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.
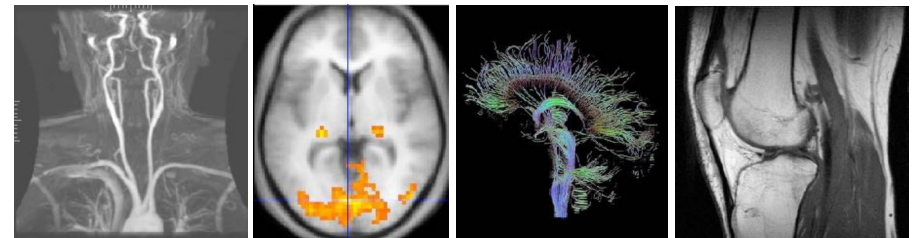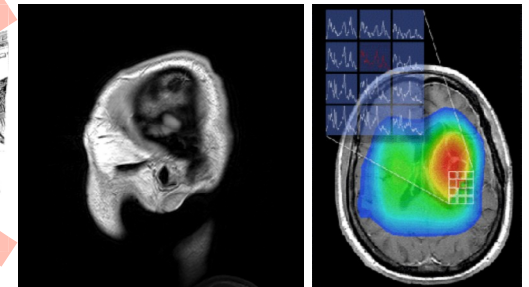
MRI is a revolutionary device

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
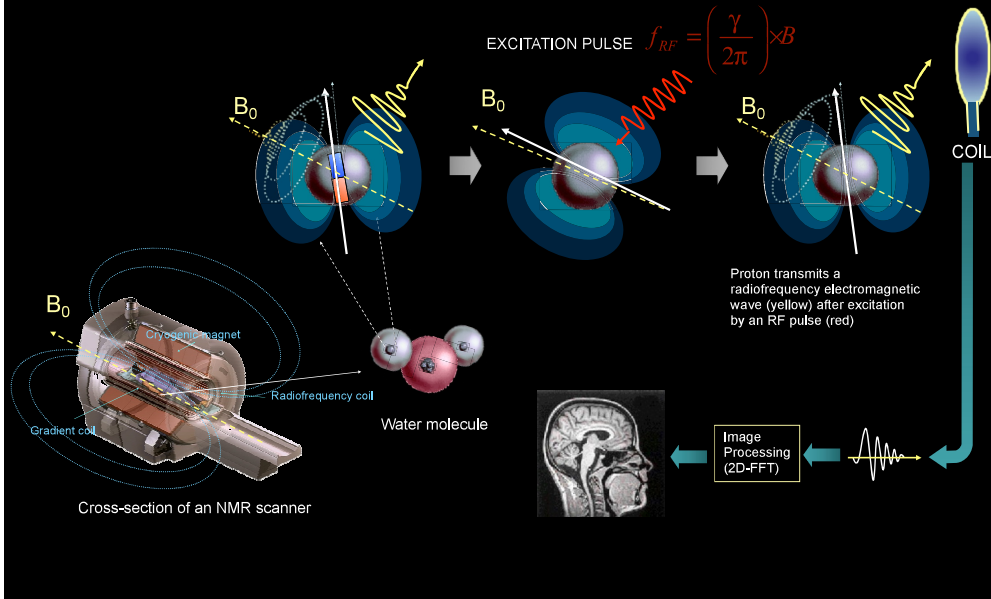
MRI History

- 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)
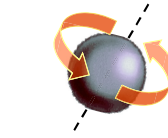
Nuclear Magnetic Resonance Imaging: Basic principle

EXCITATION PULSE $f_{RF} = \left(\dfrac{\gamma}{2\pi}\right) \times B$

B_0

COIL

Proton transmits a radiofrequency electromagnetic wave (yellow) after excitation by an RF pulse (red)

B_0

Cryogenic magnet

Radiofrequency coil

Gradient coil

Water molecule

Cross-section of an NMR scanner

Image Processing (2D-FFT)

MRI FUNDAMENTALS
I. atomic nuclei with nuclear spin are elementary magnets

Otto Stern

W. Gerlach

Atomic nuclei have mass:
$$m_{proton} = 1{,}67.10^{-24} \text{ g}$$
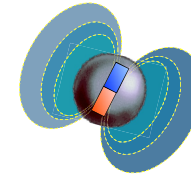
Atomic nuclei carry angular momentum:
$$L = \sqrt{l(l+1)\hbar}$$
l = spin quantum number

