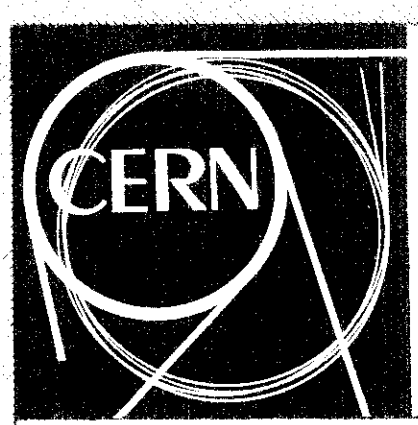

à scanner

398

#2309926

Cours/Lecture Series

2001-2002 ACADEMIC TRAINING PROGRAMME

LECTURE SERIES

TITLE	:	**Physics Technologies in Medicine**
SPEAKERS	:	G. K. Von Schulthess, Univ. of Zürich.
		S. Wildermuth, A. Buck, Univ. Hospital Zürich
		K. Jäger, Univ. Hospital Basel, R. Kreis, Univ. Hospital Bern
TIME	:	10, 11, 12, 13, 14 June, from 11.00 to 12.00hrs
PLACE	:	Auditorium, Bldg 500

ABSTRACT

Modern medicine is a large consumer of physics technologies.
The series of lectures covers medical imaging starting with an overview and the history of medical imaging. Then follows four lectures covering

- x-ray imaging
- positron emission tomography
- imaging blood flow by ultrasound
- magnetic resonance

10 June 2002 100 Years of Medical Imaging
Pr. Gustav K. von Schulthess MD, PhD, University of Zurich
History and overview of Medical Imaging

11 June 2002
X-rays: still going strong
Dr. Simon Wildermuth, MD, University Hospital Zurich
Multidetector computed tomography: New developments and applications

12 June 2002
Nuclear Medicine: PET Positron Emission Tomography
Dr. Alfred Buck, MD, MSc, University Hospital Zurich
Elucidating healthy and pathological human physiology with PET

13 June 2002 Ultrasound
Pr. Kurt Jäger, MD, University Hospital Basel
Imaging blood flow with ultrasound

14 June 2002 Magnetic Resonance
Pr. Roland Kreis, M.Sc., PhD, University Hospital Bern
Magnetic Resonance in Medicine: Morphology and Way Beyond

One Century of Medical Imaging an Overview

CERN, Geneva, June 10, 2002

Gustav K. von Schulthess, MD, PhD

[redacted]
Nuclear Medicine
and
MR Center
University Hospital
Zurich, Switzerland

Acknowledgements

-Thomas Berthold, BS
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- Thomas Hany, MD
- Gerhard Goerres, MD
- Ehab Kamel, MD
- Philipp Kaufmann, MD
-Jürg Schwitter, MD
- Hans Ch. Steinert, MD
and many others

A Century of Medical in-vivo Imaging

Table of Contents

Man as Creator of Images I

Early images: Making images is related to human conciousness

the awakening of human conciousness

recognizing the other

animals were painted to perfection even 15'000 years BC

Murals in Altamira, Spain

Man as Creator of Images II

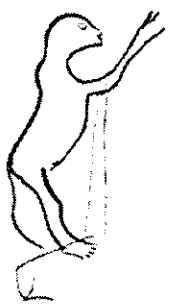
Early images

the awakening of human conciousness

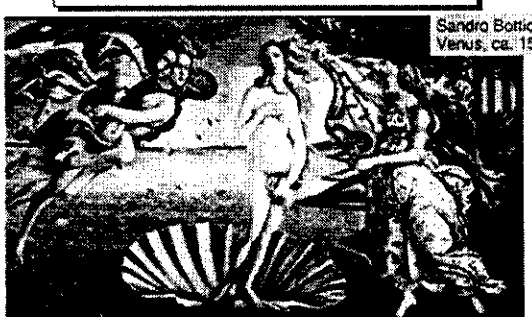
recognizing the self is apparently more difficult than recognizing the other

humans were not depicted well 15'000 years ago

Murals in Altamira, Spain



Man as Creator of Images III



Sandro Botticelli
Venus, ca. 1550

Recognition of the external self: from ~ 2000 BC to Renaissance perfection: anatomic imaging perfected!

Man as Creator of Images IV

Edvard Munch
Jealousy, ca. 1890

Using images to depict the internal self: 19th century

Medical Images
Patient Anatomy from Without

Recognizing disease by looking at and examining the patient

Inspection of patients:
an important means to diagnose disease

Greek physician examining a patients' abdomen (ca. 300 BC)

Medical Images
Anatomy of the Dead from Within

Recognizing disease by exploring the internal anatomy of the patient

Dissecting deceased humans to study disease

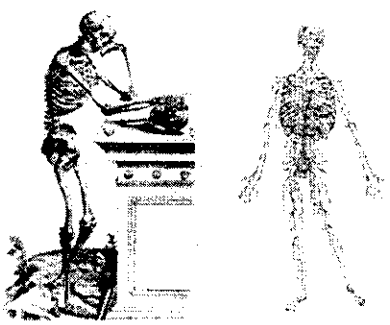
Antonius Vesalius, 1514-1564
famous 16th century anatomist
(around 1540)

Medical Images
Anatomy of the Dead from Within

Recognizing disease by exploring the internal anatomy of the patient

Depicting human anatomy

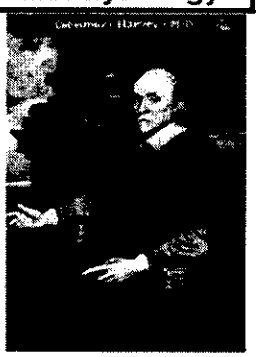
Antonius Vesalius, -
standing skeleton
- arterial system



Medical Images
Understanding Human Physiology

Understanding function by combining
- anatomical insights from within
- function information from without

William Harvey, 1578-1657
the discoverer of the blood circulation
(around 1650)



Medical Images
Gaining Pathophysiological Insights

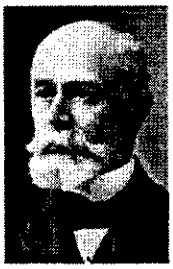
Understanding disease by examining human excretions

Viewing of urine
(around 1750)

The Revolution - Anatomy of the Living from Within

C. W. Roentgen (around 1885)

X-ray hand of Emma Roentgen
Never experiment with your wife!



Marie Curie
Nobel prize physics, 1903

Henry Becquerel
Nobel prize physics, 1903

Albert Einstein
Nobel prize physics, 1921

Discovery of Radioactivity
- Nuclear Medicine
- PET

Discovery
- of photo effect
- mass-energy equivalence

PET

Imaging Methods - Morphology

Radiology *X-rays*

- conventional x-rays
- (conventional tomography)
- x-ray angiography
- digital subtraction angiography
- (x-ray) computed tomography

-interventional radiology
(fluoroscopically guided instruments)

More by Simon Wildermuth, MD

A first revolution - conventional X-rays

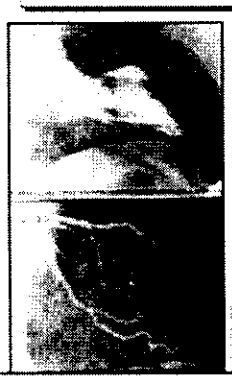
conventional chest x-ray:
excellent
air-soft tissue contrast

conventional bone x-ray:
excellent
bone-soft tissue contrast

Not a revolution - poor soft tissue contrast

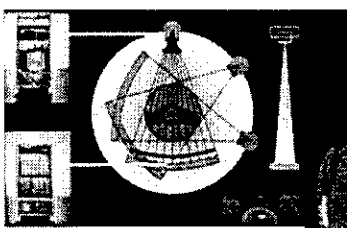
conventional abdominal x-ray: conventional skull x-ray:
excellent air-soft tissue contrast, excellent bone-soft tissue contras
but no contrast between soft tissues

A second revolution - contrast agents



Cardiac ventriculography, coronary ar
pelvic angiography:
excellent vessel-soft tissue contrast

A third revolution
cross secional images & computers



CT-principle:
reconstruction of
section from
projection images

CT-section through upper abdomen

Imaging Methods

Sonography *sound waves*

Imaging

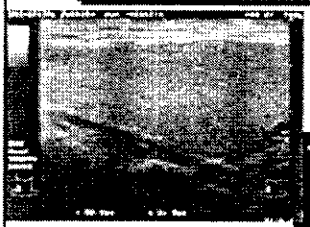
- 2D Sonography
- 3D Sonography
- harmonic imaging

Doppler sonography

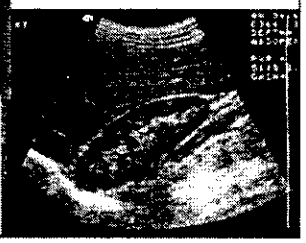
- continuous wave Doppler
- pulsed Doppler

More by Kurt Jäger, MD

Sonography
Sound waves & piezo crystals



Sonography: Thyroid disease
Soft tissue contrast



Sonography: kidney imaging
soft tissue contrast

Imaging Methods

Magnetic Resonance *radio waves*

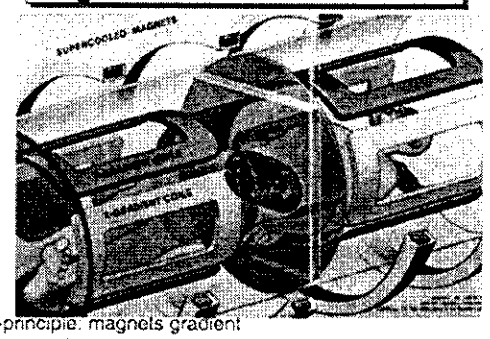
MR imaging

- static MR
- dynamic contrast enhanced MR (Perfusion)
- MR angiography (contrast enhanced, TOF, PC)
- MR flow imaging
- MR diffusion imaging

MR spectroscopy with P-31, H-1, C-13

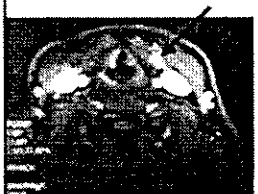
More by Roland Kreis, MD

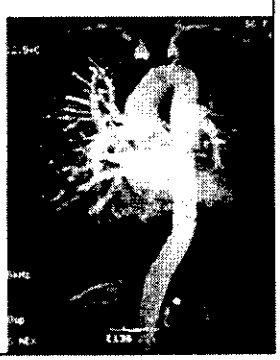
MR Imaging
Magnetic fields & radio waves



MR-principle: magnets gradient fields and short rf-pulses

From MR imaging to 3D MR angiography

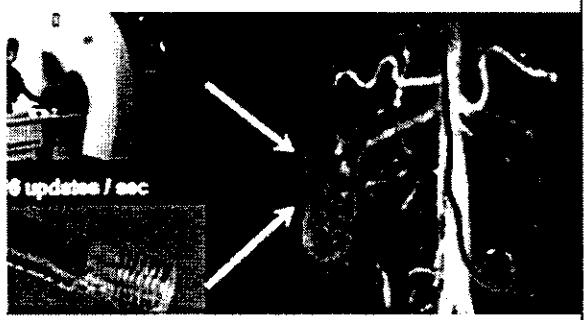




Contrast media enhanced MR scans

- thyroid carcinoma (arrow)
- contrast media enhanced MRA of the aorta (Takayasu's arteritis: arrows)

Image guided interventions today by x-ray, tomorrow by MR?



Morphology and function are different things

Sagittal MR scan through the brain of a „genius" Prof. Richard R. Ernst, Nobel laureate

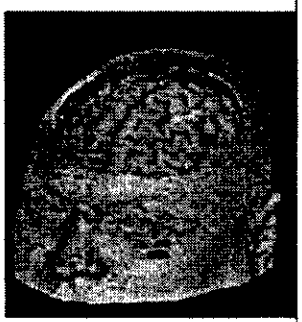
Morphology and Function are different things we cannot recognize the genius on a morphological scan

Morphology and function are different things

3D reconstruction of a brain MR scan

Despite the interesting anatomy, the only conclusion there is to be made:

The speaker has a brain!!!



Imaging of Function by examining anatomy is futile

Johann Caspar Lavater, 1741 - 1801

Judging the human character from shadow drawings of individuals

Imaging Methods Perspective

function imaging redefined

=> MOLECULAR IMAGING

- perfusion imaging
- metabolic imaging (glucose, amino acids, nucleic acids)
- gene expression imaging

Suitability of available methods

PET > NUC > MR (**MRS>fMRI>MRI**) > US > CT
optical???

Imaging Methods Imaging of Function

Nuclear Medicine *gamma rays*

single photon imaging

- static scintigraphy
- dynamic scintigraphy
- SPECT (Single Photon Emission Computed Tomography)

positron annihilation imaging *positrons*

- PET (Positron Emission Tomography) ↓

two 511keV γ rays

More by Alfred Buck, MS, MD

Imaging of function: nuclear medicine METABOLIC SPIES

Imaging of function is much more difficult than imaging of anatomy

Medical imaging over five centuries

from the anatomy of the dead to skeletal function of the living

G. K. von Schulthess: bone scan à la

Comparing imaging methods

Method	spatial resolution	temporal resolution	function* mol. Imaging
Sono	+++ ≥ 2mm	+++++ ≥ 10 ms	++
CT	+++++ ≥ 0.3mm	+++ ≥ 300 ms	+
Nuc Med	+ ≥ 10 mm	+ ≥ 5 s	++++
PET	++ ≥ 5mm	+ ≥ 5 s	+++++
MRI	++++ ≥ 0.8 mm	++++ ≥ 50 ms	+++
MRS	+ ≥ 10 mm	+ ≥ 60 s	++++

Comparing imaging methods

Imaging Method	contrast media concentration (mol/kg BW)
Sono	10^{-3}
CT	10^{-3}
Nuc Med	10^{-9}-10^{-12}
PET	10^{-9}-10^{-12}
MRI	10^{-2}
MRS	10^{-3}

MR high concentration – low affinity receptors
NUC/PET low concentration – high affinity receptors

„Bermuda Triangle" of Imaging

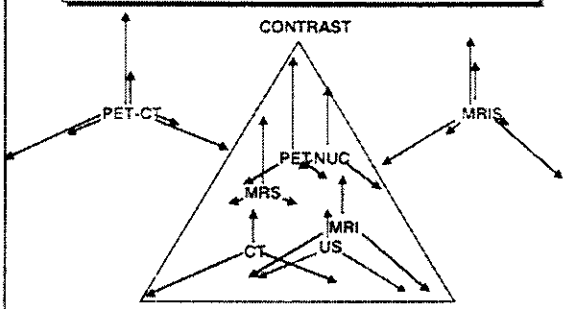
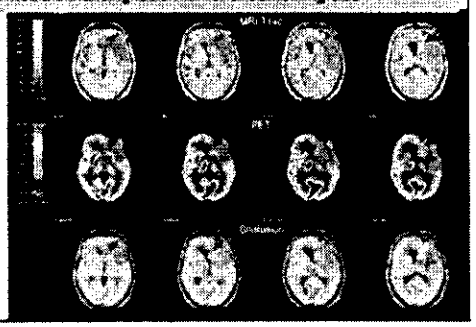
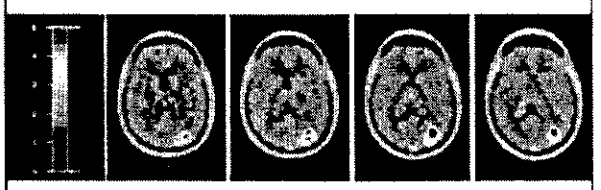


Image Fusion PET - MRI

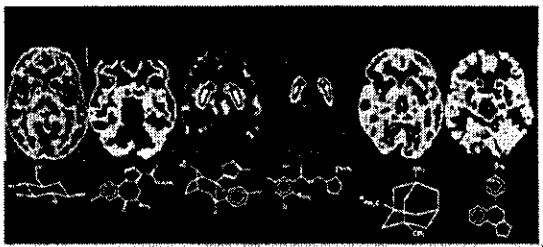
Brain tumor recurrence:
is the contrast media enhancing lesion tumor or something else



Brain imaging: Tyrosine-PET



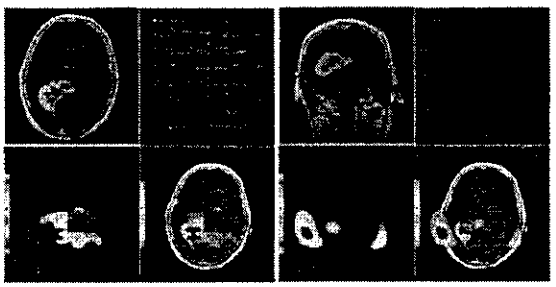
A gallery of images brain metabolism and receptor systems



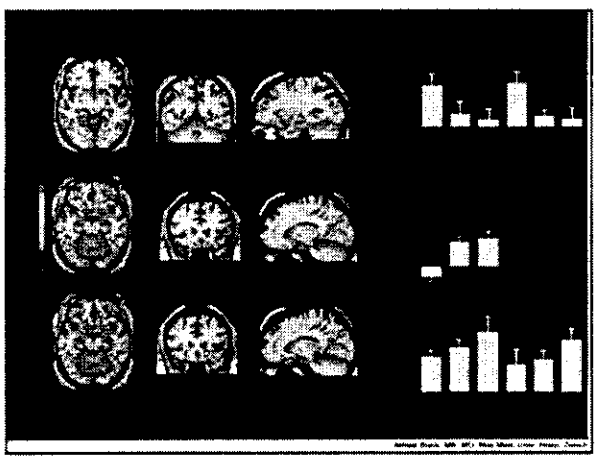
imaging of brain function: the extremely high signal/noise in nuclear studies and the use of highly specific tracers of properties of brain receptor systems opens new frontiers in drug design

© PET Center, University Hospital, Zurich

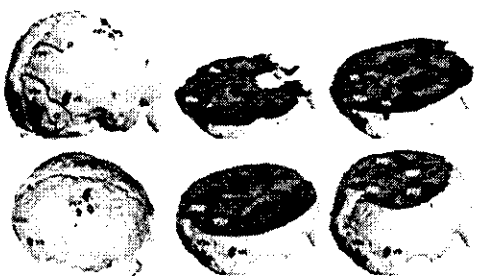
Brain tumor example



NAA(left), Lactate (right) and Choline (next slide) maps, overlayed on post-contrast axial T1-weighted MR images were generated from a 4:20 min PRESS acquisition (TE=144ms) and a 16x16 voxel resolution.

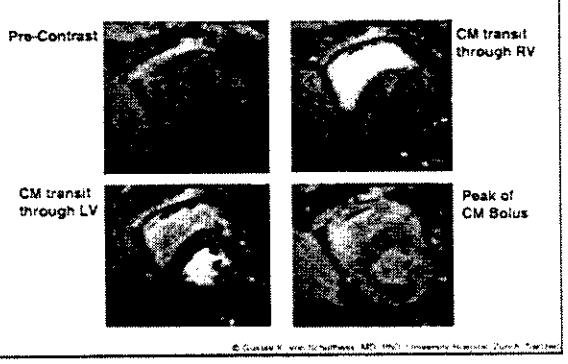


fMRI and fPET clues to the functioning of the brain

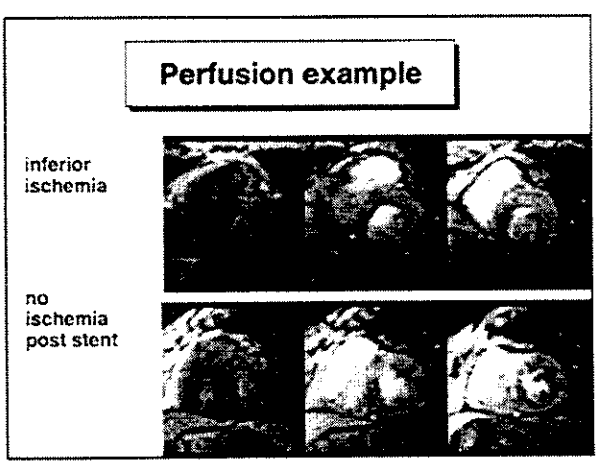


Will we be able to understand conciousness using PET and fMRI?

