice between $z_0-\Delta z$ and $z_0+\Delta z$.

Slice selection ("encoding")

- The field gradient changes the static magnetic field along a direction perpendicular to the slice selected: *only in the middle of the slice the magnetic field coincides with B_0*
- At the same time, an RF pulse is generated with frequency $\omega_L = \gamma B_0$ and *time profile close to the Fourier transform od the slice*

Slice selection:RF pulse

- It should be infinitely long (in time) to have the “exact” profile, but
- It cannot last for more than some *ms*, then
- There is an *intrinsic* limit to the spatial risolution

Slice selection: dephasing and rephasing

- The gradient G_z provokes a position-dependent deformation of the magnetic field, therefore:
- Spin dephase along z (in z_0-Δz they have smaller frequency than those in z_0 and even smaller than those in z_0+Δz)
- To correct this error: “counter”-gradient at the end of the RF-pulse to rephase all spins

Slice encoding: $B_1(t)$ and $G_z(t)$

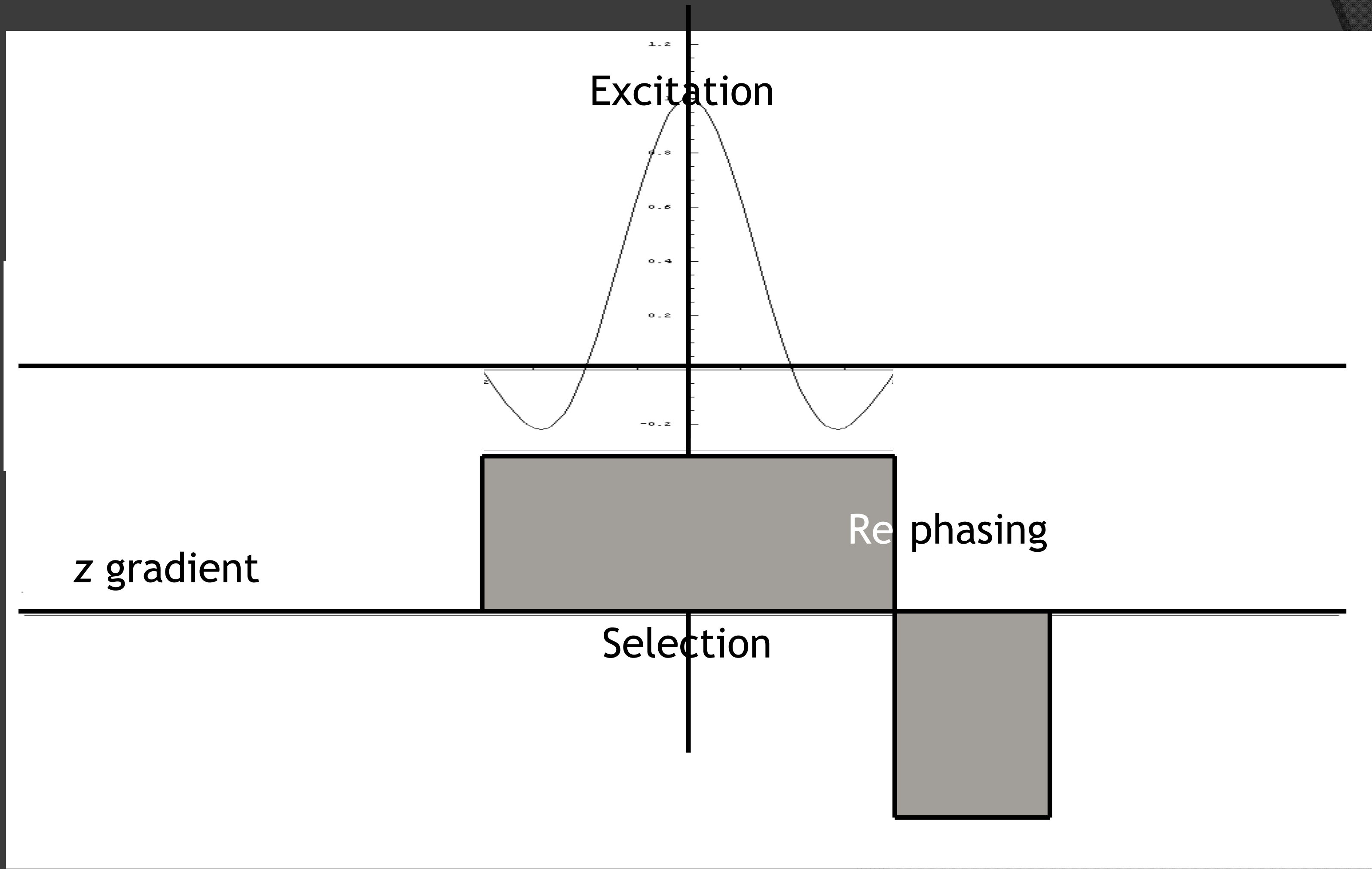


Image construction – 3

- Slice gradient
- 90° RF pulse

- Phase encoding (pixel phase proportional to its position along the gradient)

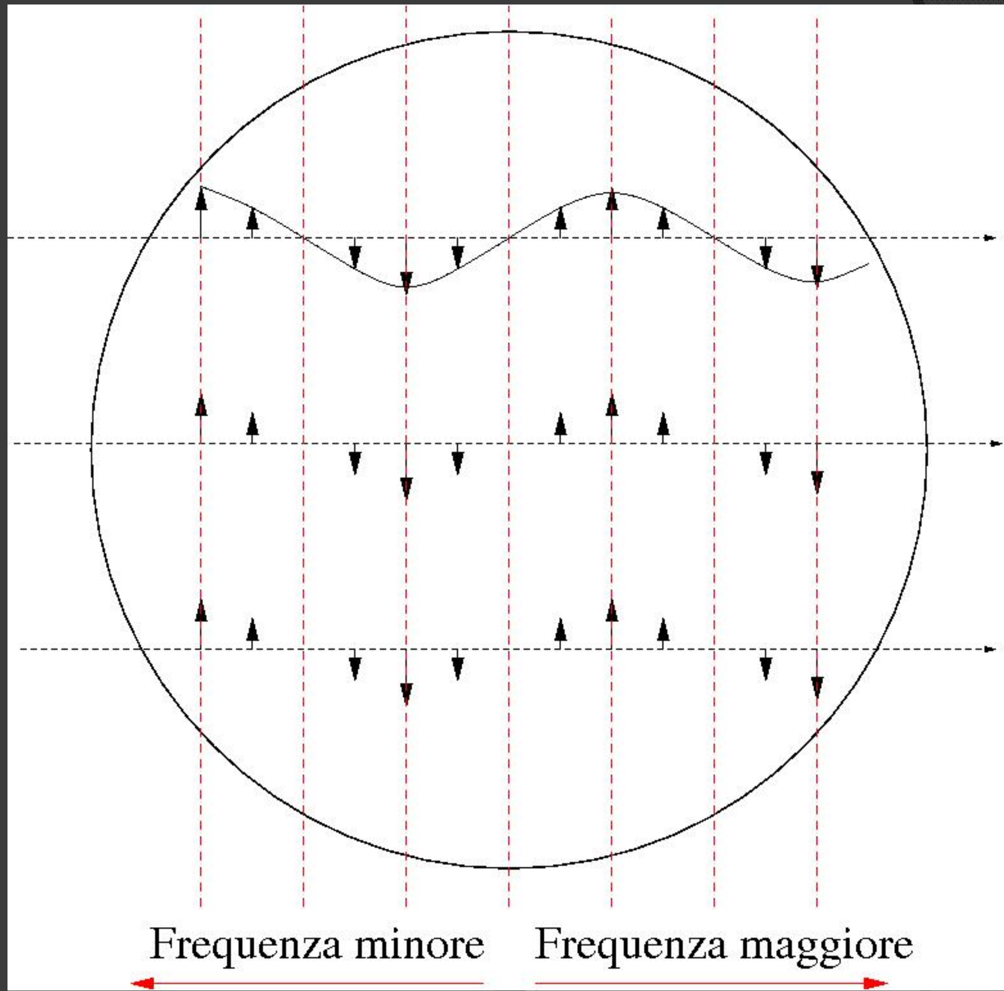


Image construction – 3

- Slice gradient
- 90° RF pulse

Selective excitation of a slice (with definite thickness) with generation of a trasverse magnetization rotating around the static field

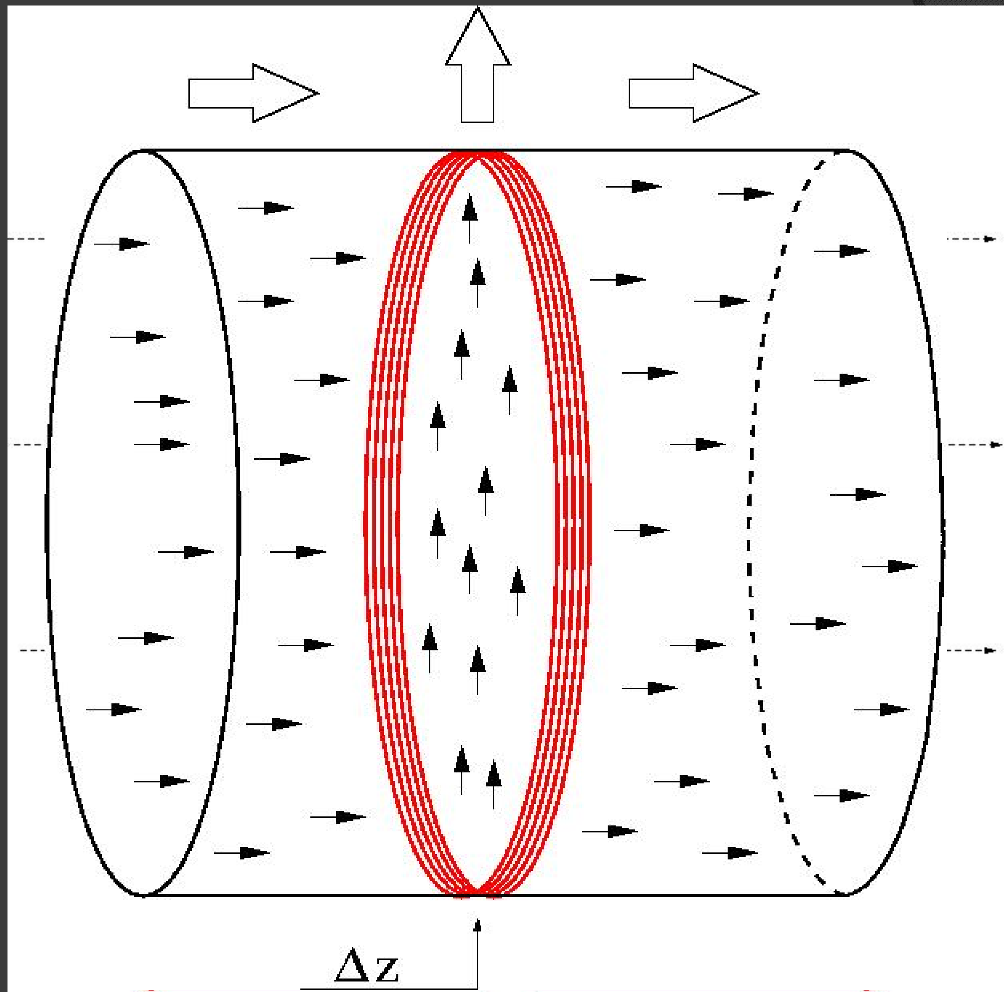
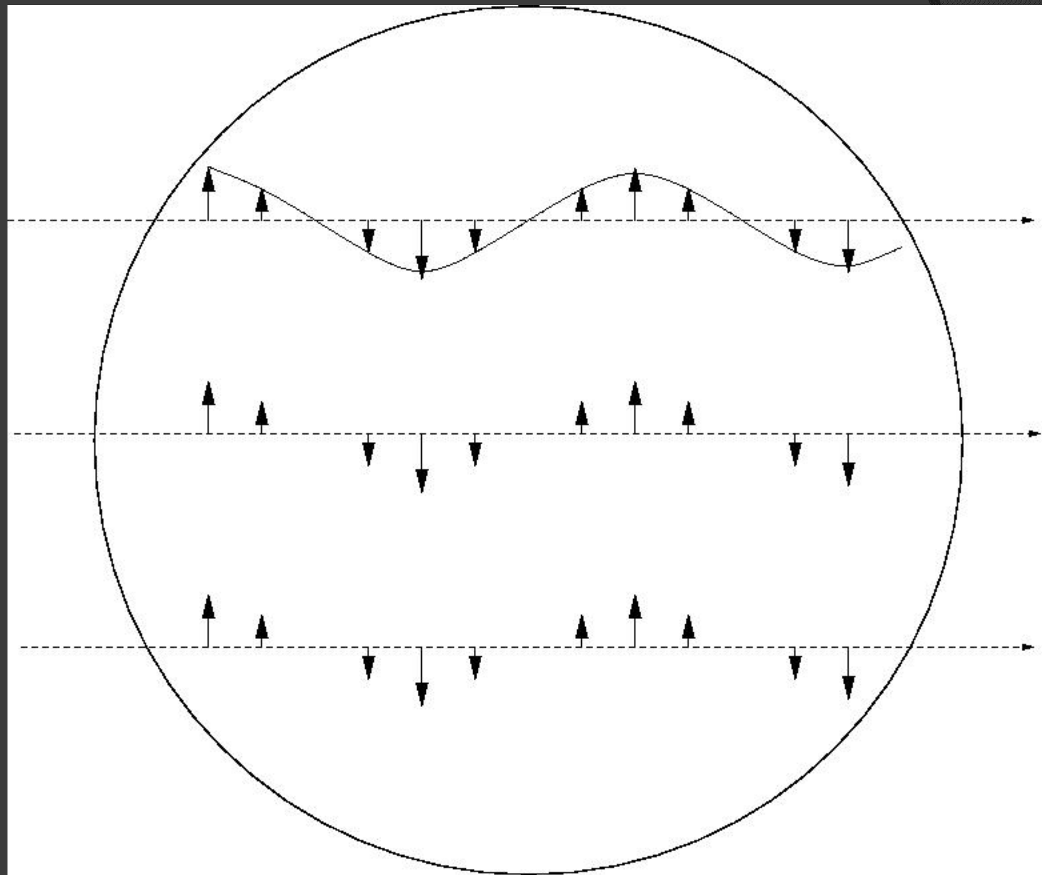


Image construction – 3

- Slice gradient
- 90° RF pulse



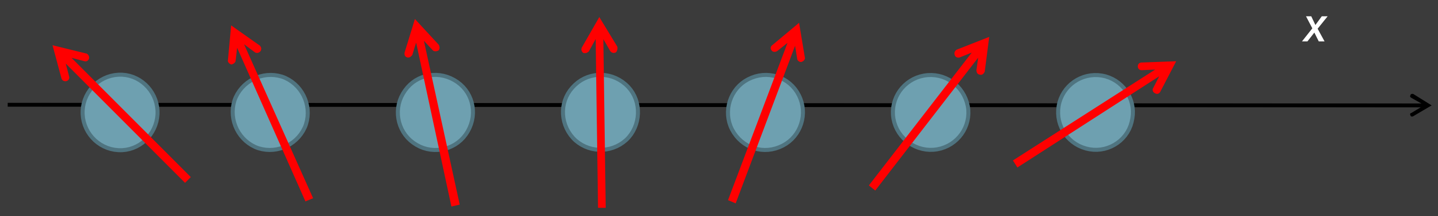
- Frequency encoding
- Signal detection

Encodings

- In a slice, each pixel is identified by two coordinates *(x,y)*
- We need to associate each coordinate to a measurable (independent) quantity
- In MRI, the receveid signal has already two intrinsic parameters: *phase* φ and *frequency* ω
- We need only to find a way to associate $(\varphi,\omega)\rightarrow(x,y)$

Phase encoding

- If we switch on a gradient (say, G_x) for a time T_φ, the spins will acquire different phases depending on their position along x



