Times, October 9, 2003

This Year's Nobel Prize in Medicine

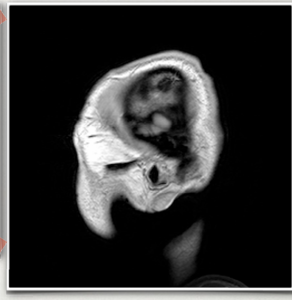
The Shameful Wrong That Must Be Righted

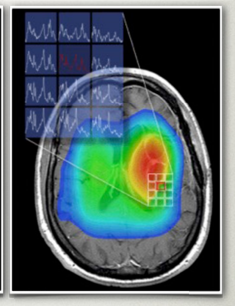
This year the committee that awards The Nobel Prize for Physiology or Medicine did the one thing it has no right to do: it ignored the truth. Eminent scientists, leading medical textbooks and the historical facts are in disagreement with the decision of the committee. So is the U. S. Patent Office. Even Alfred Nobel's will is in disagreement. The committee is attempting to rewrite history.

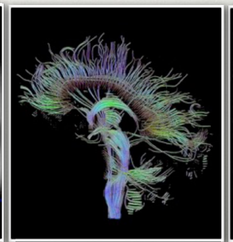
The Nobel Prize Committee to Physiology or Medicine chose to award the prize, not to the medical doctor/research scientist who made the breakthrough discovery on which all MRI technology is based, but to two scientists who later made technological improvements based on his discovery.

MRI is a revolutionary device

Non-invasive







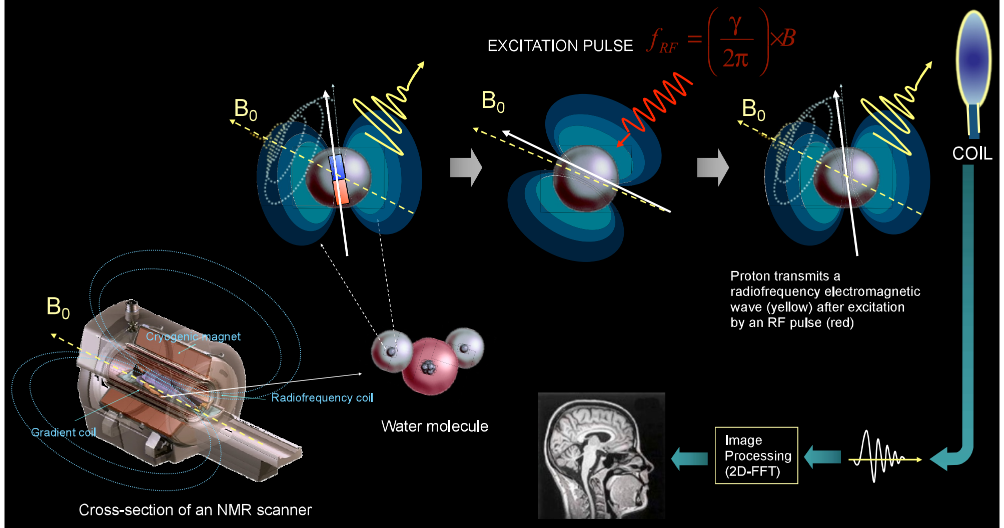
MRI

- History
- Fundamental processes
  (nuclear spin, precession, resonance, excitation-relaxation)
- Imaging
  I. Spatial coding
  II. Image reconstruction
  III. Color contrast
  IV. Scanners
  V. Contrast agents
  VI. Artifacts
  VII. Dangers, contraindications
- Applications, future trends

MRI History

- 1970 - Raymond Damadian: T1 and T2 relaxations of neoplastic and normal tissues are different.
- 1972 - Raymond Damadian: US patent
- 1973 - Paul Lauterbur: 2D MR imaging method
- 1974 - Peter Mansfield: 3D MR imaging method
- 1977 - Raymond Damadian: first MR scanner ("focused field" method)
- 2003 - Nobel-prize: Lauterbur, Mansfield
- NMR: method which has received the most Nobel-prizes (6)
  Otto Stern (1942), Isidor Rabi (1944), Felix Bloch, Edward Purcell (1952), Richard Ernst (1991), Kurt Wüthrich (2002)

Nuclear Magnetic Resonance Imaging: Basic principle

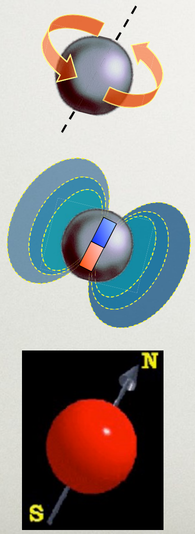


MRI fundamentals

I. Atomic nuclei with nuclear spin are elementary magnets

Otto Stern

W. Gerlach



Atomic nuclei have mass: $m_{proton} = 1{,}67.10^{-24}$ g

Atomic nuclei carry angular momentum: $L = \sqrt{l(l+1)}\hbar$

l = spin quantum number

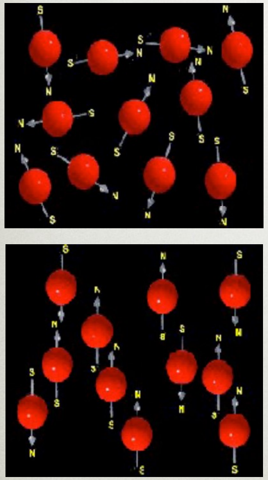
Atomic nuclei carry charge: $q_{proton} = 1{,}6.10^{-19}$ C

Atomic nuclei possess magnetic moment: $\mu_i = \gamma L$

γ = gyromagnetic ratio
L = angular momentum

MRI fundamentals

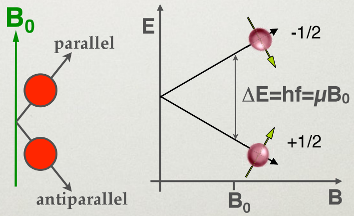
II. Nuclear spins orient in a magnetic field