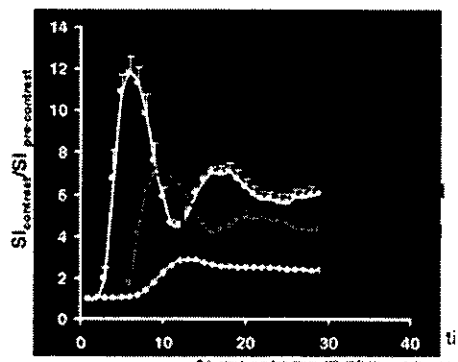
CM first pass in normal myocardium



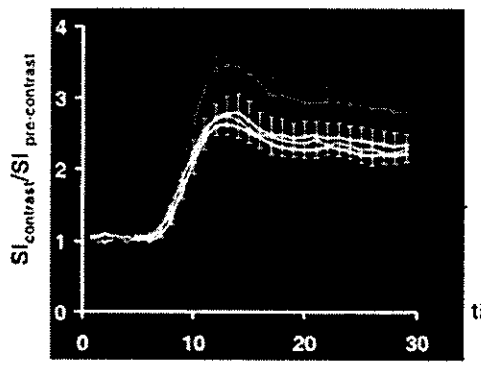
Perfusion example



MR PERFUSION



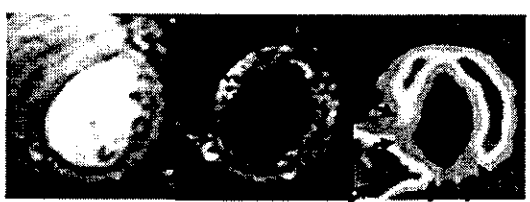
Peak of Bolus



Perfusion example

infero-posterior ischemia (top row)
recovery after dilatation and stenting (bottom row)

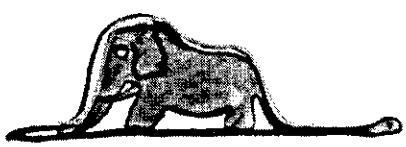
MR perfusion imaging vs PET

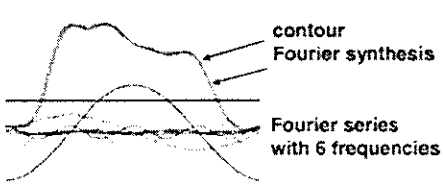


MR peak of bolus | **MR** parametric image | **PET** stress ammonia

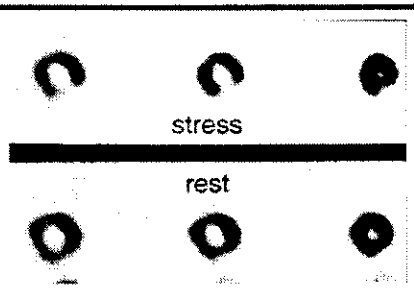
Fourier Elephant

drawing from: A. de St. Exupéry; the Little Prince





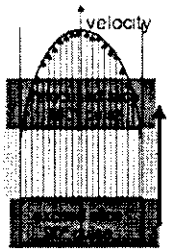
Nuclear cardiology: ischemia



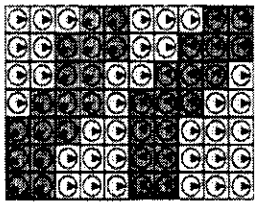
Inferior defect under stress, which is virtually absent under rest conditions: inferior ischemia

Two basic types of motion effects

Measurements of distance and time



Measurements of orientation of pixel magnetization



Richard Scarry: Children's Book This is CT

Richard Scarry: Children's Book This is PET

„ Smart" contrast agents the power of fluorodeoxyglucose (FDG)

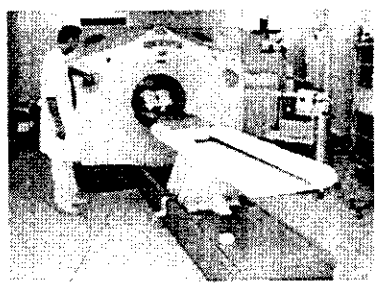
Recognition of metastases can be done elegantly with FDG-PET

extremely high signal to noise ratio:
virtually no background makes the lesion stand out brightly

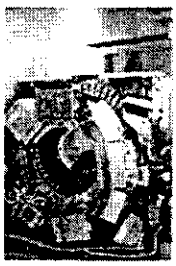
Tumor-PET in a patient with thyroid carcinoma

Richard Scarry: Children's Book This is PET/CT

In-line PET/CT



What do we have ?

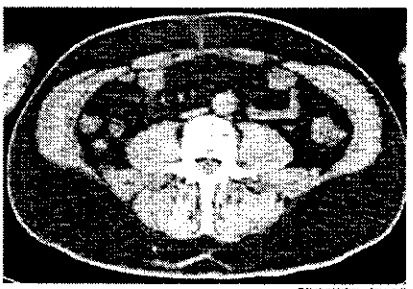


State-of-the-art CT scanner
State-of-the-art PET scanner

integrated into one PET-CT machine

MDCT: Where is the Lesion in this Image?*

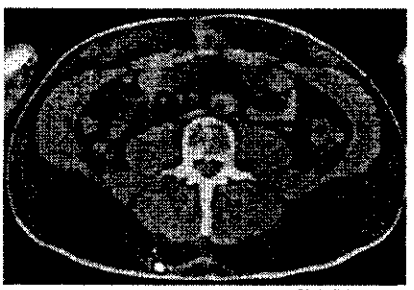
*Note: you get typically 200 of Those!



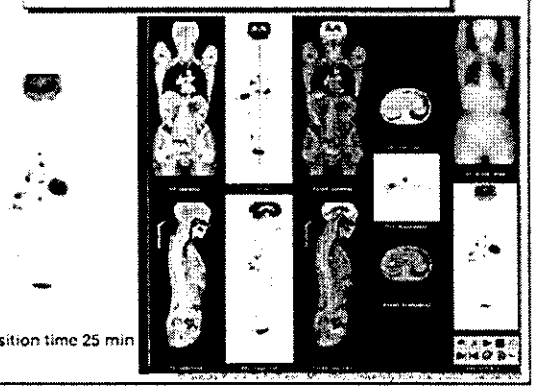
FDG-PET: The Lesion is Here!

metastatic melanoma
single manifestation ↘

PET-CT: Subcutaneous Metastasis of Melanoma



Integrated PET/CT



Acquisition time 25 min

Increase in specificity
NSCLC without mediast. involvement

Conclusions 1

Extensive imaging of human anatomy started in the Renaissance

There have been several medical imaging revolutions
- the discovery of x-rays
- the introduction of contrast media
- the use of reconstruction mechanisms to obtain tomograms
- the use of imaging to guide instruments for interventions

There are few anatomical details of relevance which modern imaging still needs to provide

Image guidance of minimally invasive procedures is used with increasing frequency

Conclusions 2

The 3rd millennium challenge: development of function imaging

Imaging of function is still in its infancy
- nuclear medicine has provided such information for 40 years
- PET imaging is being introduced on a large scale because of its impressive clinical capabilities
- MRI and US provide some functional information

Imaging of in-vivo physiology is slowly becoming a reality

Modalities are
- **NM**, **PET** and **fPET**, **MRI** and **fMRI**, US, MRS??
- optical imaging???

CERN ACADEMIC TRAINING LECTURE 2002

Physics Technologies in Medicine - June 11, 2002

X-rays: still going strong:

Multidetector computed tomography: New developments and applications

Simon Wildermuth, M.D.

U Institute of Diagnostic Radiology
University Hospital Zurich

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Jürgen K. Willmann, M.D.
Thomas Frauenfelder, M.D.
Borut Marincek, M.D.
Siemens Medical Systems

OUTLINE

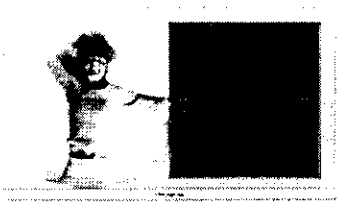
- Technical Considerations
- Imaging Protocols
- Clinical Applications
- Image Postprocessing
- Summary

1974: Siretom 80/80 Matrix 5min/Bild

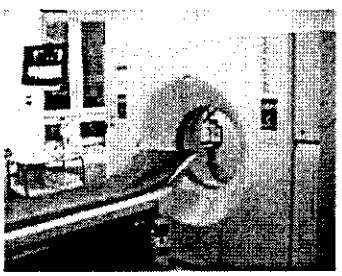
1987. Somatom+ /512Matrix 8Sec/Image

1989: first Spiral-CT Somatom+S

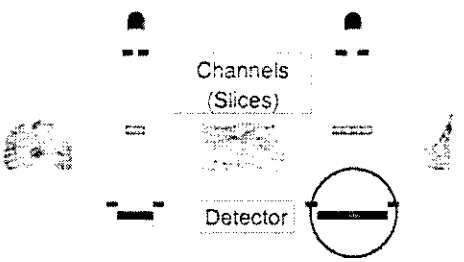
1994: Somatom Plus 4 first Subsecond-CT



1998: Somatom Volume Zoom 4 Images/ Rotation Rotation-Time: 0.5 Seconds



MULTIDECTOR TECHNOLOGY



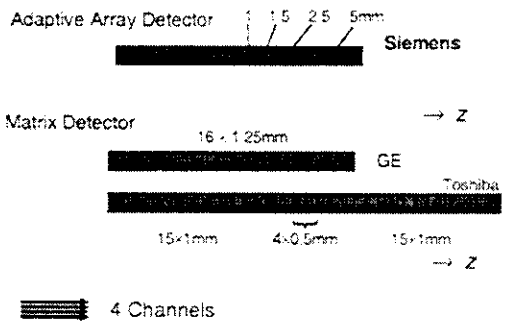
Multidetector CT

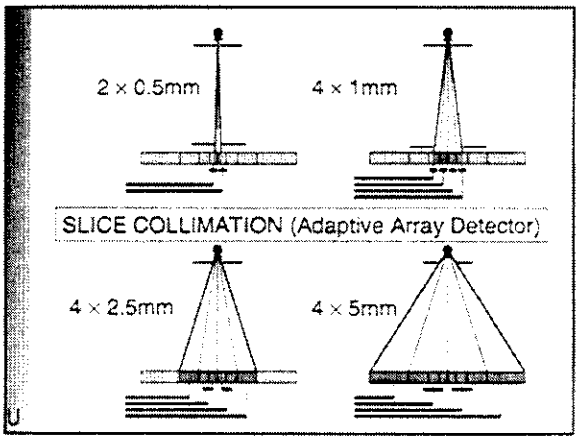
- fast volume scans
- thin collimation for entire volume
- better patient comfort
- shorter breathhold period
- isotropic resolution
- improved image quality
- less artifacts
- perfusion studies

GE- AND SIEMENS MSCT: THE DIFFERENCES

- Detector Design
- Use of Pitch
- Image Interpola-tion/Reconstruction

DETECTOR DESIGN





PITCH - SSCT

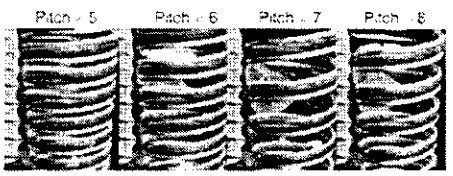
$$\text{Pitch} = \frac{\text{Table travel (mm) per gantry rotation}}{\text{Slice collimation (mm)}}$$

Pitch = 1 Pitch = 1.5 Pitch = 2 Pitch = 2.5 Pitch = 5

- Pitch (with constant mAs, kV, collimation)
  - ➢ Table Speed increases
  - ➢ mAs-value decreases
  - ➢ Patient dose decreases
  - ➢ Section thickness increases
  - ➢ Image noise increases

PITCH - MSCT

$$\text{Pitch} = \frac{\text{Table travel (mm) per gantry rotation} \quad 15\ \text{mm}}{\text{Slice collimation (mm)} \quad 2.5\ \text{mm}}$$



$$\text{Pitch} = \frac{\text{Table travel (mm) per gantry rotation} \quad 15\ \text{mm}}{\text{Nominal section thickness (mm)} \quad 4 \times 2.5\ \text{mm}}$$

INTRAVENOUS CONTRAST AGENT

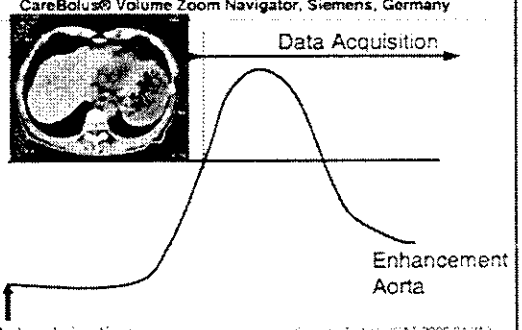
Automated Injection Pump

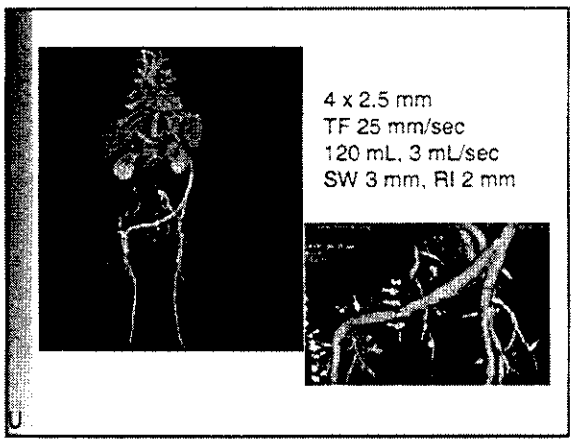
• Quantity	[ml]	:	120-150
• Nacl Flush	[ml]	:	30-50
• Iodine	[mg/ml]	:	300
• Flow	[ml/s]	:	3,0 – 4,0
• Delay	[s]	:	25-35 arterial 70 portovenous

Bolus Tracking?

AUTOMATED BOLUS DETECTION

CareBolus® Volume Zoom Navigator, Siemens, Germany





Workflow

Multislice CT < > Singleslice CT

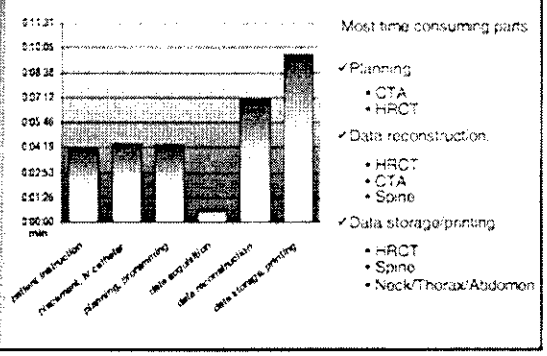
- ✓ Faster scanning time
- ✓ Extended volume coverage
- ✓ Increased spatial and temporal resolution

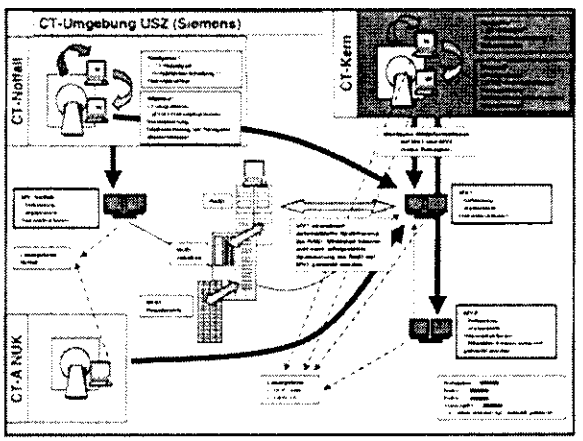
⇒ CT-books need rewriting

Quality management ?

- ✓ Technical environment
- ✓ Personnel

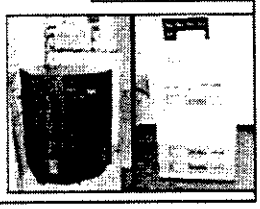
Workflow ∑Step 1-6



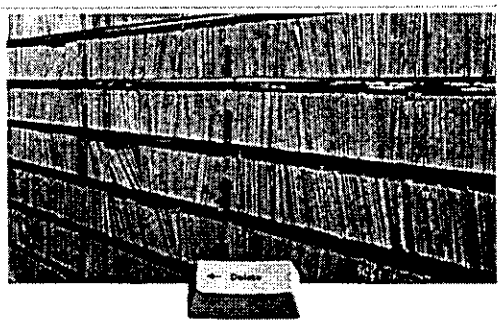


Technical Requisites

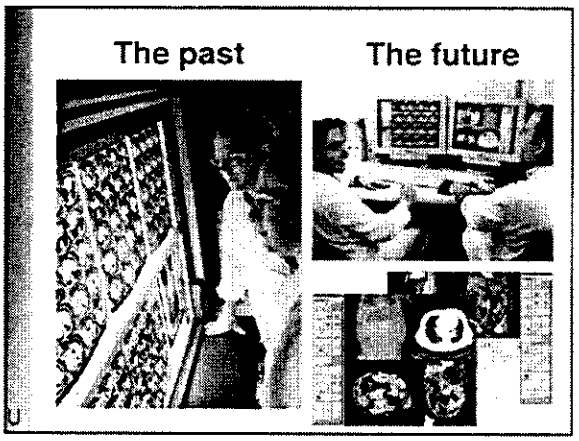
Second workstation (Volume Wizard")	• Storage and Printing • Data Transfer
Storage	• "Juke Box" 0.75 TB
Printing	• Laserprinter



The time has come...