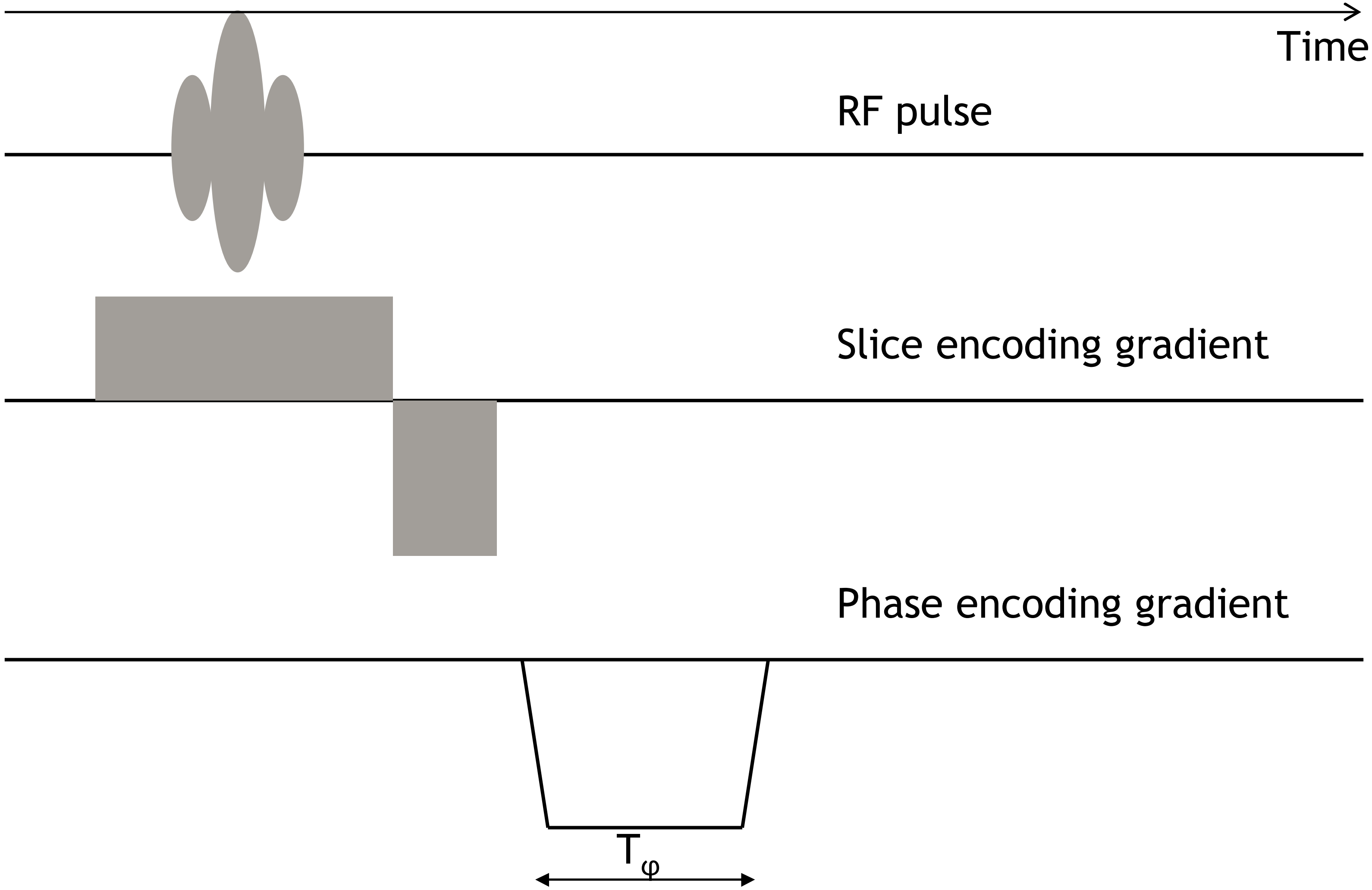
i.e.: after a time T_φ, they will all rotate at the same speed but some will be "ahead" and others will be be "behind". A spin in x will have phase

$$\varphi(x) = -\gamma G_x x T_\varphi$$

Phase encoding – 2

- Having an RF detector "in quadrature" (two coils at π) x, it is possible to determine from where a wave has come…
- Now, we need the y coordinate…

Slice and phase encoding



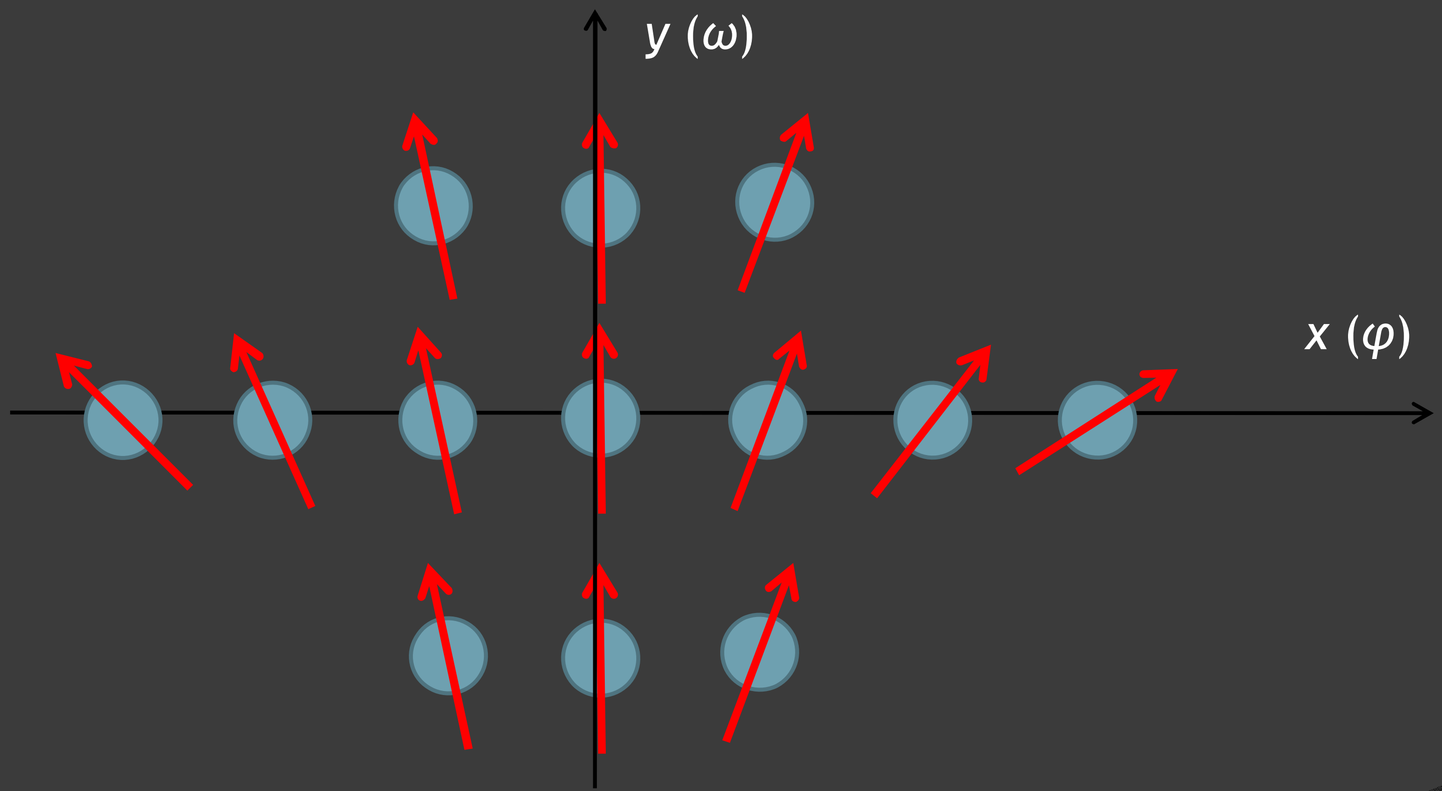
Frequency encoding (read-out)

- We excited selectively a slice (using B_1+G_z) keeping the spins in phase
- Next, we assigned a position-dependent phase at each spin along x (using G_x for a time T_φ)
- It remains to encode y: we obviously use the second independent parameter of a wave, *i.e.*, the *frequency*
- Finally, we will find a way to register the signal…

Frequency encoding

- Switching on the G_y-gradient, spins along y will feel a different magnetic field in different positions
- As a consequence, they will have different Larmor frequency!

Frequency encoding



In other words: we associated to each volume element (*voxel*) 2 coordinates (phase, frequency)

Read-out…

- We need now to register the signal…
- But we spent *a lot of time* for the spatial encoding…
- The signal has decayed exponentially with time as e^{-t/T_2^*} and we don't have anything to read…

Hahn echoes…

- In 1950, Erwin Hahn excited a sample with *two* 90° RF pulses separated in time by τ
- *Incidentally*, he observed an intense signal at time 2τ
- He called it *spin echo*…

Spin echoes

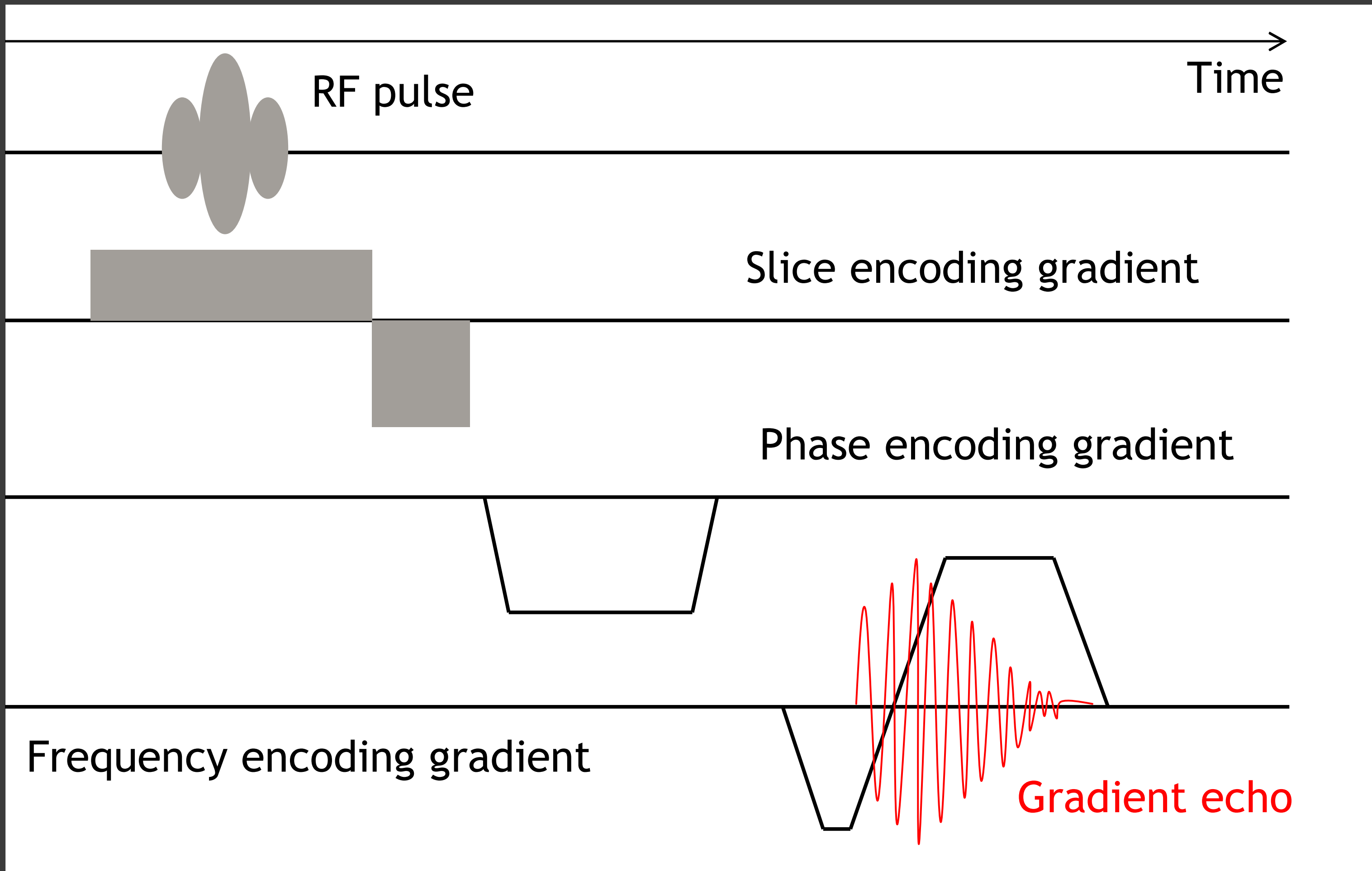
- In MRI, the pulse sequence used to generate echoes has been designed by Purcell and realized by Carr (90°-180°)

- The 180° pulse is called *refocusing pulse* and has the effect to cancel out the decay due to inhomogeneities and disuniformity (T_2^*)

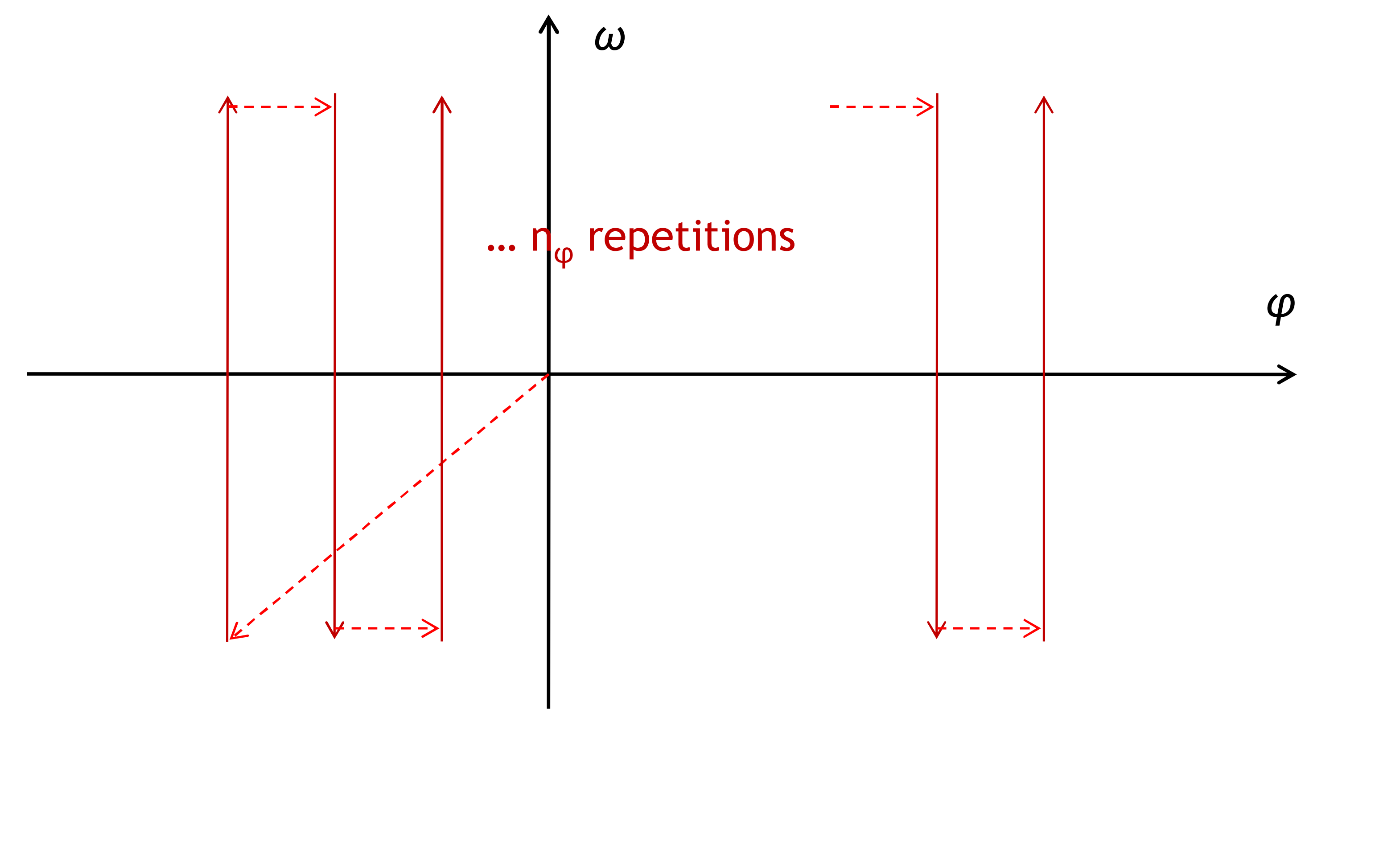
Read-out - 2

- The frequency-encoding gradient has two uses:
  - If inserted in a 90°-180° sequence, it is applied *at* the Echo time
  - If inserted in a suequence without the 180° pulse, it is deformed in such a way *to generate itself a spin echo* (called gradient-echo)

Gradient Recalled Echo – GRE



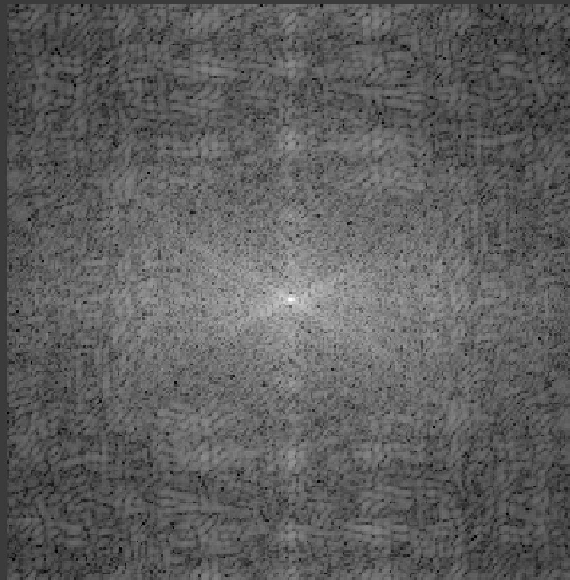
“*k* space”



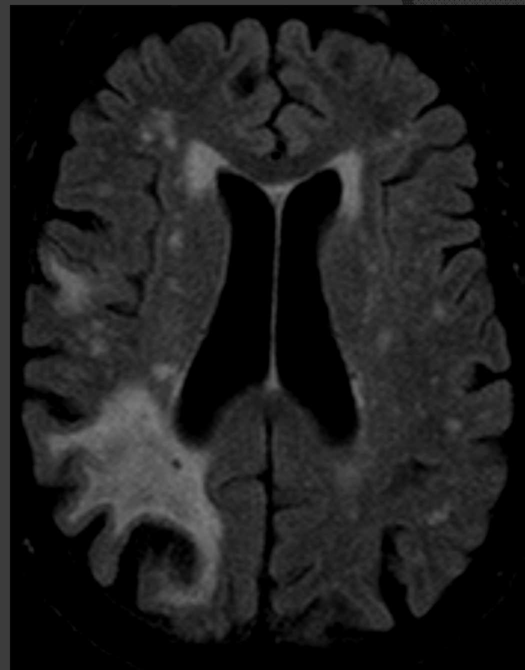
- *k* – space has a simple interpretation (similar to "normal modes in phase transitions")
- Low frequency→long waves: no spatial details, properties common to large regions (contrast resolution)
- High frequency→short waves: great detail but no information at large distance (spatial resolution)

Image construction - 4

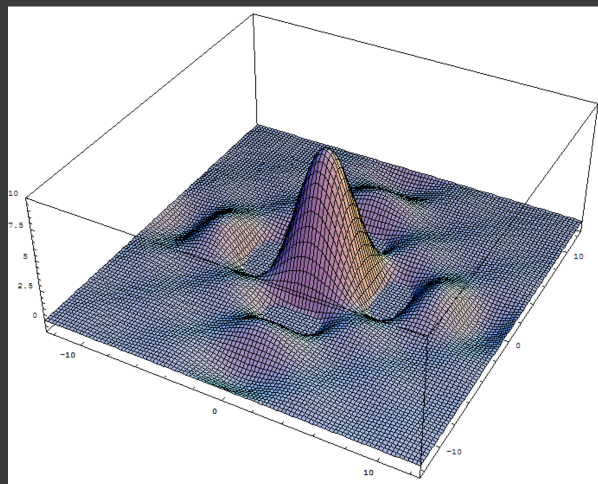
- Slice gradient
- 90° RF-pulse



- Phase encoding



- Frequency encoding
- Read-out



Fourier… what?