In absence of magnetic field:
random orientation of elementary magnets

In magnetic field:

elementary magnets orient — energy levels split

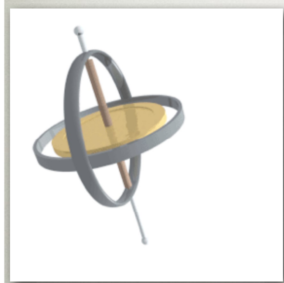


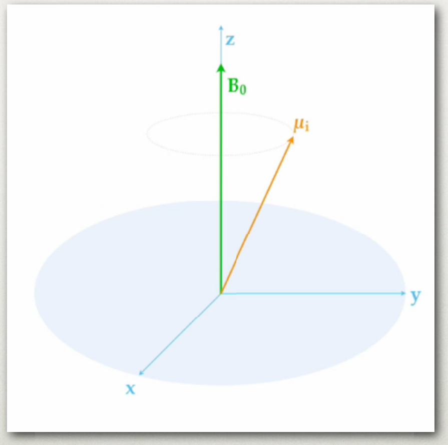
Edward Purcell, 1946

Useful nuclei in MRI: ^{1}H, ^{13}C, ^{19}F, ^{23}N, ^{31}P

MRI fundamentals

III. Oriented nuclear spins display precessional motion

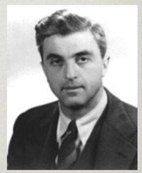




Precession or Larmor frequency:

$$\omega_0 = \gamma B_0$$

$$f_{Larmor} = \frac{\gamma}{2\pi} B_0$$

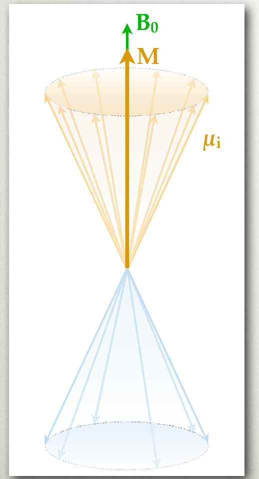


Felix Bloch, 1946

Net magnetization

Due to spin access in different energy states

Low energy state
parallel in case of proton



High energy state
antiparallel in case of proton

B_0 = magnetic field
M = net magnetization

Ratio of magnetic spins in high- (antiparallel) and low-energy (parallel) states:

$$\frac{N_{antiparallel}}{N_{parallel}} = e^{-\frac{\Delta E}{k_B T}}$$

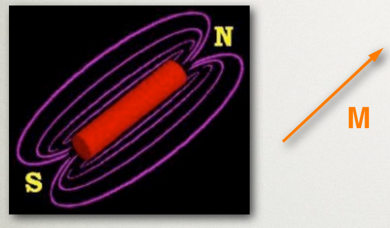
Boltzmann distribution

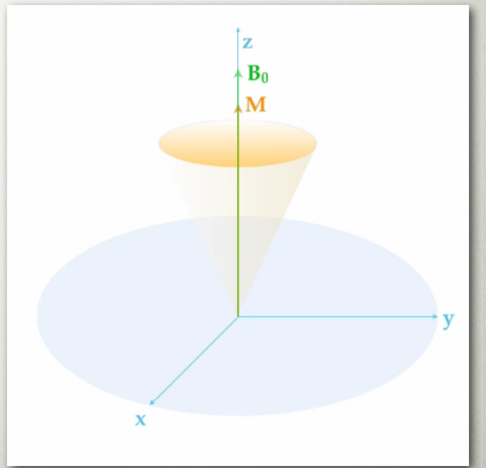
Magnetic field in MRI:
20-50 thousand times that of the Earth's magnetic field

MRI fundamentals

IV. The system may be excited with radio frequency radiation

Resonance condition: Larmor frequency



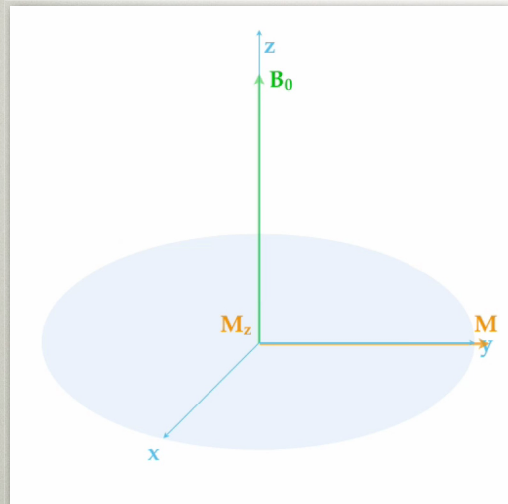


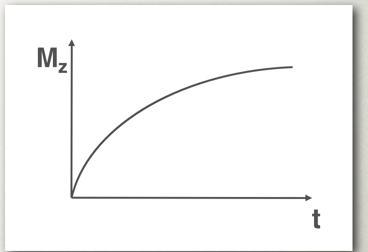
B_0 = magnetic field
M = net magnetization
B_1 = irradiated radio frequency wave

Electromagnetic radiation in MRI:
Radio waves

Spin-lattice relaxation

T1 or longitudinal relaxation

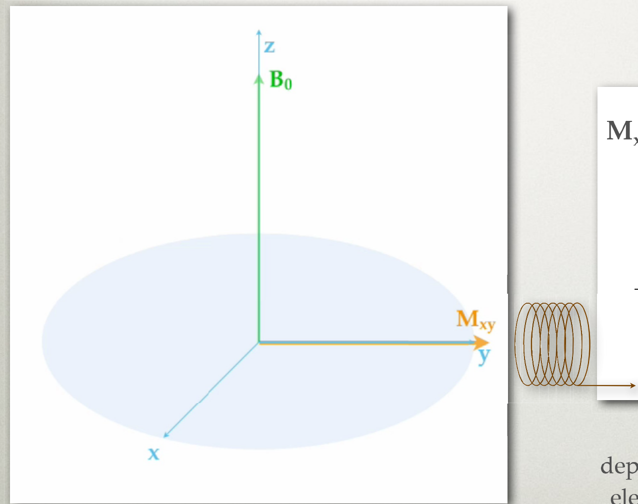


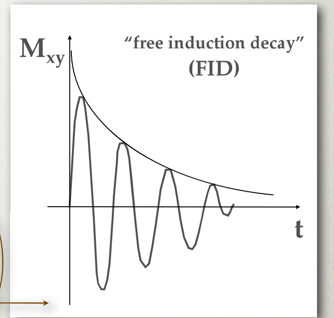


T1 relaxation time:
depends on interaction between elementary magnet (proton) and its environment

Spin-spin relaxation

T2 or transverse relaxation



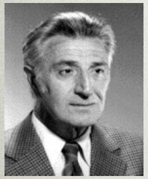


T2 relaxation time:
depends on interaction between elementary magnets (protons)