IMPROVE YOUR ARCHIVE



4 parallel detectors

Improvements:
- spatial resolution
- temporal resolution

Disadvantages:
- large data volume
- postprocessing time

two- and three dimensional data-processing

MD-CT: Postprocessing

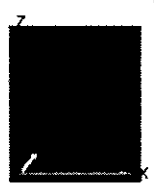
- diagnostic information in CT = far more than the sum of the individual slices
- main advantage:
  nearly isotropic resolution

2D: Multiplanar Reformatting (MPR)
2D, 3D: Max/Min Intensity Projection (MIP)
3D: Surface Rendering (SR)
Volume Rendering (VR)
Virtual Endoscopy (VIE)

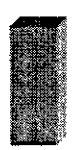
3D Reconstruction

- **data acquisition**
  optimize parameters:
  spatial resolution
  examination time
  radiation exposure
- **data management and display**
- **information distribution and management**

Isotropic Voxel



Isotropic Voxel
=
Volume Voxel is cubic

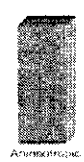


Aninsotropic Voxel
FOV 40 cm
Matrix 512x512
Slice th. 3mm

Isotropic voxel
FOV 40 cm
Matrix 512x512
Slice th. 1mm

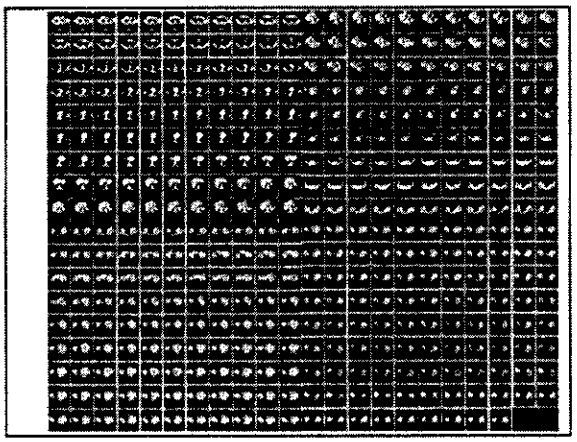
Important factor for high quality 3D reconstructions:
Longitudinal resolution in (z-axis)

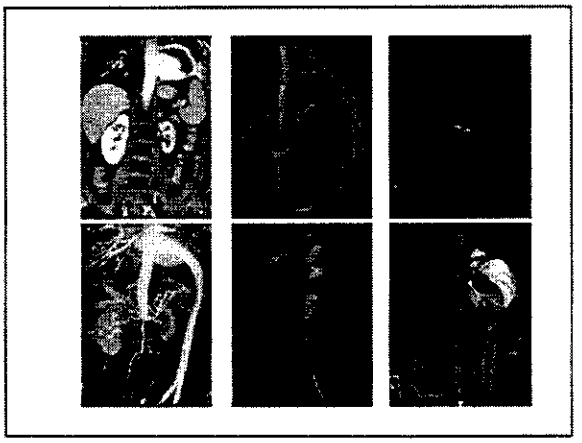
Isotropic Voxel



A: spatial interpolation methods
resample reconstruction interval
decrease pixel resolution (512 > 256)
increase FOV

B: true istotropic imaging
MD-CT imaging



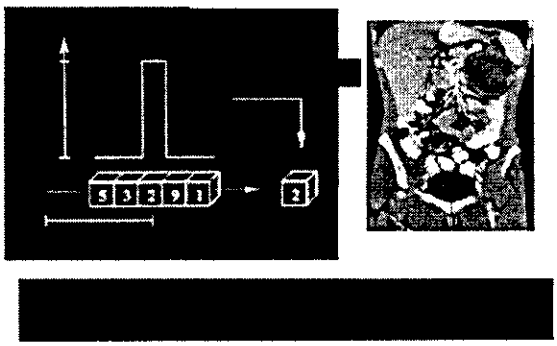


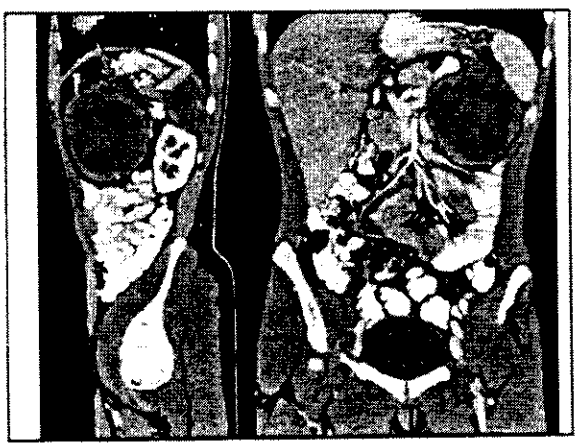
Multiplanare Reformation (MPR)

curved Reformation (cMPR)

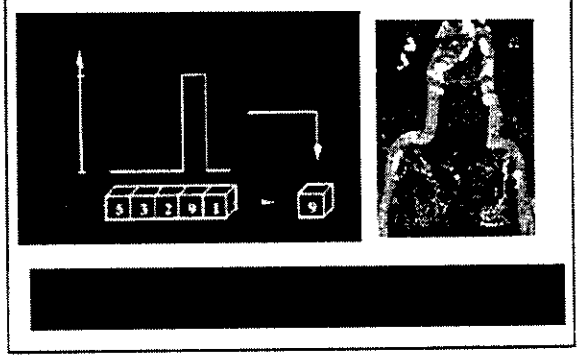
Max-/Minimum-Intensitätsproj. (MIP)

Multiplanar Reconstruction (MPR)

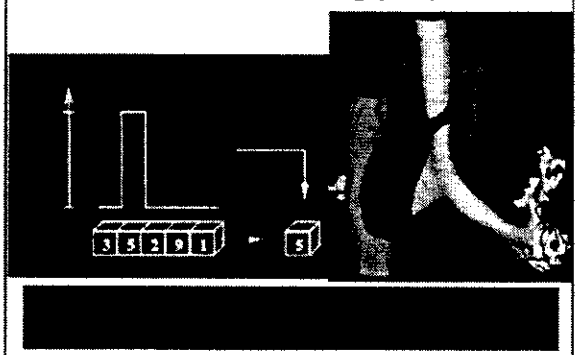


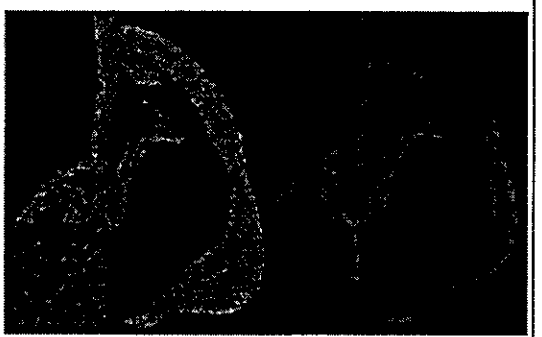


Maximum Intensity Projection (MIP)

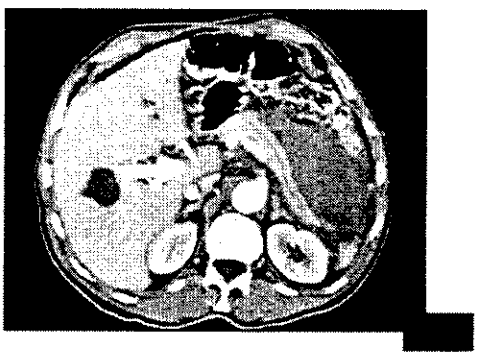


Surface Rendering (SSD)



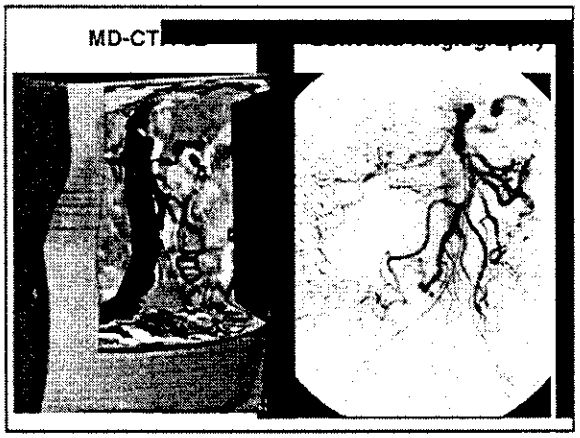


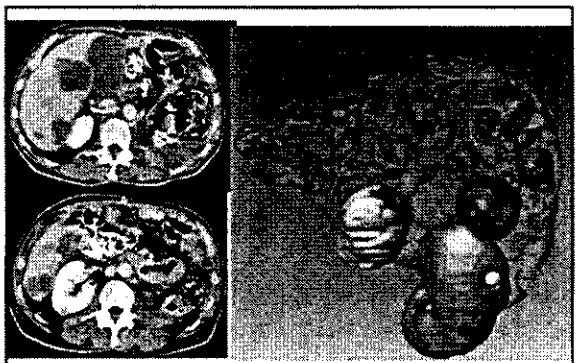
Retroperitoneal Bleeding



Segmental Arterial Mediolysis (SAM)

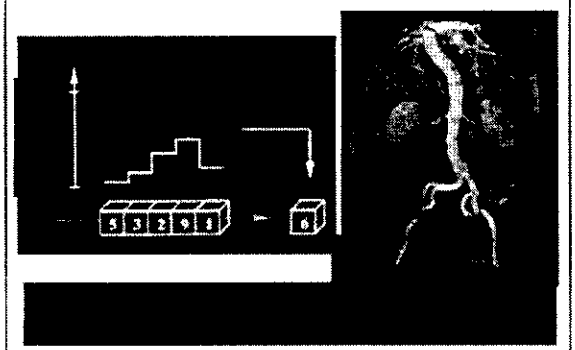
MD-CT

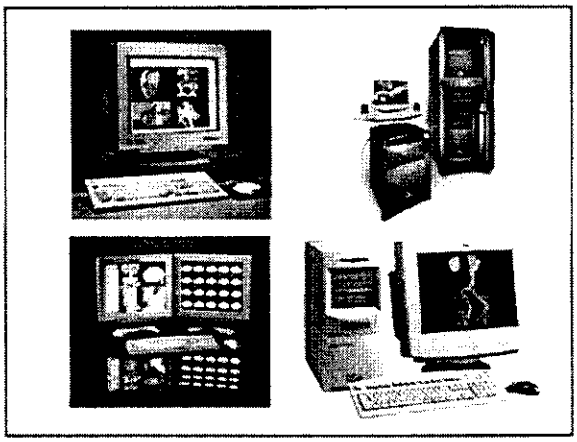


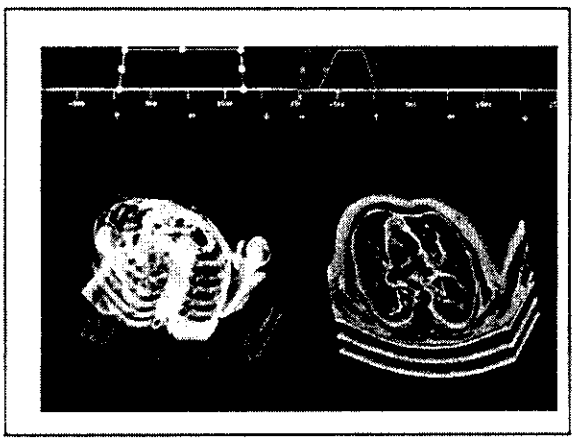


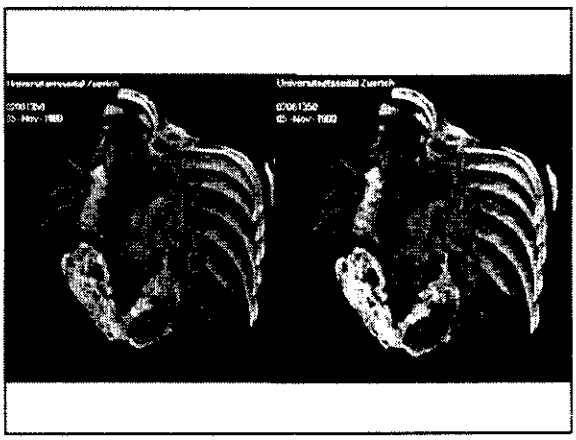
Quantification (Tumor Volume)

Volume Rendering (VR)







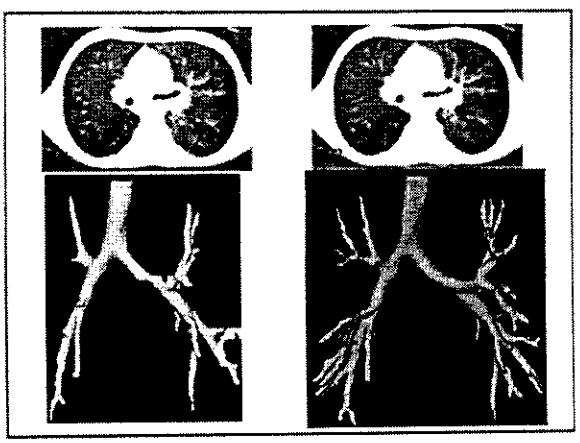


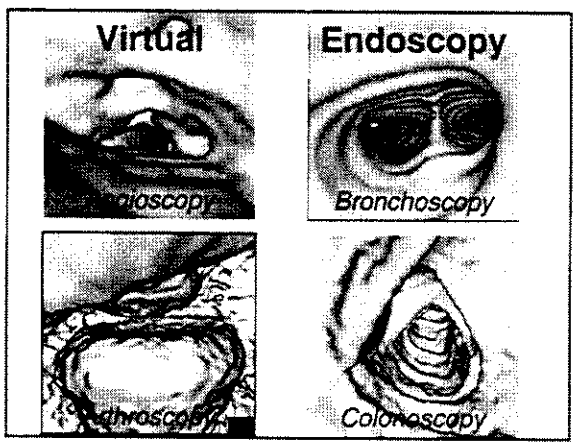
Volume- vs Surface-Rendering

Volume Rendering
- *high perf. workstation*
- *VR graphics card*
- *no distortion*
- *internal structures vis.*
- *several structures jointly displayed*
- *volume visulisation of volumetric data*
- *better diagnostic quality?*

Surface Rendering
- *binary segment. requ.*
- *only surfaces displayed*
- *generally fast techn.*
- *polygon > VMRL exp.*
- *selective display*
- *measurements*
- *soft tissue modeling*
- *surgical planning*

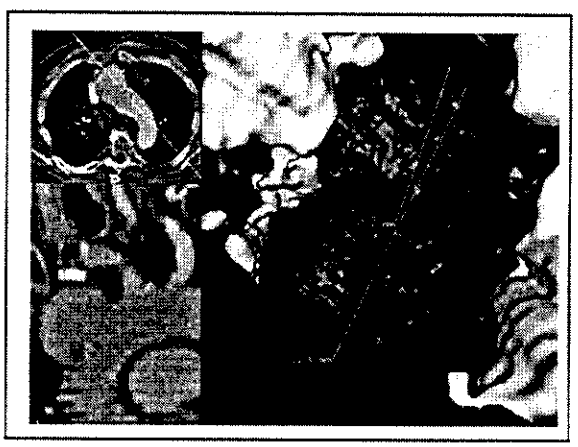
both methods need segmentation !!!!

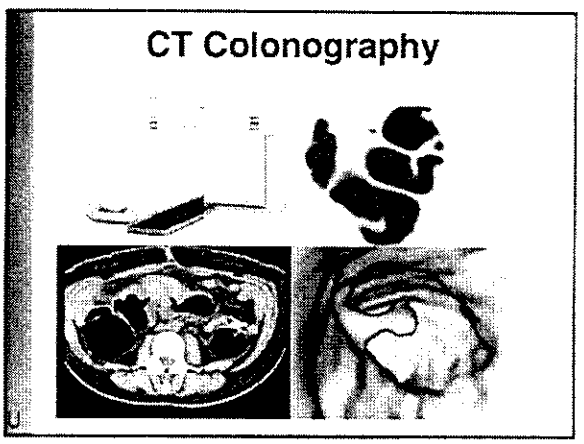


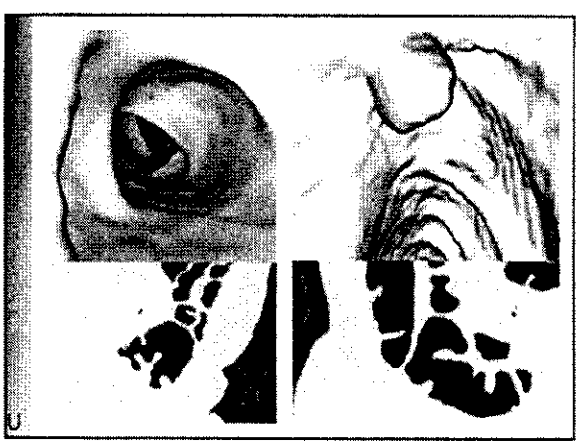


Virtual Angioscopy

- Virtual colonoscopy and bronchoscopy have fiberoptic correlates
- There is no means of directly visualizing the inner walls of blood vessels with optical technique (opaqueness of blood)







CT Colonography

Single Detector CT-Colonography (CTC)

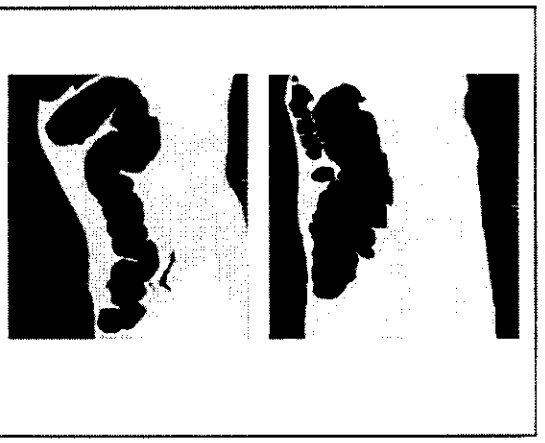
patient position prone and supine	tube current	voltage	collimation	table feed/rotation	rotation time	reconstruction increment
	70-110 mA	120 kVp	3-5 mm	3, 7.5, 10 mm	1 sec	1.5-5 mm

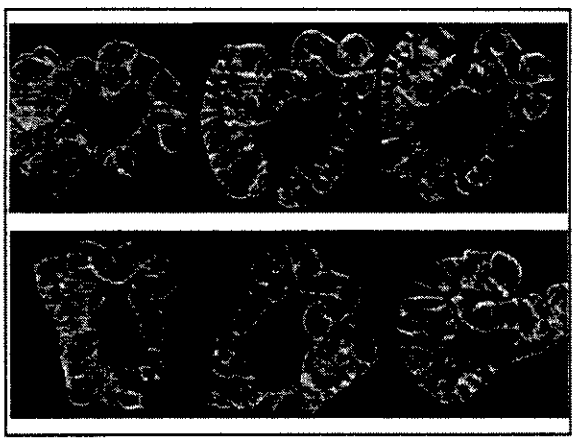
Multidetector CT-Colonography (MD-CTC): LOW DOSE PROTOCOL

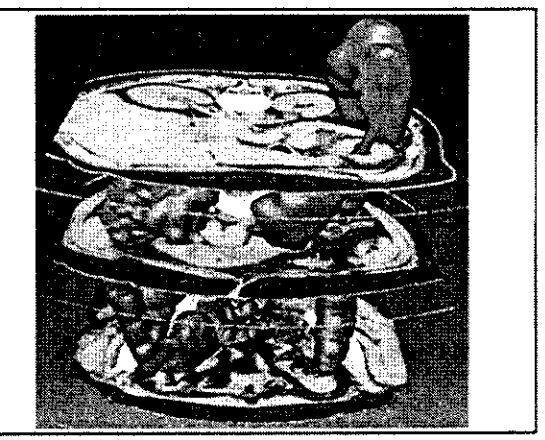
patient position prone and supine	tube current	voltage	collimation	table feed/rotation	rotation time	reconstruction increment
	165 mA	120 kVp	1 or 2.5 mm	7 mm/1 or 12.5 mm/s	0.5 sec	1-3 mm

Multidetector CT-Colonography (MD-CTC): HIGH RESOLUTION PROTOCOL

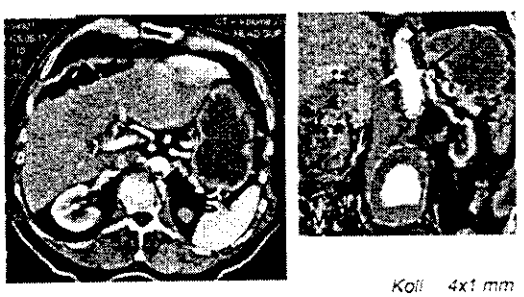
patient position prone and supine	tube current	voltage	collimation	table speed	rotation time	reconstruction increment
	210 mA	140 kVp	1.0 mm	5 mm/s	0.5 sec	1 mm





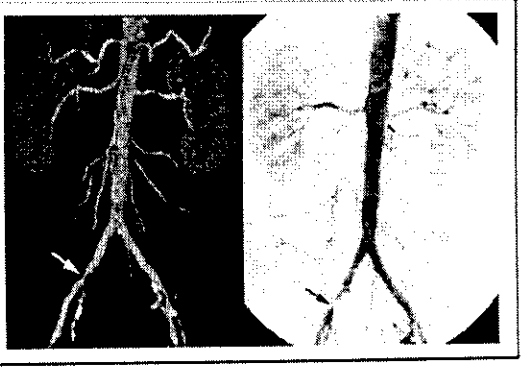


RENAL ARTERY CLOT



Koll 4x1 mm
SW 1.25 mm
RI 1 mm

ABDOMINAL CTA



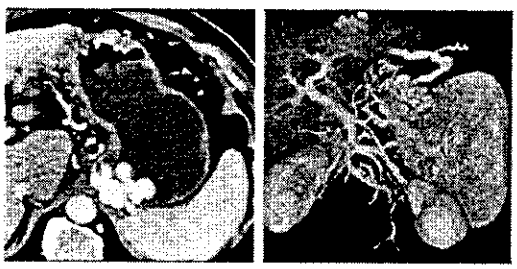
GASTRIC FUNDAL VARICES

- May cause severe variceal bleeding
- Sequelae of portal hypertension
- Establishing diagnosis is difficult