- mathematical operator able to extract the frequency content of a function

- function $f(x) \rightarrow$ "symphony"

- Fourier-transformed function $F(k)=F[f(x)](k) \rightarrow$ "sheet music"

- Fourier transform $\rightarrow$ "orchestra"

The orchestra change a mysterious ensemble of symbols (frequencies, Intensities…) in a easily recognizable entity…

Modern *3T* MRI

Three-parameter imaging (at least…)

- Repetition Time: T_R
  - Interval between two RF excitation pulse
    - Parameter: T_R / T_1

- Echo Time: T_E
  - Interval between excitation and read-out (peak of the echo)
    - Parameter: T_E / T_2

- Proton Density: ρ

“Contrast”

- Possibility to distinguish different structures by difference in signal intensity (i.e.: water vs lipids –*chemical shift*; water vs blood –*Iron content*…)

- Higher $S/R \rightarrow$ higher C/R

- Sequence-dependent (*Spin Echo, Gradient-Recalled Echo, Turbo Spin Echo, Spoiled-Gradient 3D Echo…*)

- Parameter-dependent (Repetition Time, Echo Time, Inversion Time, Flip angle, Echo-Train Length…)

GRE: contrast

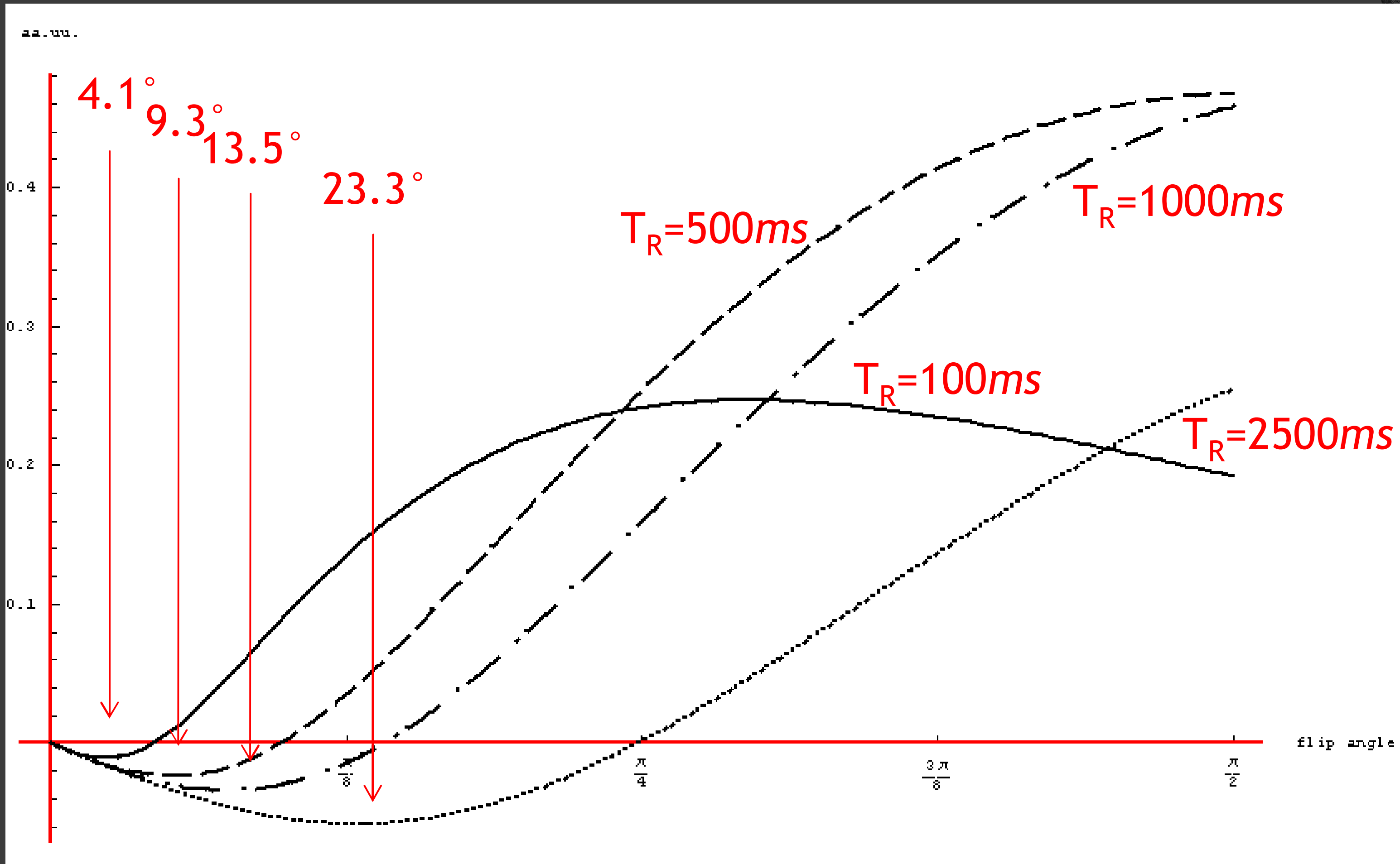
$$\mathcal{S}^{(x)} \propto \rho_{DP,x} \frac{1-e^{-T_R/T_{1,x}}}{1-\cos\alpha e^{-T_R/T_{1,x}}} \sin\alpha e^{-T_E/T^*_{2,x}}$$

$$\mathcal{S}^{w+f} = \rho_{DP} \frac{1-e^{-T_R/T_{1,w}}}{\qquad\qquad {}_{1,w}} \sin\alpha e^{-T_E/T^*_{2,w}}$$

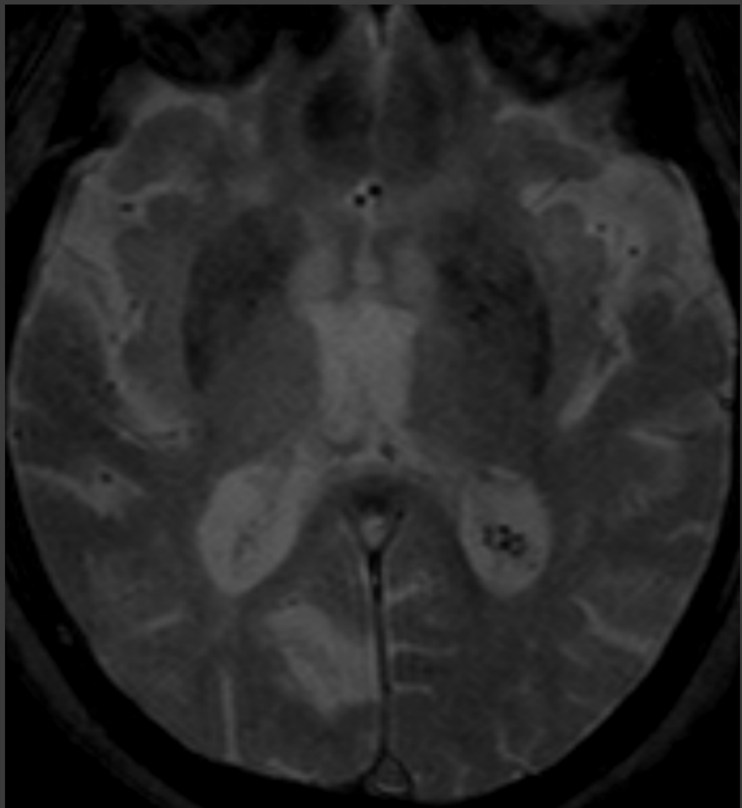
$$\frac{1}{T_2^*} = \frac{1}{T_2} + \frac{1}{\gamma \Delta B}$$

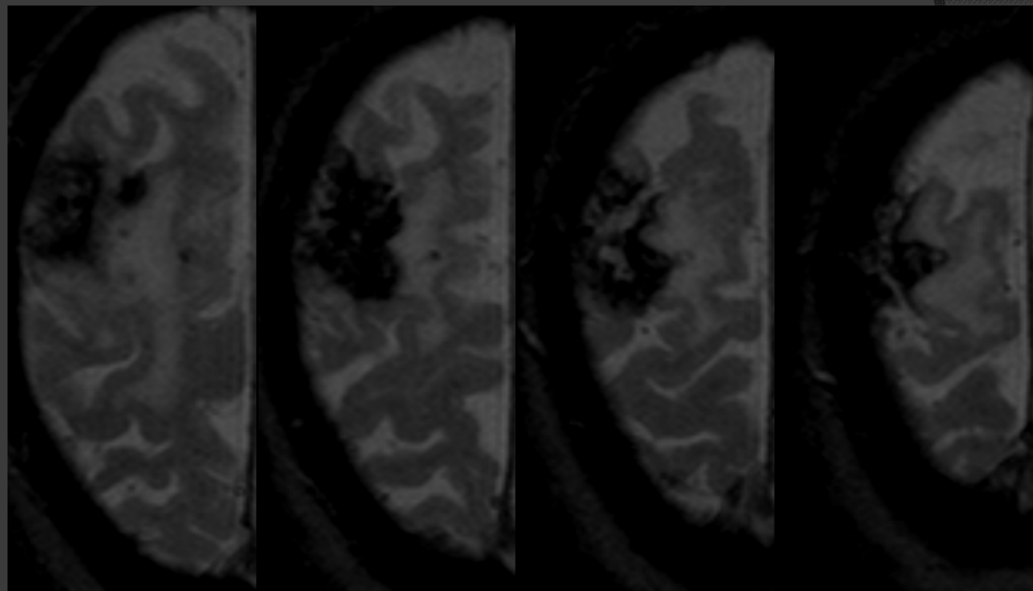
$$+ \quad \rho_{DP,f} \frac{1-e^{-T_R/T_{1,f}}}{1-\cos\alpha e^{-T_R/T_{1,f}}} \sin\alpha e^{-T_E/T^*_{2,f}}$$

GRE contrast: $T_E \approx 24ms$

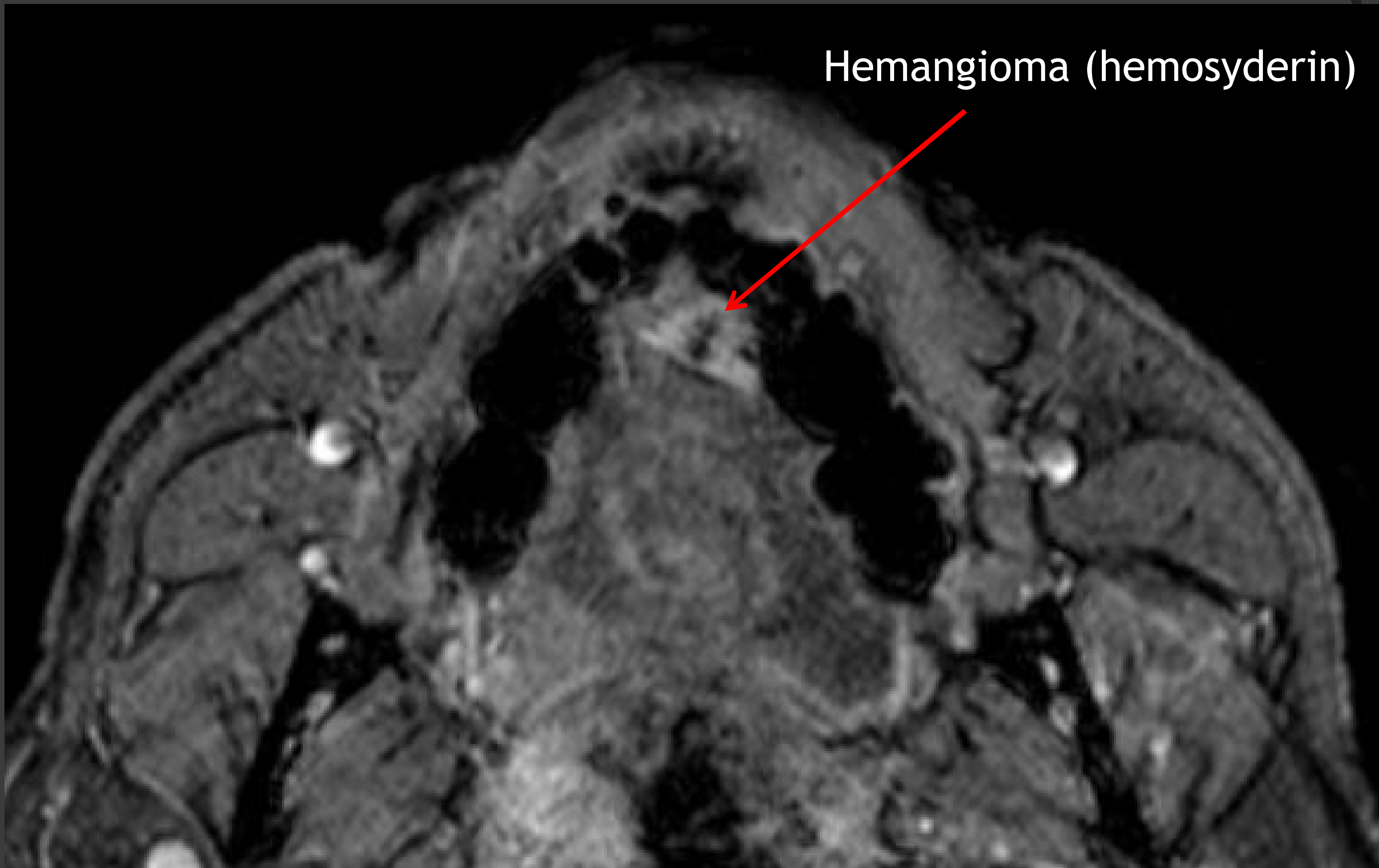


GRE: T_2-weighting (low flip)

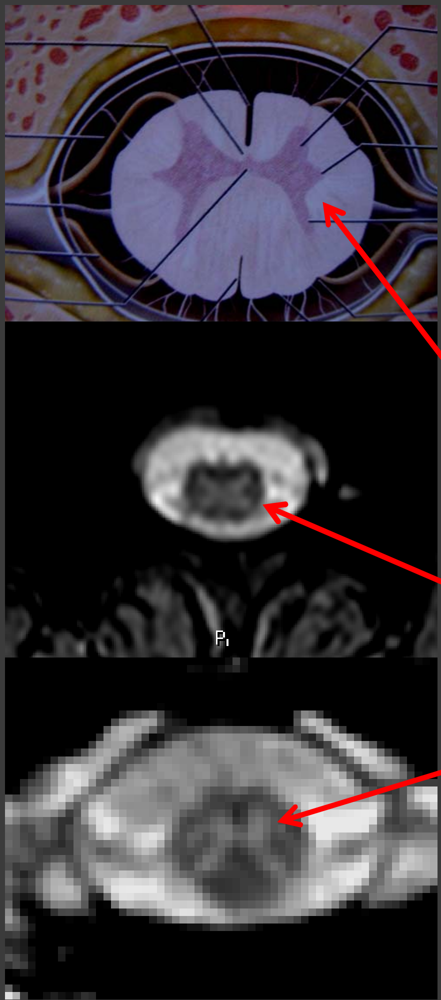




GRE: T_2-weighting



GRE: T_2-weighted



Anatomical description

Trans-axial MRI image of the spinal chord

Central medullary gray matter
(medullar “butterfly”)