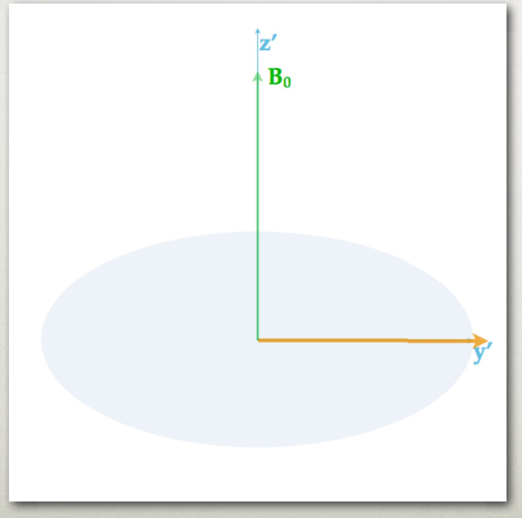
Spin-spin relaxation

T2 or transverse relaxation

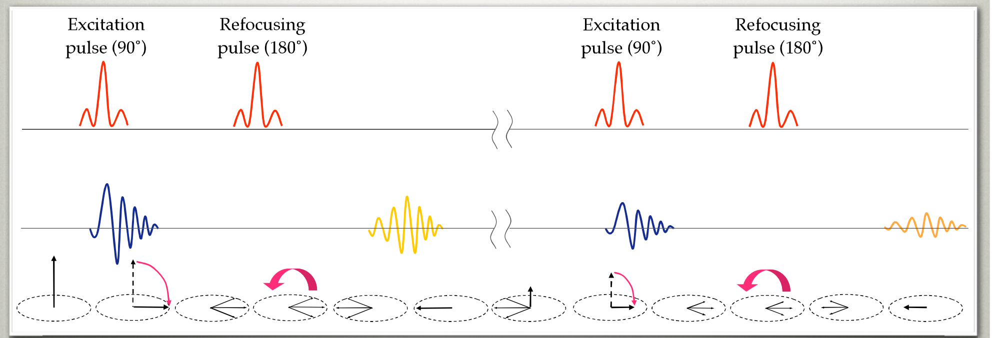
Repetitive pulses of excitation and subsequent relaxation: spin-echo sequence

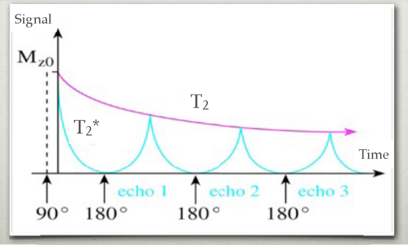


Erwin Hahn, 1949

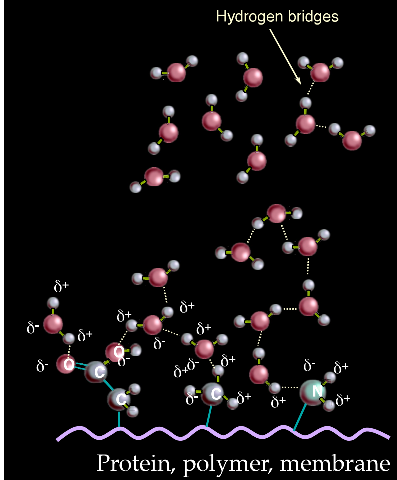


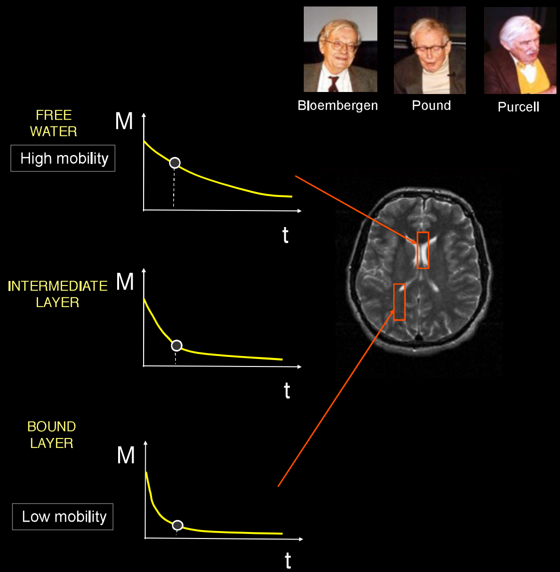
The spin-echo experiment



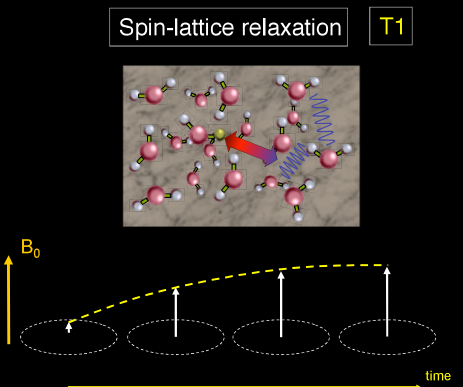


Contrast in MR images is determined by the interaction of spin systems





Nuclear Magnetic Resonance Imaging: Two important relaxation mechanisms



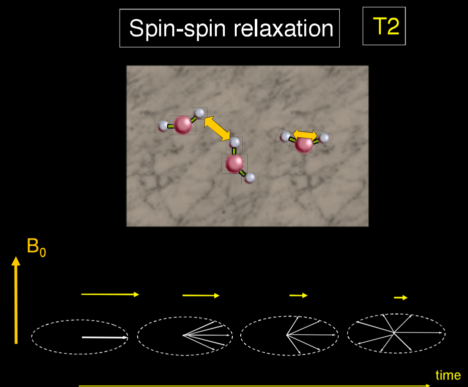
Restoration of longitudinal magnetization

Energy transfered to lattice (phonons)

Entropy increases

Repopulation of spins between spin energy levels

Interactions with magnetic field fluctuations at Larmor frequency



Dephasing of transverse magnetization

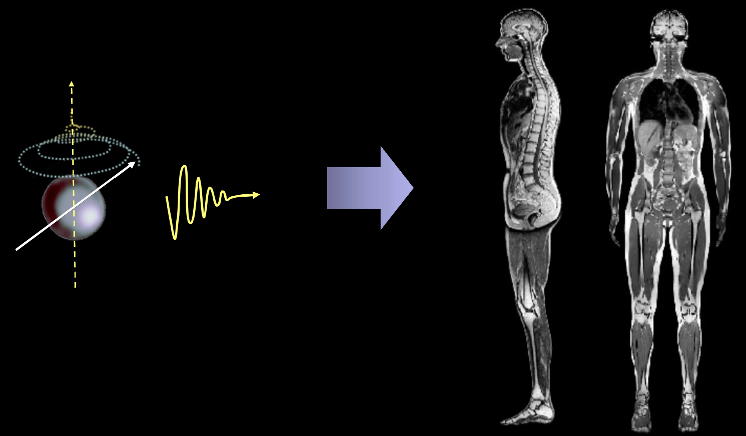
Energy transferred between spins

No entropy change of total spin system

No repopulation of spins between spin energy levels

Interactions with magnetic field fluctuations at low frequency

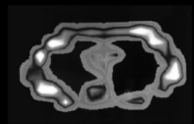
From nuclear magnetic resonance signal to Magnetic Resonance Imaging