GASTRIC FUNDAL VARICES

Coll 4x1 mm
SW 1.25 mm
RI 1 mm

GASTRIC FUNDAL VARICES

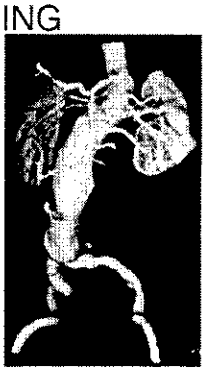


AAA IMAGING

3D MR-Angiography
- fast spoiled 3D MRA
- Gd-DTPA iv

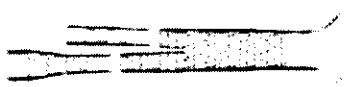
Spiral CT-Angiography

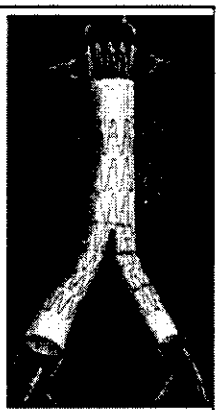
MD CT-Angiography



ENDOVASCULAR AAA REPAIR

- **covered stent used for AAA treatment**
  - **–less invasive**
  - **–less morbidity/mortality**
- **appropriate endov. stent-graft technology requires high accuracy imaging system**



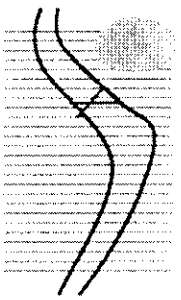


VASCULAR STENTS

- requires length/diameter measurements of
  - proximal neck
  - distal cuffs and graft limbs
- undersizing endograft diameter may have
  - endoleak (perigraft flow)
  - migration
- under-/oversizing endograft length may have
  - endoleaks, occlusion of branches
  - kinking

MEASUREMENT DIFFICULTIES

- axial CT sections do not provide perpendicular planes to the vessel
- diameter measurements difficult

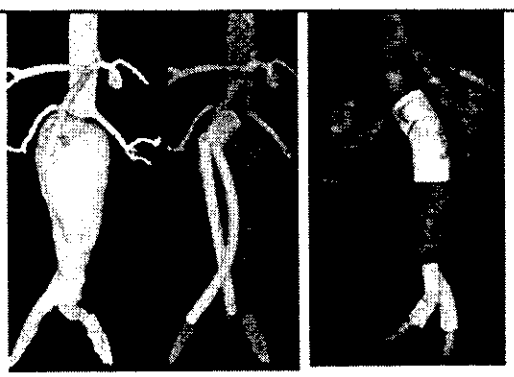


MEASUREMENT DIFFICULTIES

- conventional angiography provides a 2D projection of a complex 3D structure
- catheter does not follow the centerline of blood flow channel or proposed graft path
- length determination difficult

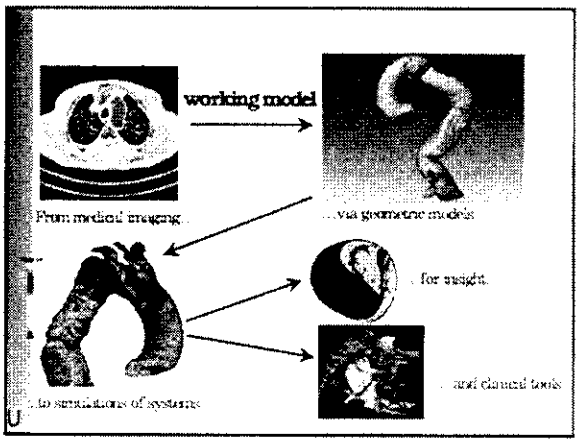
VIRTUAL ANGIOSCOPY (MedIS)

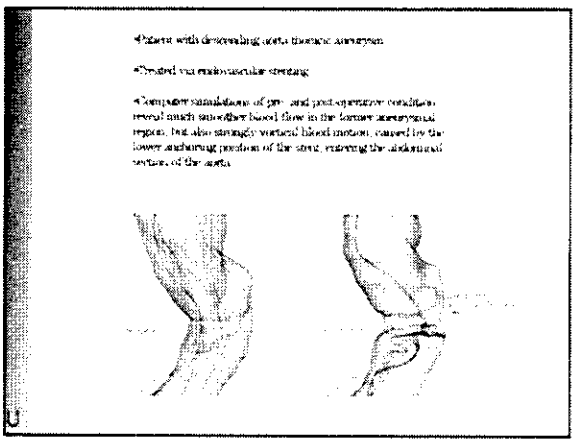
- highly generic and flexible system
- combined surface and volume rendering
- recording and measur. of different exploring paths
- multiple stent placement and measurements

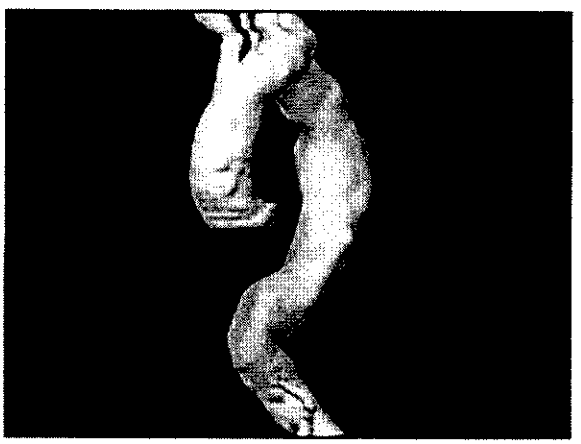


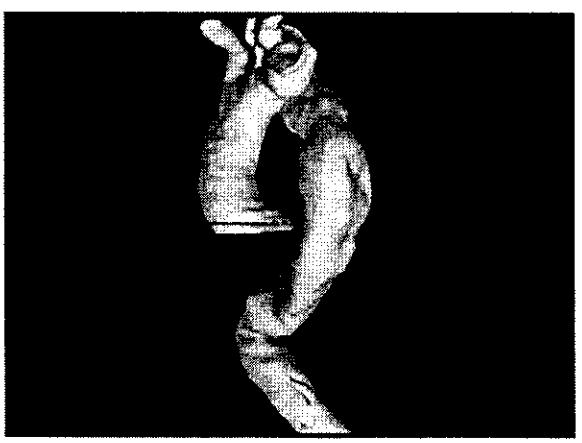
virtual stent graft adjustment

- Multislice CTA (or MRA) is well suited for planning of endovasc. aortic stent implants
- virtual endoluminal approach provides direct data of the stent itself, resulting in accurate diameter and length measurements



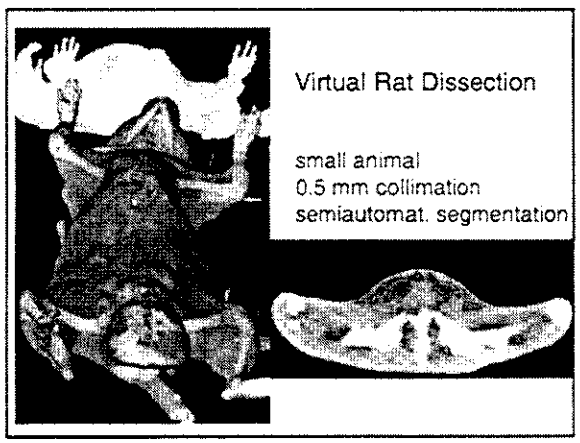


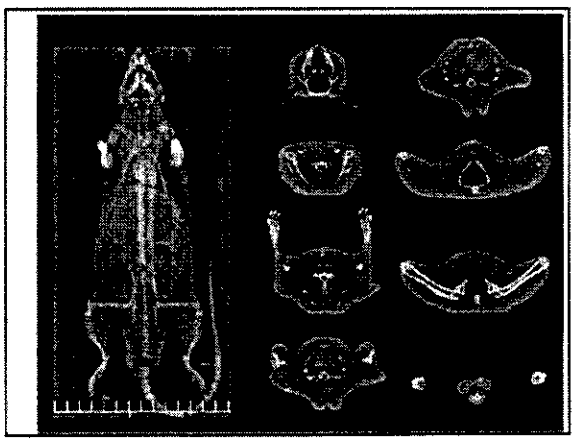


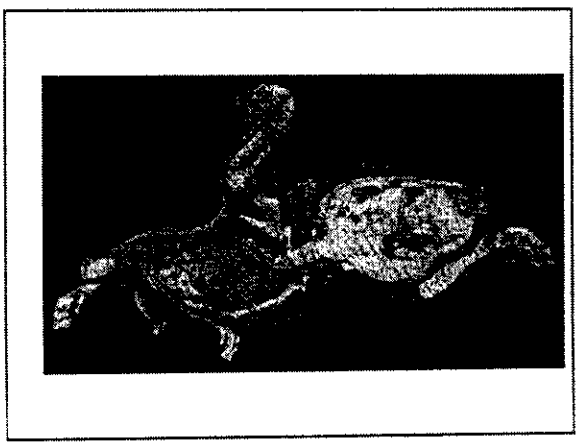


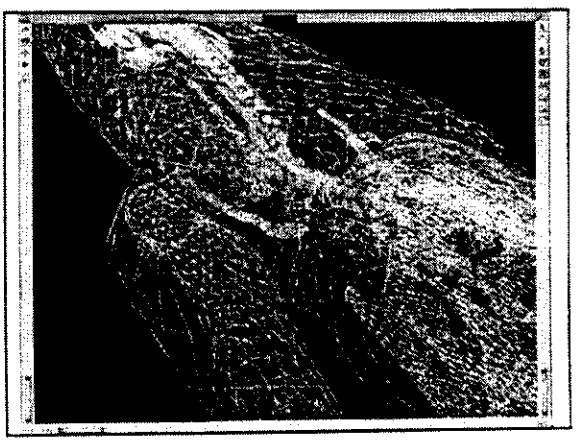
Surgical Planning

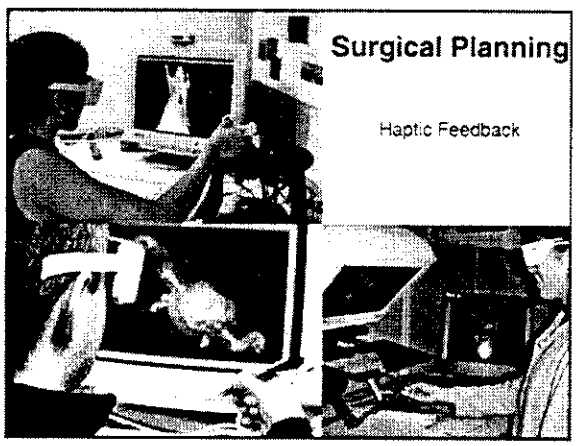

DINOSAURS
NAME: ALADAR
IGUANODON

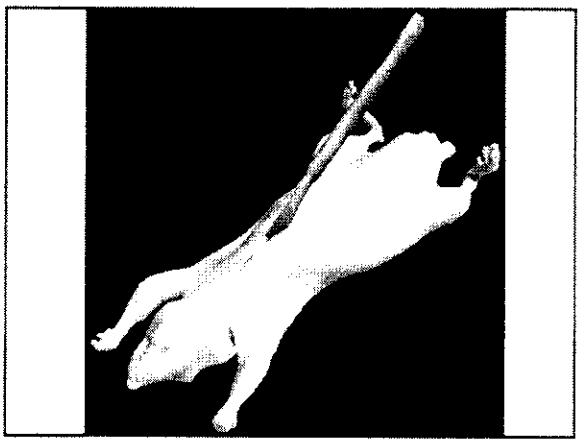

Virtual Rat Dissection
small animal
0.5 mm collimation
semiautomat. segmentation

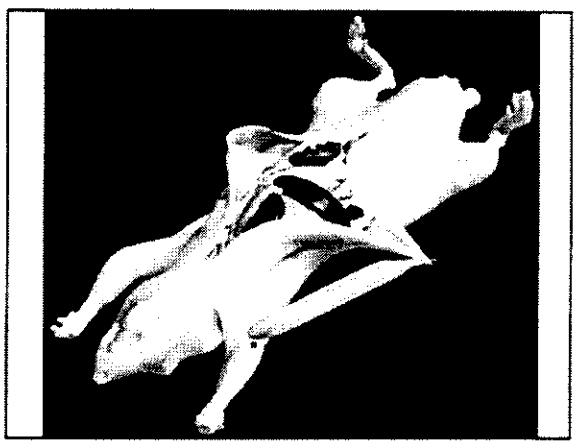












Conclusion

- multidetector CT allows nearly true isotropic imaging
- major impact for most image postprocessing modalities
- multidetector CT is well suited for planning of endoluminal stent implants and surgical planning

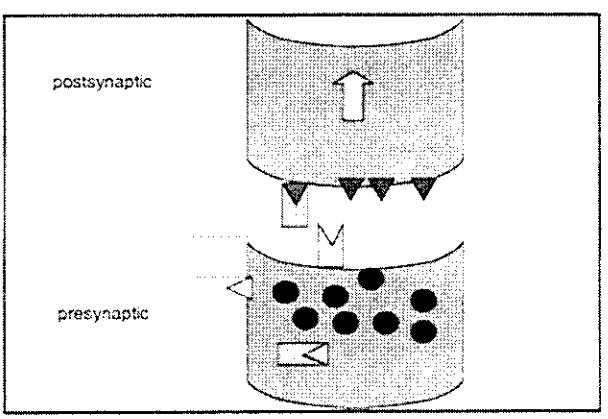
Elucidating healthy and pathological human physiology with PET

Alfred Buck
PET Center
University Hospital Zürich

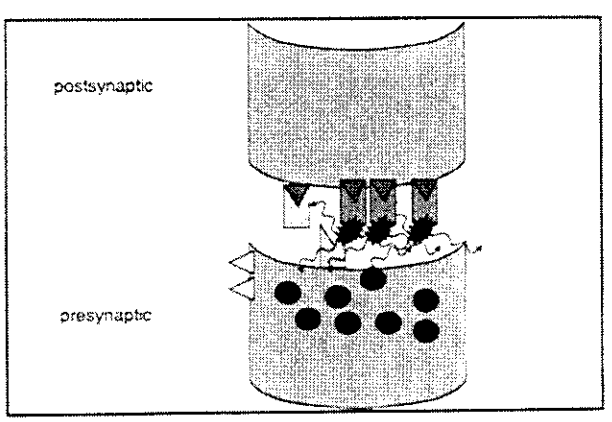
Positron emission tomography (PET)

Fluoro Deoxy Glucose (FDG)

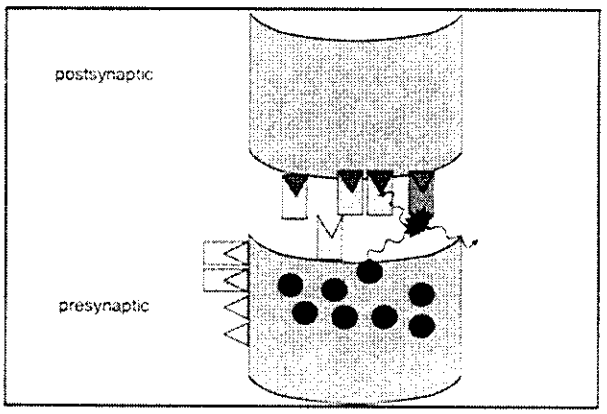
Neurotransmission



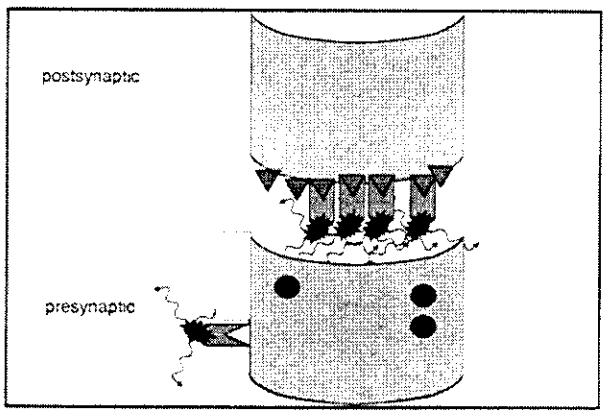
Imaging Neuroreceptors

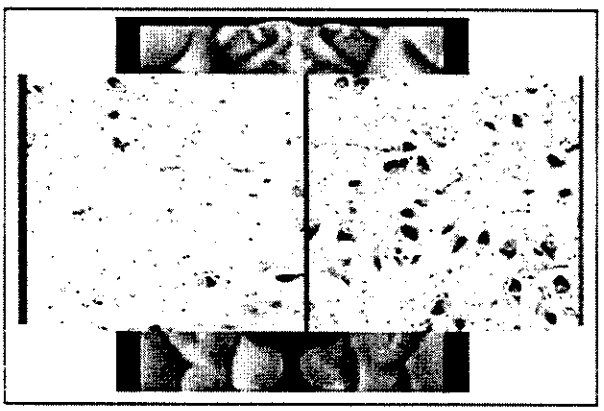


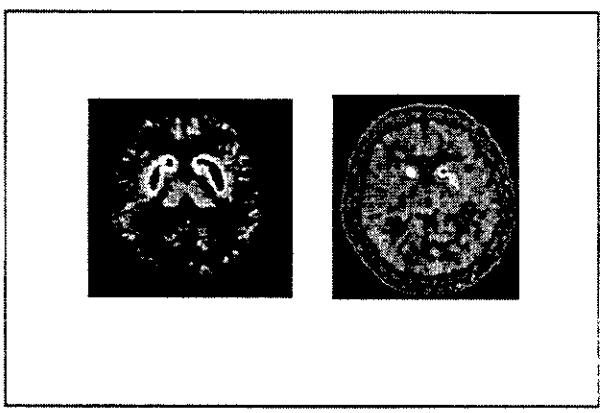
Blockade of uptake sites

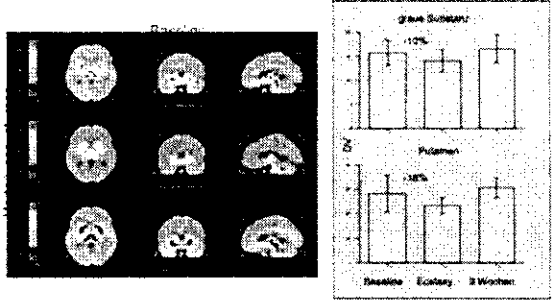


Parkinson's Disease









Normal [F-18]FDG PET

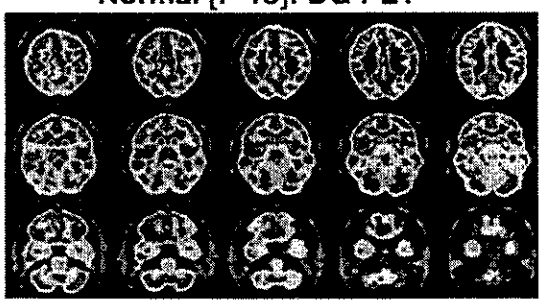
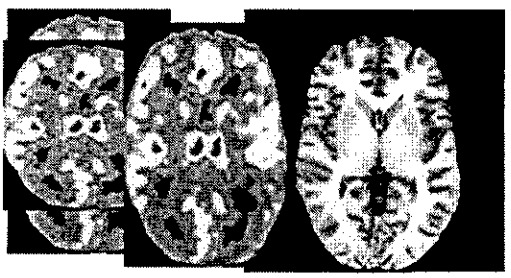
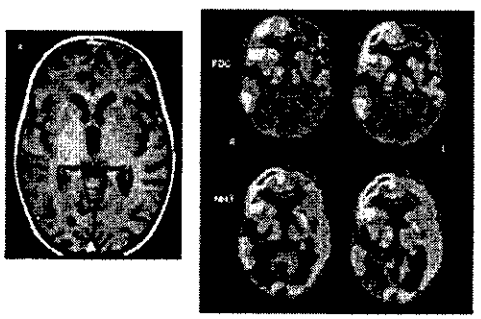