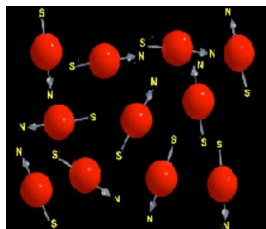Atomic nuclei carry charge:
$$q_{proton} = 1{,}6.10^{-19} \text{ C}$$
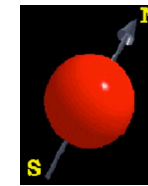
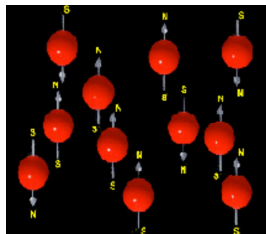Atomic nuclei possess magnetic moment:
$$\mu_i = \gamma L$$
γ = gyromagnetic ratio
L = angular momentum

N

S

MRI FUNDAMENTALS
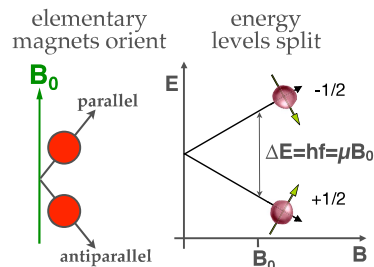## II. nuclear spins orient in a magnetic field

In absence of magnetic field:
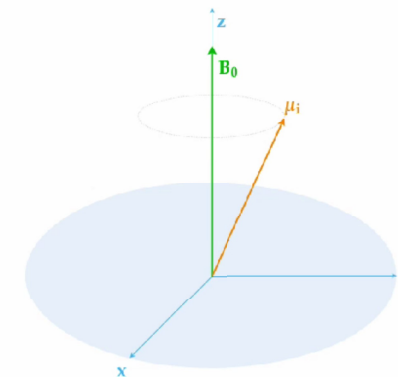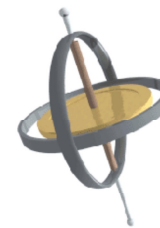random orientation of elementary magnets

In magnetic field:

elementary magnets orient

energy levels split

B_0

parallel

antiparallel

E

-1/2

$\Delta E = hf = \mu B_0$

+1/2

B_0

B

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

z

B_0

μ_i

y

x

Precession or Larmor frequency:
$$\omega_0 = \gamma B_0$$
$$f_{Larmor} = \frac{\gamma}{2\pi} B_0$$

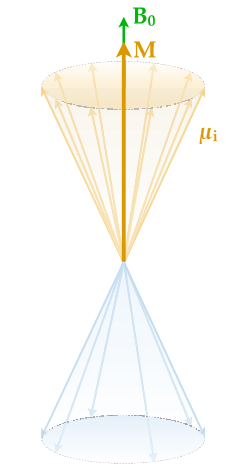Felix Bloch, 1946

Net magnetization
Due to spin access in different energy states

Low energy state
parallel in case of proton

B_0
M

μ_i

B_0 = magnetic field
M = net magnetization

High energy state
antiparallel in case of proton

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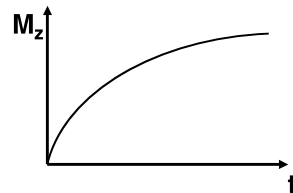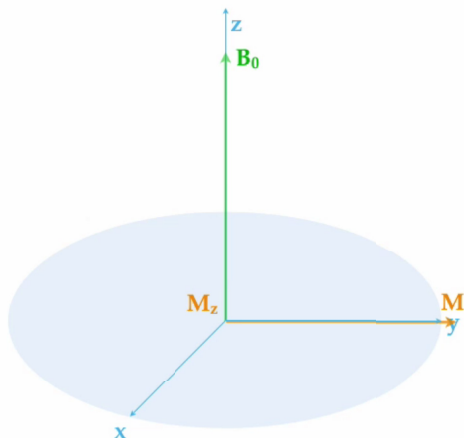
Magnetic field in MRI:
20-50 thousand times that of the Earth's
magnetic field

MRI fundamentals
IV. The system may be excited with radio frequency radiation

**Resonance condition: Larmor frequency**

N

S

M

z
B_0
M

x

y

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

z
B_0

M_z

x

M_z

M
y

M_z

t

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

Spin-spin relaxation
T2 or transverse relaxation

z
B_0

x

M_{xy}
y

M_{xy}

"free induction decay"
(FID)