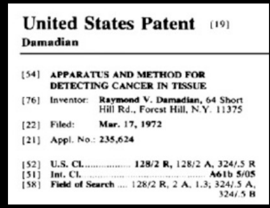
MRI: net magnetization of the human body is generated

Downstate Medical Center - Brooklyn, 1972

Raymond V. Damadian

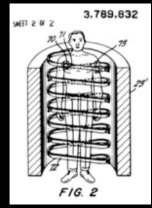


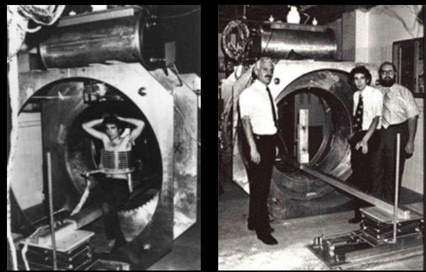
First MRI scan



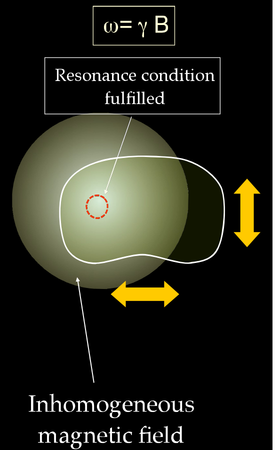
United States Patent [19]
Damadian

[54] APPARATUS AND METHOD FOR DETECTING CANCER IN TISSUE
[76] Inventor: Raymond V. Damadian, 64 Short Hill Rd., Forest Hill, N.Y. 11375
[22] Filed: Mar. 17, 1972
[21] Appl. No.: 235,624



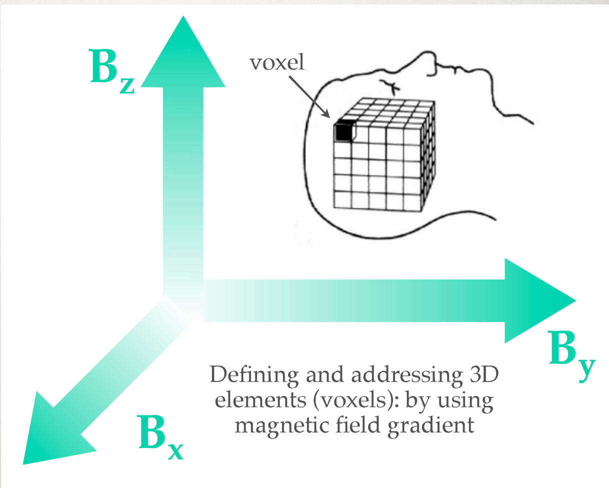


1970: detection of lengthened relaxation times in cancerous tissues
1972: theoretical development of human in vivo 3D NMR
1977: first human MRI image