Image coregistration

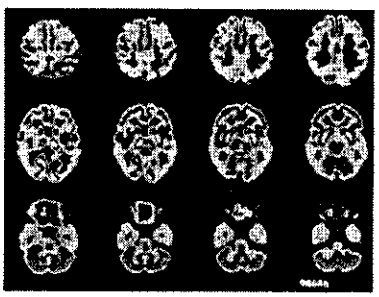


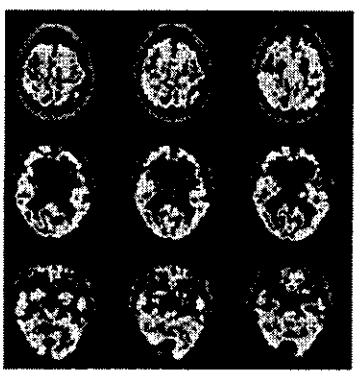
Epilepsy



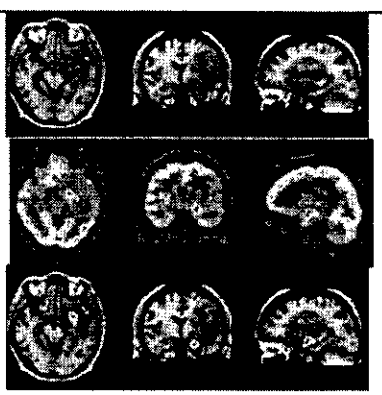
Dementias

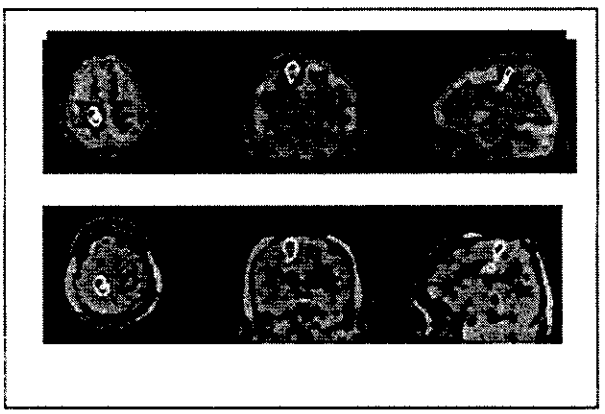
- Confirmation of Alzheimer's

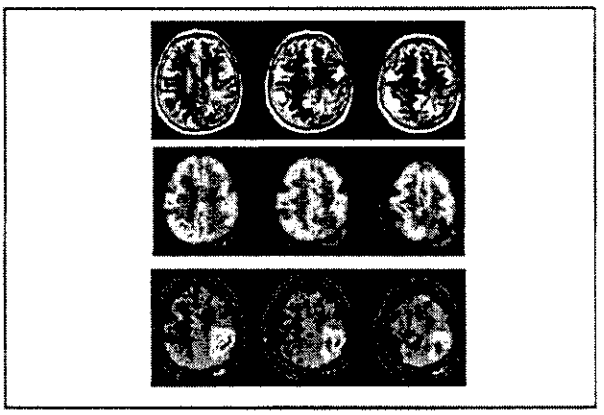


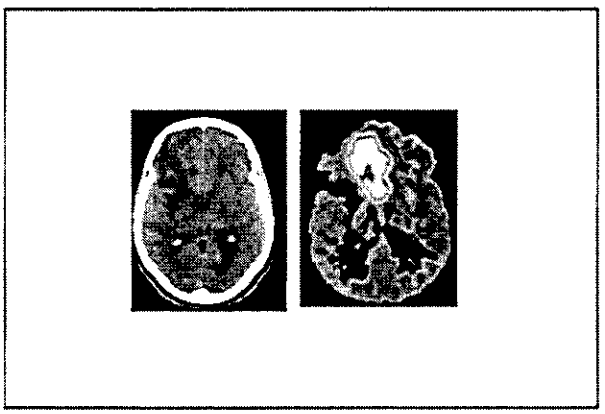


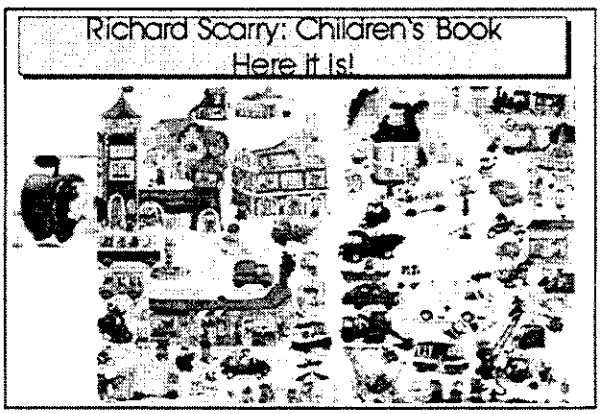
Brain Tumors

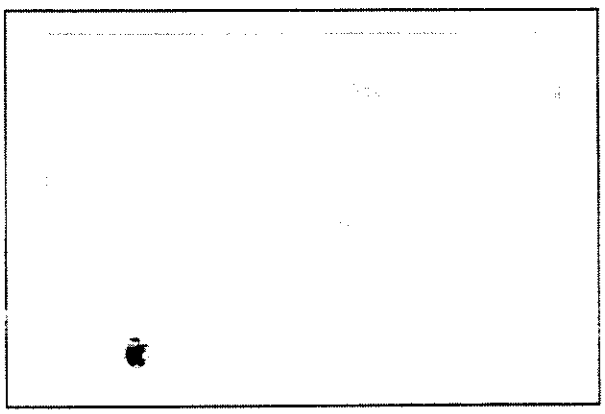






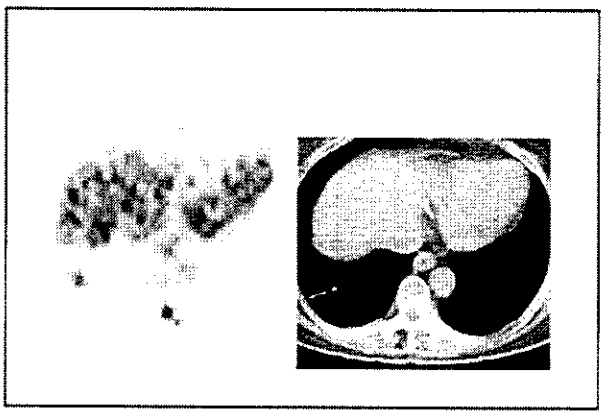


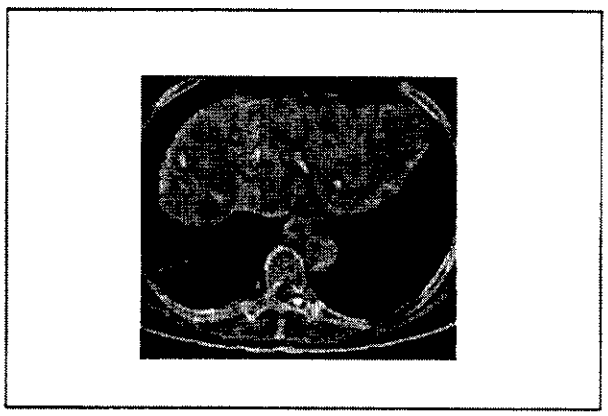


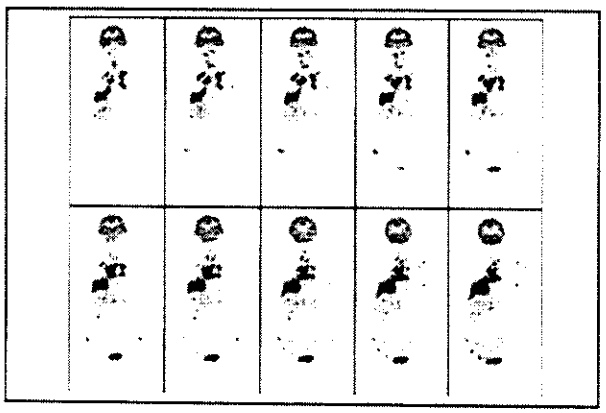


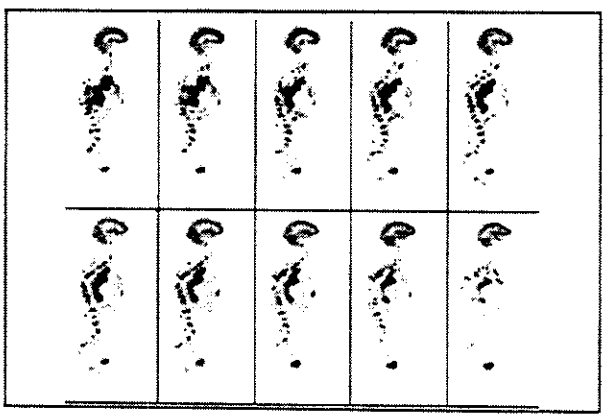
Positron emissions tomographie (PET)

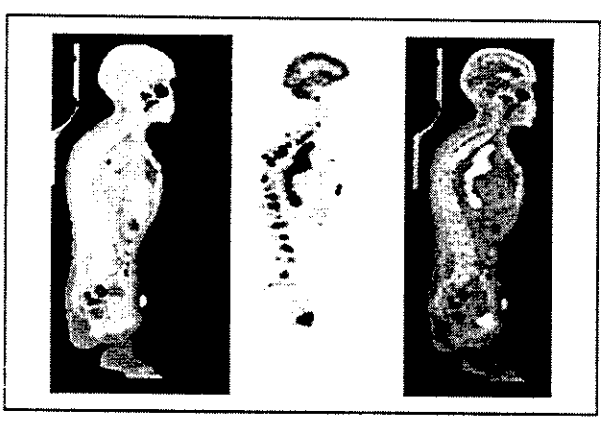
Fluoro Deoxy Glucose (FDG)





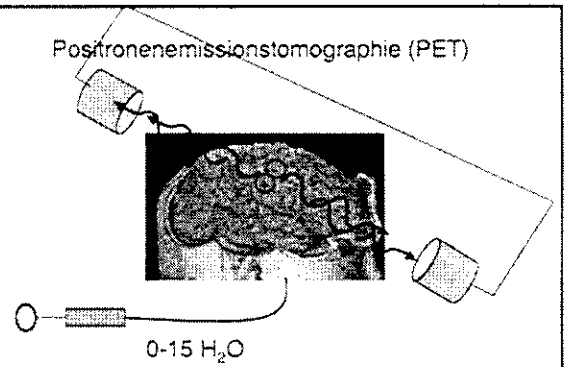




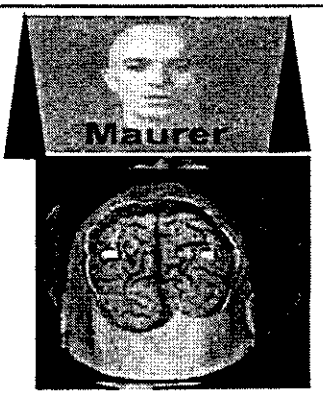


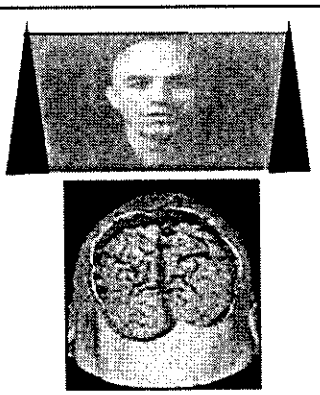
Elucidating brain function

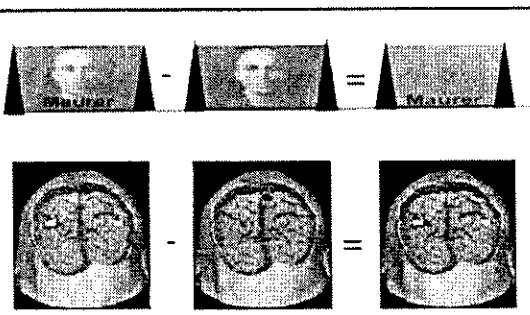
Alfred Buck
PET Center
University Hospital Zürich

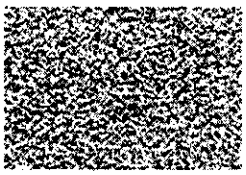


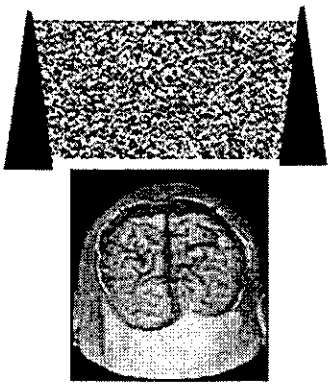
Experiment 1

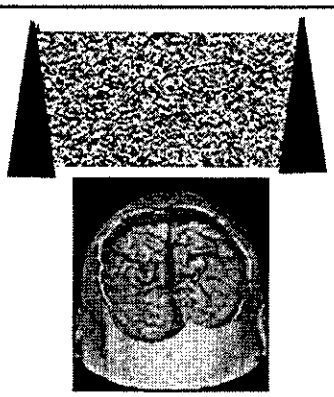


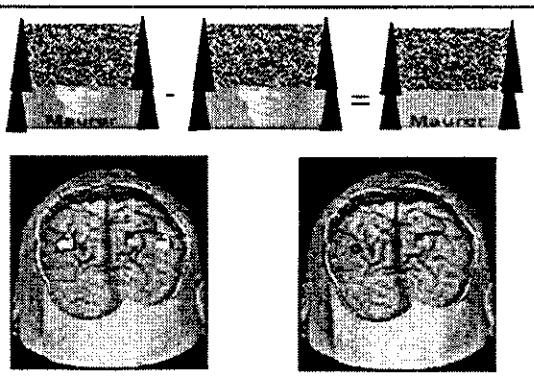






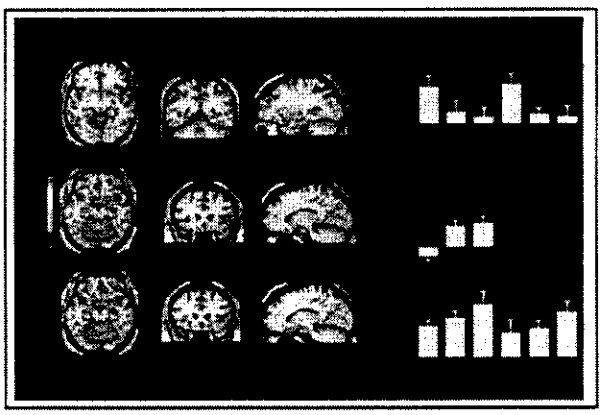


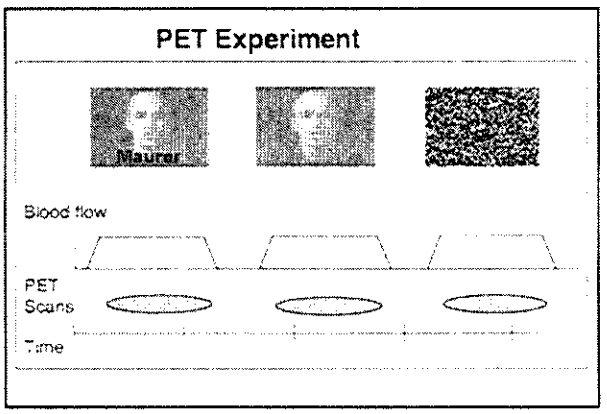


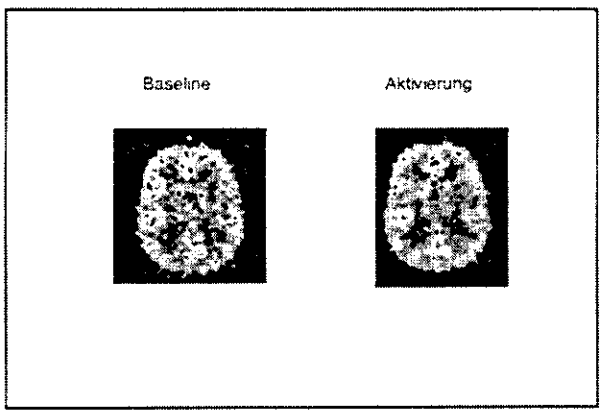


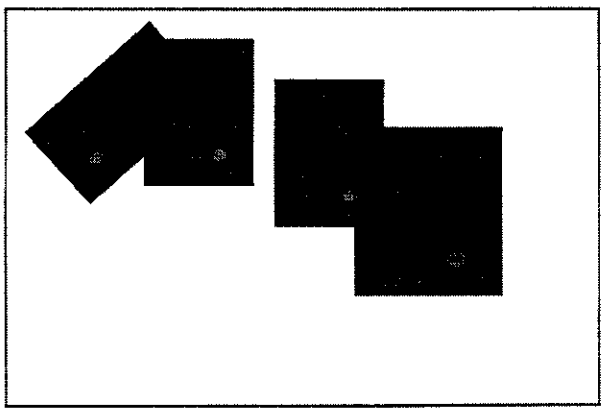
Experiment 2

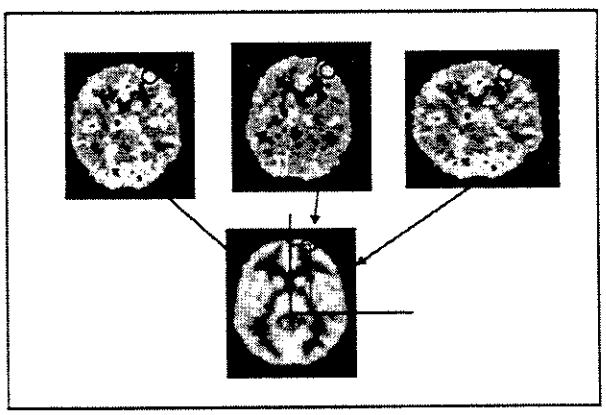
How the brain navigates through the information jungle

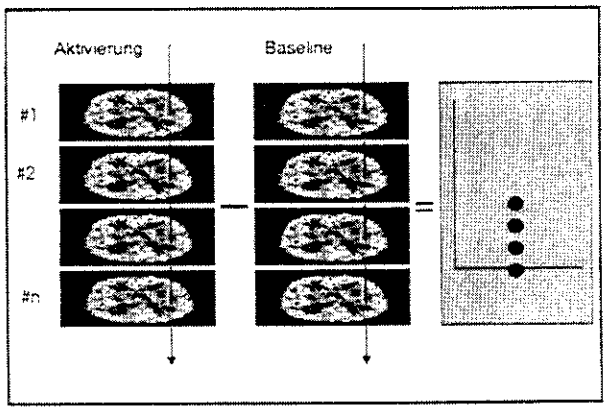



PET Experiment
Maurer
Blood flow
PET
Scans
Time

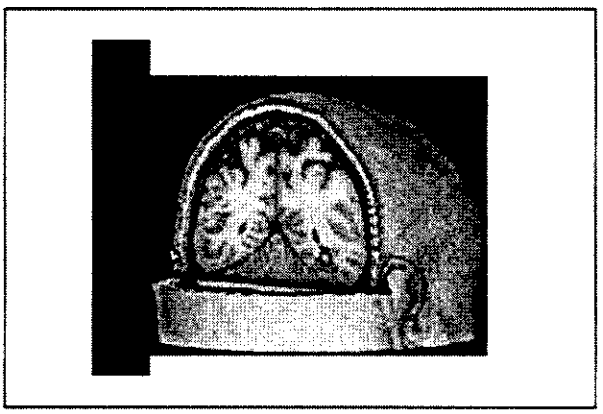

Baseline
Aktivierung



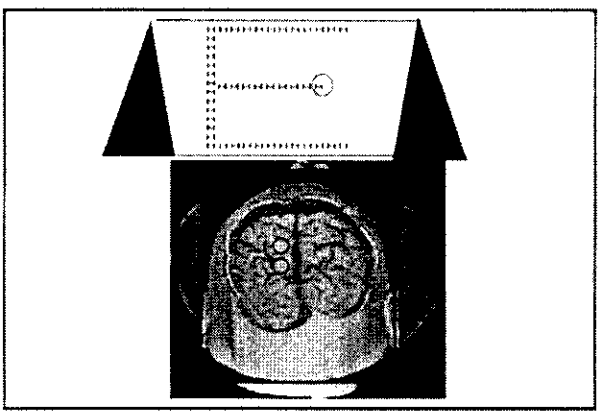


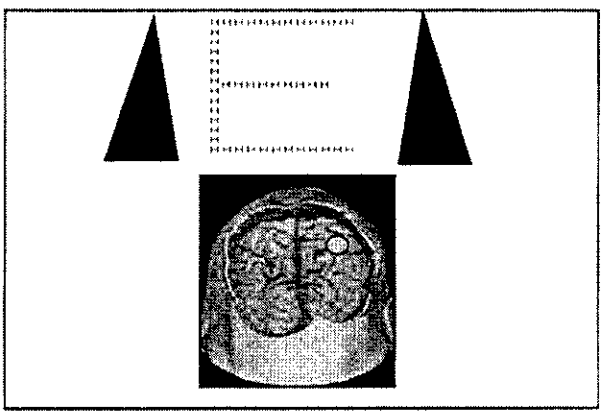

Aktivierung
Baseline
#1
#2
#n

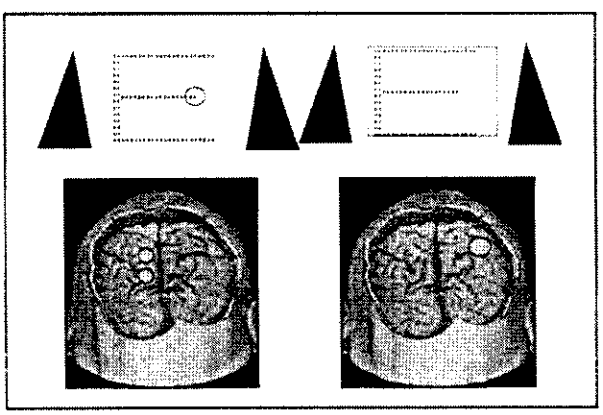
Experiment 3



Experiment 4







Ultrasound: Imaging Blood Flow

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University Hospital
Basel/Switzerland