t
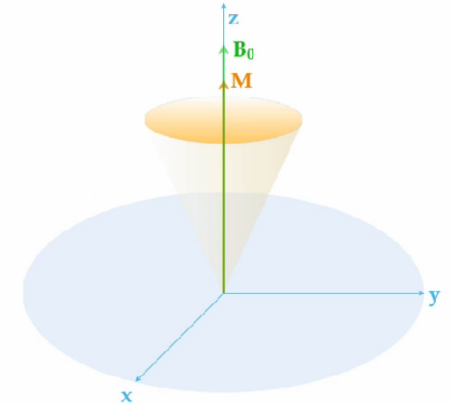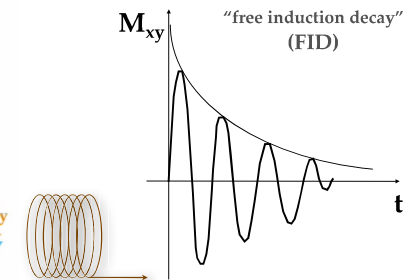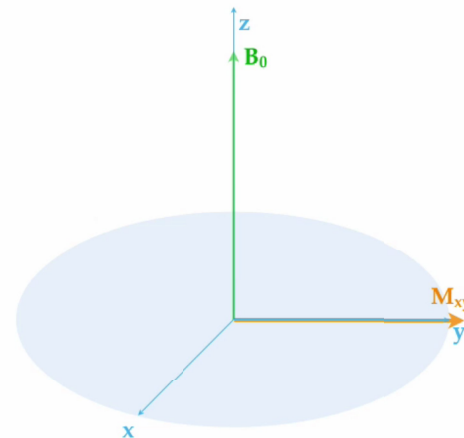
T2 relaxation time:
depends on interaction between
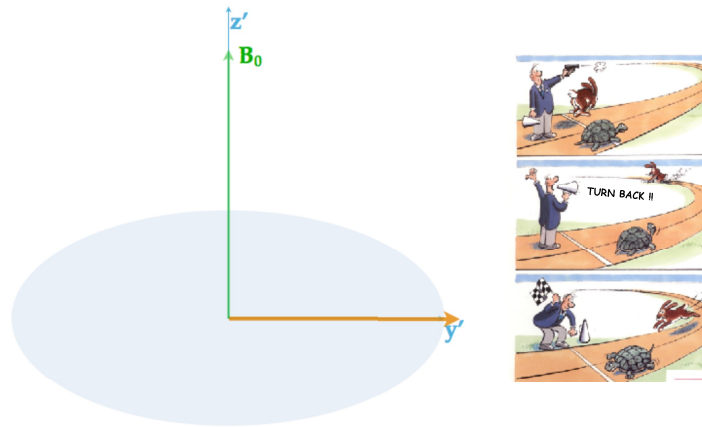elementary magnets (protons)
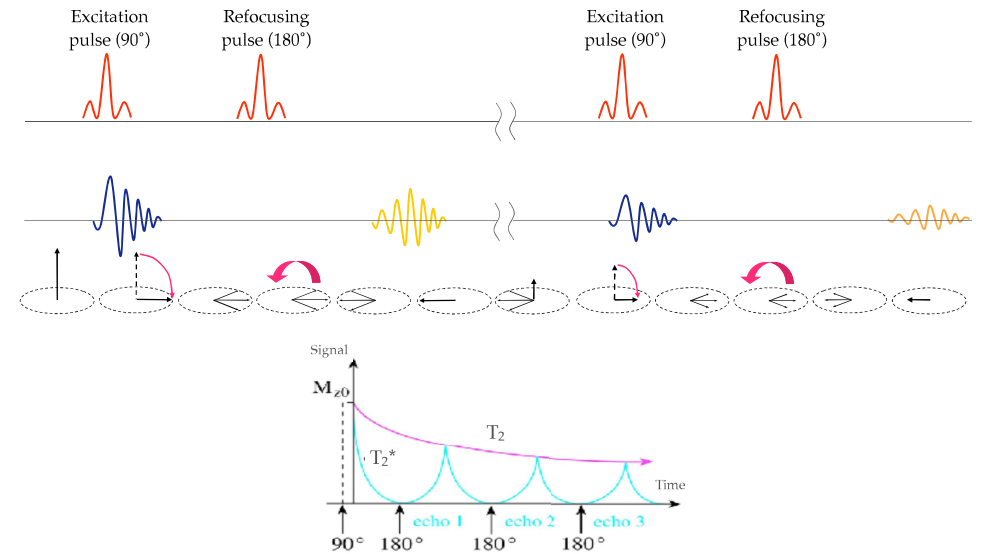
Spin-spin relaxation
T2 or transverse relaxation

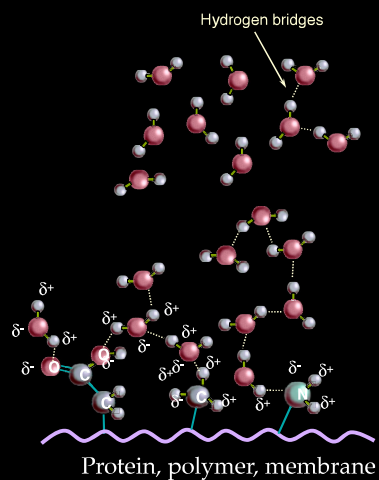Repetitive pulses of excitation and subsequent relaxation: spin-echo sequence