GRE: T_1-weighting (flip 90°)

"Whole-Body" MRI

4 "stacks" (coronal plane), 20 seconds each

SE: Contrast

$$\mathcal{S}^{(x)} \propto \rho_{DP,x} \left(1 - e^{-T_R/T_{1,x}}\right) e^{-T_E/T_{2,x}}$$

$$\begin{aligned}\mathcal{S}^{w+f} &\propto \rho_{DP,w} \left(1 - e^{-T_R/T_{1,w}}\right) e^{-T_E/T_{2,w}} + \\ &+ \rho_{DP,f} \left(1 - e^{-T_R/T_{1,f}}\right) e^{-T_E/T_{2,f}};\end{aligned}$$

Contrast: short T_E, T_R

- T_R=500*ms*; T_E=10*ms*
  - $T_{1,w}$=4000*ms*, $T_{2,w}$=2000*ms*; $T_{1,f}$=700*ms*, $T_{2,w}$=80*ms*
- $S_w \approx 0.117 * 0.995 \approx 0.117$
- $S_f \approx 0.853 * 0.882 \approx 0.750 > S_w$

- The weighting is dictated by the difference in relaxation time: "T_1-weighted" sequence
  - Fat (fast relaxation) brighter than water (slow relaxation)

Contrast: long T_E , T_R

- T_R=3000*ms*; T_E=120*ms*
  - $T_{1,w}$=4000*ms*, $T_{2,w}$=2000*ms*; $T_{1,f}$=700*ms*, $T_{2,w}$=80*ms*
- $S_w \approx 0.527*0.941 \approx 0.497$
- $S_f \approx 0.999*0.223 \approx 0.223$ $<S_w$

- The weighting is dictated by the difference in dephasing time: "T_2-weighted" sequence
  - Fat (fast dephasing) darker than water (slow dephasing)

Contrast: short T_E, long T_R

- T_R=3000*ms*; T_E=30*ms*
  - $T_{1,w}$=4000*ms*, $T_{2,w}$=2000*ms*; $T_{1,f}$=700*ms*, $T_{2,w}$=80*ms*
- $S_w \approx 0.527 * 0.985 \approx 0.520$
- $S_f \approx 0.999 * 0.687 \approx 0.687 \approx S_w$

- The weighting is dictated by the difference in proton density: "PD-weighted" sequence

Spin-Echo: T_1-weighted

Renal cyst

Slow relaxation (long T_1)

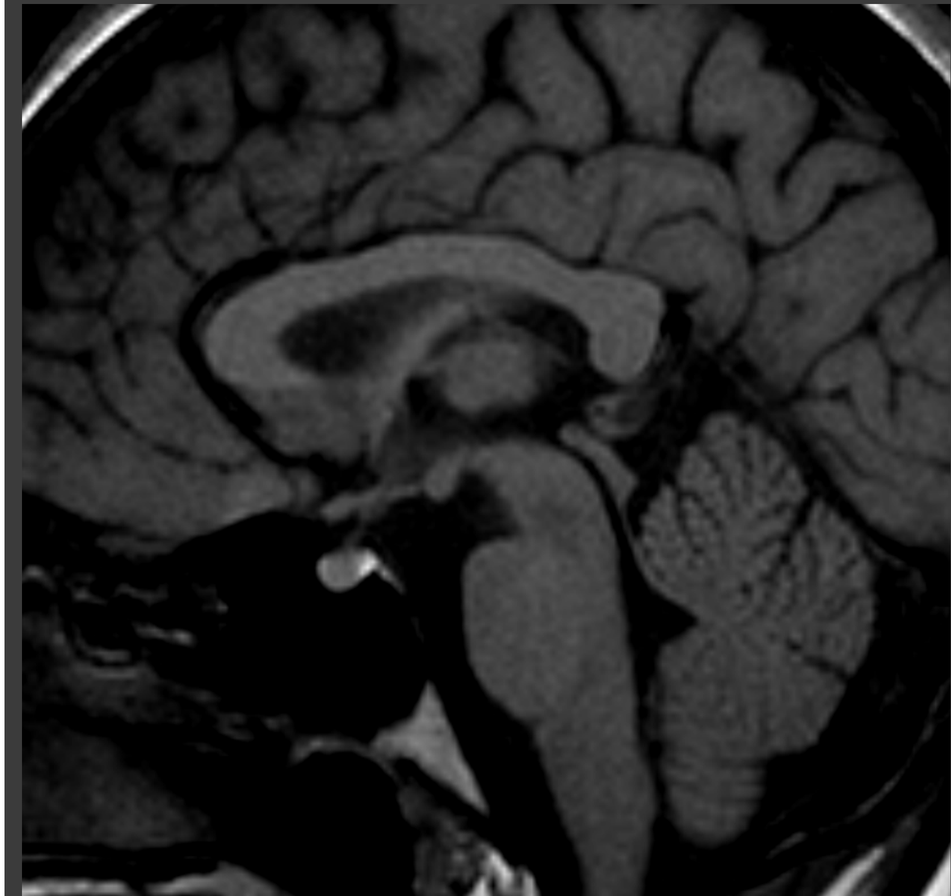
Cerebro-spinal fluid

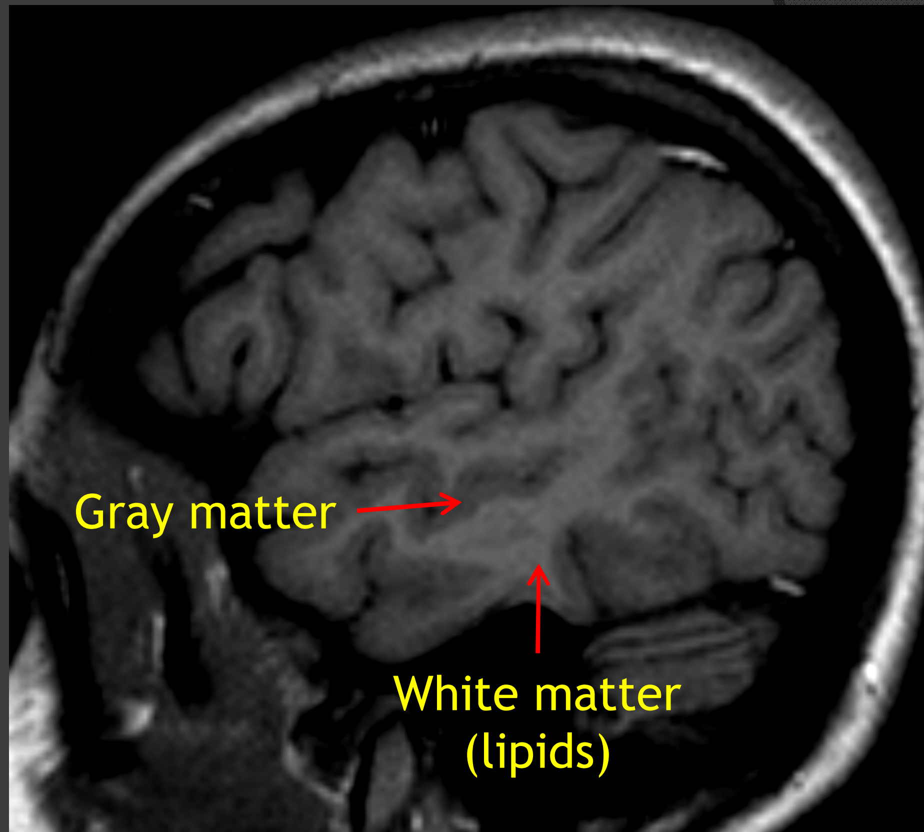
Fat

Fast relaxation (short T_1)

Yellow bone marrow (fat cells)

Spin-Echo: T_1-weighted





Spin-Echo: T_2-weighted

Retro-ocular fat

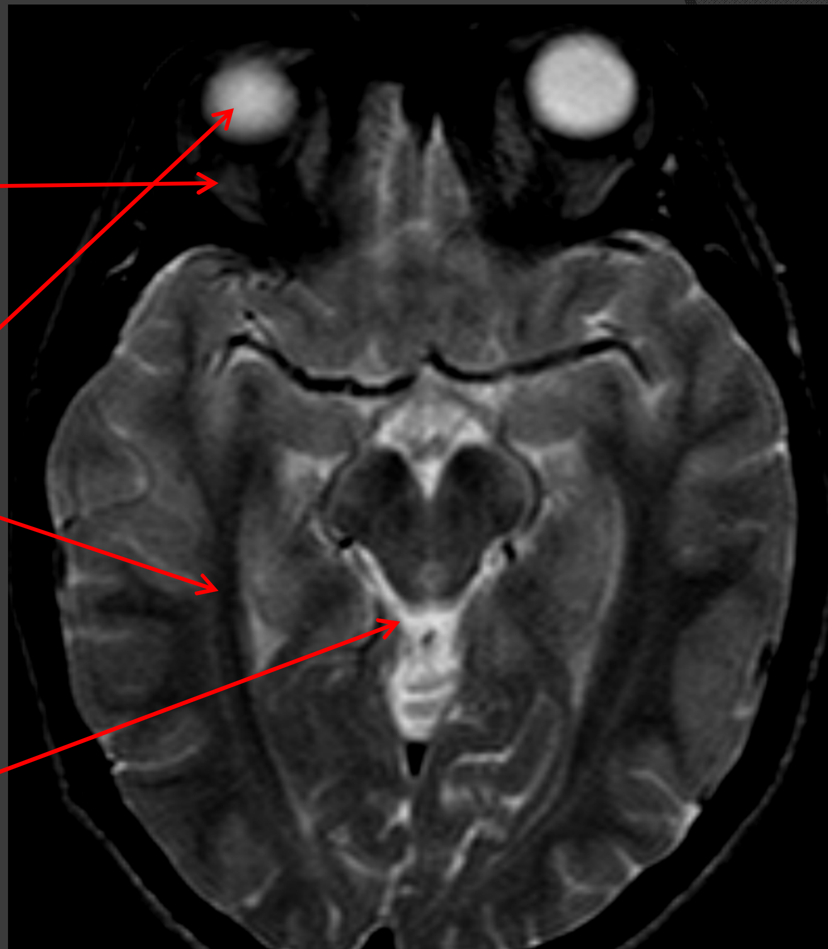
Fast dephasing (short T_2)

White matter (lipids)

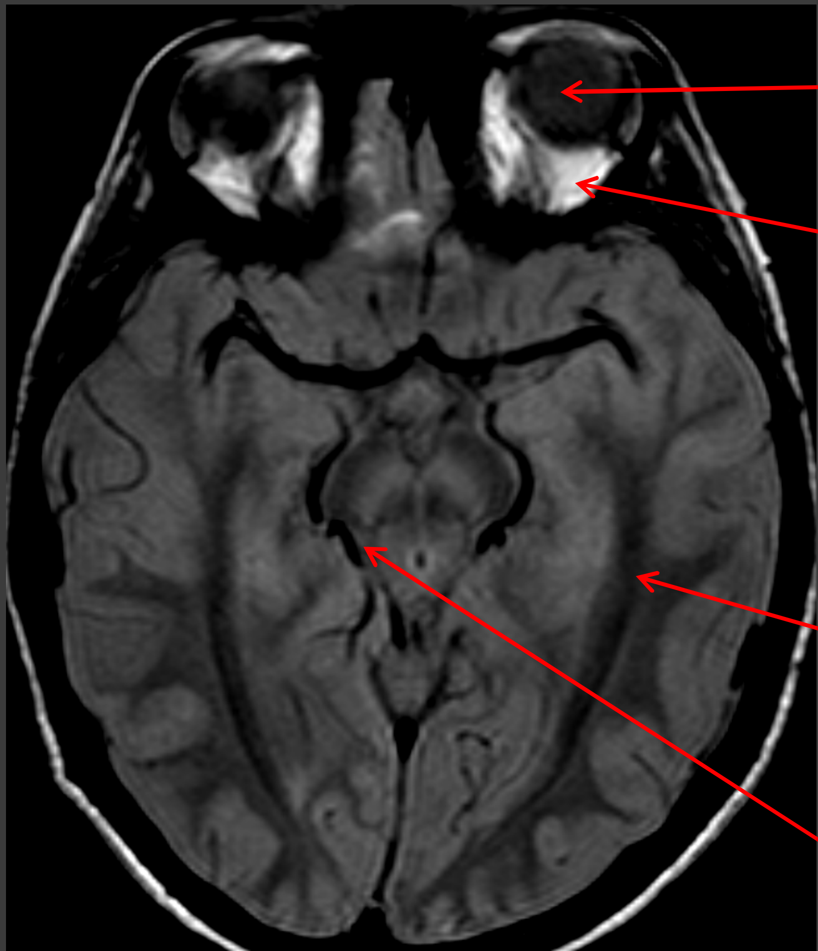
Intra-ocular water

Slow dephasing (long T_2)

Cerebro-spinal fluid



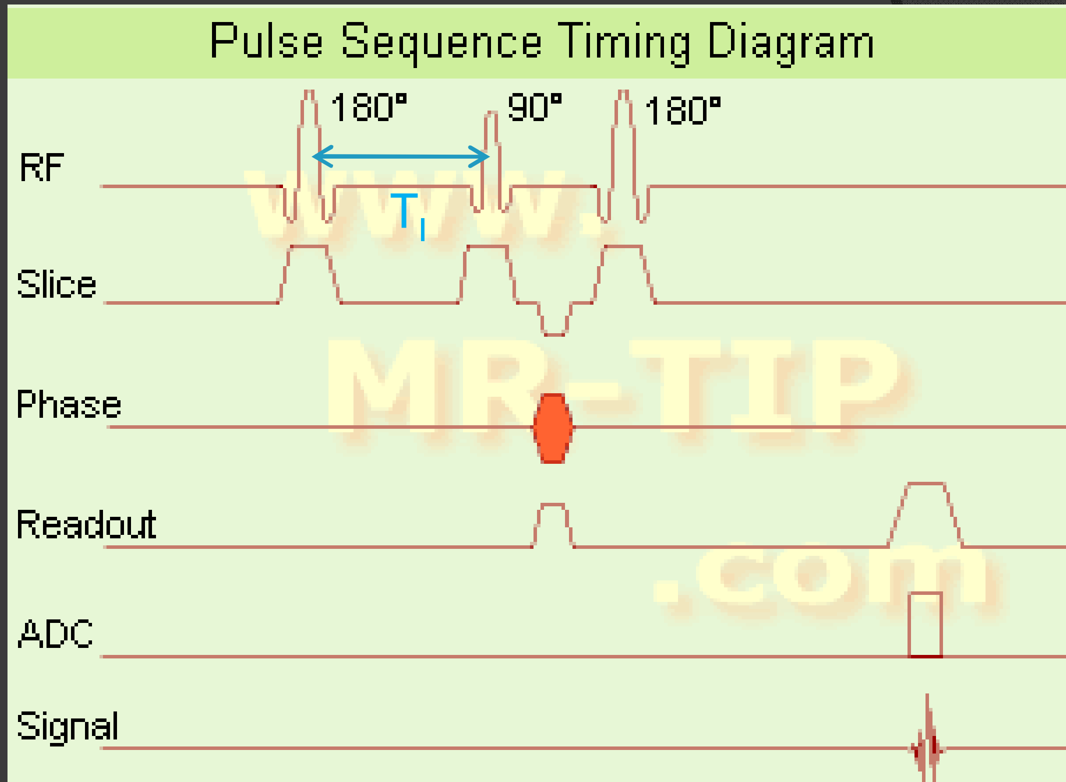
Spin-Echo: PD-weighted



Other possibilities?

- Tissue-selective saturation pulses

Fat signal nulling



T_I is the time to relax the magnetization of the selected tissue from the inverted position until the *xy* plane (at *1.5T*, *180ms* for fat, *2500ms* for water…)

Water signal nulling

- *Free* water relax in *2500ms*
  - CSF is dark
- *Constrained* water relax much faster
  - *Lesions are bright*
    - Creuzfeldt-Jakob disease (hyperintensity in basal ganglia)

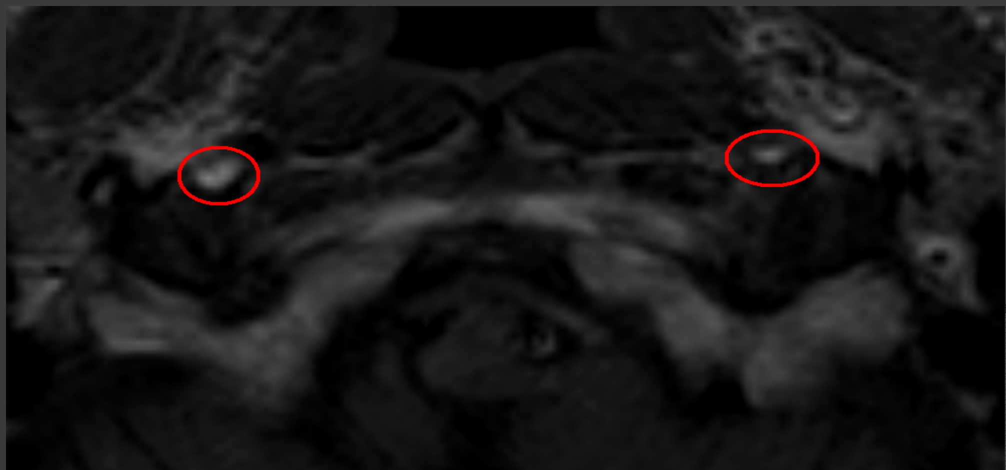
Other possibilities?