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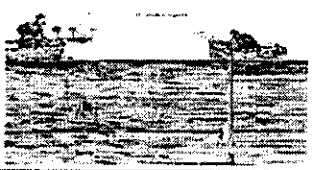
Diagnostic ultrasound

Reflection of short pulses of sound waves (2 - 20 MHz)

Synonym: Sonography

Some major early developments

1822 Colladen Daniel calculated speed of sound in water



Some major early developments

1822 Colladen Daniel calculated speed of sound in water

1877 Lord Rayleigh „The theory of sound" wave transmission and reflection

1880 Curie Pierre and Jacques discovered piezo-electric effect

Some major early developments

1912 Richardson files first patent for under-water echoranging sonor (icebergs)

1938 Pierce and Griffin detect ultrasonic cries of bats

Some major early developments

1939 Pohlman describes therapeutic use of ultrasound

1942 Dussik Karl Theodor: Hyper-phonography of the brain

Some major early developments

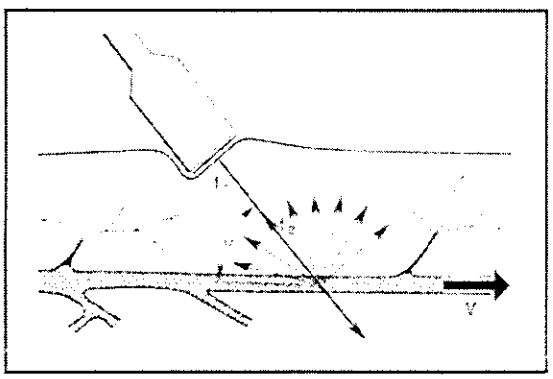
1939 Pohlman describes therapeutic use of ultrasound

1942 Dussik Karl Theodor: Hyper-phonography of the brain

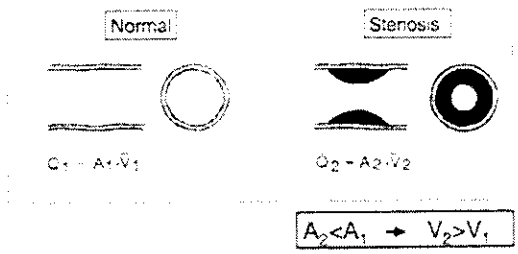
1955 Satomura Shigeo: Application of Doppler effect

$$\Delta f = \frac{2 \cdot f_0 \cdot v \cdot \cos \alpha}{c}$$

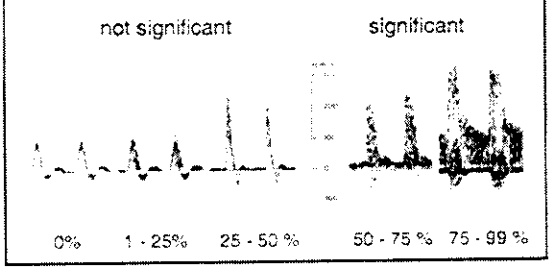
$$V = \frac{\Delta f \cdot c}{2 f_0 \cdot \cos \alpha}$$



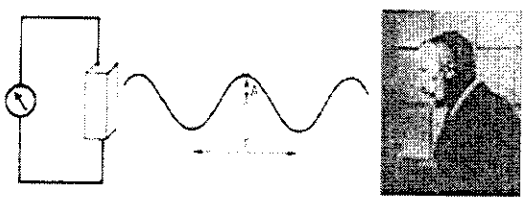
Increase in flow velocity in a stenosis

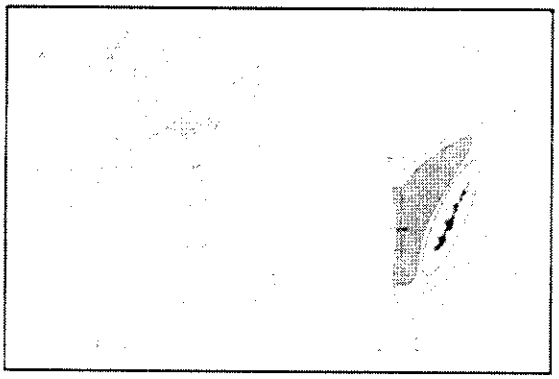


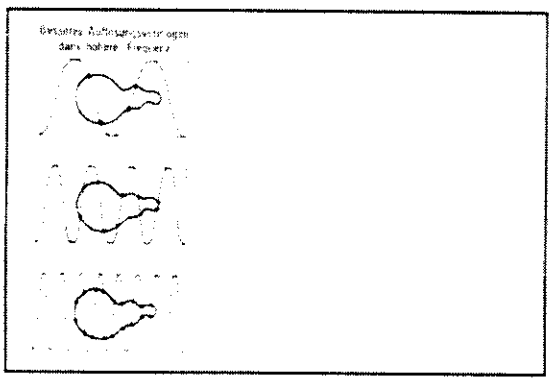
Grading of stenoses

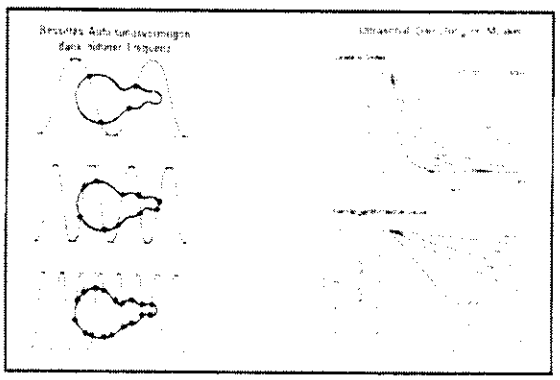


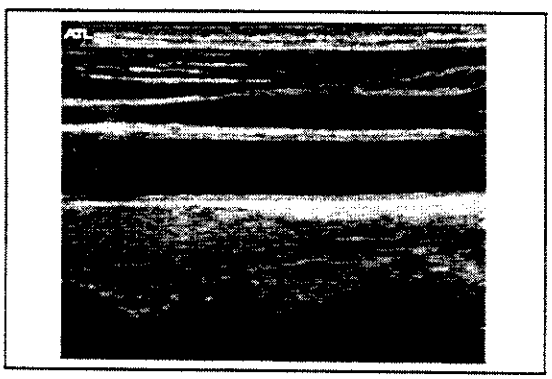
Piezo-electric effect

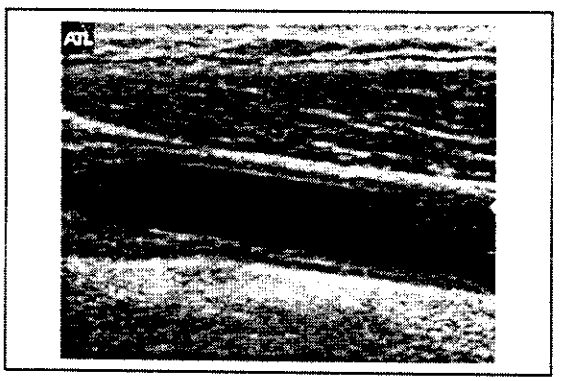


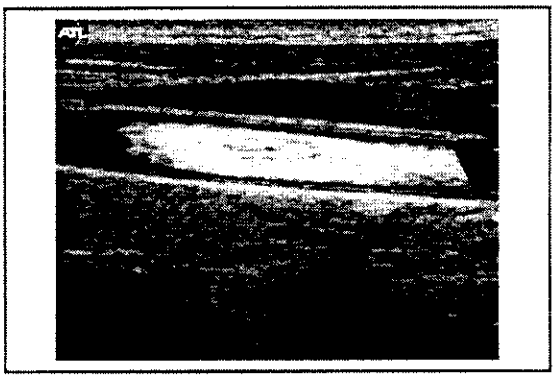


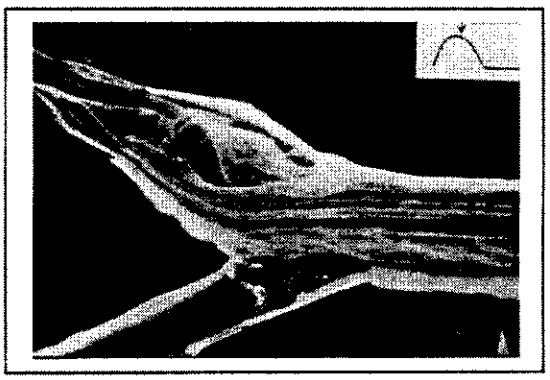


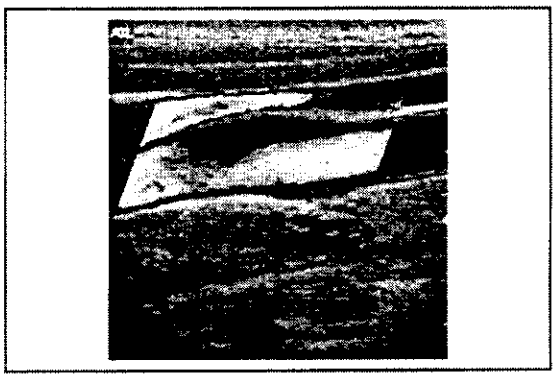


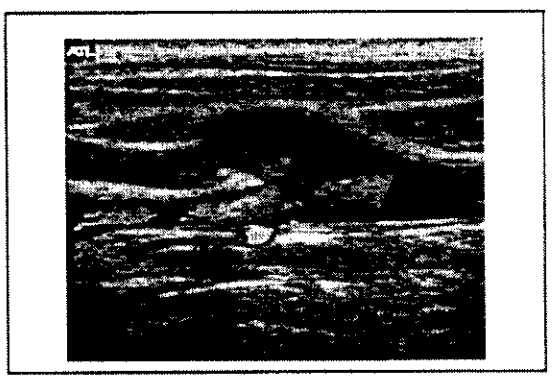






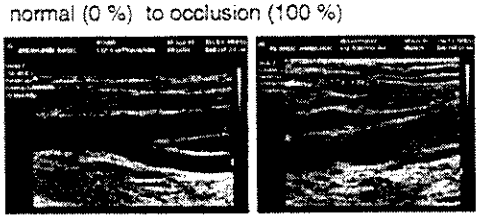






Reliable grading of stenoses

- Narrowing of vascular lumen from normal (0 %) to occlusion (100 %)



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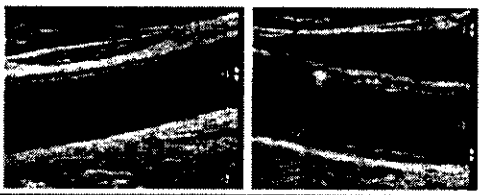
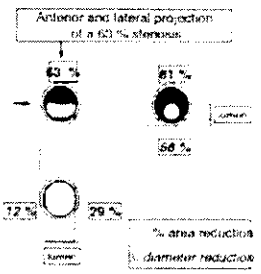


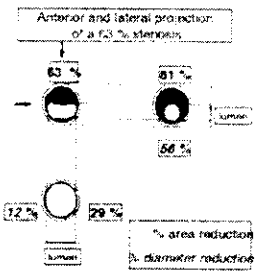
Arteriography

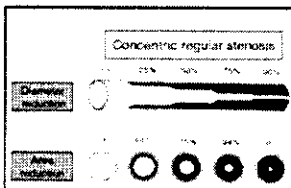
- Cast a shadow of the residual lumen upon an X-ray film

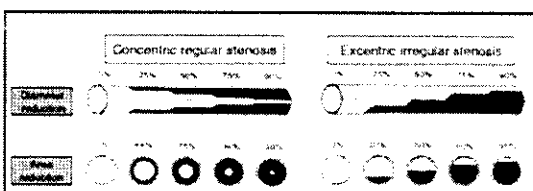


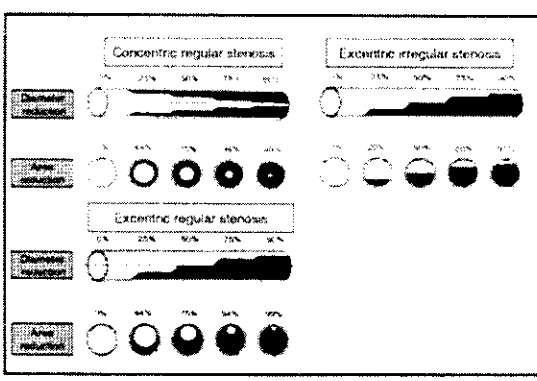
Arteriography

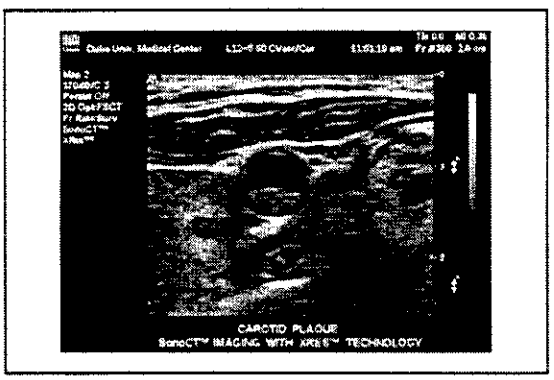
- Cast a shadow of the residual lumen upon an X-ray film
- Diameter reduction v.s. area reduction

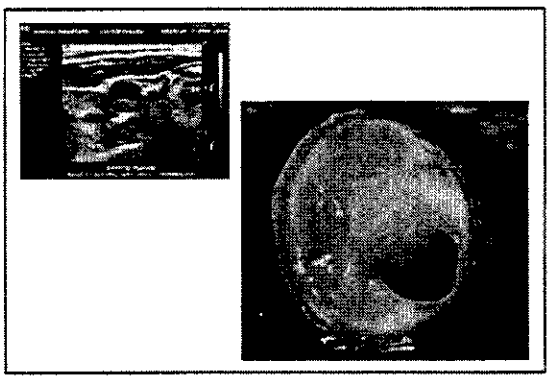


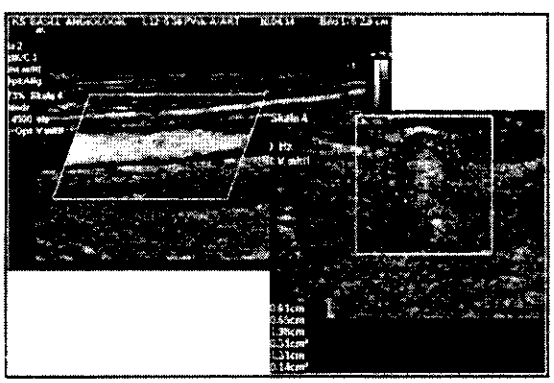




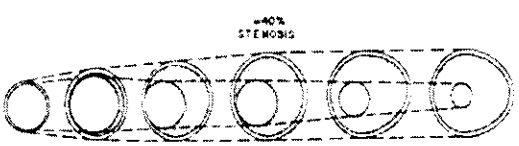








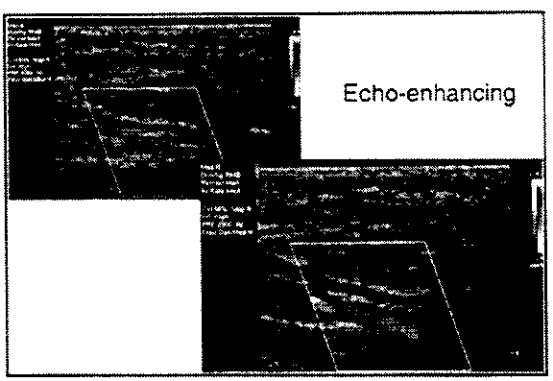
The artery initially enlarges in response to plaque accumulation



Flow through stenoses

Factors influencing flow:

- degree of stenosis
- morphology: length, surface, shape
- inflow
- outflow resistance

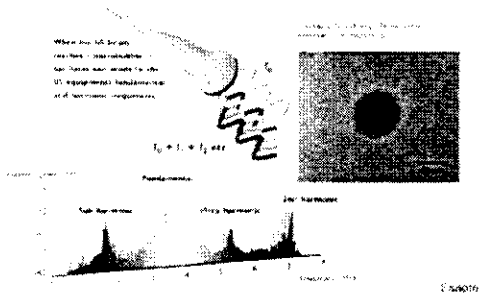


Echo-enhancing

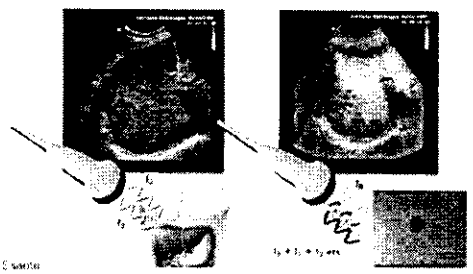
Second generation contrast agents

- Soft shell
- Oscillate and give characteristic responses at low pressure levels
- Distinguish echo from CA and tissue
- Perfusion measurements

Harmonic imaging



Harmonic imaging



Blood flow

Arterial system

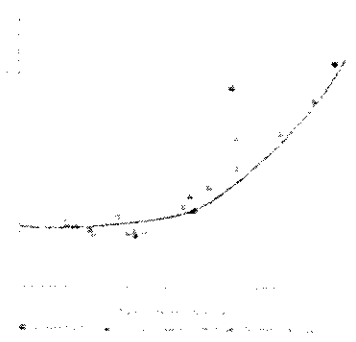
- arteries carry blood to the organs
- occlusive disease mainly due to arteriosclerosis (heart, brain, abdomen, extremities)

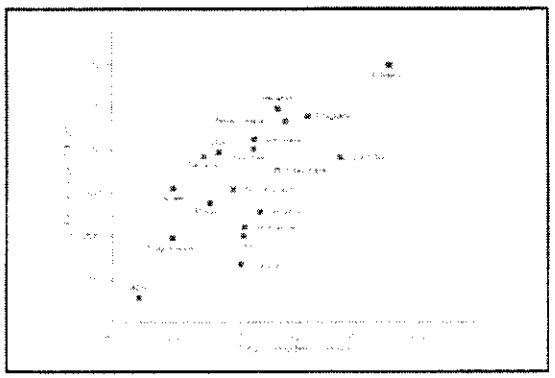
Venous system

- returns blood to heart and lungs
- thrombosis may result in embolism and chronic venous insufficiency

Arteriosclerosis

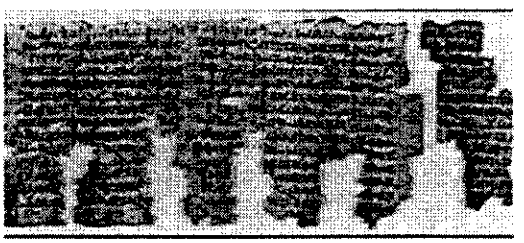
- Civilization disease
  Problem of our modern day society
- Caused by known risk factors
  - smoking
  - cholesterol
  - diabetes
  - high blood pressure





Arteriosclerosis

- An ancient disease



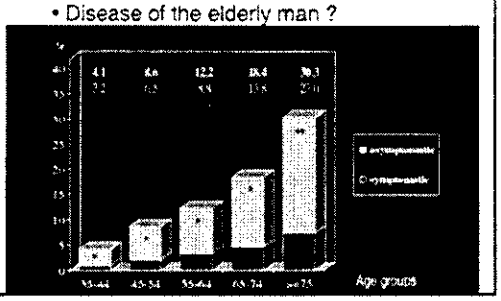
Arteriosclerosis

- An ancient disease

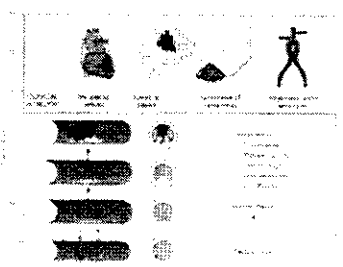
  Egyptian papyrus and mummified human remains ⟶ arterial disease
  - was not uncommon
  - was not different

Arteriosclerosis

- Disease of the elderly man ?