Erwin Hahn, 1949

The spin-echo experiment

Excitation pulse (90°) Refocusing pulse (180°) Excitation pulse (90°) Refocusing pulse (180°)

Signal

M_{z0}

T_2

T_2^*

Time

90° 180° 180° 180°

echo 1 echo 2 echo 3

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

Hydrogen bridges

FREE WATER
High mobility

INTERMEDIATE LAYER

BOUND LAYER
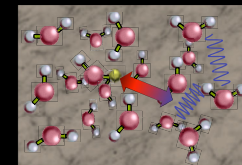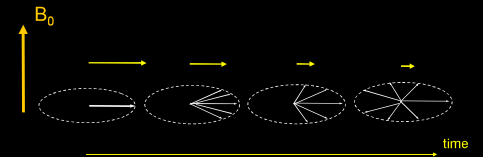Low mobility

Protein, polymer, membrane
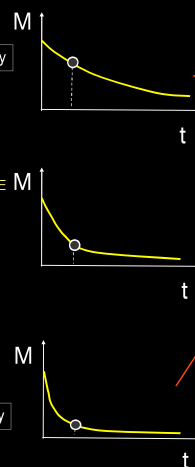
Bloembergen Pound Purcell
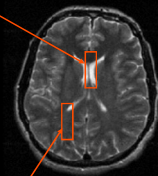
Nuclear Magnetic Resonance Imaging: Two important relaxation mechanisms

| Spin-lattice relaxation	T1	Spin-spin relaxation	T2

B_0 time B_0 time
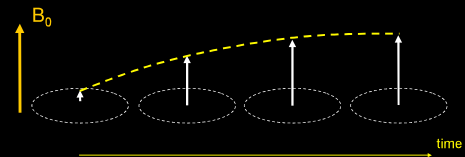
Restoration of longitudinal magnetization	Dephasing of transverse magnetization
Energy transferred to lattice (phonons)	Energy transferred between spins
Entropy increases	No entropy change of total spin system
Repopulation of spins between spin energy levels	No repopulation of spins between spin energy levels
Interactions with magnetic field fluctuations at Larmor frequency	Interactions with magnetic field fluctuations at low frequency

From nuclear magnetic resonance signal to Magnetic Resonance Imaging
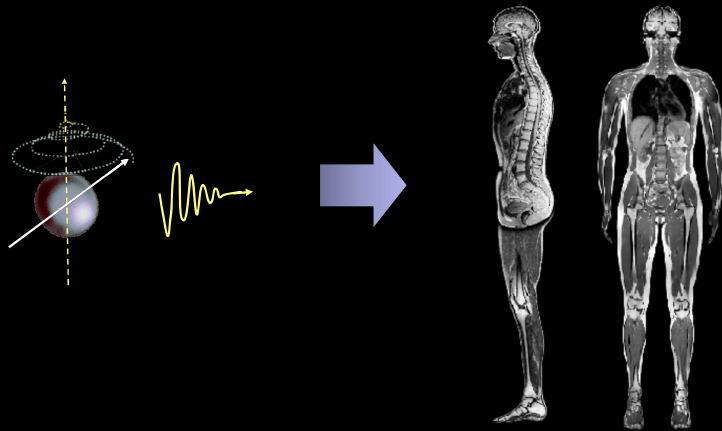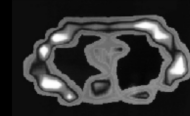

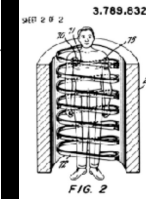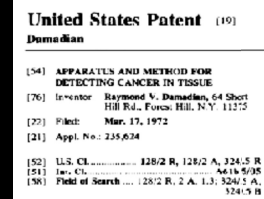# MRI: net magnetization of the human body is generated

Downstate Medical Center - Brooklyn, 1972

Raymond V. Damadian

First MRI scan

United States Patent
Damadian
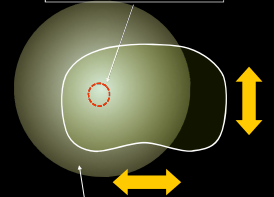[54] APPARATUS AND METHOD FOR DETECTING CANCER IN TISSUE