- Tissue-selective saturation pulses
- Velocity-weighted imaging

"Flow-Related Enhancement"

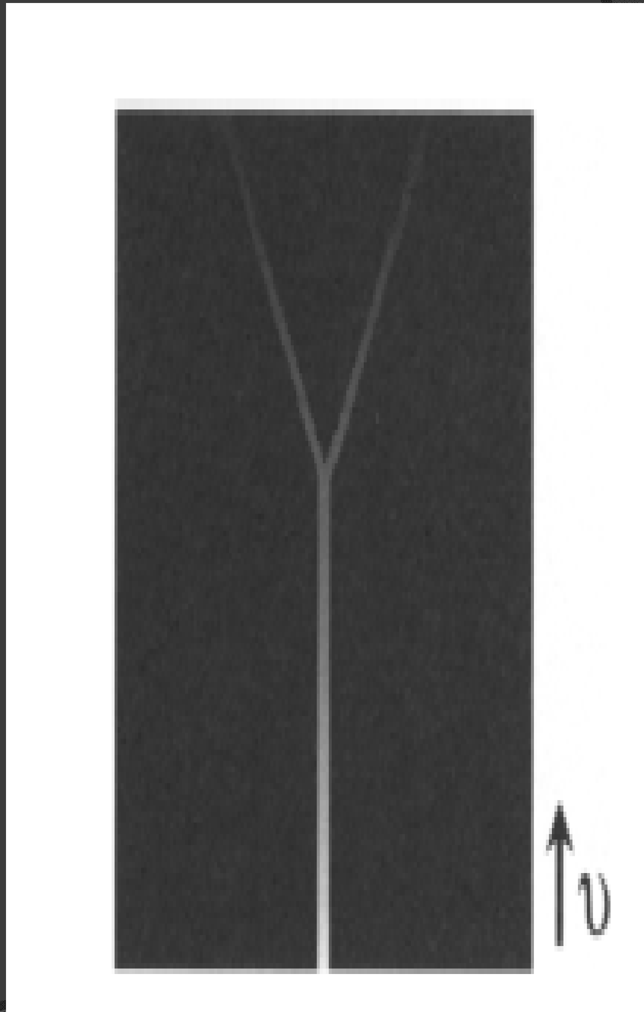
T_1-weighted	FAT	WATER	FLOW
T_2-weighted	FAT	WATER	FLOW
DP-weighted	FAT	WATER	FLOW

In fact…

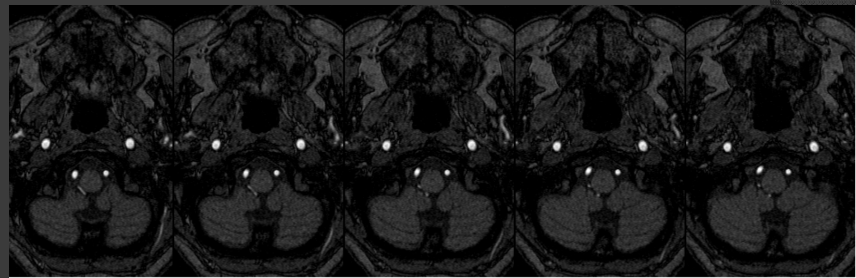


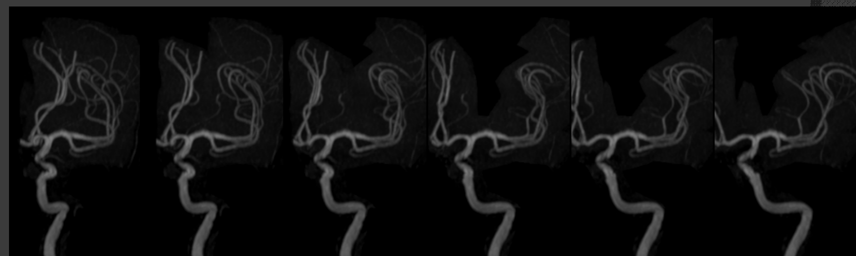
Time-of-flight weighted imaging

- A series of RF pulses "saturate" the M_+ of a slice
- *Moving* spins entering the slice have a non-saturated magnetization
  - *They contribute strongly to the signal*
- If the slice is *very* thick (3D acquisition), even moving spins get saturate during their motion



Acquisition and reconstruction





Phase-Contrast Angiography

- Phase encoding reminder: application of a field gradient along -say- y for a time δ with amplitude g_y to assign a definite phase to the spins in the pixels along such axis
- The phase of a spin in the position y_0 results as:

$$\varphi = y_0 k_y$$

where

$$k_y = g_y \delta \gamma$$

- If the spin is moving along y…

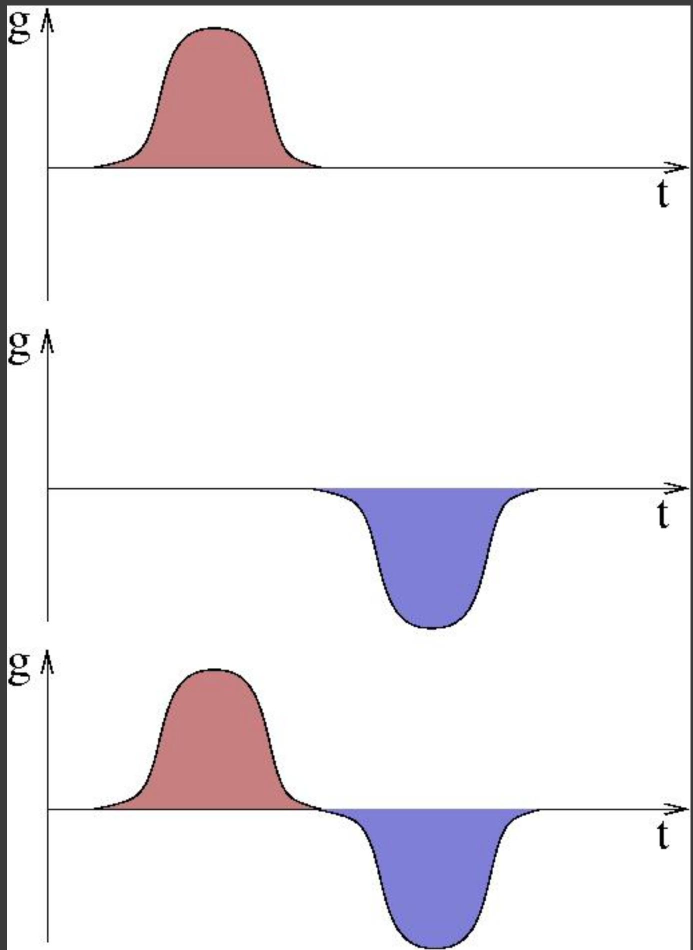
$$\varphi = \left(y_0 \pm vT\right) k_y$$

Spin velocity

Time interval between RF and g_y

Phase-Contrast Angiography - 2

1
2
3



$$\text{fase accumulata} \rightarrow \begin{cases} \varphi_{\text{statico}} = y_0 k_y \\ \varphi_{\text{mobile}} = (y_0 + vT)\, k_y \end{cases}$$

$$\text{fase accumulata} \rightarrow \begin{cases} \varphi_{\text{statico}} = -y_0 k_y \\ \varphi_{\text{mobile}} = (-y_0 + vT)\, k_y \end{cases}$$

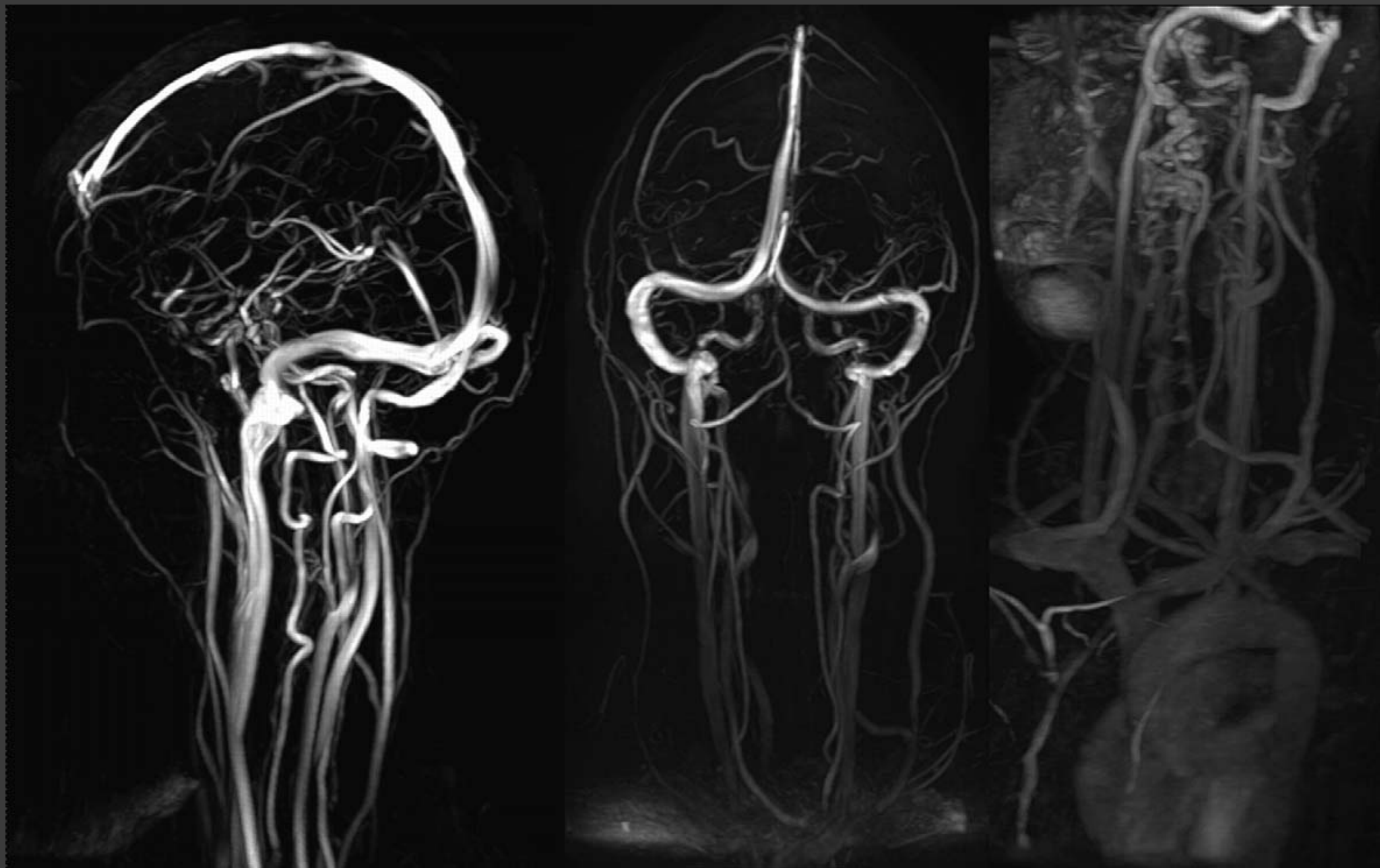
$$\text{fase accumulata} \rightarrow \begin{cases} \varphi_{\text{statico}} = 0 \\ \varphi_{\text{mobile}} = 2vTk_y \end{cases}$$

Phase-Contrast Angiography - 3

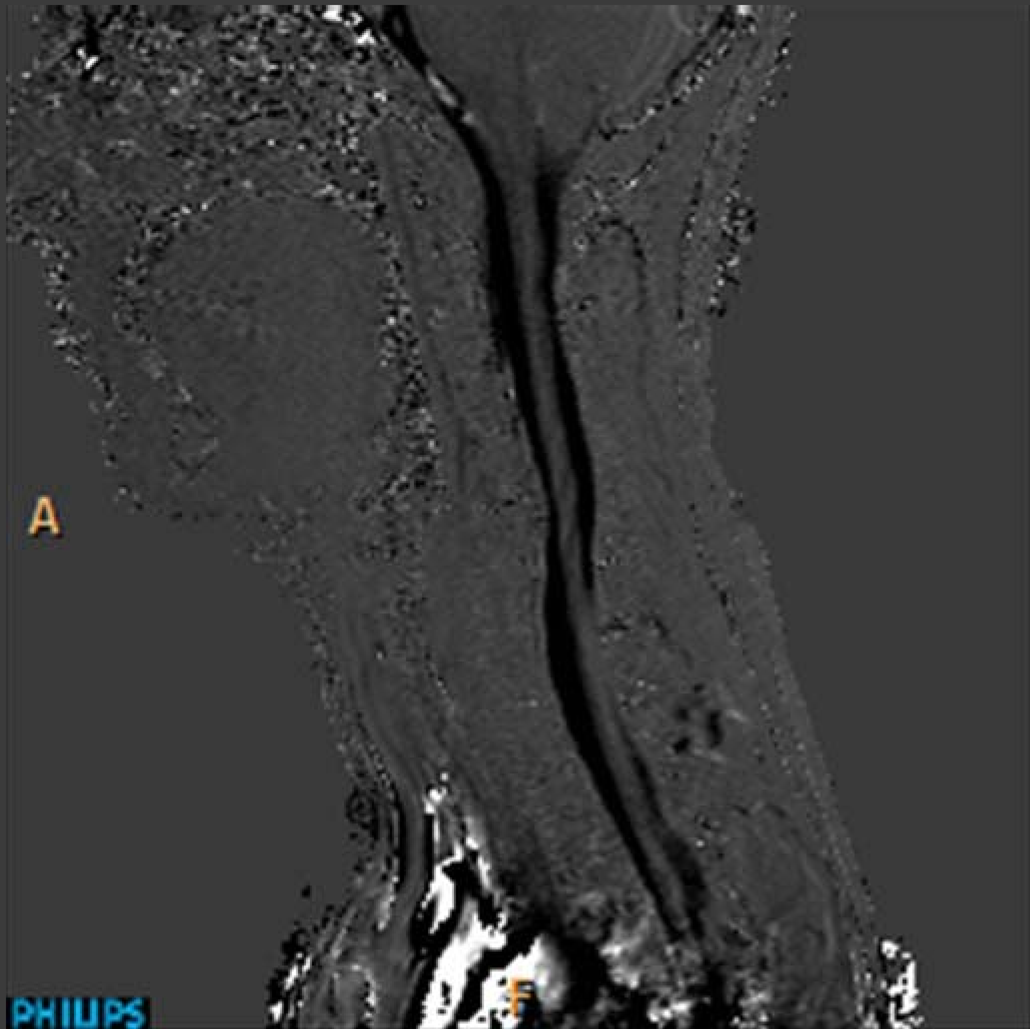
A phase-encoding gradient with two opposite lobes ("*bipolar gradient*") allows to acquire a signal whose intensity is a DIRECT MEASUREMENT of spin velocity

(analogously, a four-gradient lobes suitably designed can allow the measure of the acceleration…)

“static” PC imaging



“dinamic” PC imaging

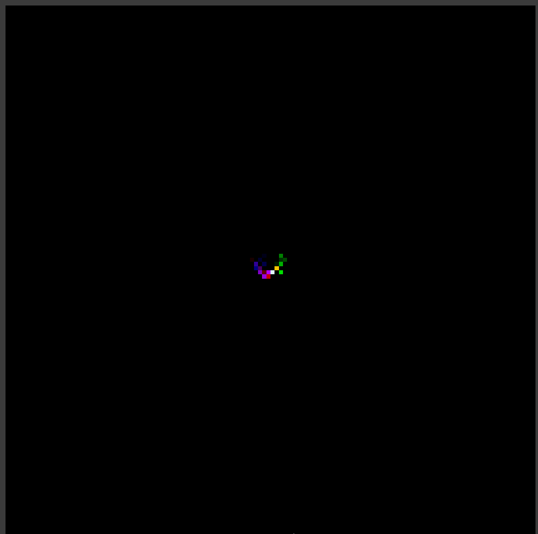


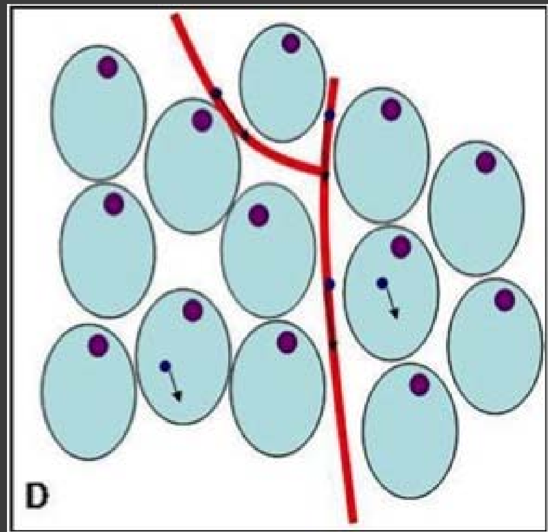
Other possibilities?