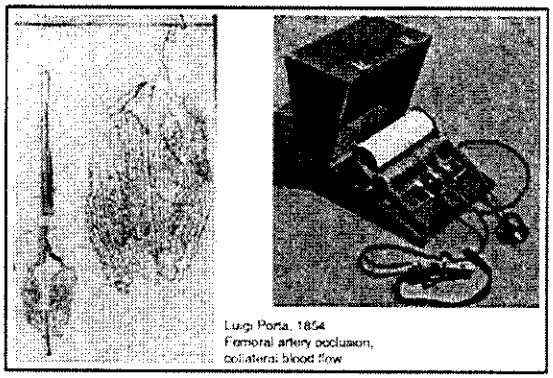
Arteriosclerosis



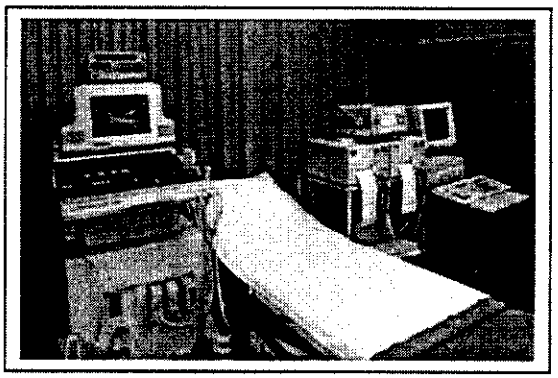
William Harvey

1578 - 1657

De motu cordis et sanguinis, 1639



Luigi Porta, 1854
Femoral artery occlusion,
collateral blood flow

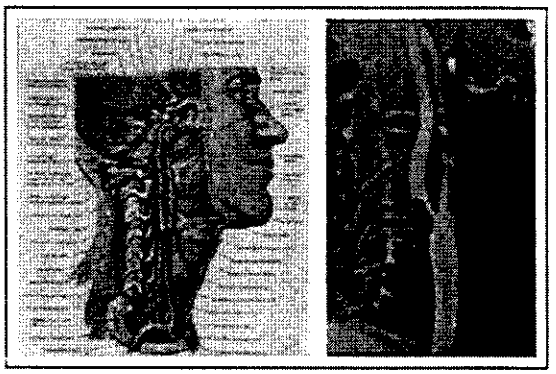


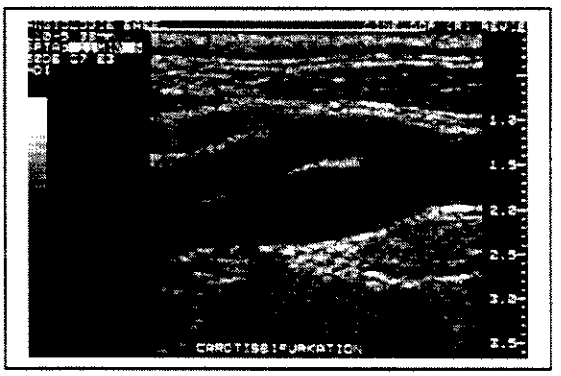
US - techniques to assess stenosis

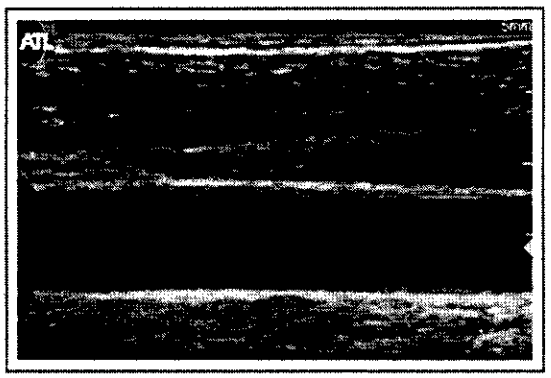
- B -Mode imaging
- B- Flow imaging
- Doppler techniques
  - Color coded imaging
  - Spectral analysis
- Echoenhancer

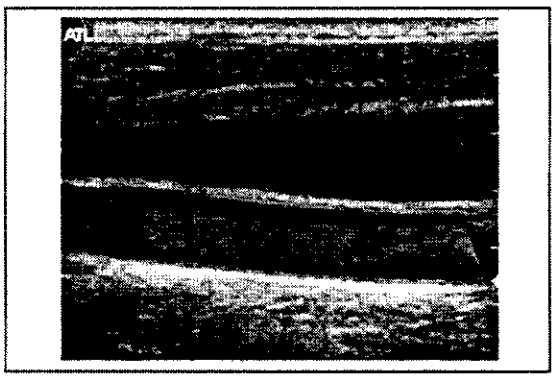
US - techniques to assess stenosis

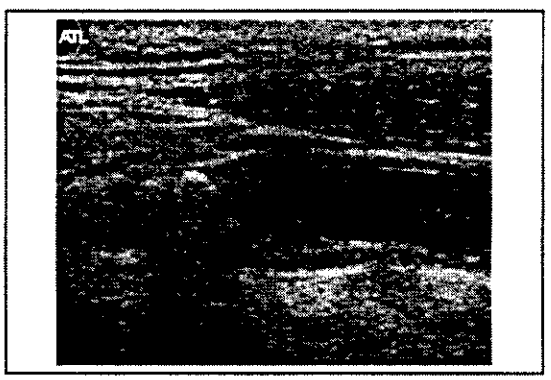
- B -Mode imaging → overestimate stenosis
- B- Flow imaging
- Doppler techniques
  - Color coded imaging → underestimate stenosis
  - Spectral analysis
- Echoenhancer





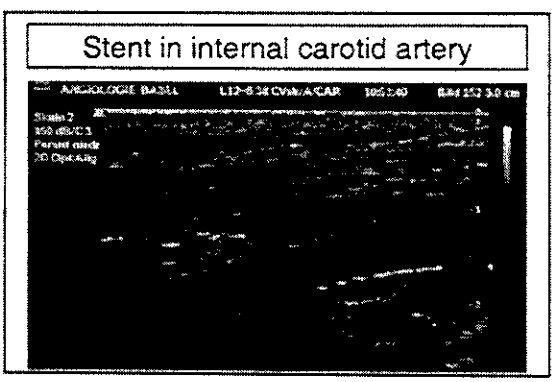

ATL

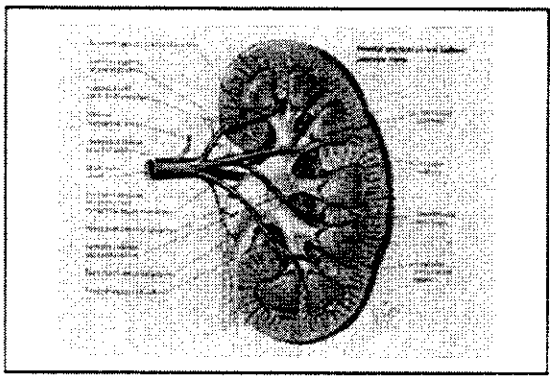

ATL

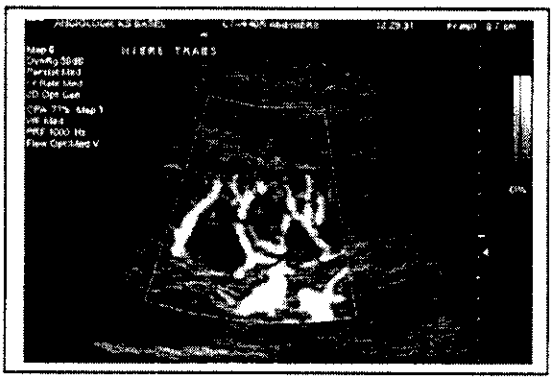

ATL

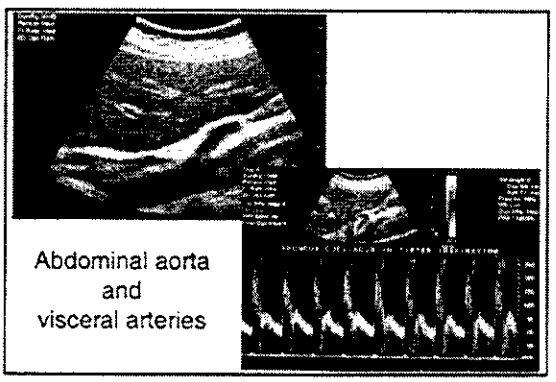

ATL


ATL


Stent in internal carotid artery

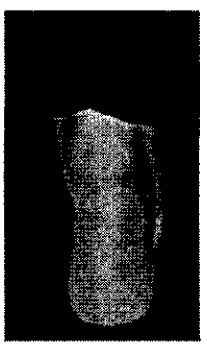


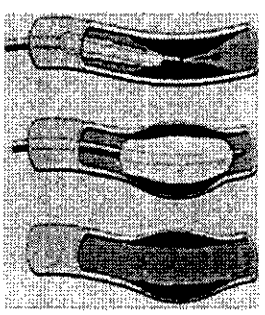


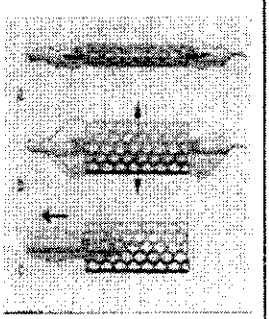


Abdominal aorta
and
visceral arteries

Improve walking capacity
and avoid amputation







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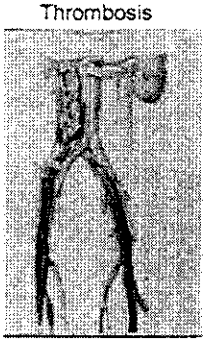
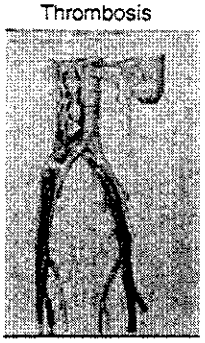
- returns blood to heart and lungs
- thrombosis may result in embolism and chronic venous insufficiency

Thrombosis



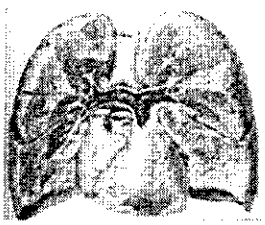
Thromboembolism

Thrombosis



Thromboembolism

Embolism



Relevance of pulmonary embolism

Rate of fatal PE in Europe:	60 / 100'000
Fatal PE in USA:	200'000 / year
In-hospital mortality due to PE :	10%

Most frequent severe in-hospital complication

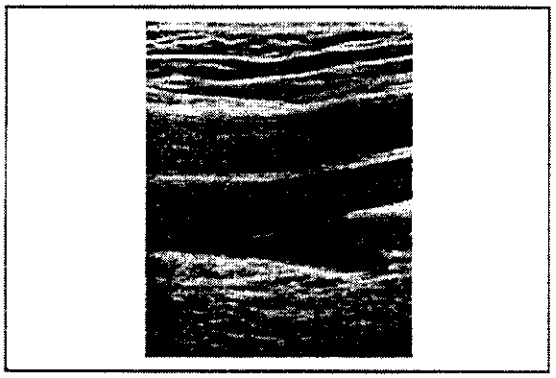
Pulmonary embolism (PE) and deep vein thrombosis (DVT)

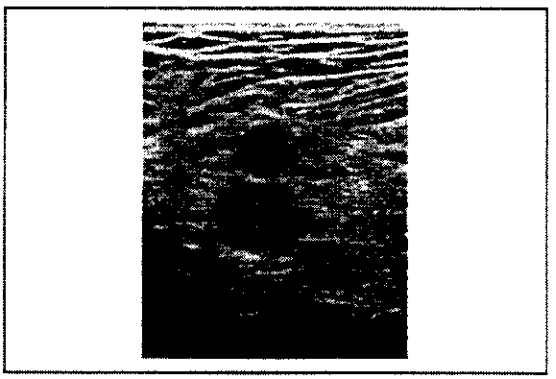
> 80 % of emboli stem from lower extremity DVT

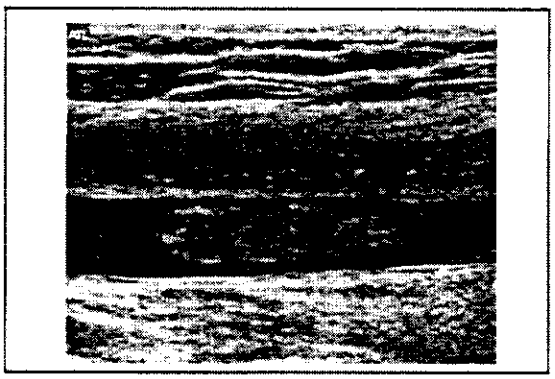
At the time of DVT-diagnosis > 50 % have PE

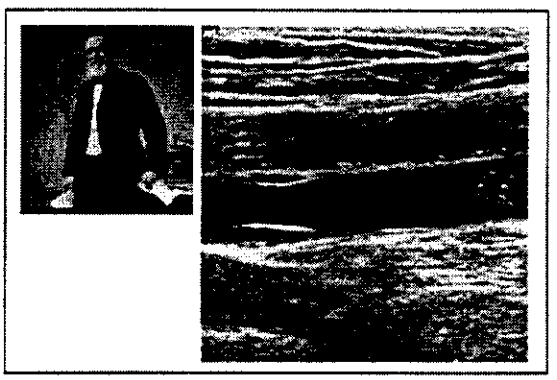
Untreated DVT results in PE in 2/3

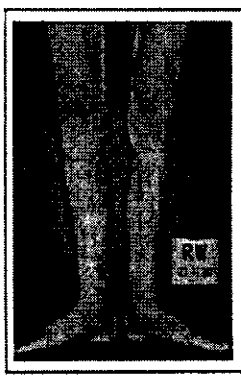
Untreated DVT results in fatal PE in > 10%









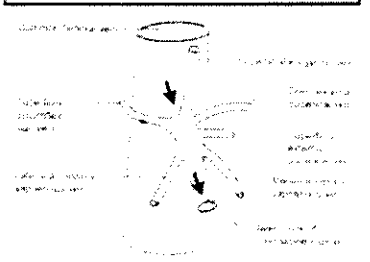


Venous insufficiency

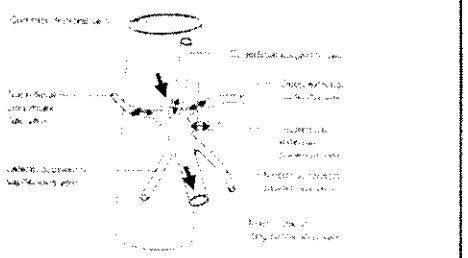
caused by

- incompetent venous valves
- increased venous distensibility
- increased intravenous pressure

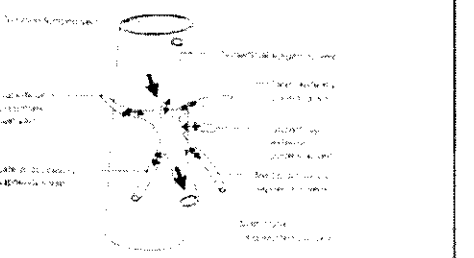
Origin of reflux



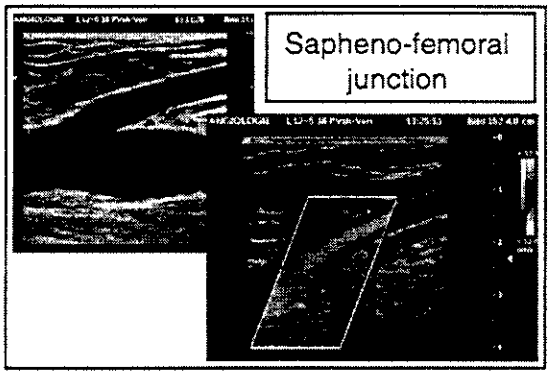
Origin of reflux



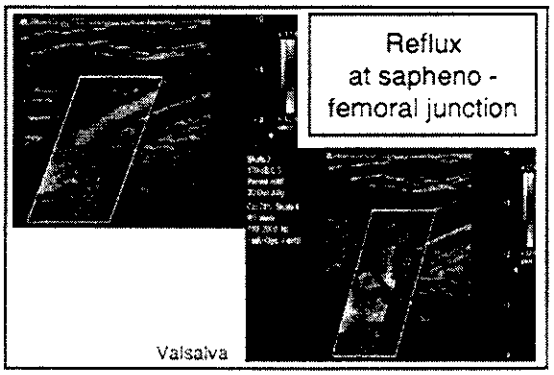
Origin of reflux

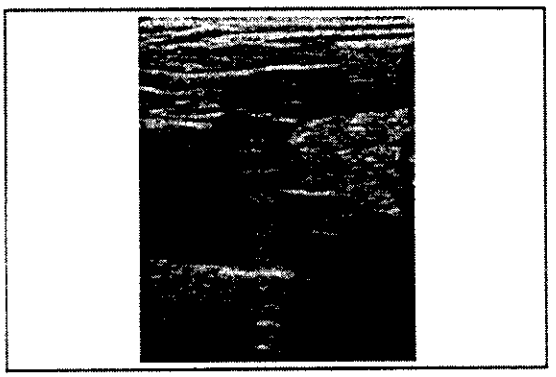


Sapheno-femoral junction

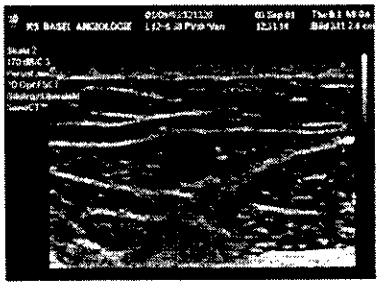


Reflux at sapheno - femoral junction





The Egyptian eye

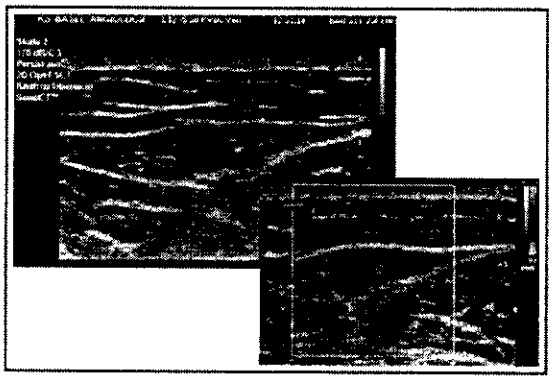


Saphenous eye

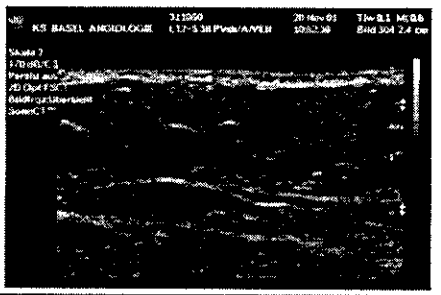
Saphenous compartment

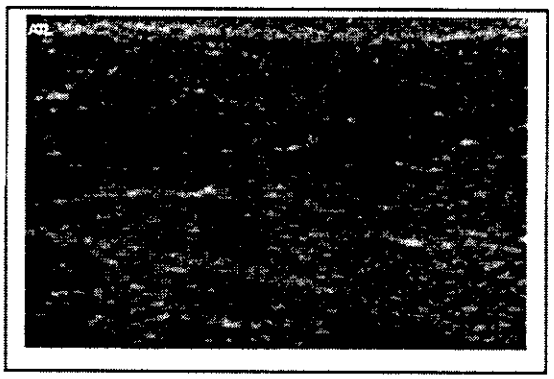
Saphenous fascia
- muscular fascia
- membranous lamina

Anchoring strands



Saphenous vein and tributaries





Duplex scanning : Conclusion

- Compares favorably with angiography in the detection and characterization of lesions

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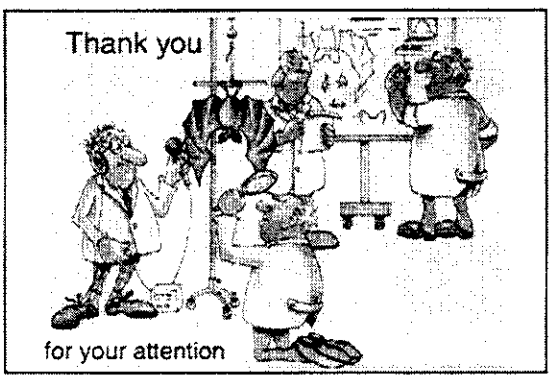
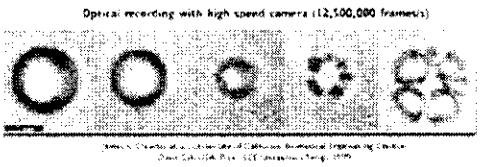
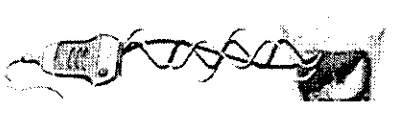
Duplex scanning : Conclusion

- Compares favorably with angiography in the detection and characterization of lesions
- Provides information needed for planing of best treatment
- Safe and reliable non-invasive diagnostic modality
- More ultrasound machines installed than all other imaging techniques combined

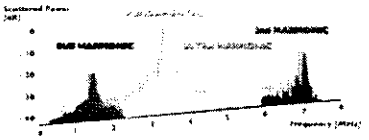


First generation contrast agents





Harmonic imaging



Magnetic Resonance in Medicine:

Morphology and Way Beyond

Roland Kreis, PhD

Dept. Clinical Research
MR Spectroscopy and Methodology
University Berne, Switzerland

How Come … ?