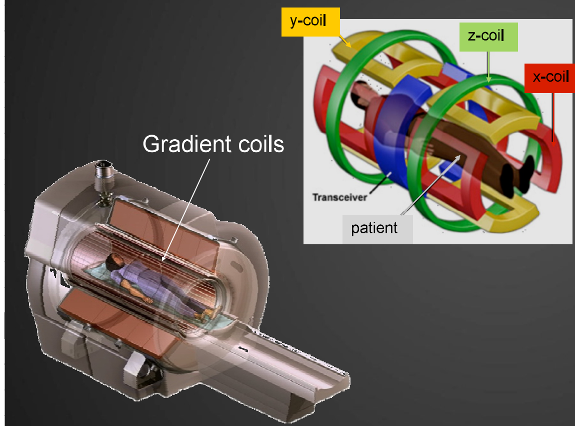


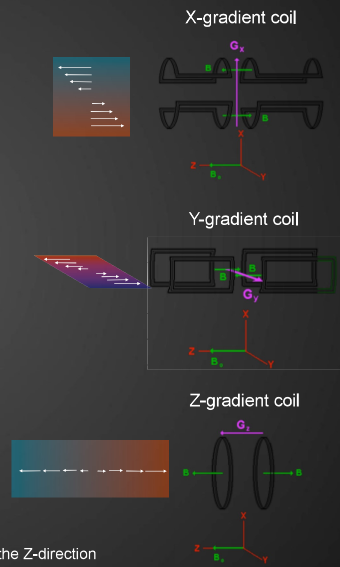
MRI Imaging
I. Spatial encoding

Paul C. Lauterbur (1929-)
Developer of spatially resolved NMR

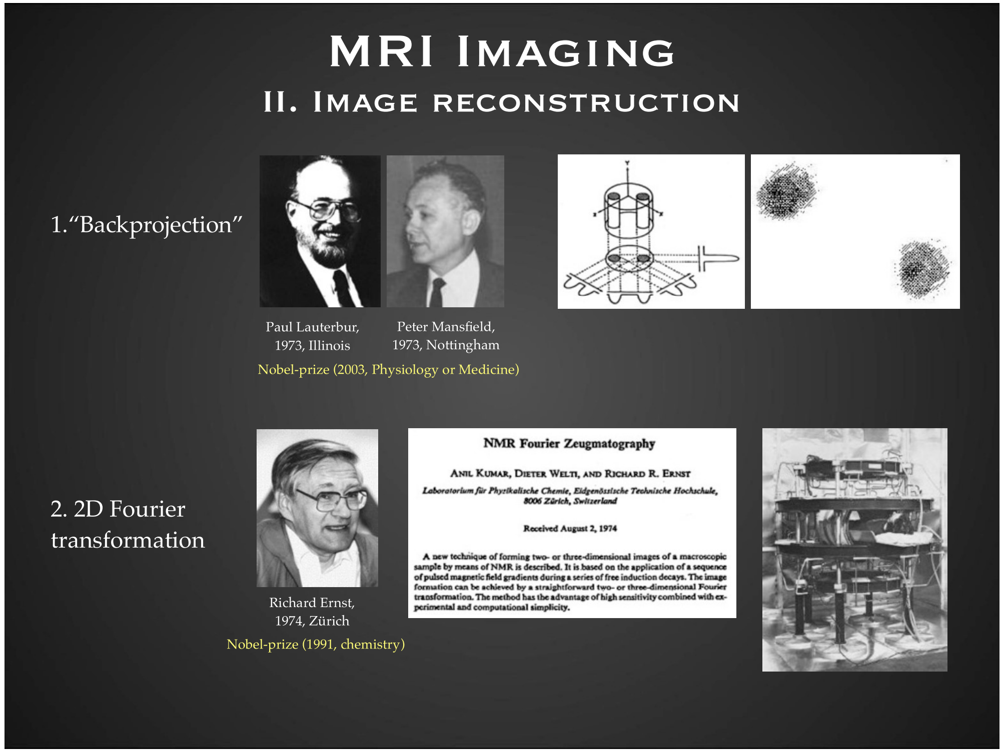


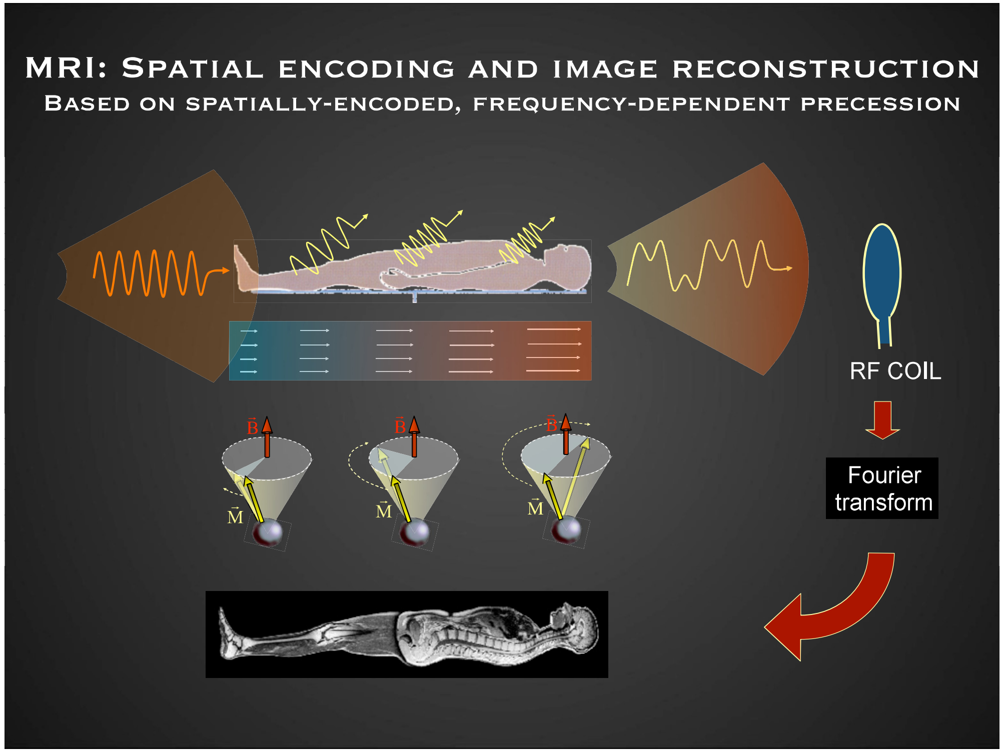
Spatial encoding of the NMR signal: Imaging gradients