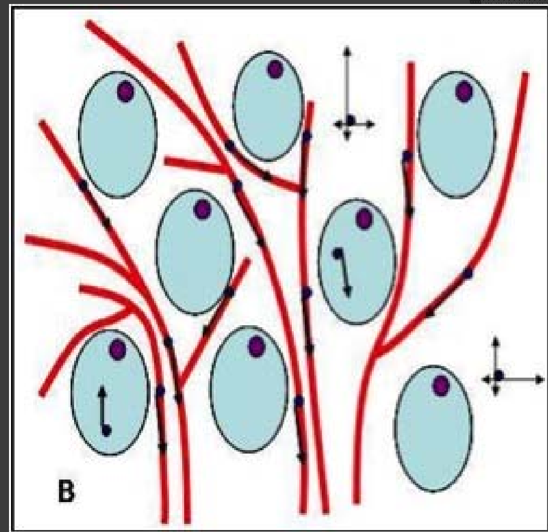
- Tissue-selective saturation pulses
- Velocity-weighted imaging
- Diffusion-weighted imaging

DwI

Tissue water molecules show this behaviour, but we have to take into account physiological constraints (cells, membrane, etc. etc.)







True random walk

Human tissues (constrained water molecules)

But…

- Can we directly measure the water diffusion coefficient in human tissue?

No

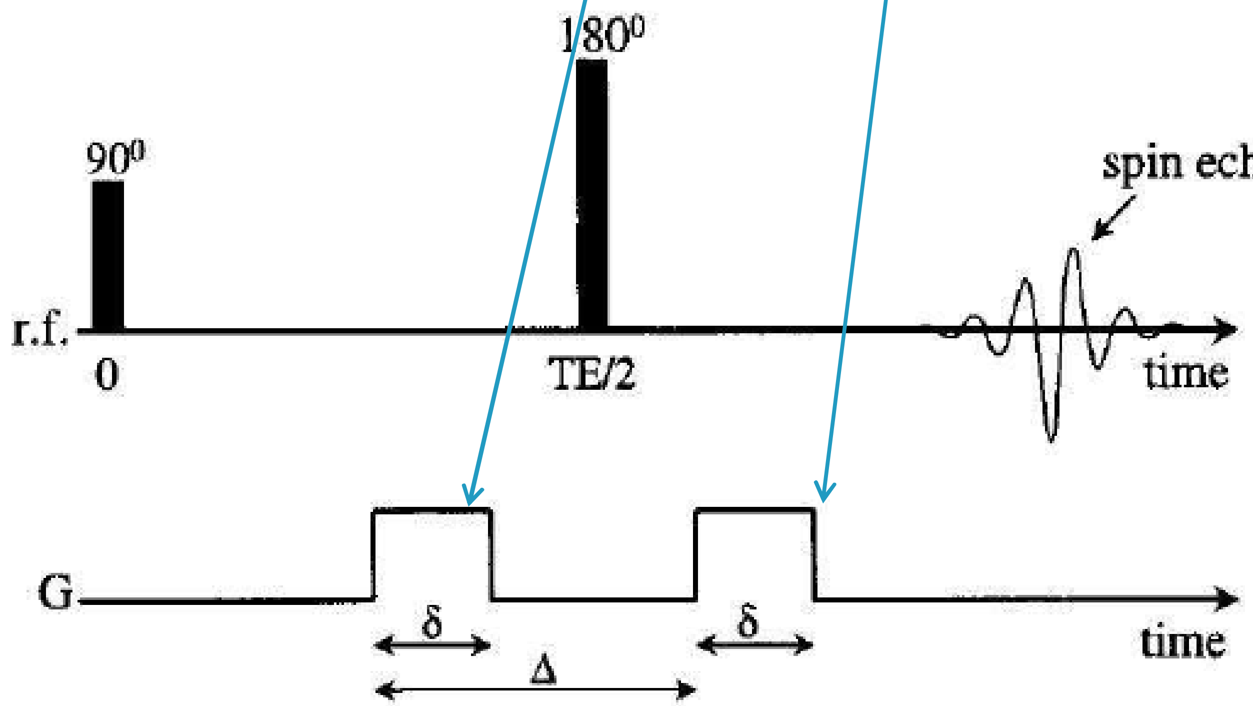
- But we can measure the diffusion effect on MR signal (Hahn 1950, Carr-Purcell 1954)

Now we have to…

- Think to spins:

Dephase all spins

Rephase all static spins: moving spins will remain dephased at a degree proportional
to their mobility



Stejskal-Tanner mechanism

DwI – 2

$$\mathcal{S}(T_E) = \mathcal{S}_0 \exp\left[-\frac{T_E}{T_2} - D\gamma G^2\delta^2\left(\Delta - \frac{\delta}{3}\right)\right]$$

Water magnetization diffusion coefficient

Gradient duration

Gradient interval

Amplitude of the *motion probing* gradient

One can calculate D with a single acquisition, but it will depend on T_E and T_2:

$$\ln\frac{\mathcal{S}(T_E)}{\mathcal{S}_0} - \frac{T_E}{T_2} = bD$$

$$\text{dove } b = \gamma\left(g\delta\right)^2\left(\Delta - \delta/3\right)$$

Dwi – 3

- With 2 acquisitions with different *b* (varying *G*, Δ or δ), one obtains *D*:
- It is sufficient to subtract (pixel by pixel) signal intensities…

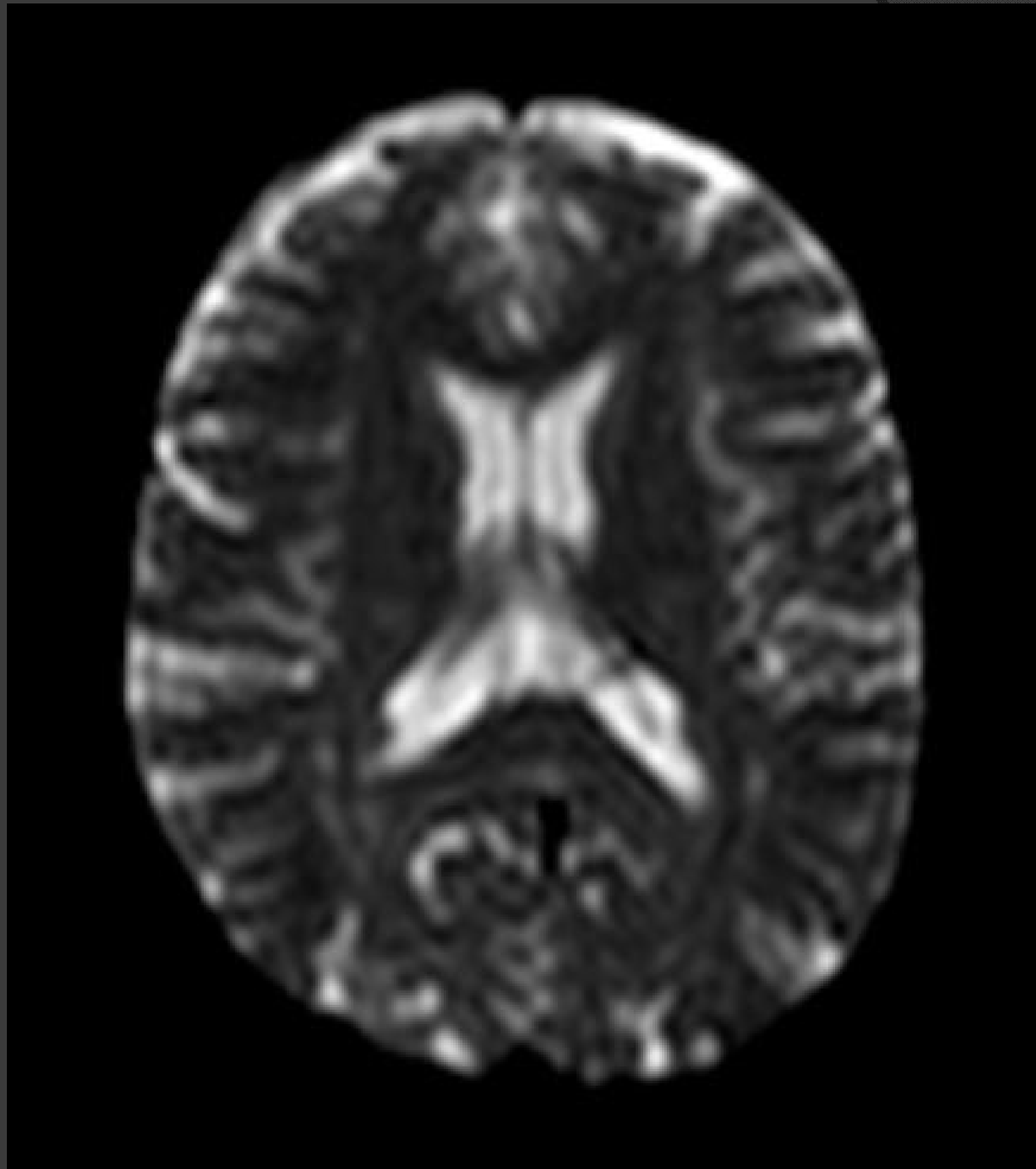
$$D = \frac{1}{b_1 - b_2} \ln \frac{S_2}{S_1}$$

- usually, $b_1=0$ and $b_2=800\text{-}1000$

b=0

T_2-weighted image
(long echo time)

CSF hyper-intense
GM iso-intense
WM hypo-intense

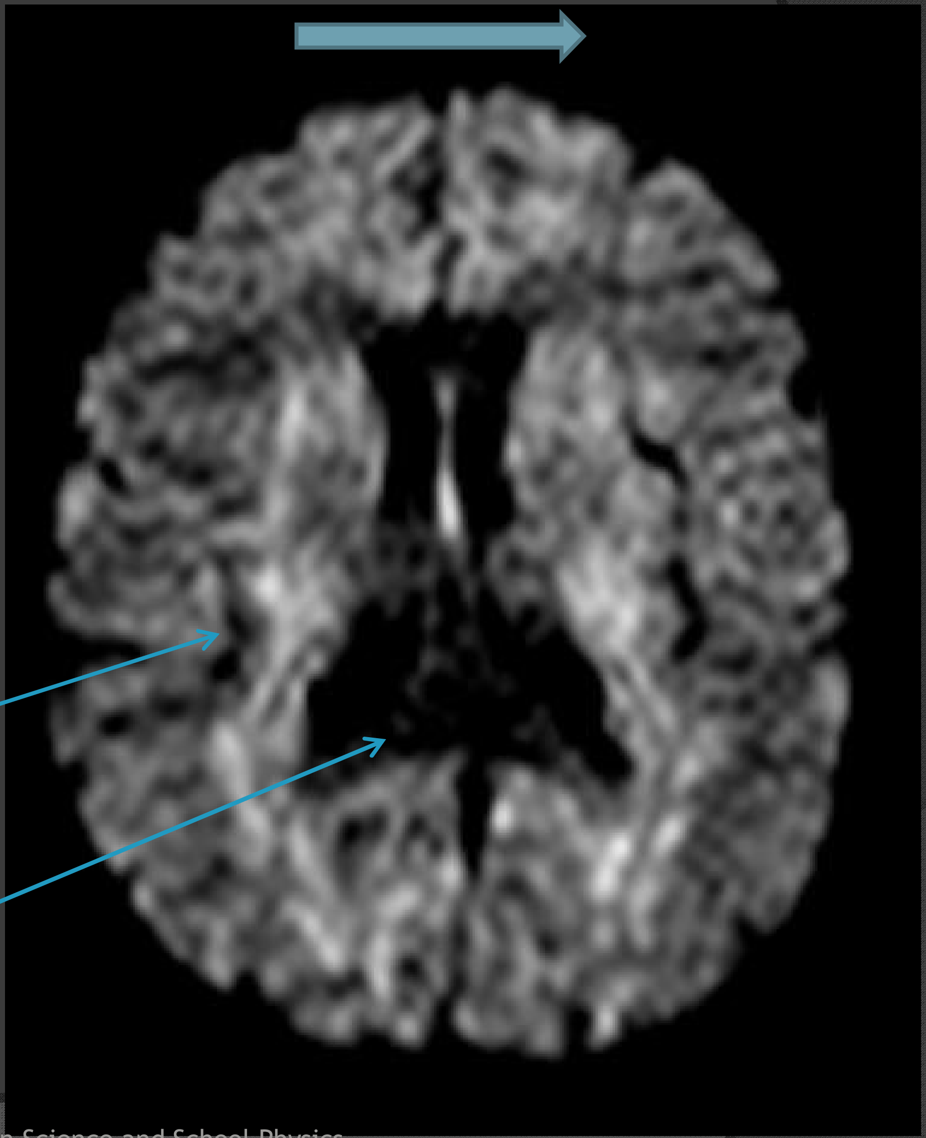


b=1000 M (measure)

Diffusion weighting along the read-out (frequency) gradient

CSF hypo-intenso (high mobility)
GM iso-intense
WM iso-intense

Hyper-intensity along fibers orthogonal to the read-out gradient (i.e. otpic radiation; geniculo-striate pathway)
Hypo-intensity along parallel fibers (i.e. splenium of corpus callosum)

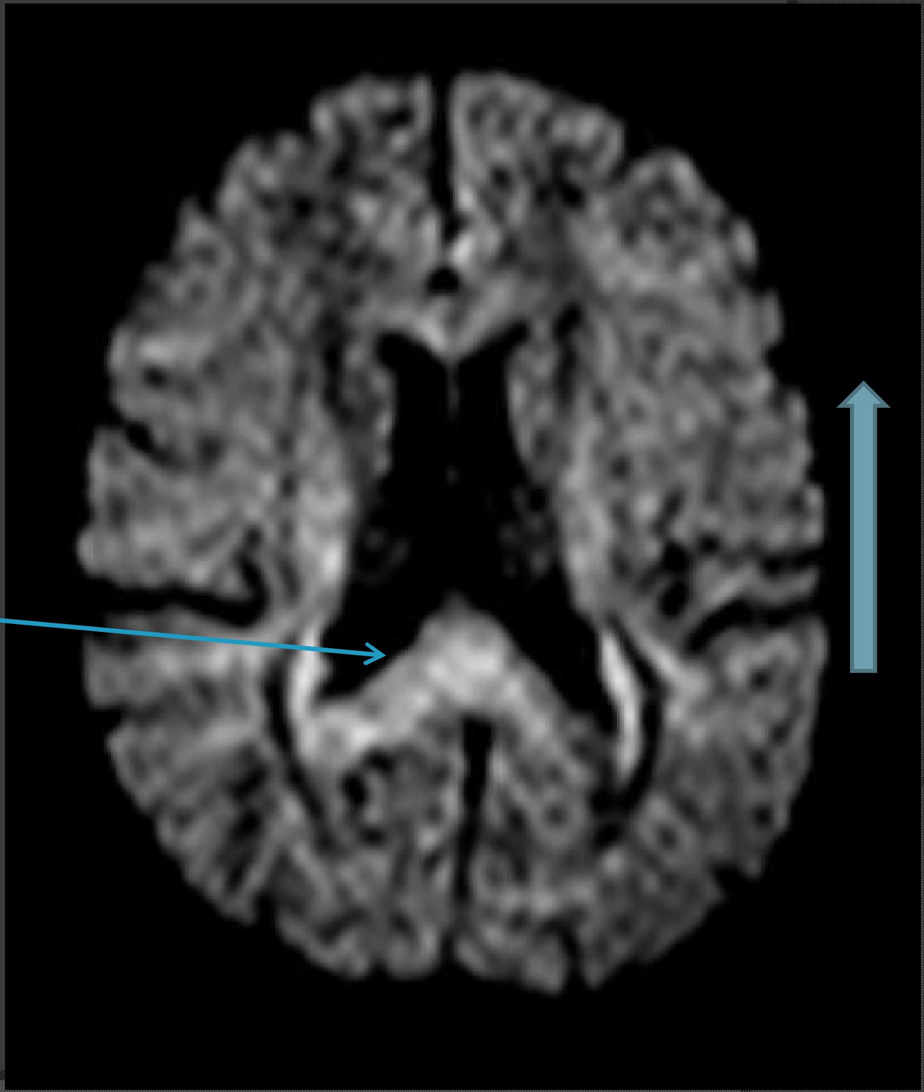


b=1000 P (phase)

Diffusion weighting
along the phase gradient

CSF hypo-intense (high mobility)
GM iso-intense
WM iso-intense

Hyper-intensity along fiber orthogonal to the phase gradient (i.e. splenium of the corpus callosum)