3.789.832

FIG. 2

$\omega = \gamma B$

Resonance condition fulfilled

Inhomogeneous magnetic field

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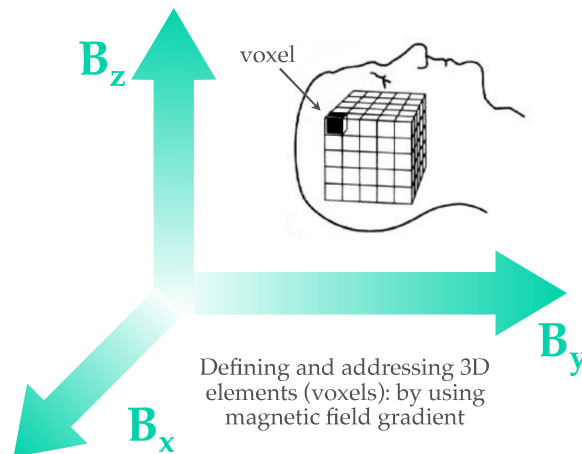1972: theoretical development of human in vivo 3D NMR
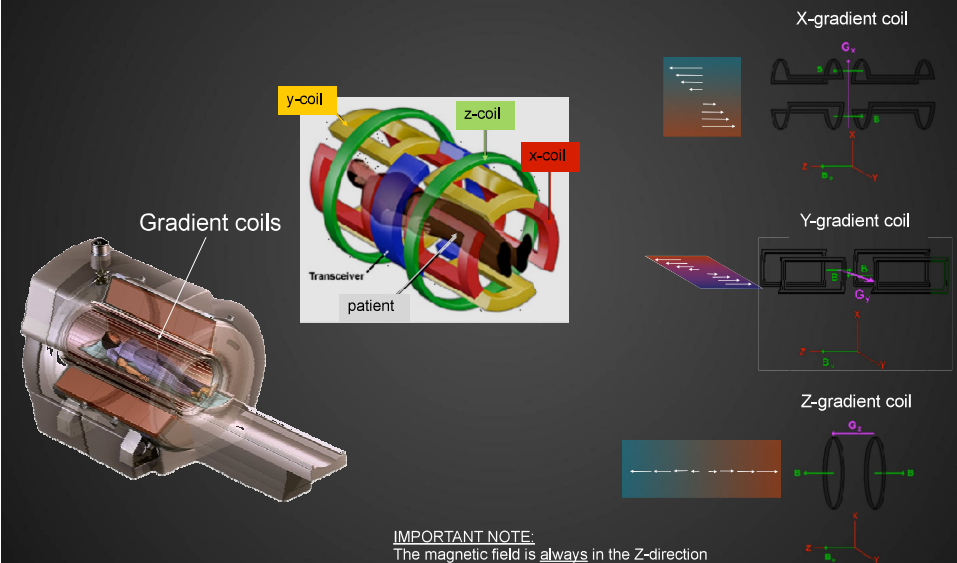1977: first human MRI image

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MRI Imaging
I. Spatial encoding

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

B_z

B_y

B_x

voxel

Defining and addressing 3D elements (voxels): by using magnetic field gradient

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Spatial encoding of the NMR signal: Imaging gradients

X-gradient coil

Y-gradient coil

Z-gradient coil

Gradient coils

y-coil

z-coil

x-coil

Transceiver

patient

IMPORTANT NOTE:
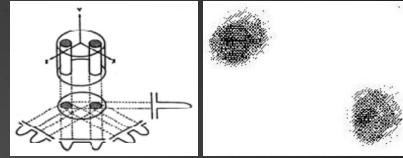The magnetic field is always in the Z-direction
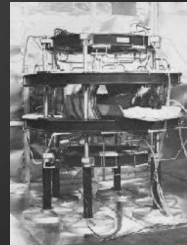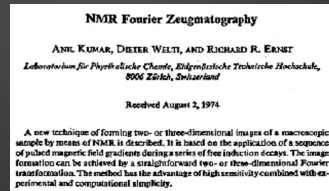
MRI Imaging
II. Image reconstruction

1. "Backprojection"

Paul Lauterbur,
1973, Illinois

Peter Mansfield,
1973, Nottingham

Nobel-prize (2003, Physiology or Medicine)

2. 2D Fourier transformation

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.

Richard Ernst,
1974, Zürich

Nobel-prize (1991, chemistry)

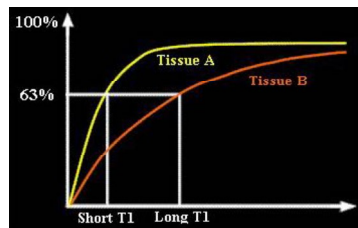# MRI: Spatial encoding and image reconstruction
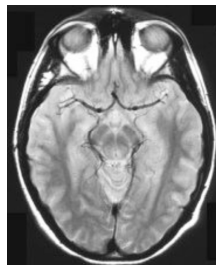## Based on spatially-encoded, frequency-dependent precession