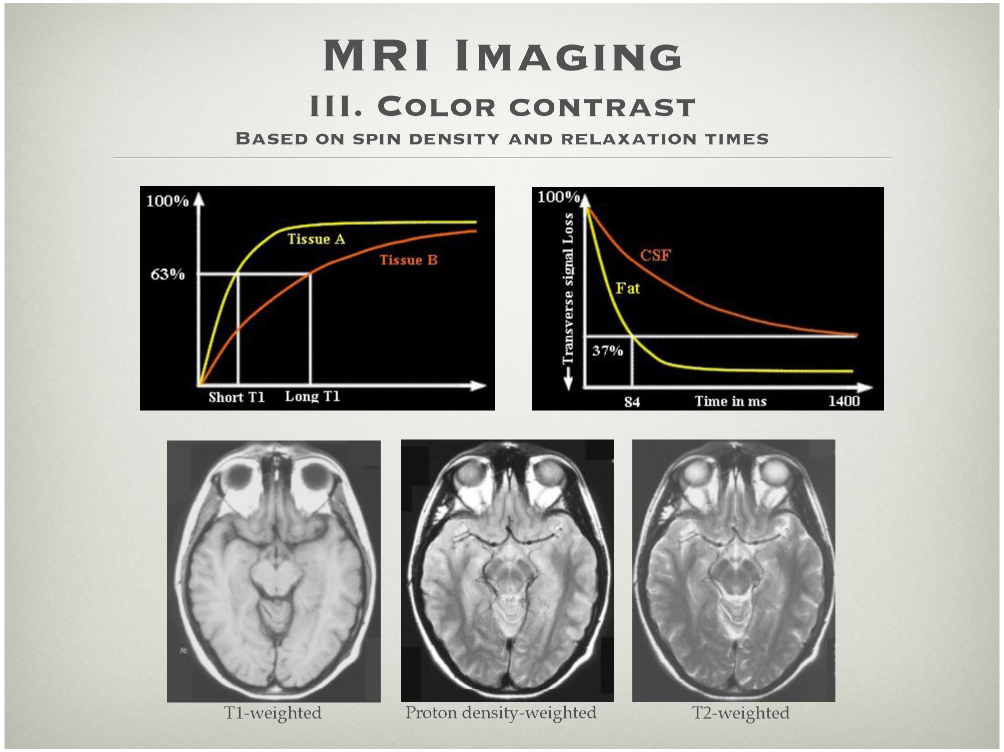


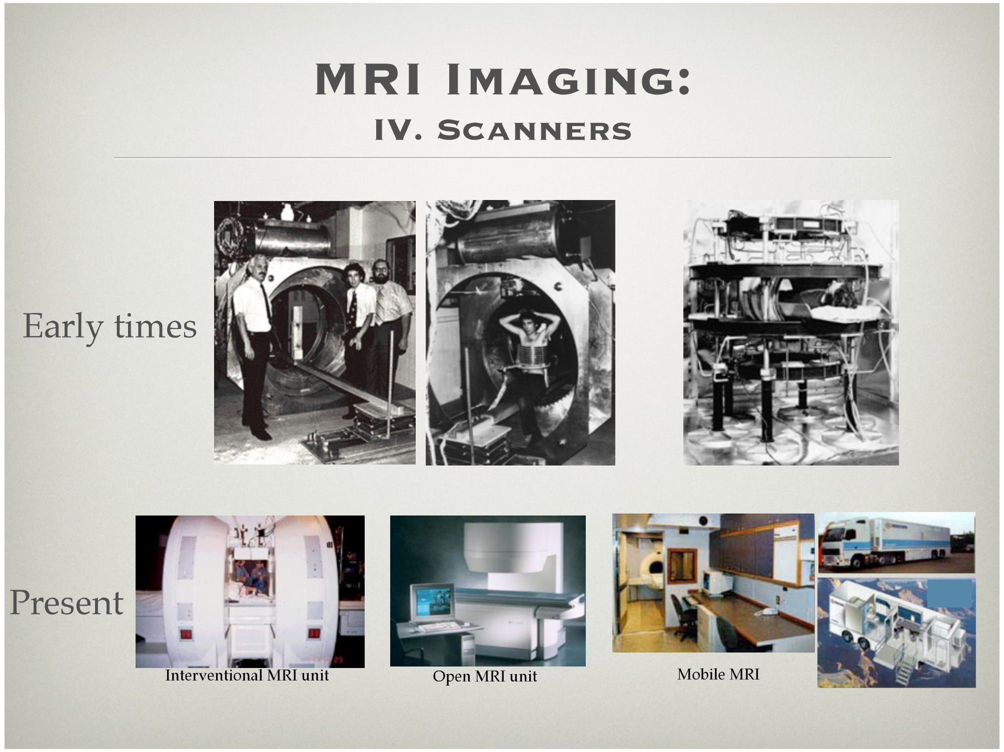


IMPORTANT NOTE:
The magnetic field is always in the Z-direction


MRI Imaging
II. Image reconstruction
1."Backprojection"
Paul Lauterbur, 1973, Illinois
Peter Mansfield, 1973, Nottingham
Nobel-prize (2003, Physiology or Medicine)
2. 2D Fourier transformation
Richard Ernst, 1974, Zürich
Nobel-prize (1991, chemistry)
NMR Fourier Zeugmatography
Anil Kumar, Dieter Welti, and Richard R. Ernst
Laboratorium für Physikalische Chemie, Eidgenössische Technische Hochschule, 8006 Zürich, Switzerland
Received August 2, 1974
A new technique of forming two- or three-dimensional images of a macroscopic sample by means of NMR is described. It is based on the application of a sequence of pulsed magnetic field gradients during a series of free induction decays. The image formation can be achieved by a straightforward two- or three-dimensional Fourier transformation. The method has the advantage of high sensitivity combined with experimental and computational simplicity.


MRI: Spatial encoding and image reconstruction
Based on spatially-encoded, frequency-dependent precession
RF COIL
Fourier transform
B
M

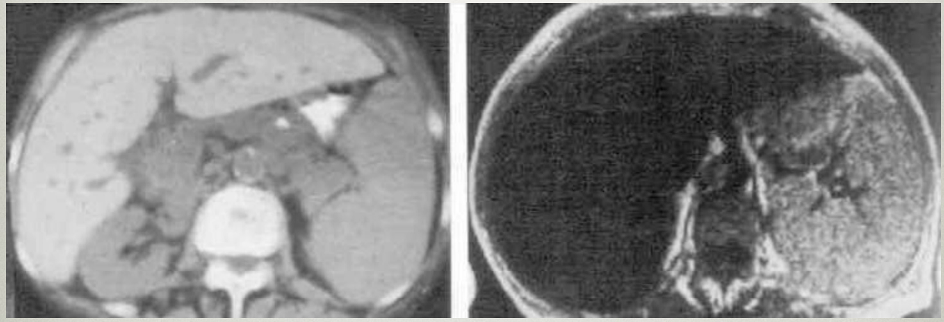

MRI Imaging
III. Color contrast
Based on spin density and relaxation times
100%
63%
Tissue A
Tissue B
Short T1
Long T1
100%
Transverse signal Loss
CSF
Fat
37%
84
Time in ms
1400
T1-weighted
Proton density-weighted
T2-weighted


MRI Imaging:
IV. Scanners
Early times
Present
Interventional MRI unit
Open MRI unit
Mobile MRI

MRI Imaging:
V. Contrast agents

Positive: paramagnetic elements (T1 contrast): Gd, Mn

Negative: superparamagnetic, ferromagnetic (T2 contrast): FeIII, MnII

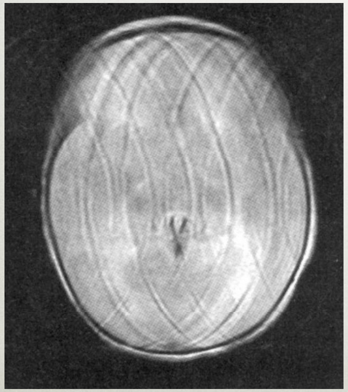


CT MR T2

Haemochromatosis hepatis

MRI Imaging:
VI. Artifacts

- Motion
- Metals (implants, injury)

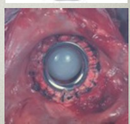


Motion artifact

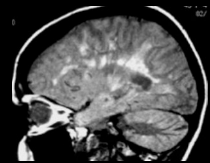
Metal in the orbit of the eye

MRI Imaging:
VII. Dangers, contraindications

- Static magnetic field - metal objects
  Contraindications: implanted devices (pacemaker, defibrillator, hearing aids, drug delivery devices), neurostimulators, brain aneurysm clamps, early cardiac valve implants
- Gradient field - induced current
- Radio frequency field - thermal effects (lens, testis)

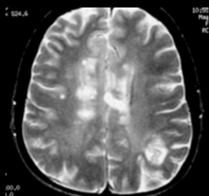


Anatomical imaging:
Multiple sclerosis

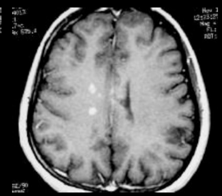


Proton density (sagital)