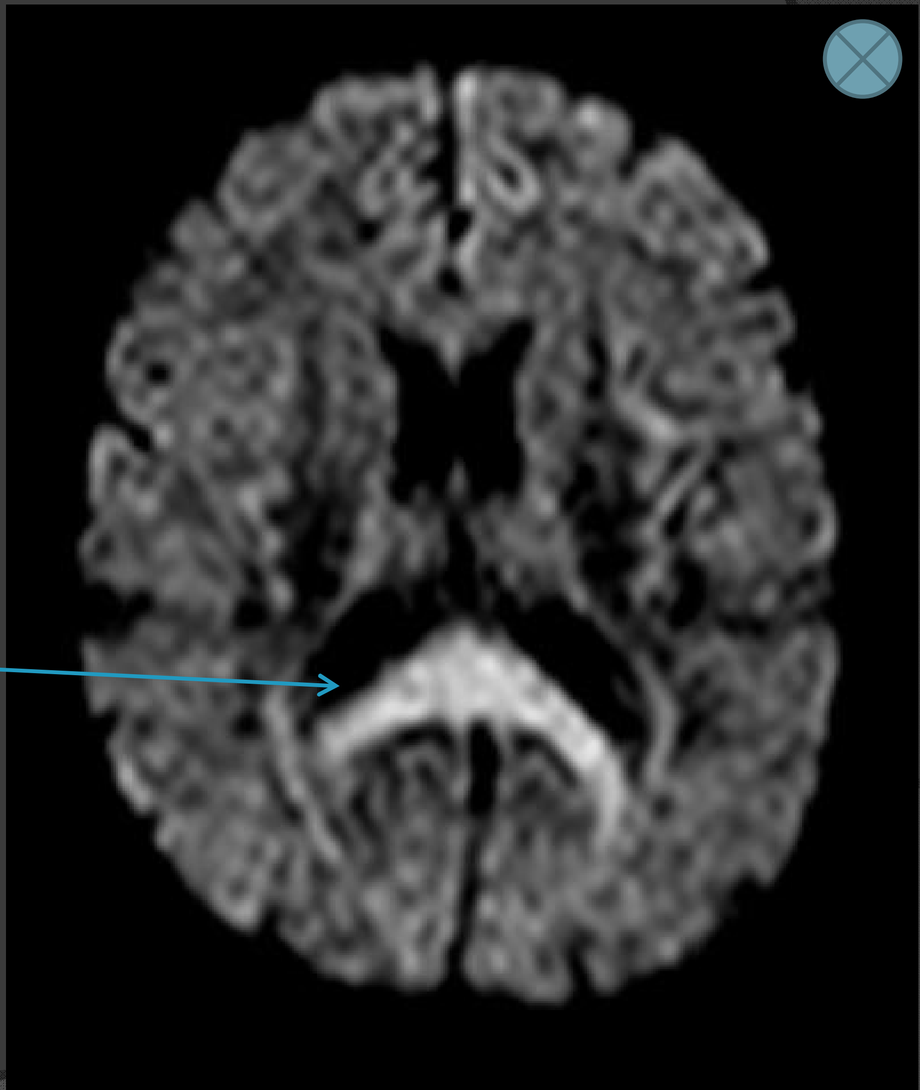


b=*1000* S (slice)

Diffusion weighting
along the slice gradient

CSF hypo-intense (high mobility)
GM iso-intense
WM iso-intense

Hyper-intensity along fibers orthogonal to the slice gradient (i.e. spenium of the corpus callosum)

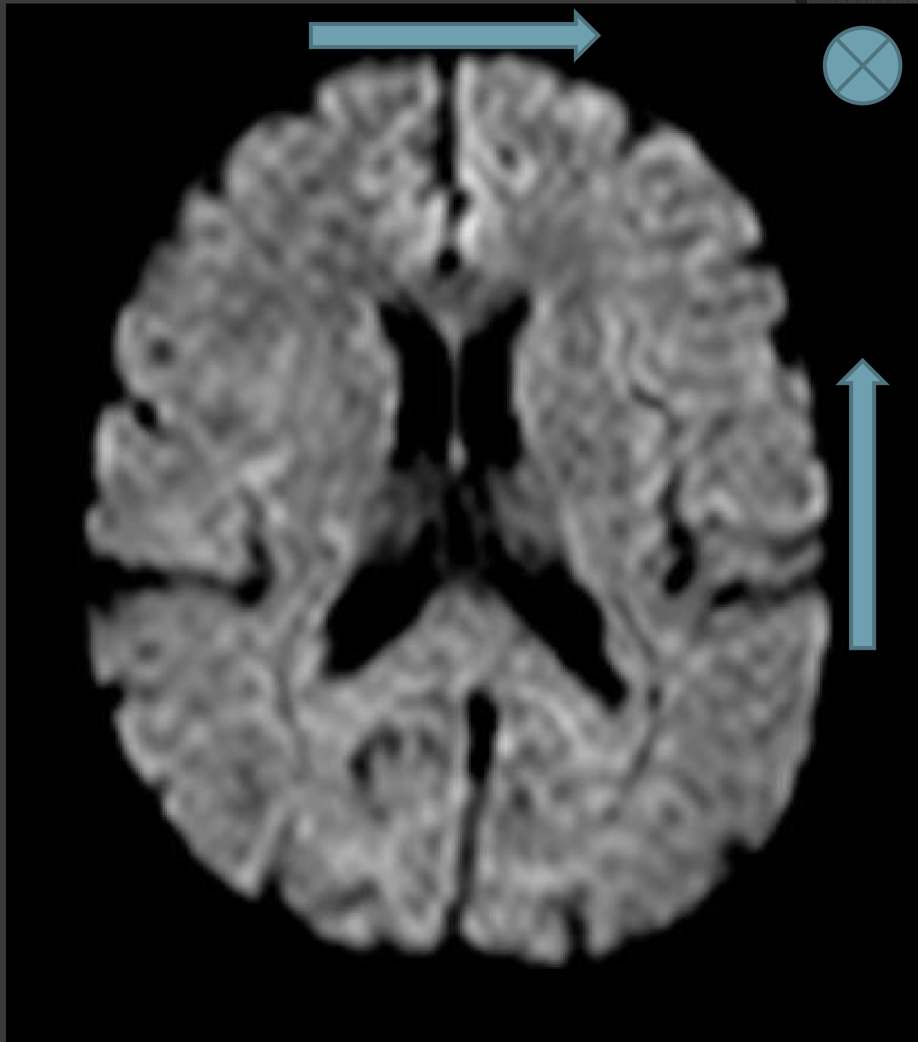


b=1000 I (isotropic o *trace*)

Sum of weightings along the three axis

CSF hypo-intense
GM iso-intense
WM iso-intense

No hyper-intensities

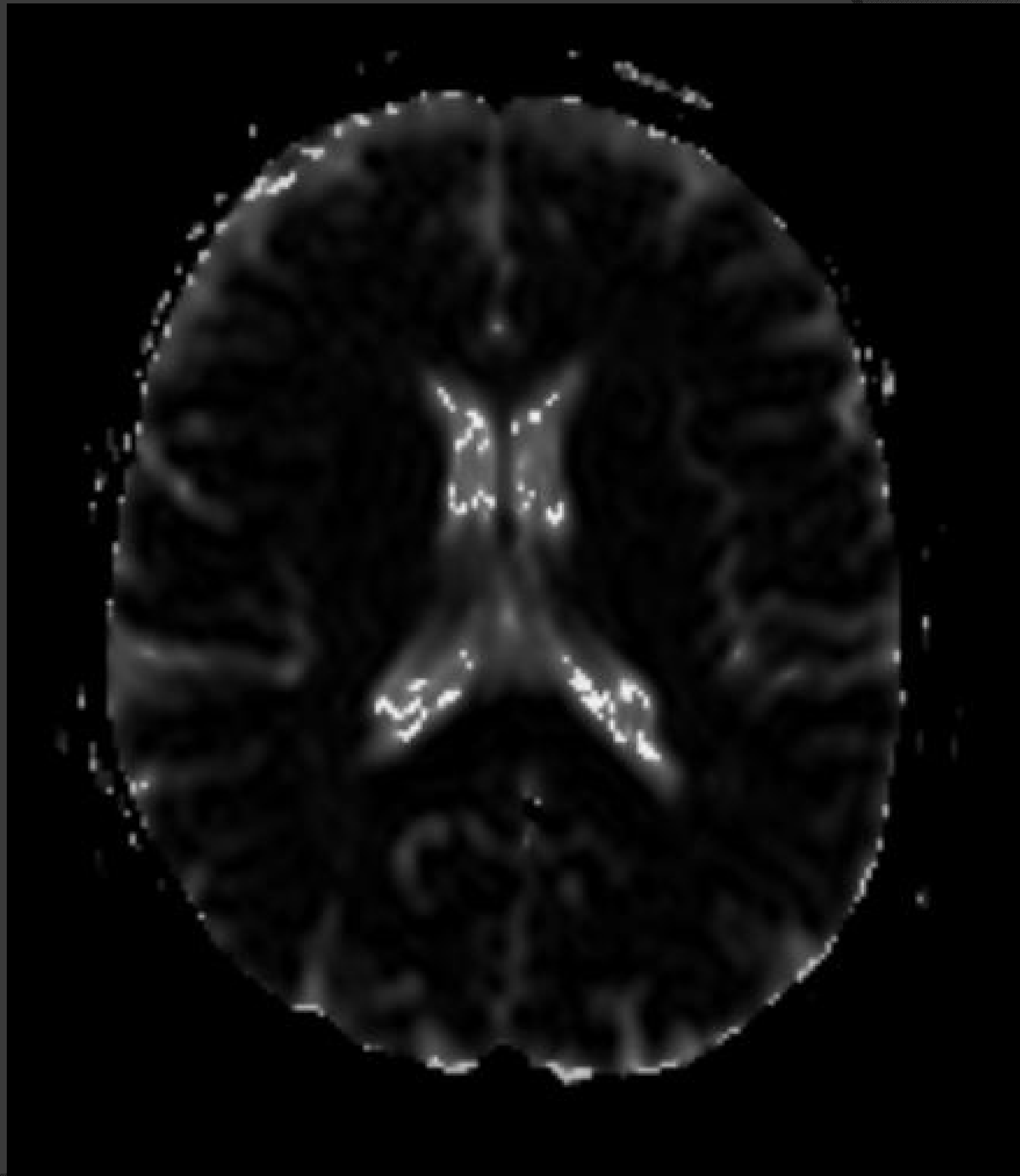


ADC map

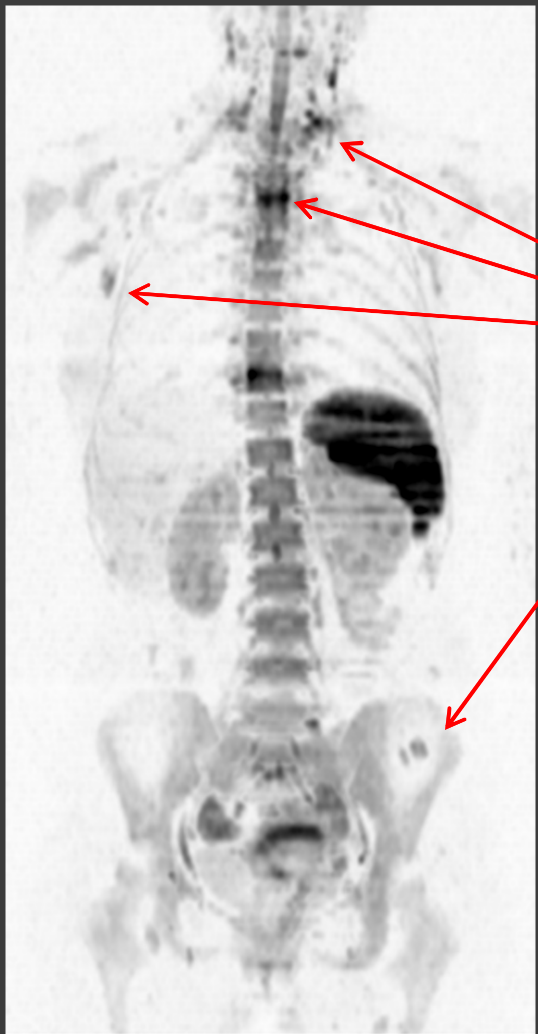
Average of the *apparent* diffusion coefficient (ADC)

CSF hyper-intense
GM iso-intense
WM hypo-intense

Why “apparent”???



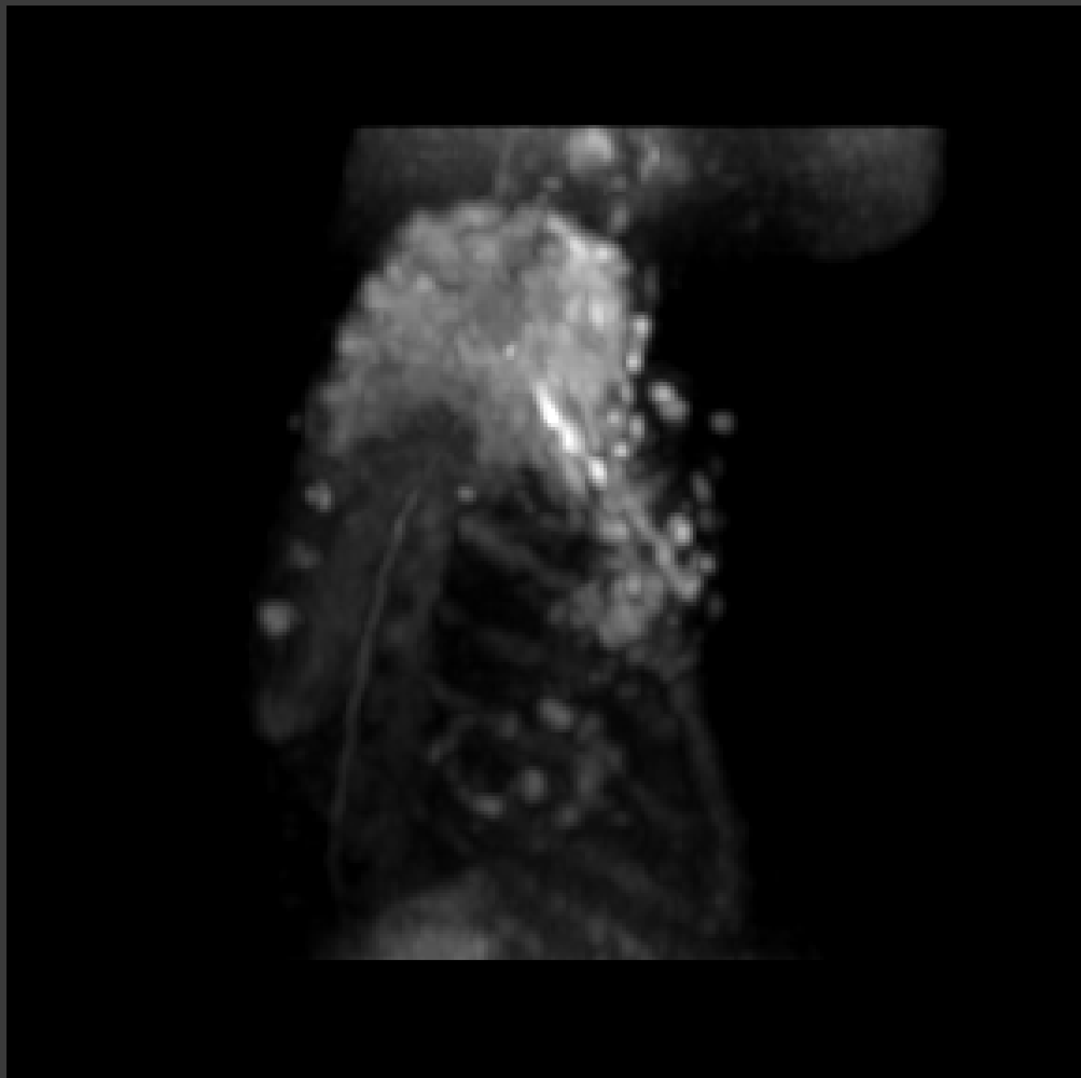
In the body…



Plexiform neurofibromas
(NeuroFibromatosis type 1)

In young patients, it allows whole-body examinations for screening in systemic and/or oncologic diseases without the use of ionizing radiation
(Lymphomas, NF1, metastasis…)

3D reconstruction… (*MIP*)



Other possibilities?