RF COIL

Fourier transform
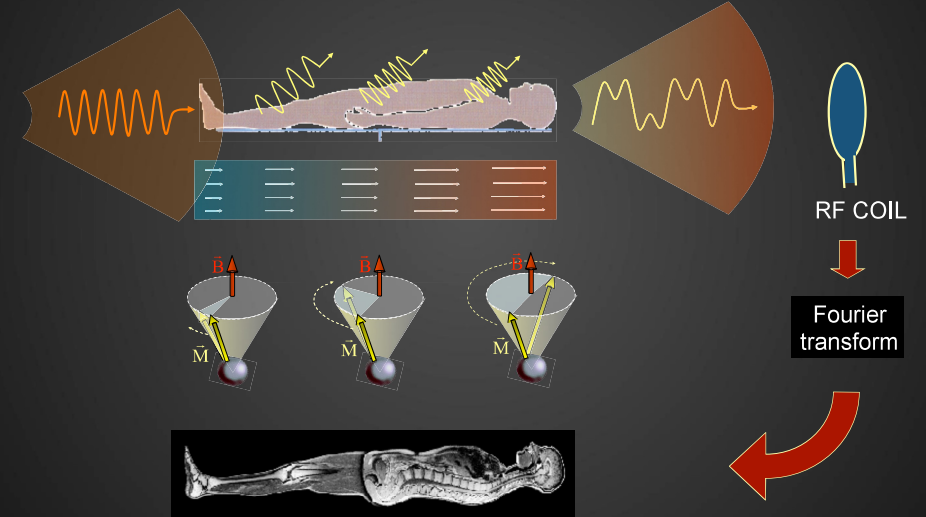
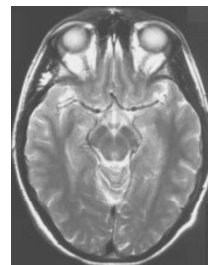# MRI Imaging
III. Color contrast
Based on spin density and relaxation times
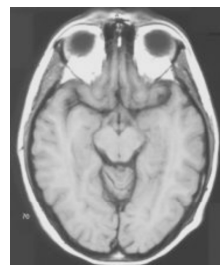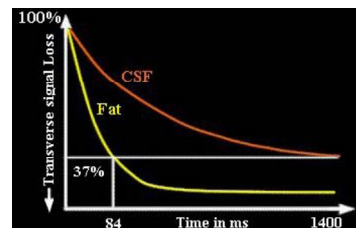
T1-weighted

Proton density-weighted

T2-weighted

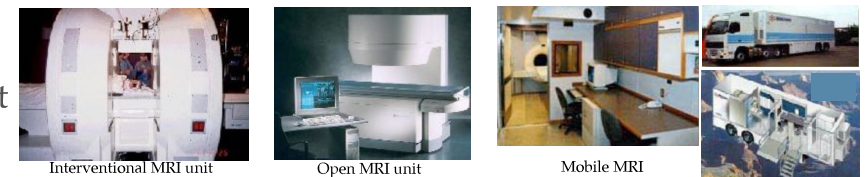# MRI Imaging:
IV. Scanners

Early times

Present

Interventional MRI unit
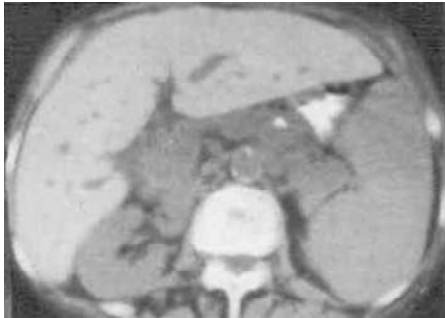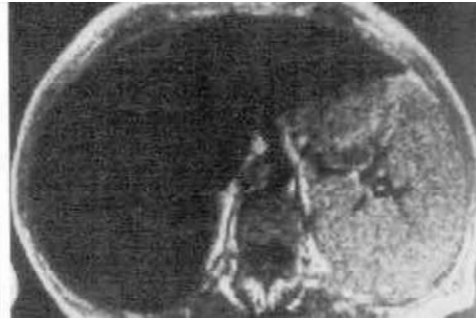
Open MRI unit

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:
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)