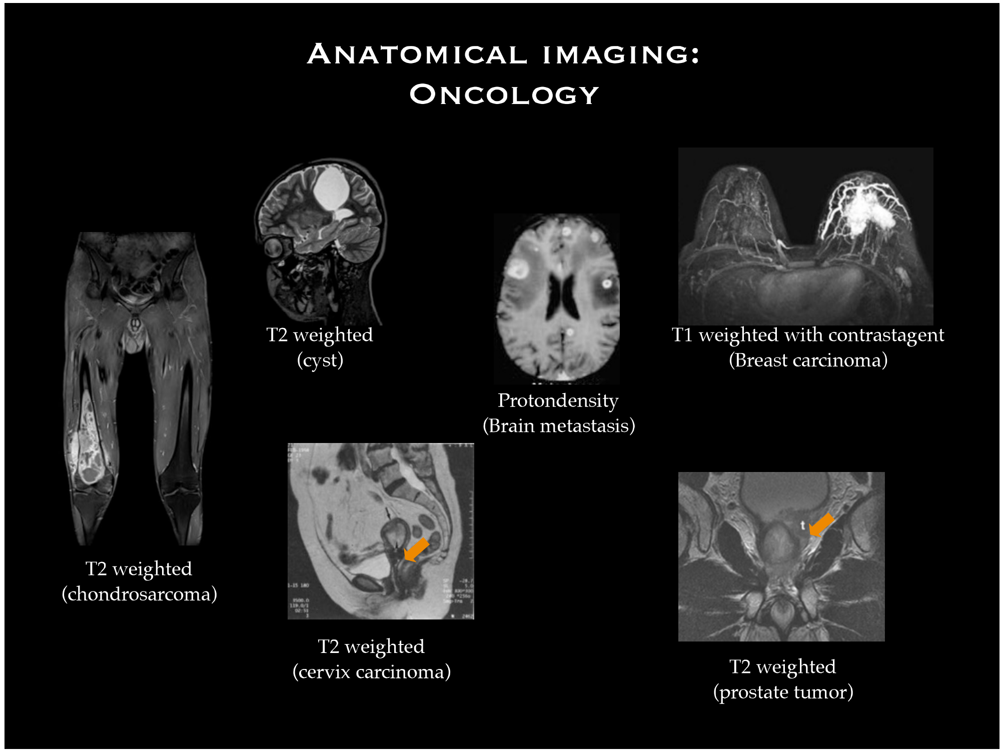
Proton density (transverse)

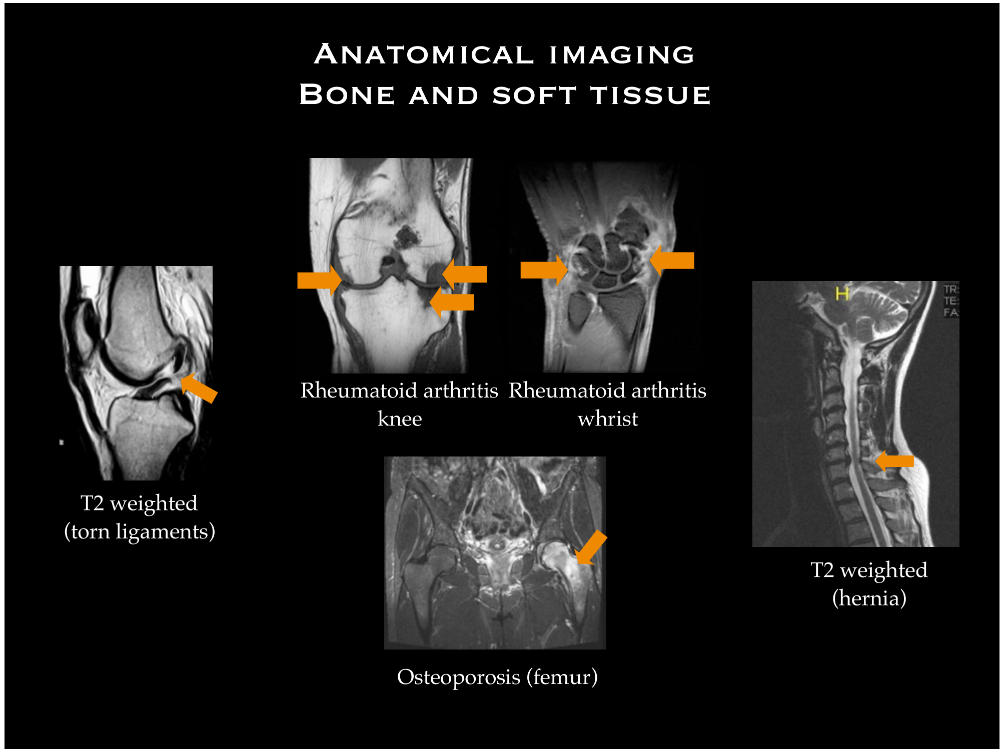


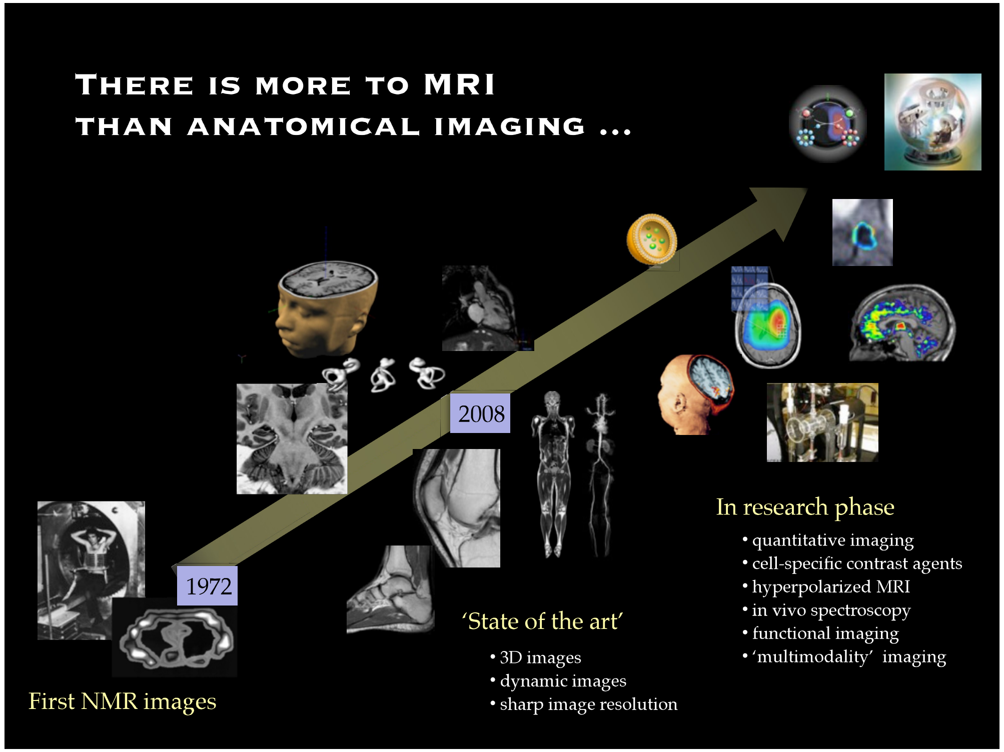
T2 weighted (transverse)