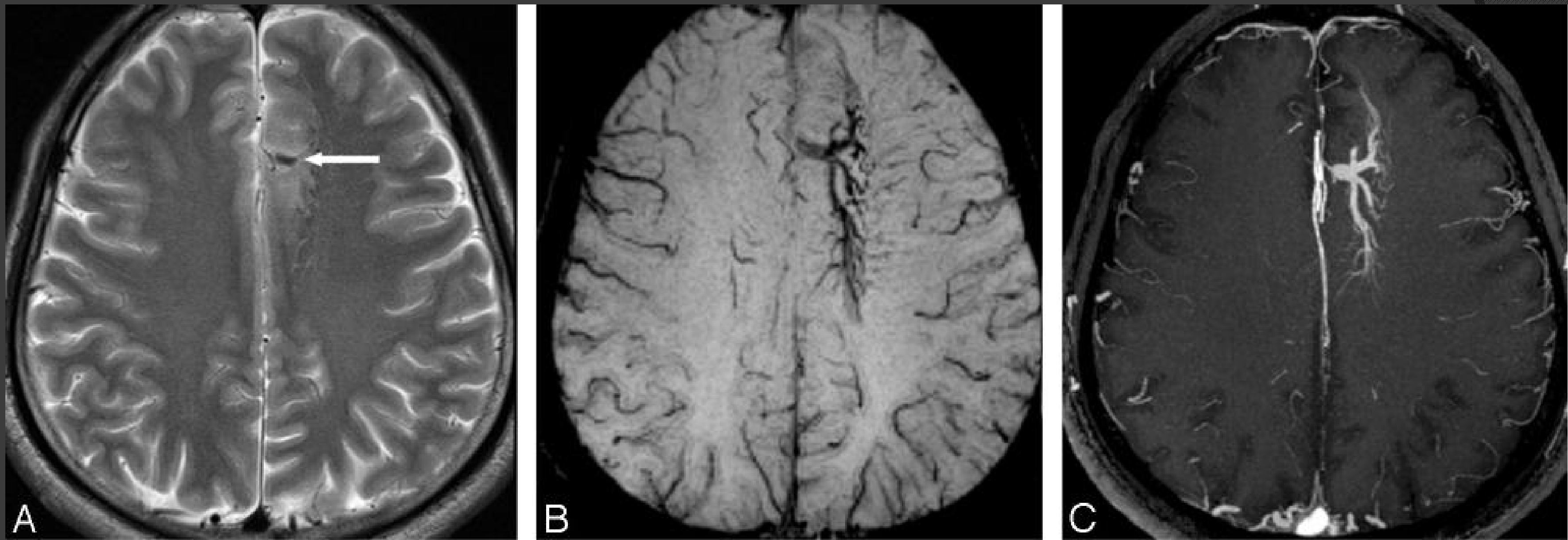
- Tissue-selective saturation pulses
- Velocity-weighted imaging
- Diffusion-weighted imaging
- Susceptibility-weighted imaging

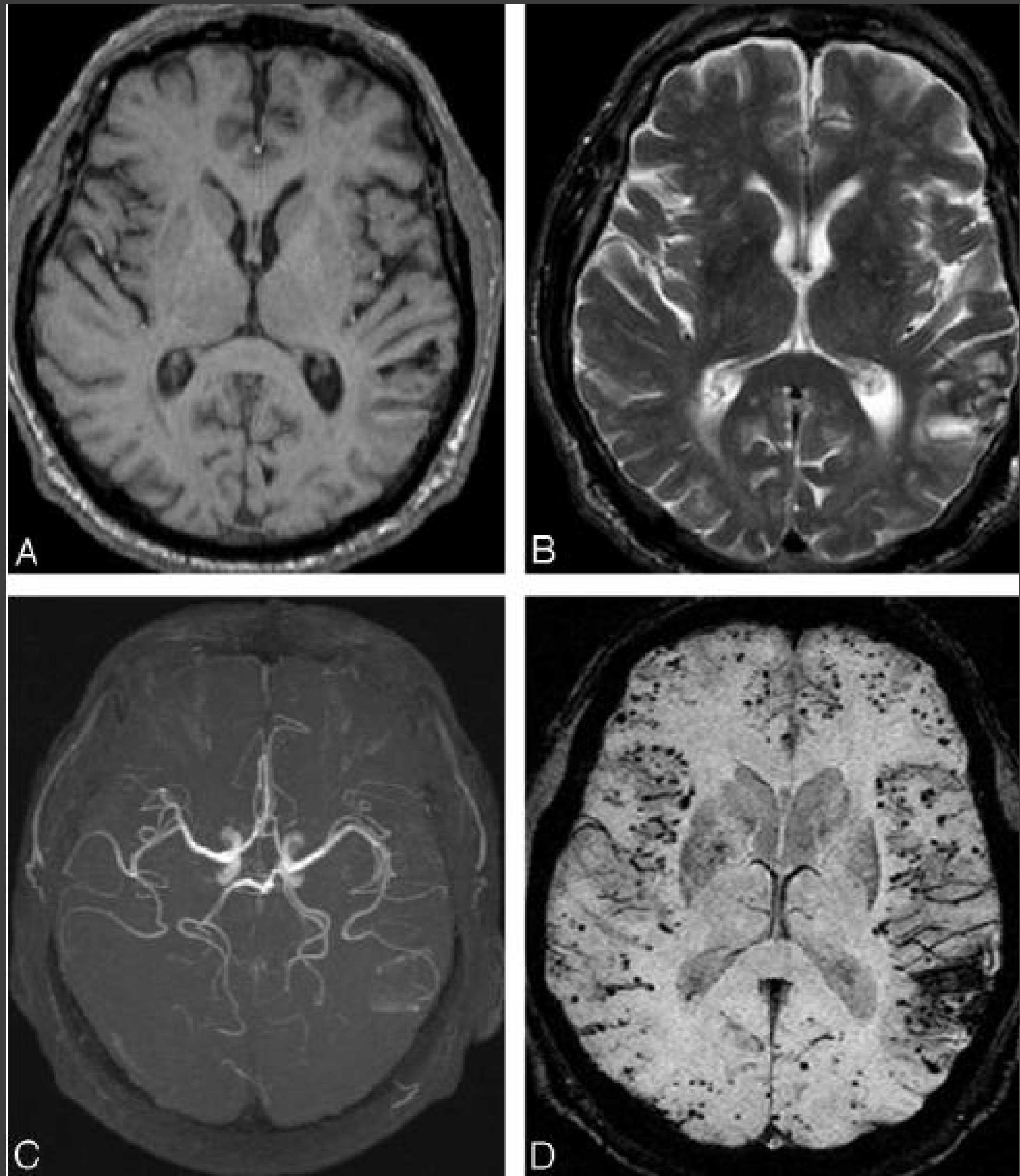
SwI

- The contrast is related to susceptibility differences

- In particular, blood “lives” in different states
  - In the arterial state, contains oxyhemoglobin (no “free” spins)
  - In the venous state, contains deoxyhemoglobin (2 free spins: paramagnetic!)
  - Outside vessels (hemorrhage): iron in tissues (ferromagnetic!)

SWI




A
B
C
D

Other possibilities?

- Tissue-selective saturation pulses
- Velocity-weighted imaging
- Diffusion-weighted imaging
- Susceptibility-weighted imaging
- Contrast media administration…

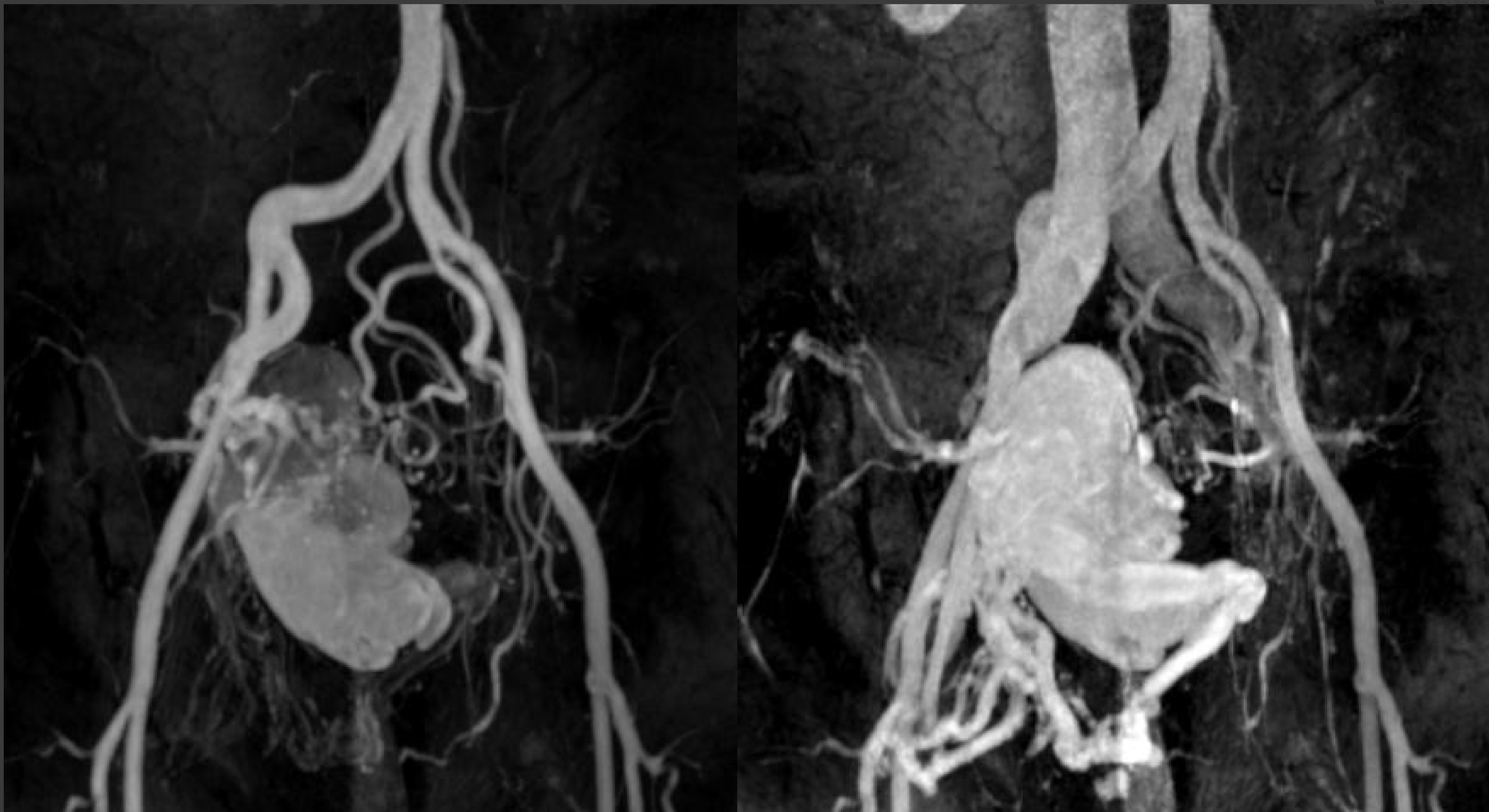
Contrast media

- T_1-shortening (most diffuse; act on T_1-weigthed sequences)
- T_2-lengthening (super-paramagnetic media; act both on T_1- and T_2-weighted sequences)
- Both (initially T_1-shortening then T_2-lengthening)

Contrast-Enhanced MRA

Arterial phase

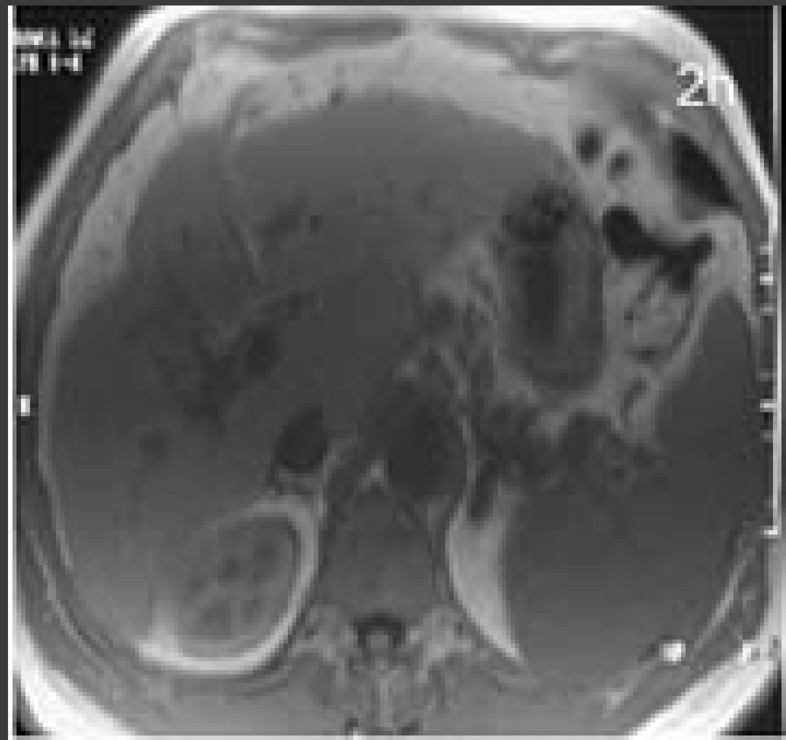
Venous phase



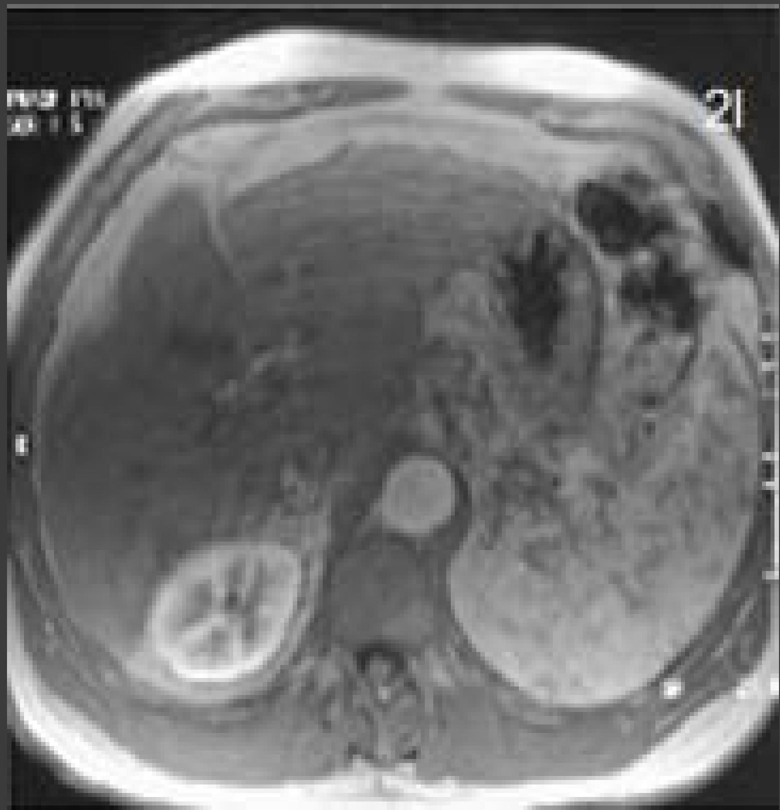
Hepatospecific contrast media

- First pass: through the vessels
  - Arterial phase (after 30’’)
  - Venous phase (after 70’’)
  - “equilibrium” phase (after 180’’)
- Usual c.m.’s are eliminated through the kidneys
- Hepatospecific c.m.’s remain in the hepatic tissue and are eliminated through *normal* hepatocities (after 30-60 mins)
  - Abnormal tissue looks darker!

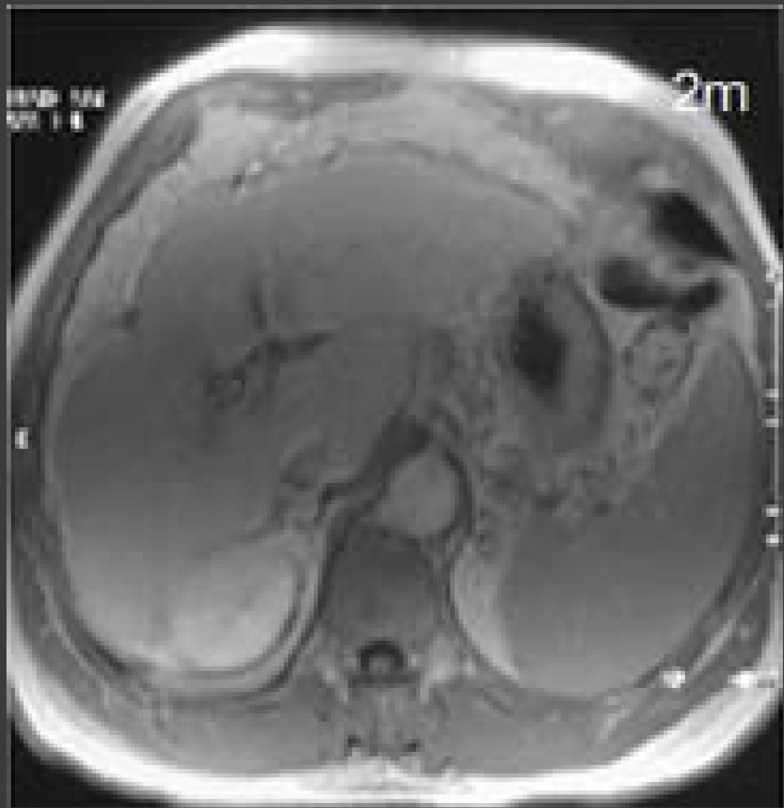
Liver: no contrast



Liver: arterial phase (30'')



Liver: equilibrium phase (180'')



Liver: hepatobiliary phase (1800’’)

Conclusions (?) in imaging

- Huge improvements in "in vivo" imaging in the last 30 years
  - Morphologic maps (CT)
  - Functional maps (PET, Nuclear Medicine)
  - "Chemical" maps (MRI, MR Spectroscopy Imaging)
  - Co-registration (CT-PET, MR-PET)
  - Fusion software (*any* two or more imaging techniques)
- Perspectives
  - MR chemical-functional maps (paramagnetic tracers)
  - ???

Just a reminder on therapy…

- Radio-therapy (oncology):
  - Fractional “dose-release” (many γ- or X-rays burst)
    - 3D conformal RT
    - Intensity Modulated RT
    - Intra-operative RT
    - Tomotherapy
  - Unique o few burst
    - Cyber-knife, γ-knife
    - Radio-surgery
- US (oncology):
  - High Intensity Focused US
- Magneto-therapy
- Laser-therapy
  - External (inflammatory disease…)
  - Endoscopic (ischemic heart attack, trombolysis…)

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- Dr. Valentino Carini (Radiologist)

- Prof. Andrei A. Varlamov

- (and many others…)

To the dear memory of

Dr. LUCA LASCIALFARI