MRI Imaging:
VI. Artifacts

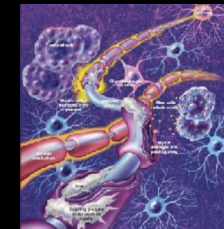- Motion

- Metals (implants, injury)
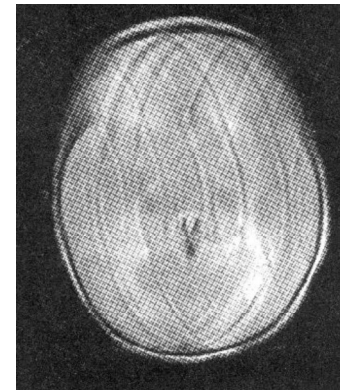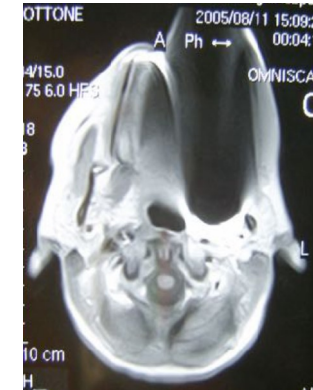
Motion artifact   *Metal in the orbit of the eye*
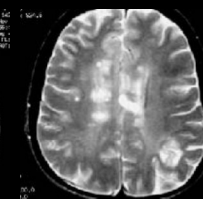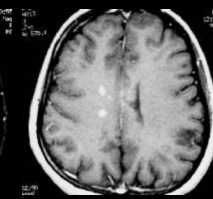
Anatomical imaging:
Multiple sclerosis
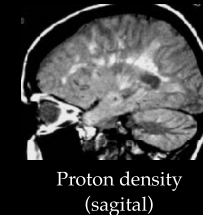
Proton density
(sagital)

Proton density   T2 weighted   T1 weighted
(transverse)   (transverse)   With contrast agent

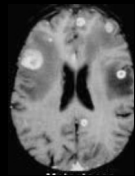**ANATOMICAL IMAGING: ONCOLOGY**
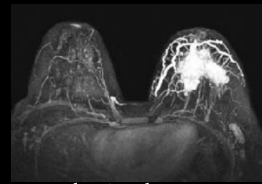
T2 weighted (cyst)

Protondensity (Brain metastasis)

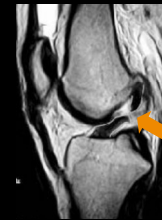T1 weighted with contrastagent (Breast carcinoma)

T2 weighted (chondrosarcoma)

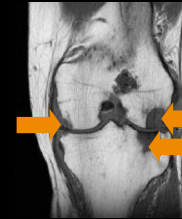T2 weighted (cervix carcinoma)

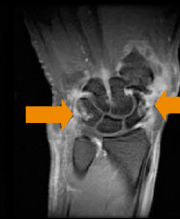T2 weighted (prostate tumor)

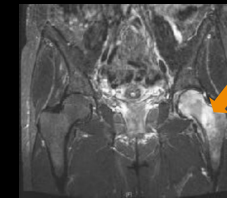

ANATOMICAL IMAGING BONE AND SOFT TISSUE

T2 weighted (torn ligaments)

Rheumatoid arthritis knee
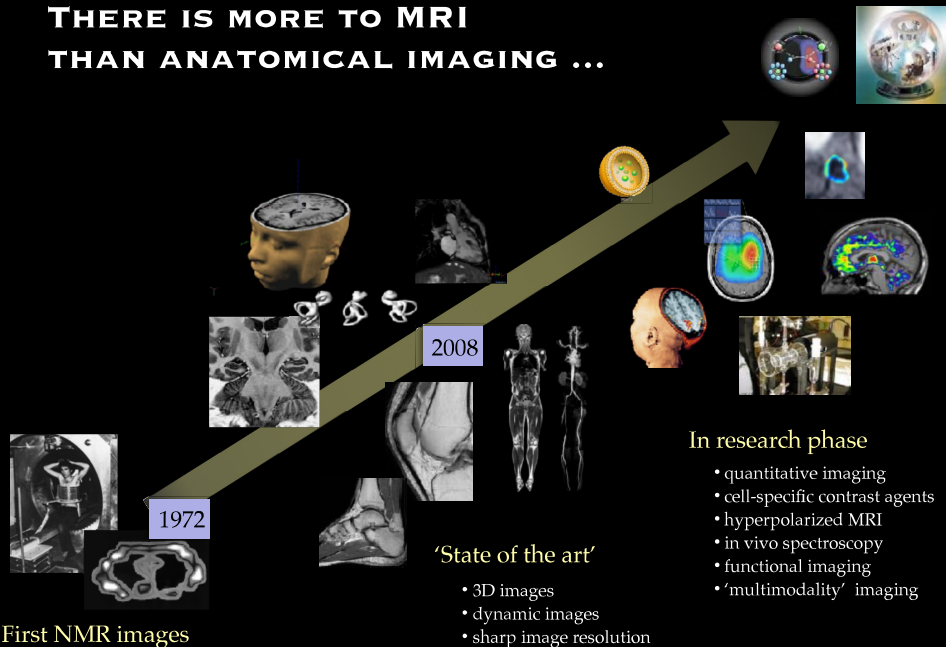
Rheumatoid arthritis whrist

Osteoporosis (femur)