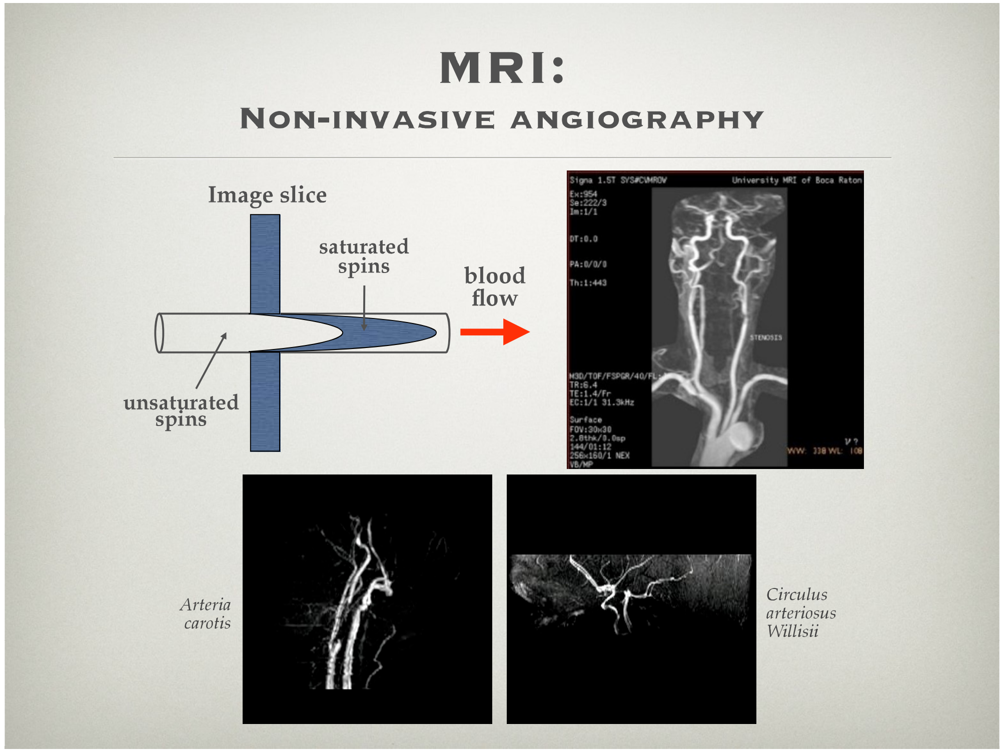


T1 weighted With contrast agent


Anatomical imaging:
Oncology
T2 weighted
(cyst)
Protondensity
(Brain metastasis)
T1 weighted with contrastagent
(Breast carcinoma)
T2 weighted
(chondrosarcoma)
T2 weighted
(cervix carcinoma)
T2 weighted
(prostate tumor)


Anatomical imaging
Bone and soft tissue
Rheumatoid arthritis
knee
Rheumatoid arthritis
whrist
T2 weighted
(torn ligaments)
Osteoporosis (femur)
T2 weighted
(hernia)


There is more to MRI
than anatomical imaging ...
2008
1972
First NMR images
'State of the art'
• 3D images
• dynamic images
• sharp image resolution
In research phase
• quantitative imaging
• cell-specific contrast agents
• hyperpolarized MRI
• in vivo spectroscopy
• functional imaging
• 'multimodality' imaging


MRI:
Non-invasive angiography
Image slice
saturated
spins
blood
flow
unsaturated
spins
Arteria
carotis
Circulus
arteriosus
Willisii

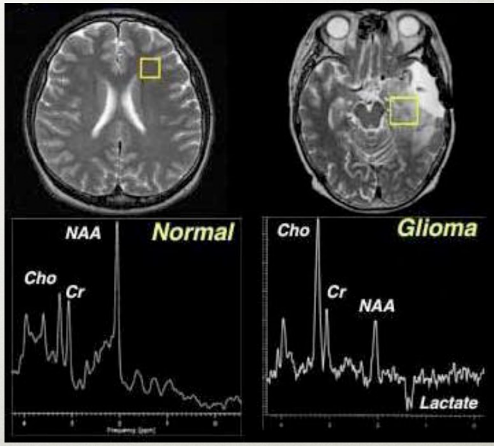
MRI movie

Based on high time resolution images

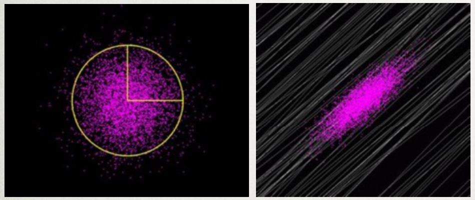
Opening and closing of aorta valve

MR Spectroscopy

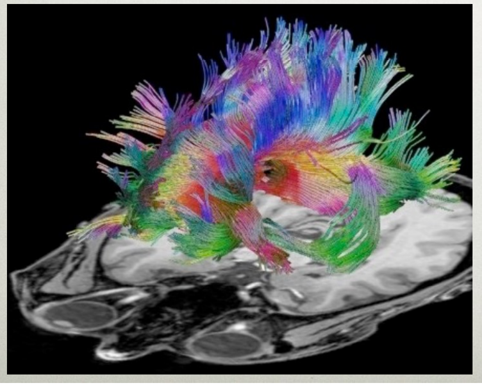
- Chemical shift
- Identification of metabolited
- Tumor diagnostics



Diffusion imaging



Anisotropic water diffusion: contrast

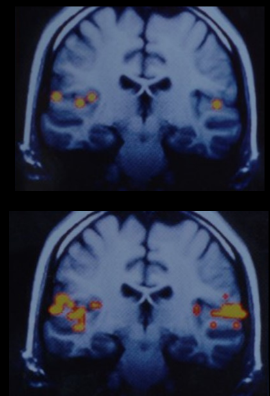


Imaging neural tracts: tractography

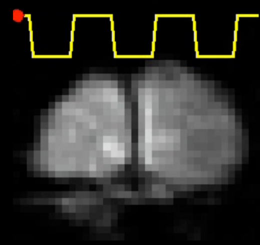
Corpus callosum

Functional MRI (fMRI)

High time resolution images recorded synchronously with physiological processes



Activation in the acoustic cortex



Effect of light pulses on visual cortex

Superposition of MRI on other information (PET)

Superimposed MRI and PET sequence

PET activity: during eye movement
Volume rendering