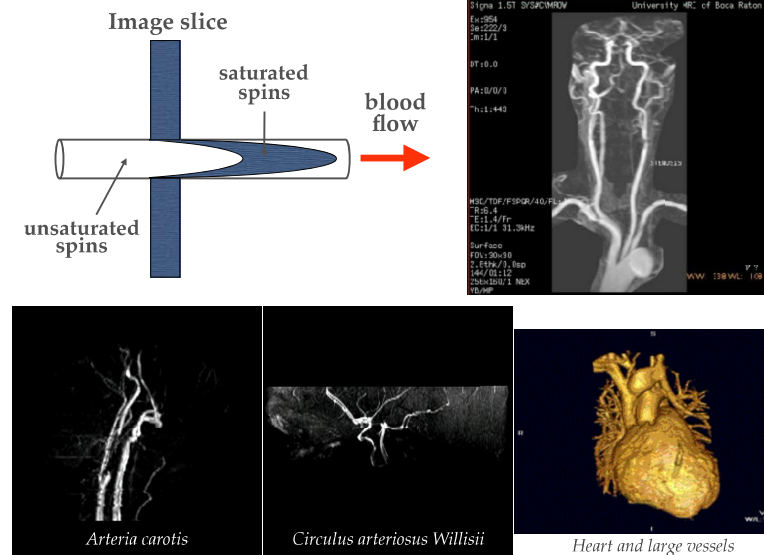T2 weighted (hernia)
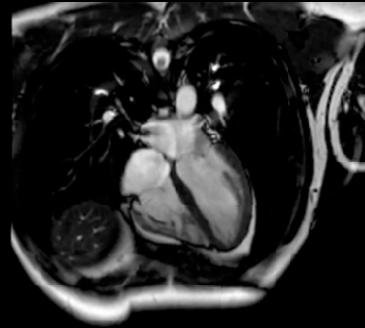

THERE IS MORE TO MRI THAN ANATOMICAL IMAGING ...

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

Heart and large vessels

MRI movie
Based on high time resolution images

Opening and closing of aorta valve

Blod flow in cardiac chambers

MR Spectroscopy

- Chemical shift
- Identification of metabolited
- Tumor diagnostics
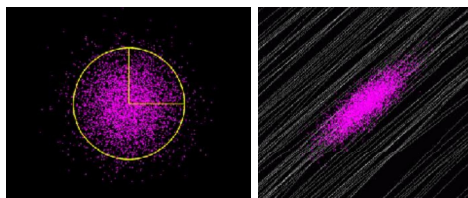
Diffusion imaging

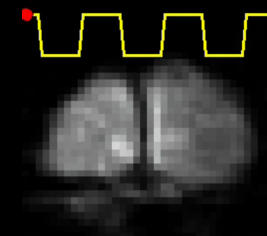Anisotropic water diffusion: contrast
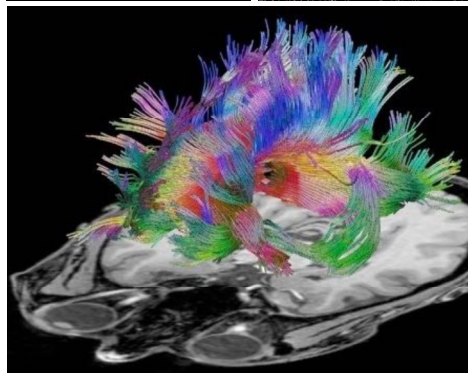
Imaging neural tracts: tractography

Corpus callosum
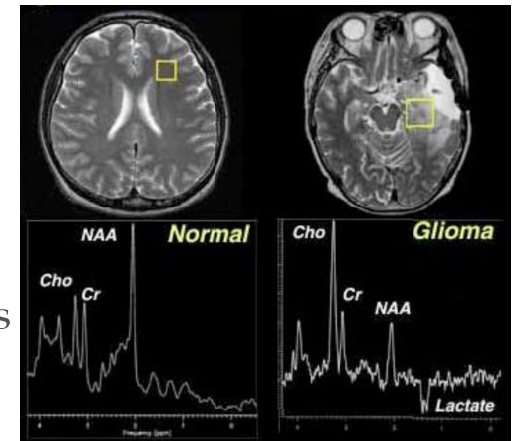
Functional MRI (fMRI)
High time resolution images recorded synchronously with physiological processes

Effect of light pulses on visual cortex

Activation in the acoustic cortex

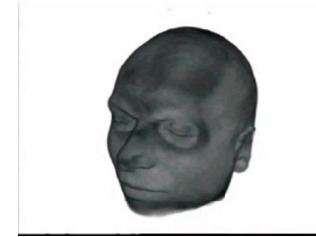# Superposition of MRI on other information (PET)

Superimposed MRI and PET sequence

PET activity: during eye movement
Volume rendering