How come, a technique

- ***using radiation with a wavelength in the meter range and***
- ***with equilibrium population differences of a few ppm***

should be useful for imaging of humans and even single cells ?

Table of Contents

- Theory
  - Quantum-mechanical Description
  - Classical Model
  - Basic MRI Sequence
  - Contrast Mechanisms

- Applications
  - Examples from Routine Radiology
  - Advanced Applications
  - Frontier

Bootstrap for Physicists 1

Nuclear Magnetic Resonance (NMR) is well-described in quantum-mechanical terms (density operator formalism)

e.g. Ernst, Bodenhausen & Wokaun,
Principles of Nuclear Magnetic Resonance in One and Two Dimensions, Oxford (1987)

Liouville-von Neuman Equation represents equation of motion for density operator of whole system

$$\frac{d}{dt}\rho(t) = -\mathrm{i}\left[\mathcal{H}(t), \rho(t)\right]$$

Bootstrap for Physicists 2

Space and spin part of density operator can usually be separated to obtain reduced equation of motion for spin system:

$$\frac{d}{dt}\sigma(t) = -\mathrm{i}\left[\mathcal{H}^{\times}(t), \sigma(t)\right] - \hat{\Gamma}\{\sigma(t) - \sigma(0)\}$$

Spin-Density-Operator

Spin-Hamiltonian

Spin-Lattice Superoperator

Bootstrap for Physicists 3

Relevant parts of Spin-Hamiltonian:

$$\mathcal{H}^{\times}(t,\vec{x}) = \mathcal{H}_{B_0} + \mathcal{H}_G(t,\vec{x}) + \mathcal{H}_{rf}(t,\vec{x}) + \mathcal{H}_J + \mathcal{H}_D + \mathcal{H}_Q$$

Interaction with static field B_0

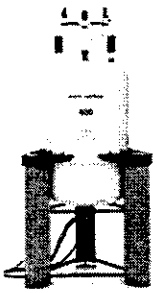
Interaction with gradient field $G(t,x)$
(time- and space-dependent)

Interaction with radio-frequency field $B_{rf}(t,x)$
(time- and space-dependent)

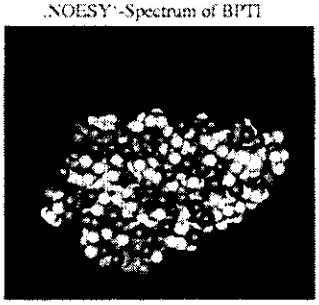
Spin-Spin Interactions
(NMR Spectroscopy + advanced applications)

High Resolution NMR Spectroscopy

Bruker Spectrospin
600 MHz = 14 Tesla



„NOESY"-Spectrum of BPTI



Courtesy of G.Wider & K.Wüthrich

Bootstrap for Physicists 4

Classical picture for ensemble of spins ½ (Bloch equations):

$$\dot{\mathbf{M}}(t) = \gamma \mathbf{M}(t) \times \mathbf{B}(t) - \mathbf{R}\{\mathbf{M}(t) - \mathbf{M}_0\}$$

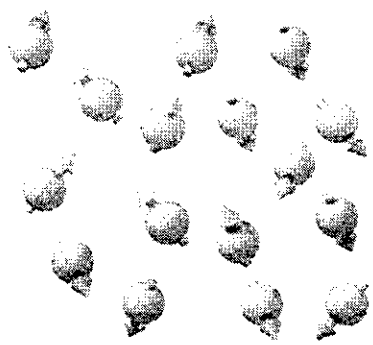
Overall Spin Magnetization

Time-varying B-field
(rf and static)

Relaxation Matrix
Spin-Lattice and Spin-Spin

Equilibrium
magnetization

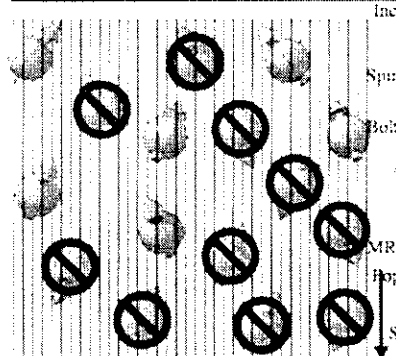
Nuclei (spins) without external B field



Random orientations:
=> no resulting
macroscopic
magnetization
(sum of all spins)
=
0

Courtesy of Ch.Leach, Berne

Nuclei (spins) with external B field



Incoherent precession
around B_0

Spins either up or down

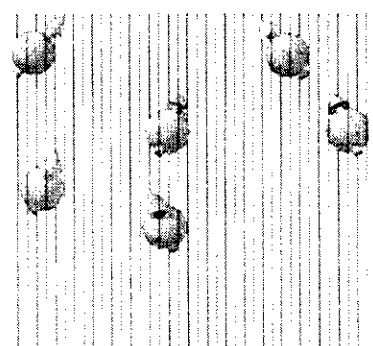
Boltzmann Distribution
of Populations
$P_i = \exp(-E_i/kT)$

$\Delta E \, h / kt << 1$
MRI perfectly safe, but
Population Difference
in ppm range

Static B_0

Adapted from Ch.Leach, Berne

Nuclei (spins) with external B field



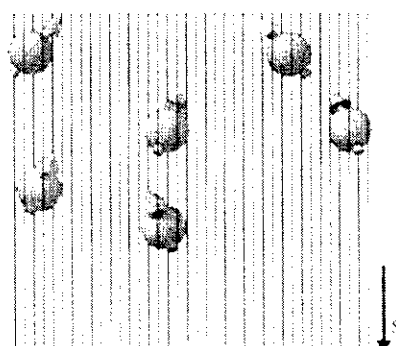
Net macroscopic
magnetization:

$M_0 = +Mz$

Static B_0

Courtesy of Ch.Leach, Berne

Effect of RF Pulses (B_π)



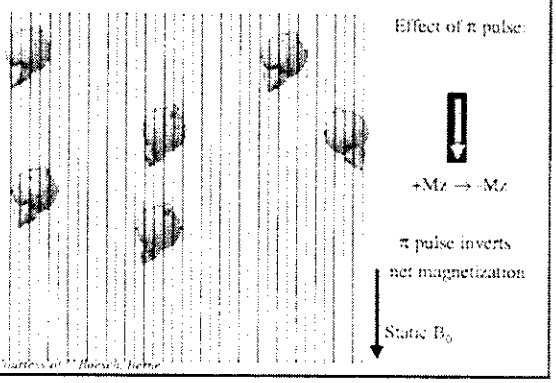
Effect of π pulse:

$+Mz \rightarrow -Mz$

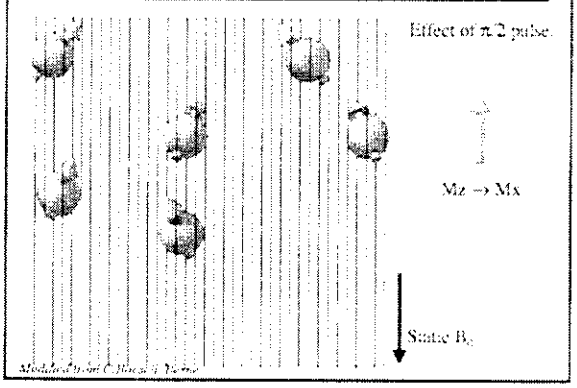
Static B_0

Courtesy of Ch.Leach, Berne

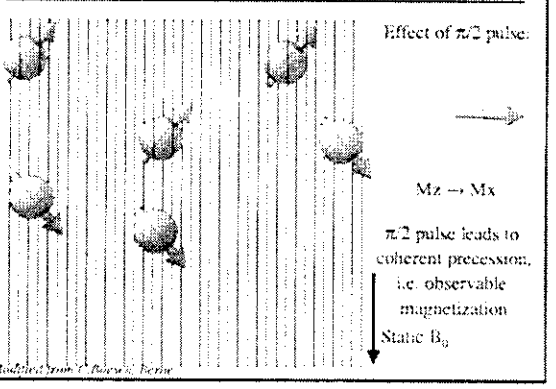
Effect of RF Pulses (π)



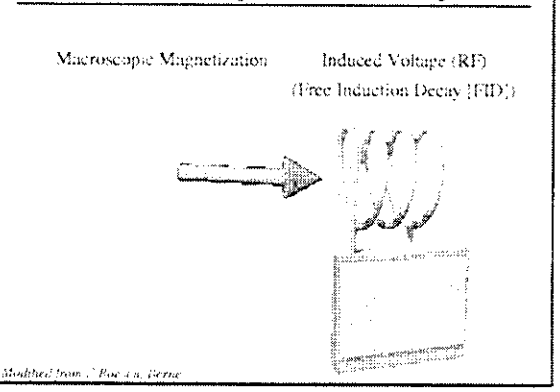
Effect of RF Pulses (π/2)



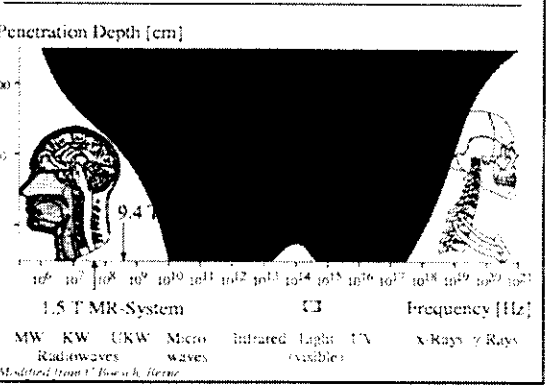
Effect of RF Pulses (π/2)



Observable Signal (induced voltage)



RF Penetrates the Human Body



The MRI Scanner

Resonance Frequency

$$= \frac{\gamma}{2\pi} *$$

Detected radiofrequencies depend on effective B-field

External: B0 + gradients

Internal: γ + electron structure

MR is based on frequency encoding

Modified from C.Boesch, Berne

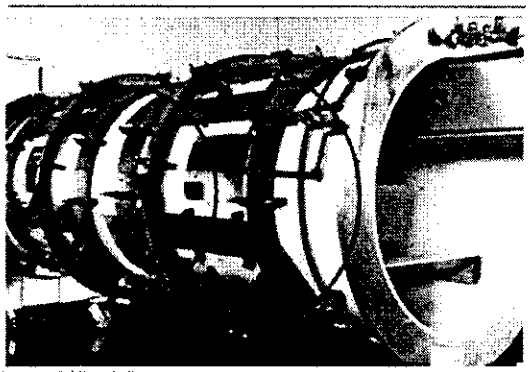
Frequency Encoding of Spatial Location

Gradients:
switchable space-dependent B fields

space-dependent resonance frequencies

Modified from C.Boesch, Berne

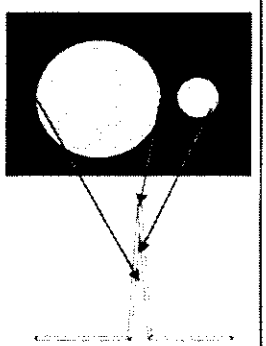
Gradient Coils



Courtesy of C.Boesch, Berne

Frequency Encoding by Projections 1

Magnetic Field



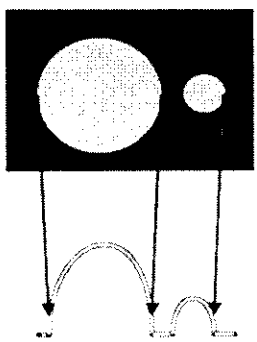
Homogeneous field
=> same resonance frequency
for whole object

Courtesy of C.Boesch, Berne

resonance frequency

Frequency Encoding by Projections 2

Magnetic field



Spatially varying magnetic field
=> Resonance frequency
depends on spatial position

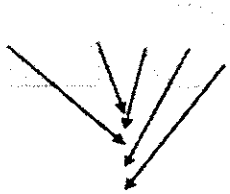
Courtesy of C.Boesch, Berne

resonance frequency => projection

Frequency Encoding by Projections 3

Gradient strength

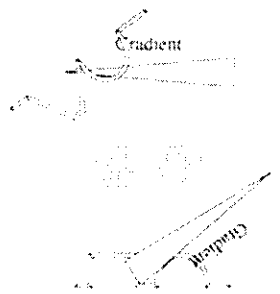
Objects



Resonance frequency =
projection

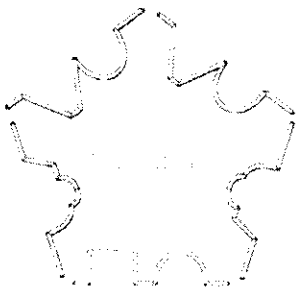
Courtesy of C.Boesch, Berne

Projection Reconstruction



Courtesy of C.Boesch, Berne

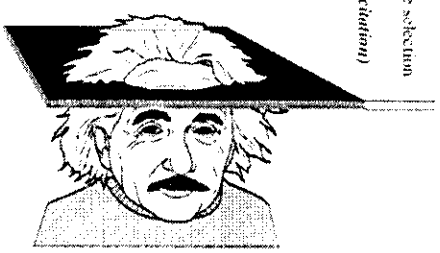
Projection Reconstruction



Projektionen

Courtesy of C.Boesch, Berne

Selection of Directions



Courtesy of C.Boesch, Berne

Slice Selection

Selective Pulse ν B

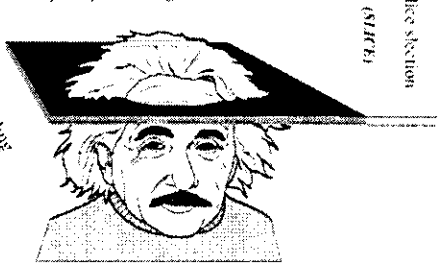
$\Delta\nu$

$B(z)$ Z-Gradient

$$\nu = \frac{\gamma}{2\pi} B$$

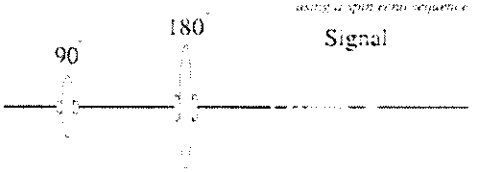
Courtesy of C.Boesch, Berne

Selection of Directions



Courtesy of C.Boesch, Berne

Frequency Encoding in X and Y ("k-space")



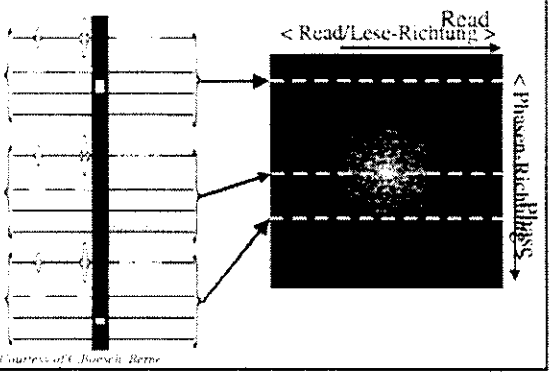
Slice

Phase

Read

Courtesy of C.Boesch, Berne

Data Storage in „k-Space"



Courtesy of C Boesch, Berne

From "k-Space" to Physical Space by Fourier-Transformation

"k-space"
< Read/Lese-Richtung >
< Phasen-Richtung >

$$\mathbf{k}(t) = \gamma \int_0^t \mathbf{G}(t')dt'$$

k: spatial frequency vector

physical space
(calculated domain)

Adapted from C Boesch, Berne

Central Part of "k-Space"

< Read/Lese-Richtung >
< Phasen-Richtung >

Courtesy of C Boesch, Berne

Peripheral Part of "k-Space"

< Read/Lese-Richtung >
< Phasen-Richtung >

Courtesy of C Boesch, Berne

Fourier Imaging

FOURIER-Imaging

NON-STANDARD MRI

Courtesy of C Boesch, Berne

Spatial Resolution

- NOT limited by wavelength
- only limited by
  - gradient strength
  - signal to noise (time)

Microimaging with λ ~0.5m

Mouse Embryo

13.5 days post-conception

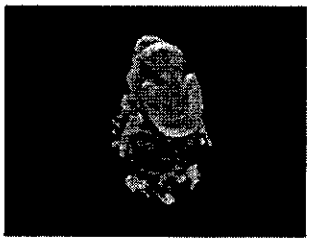
Sagittal slices

Left-right views

Marc Dhenain
Russell E. Jacobs
CalTech

http://www.mousearlas.caltech.edu

Mouse Embryo: 3D Rendering



http://www.mousearlas.caltech.edu

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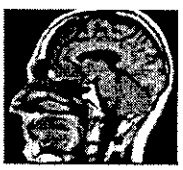


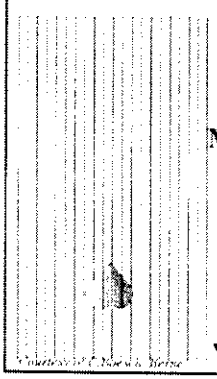
Spin-Density Contrast (ρ)

Spin-Density is

= proportional to water (and fat) content of tissue

=> ρ is tissue/pathology dependent

T_1 – Contrast (Longitudinal Relaxation)



Recovery of steady-state magnetization

(spin-lattice temperature equilibration)

=> T_1 relaxation is tissue dependent

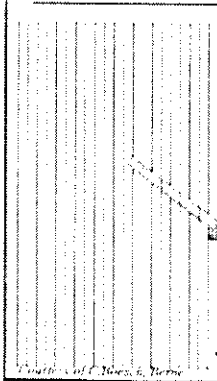
M

$M(t)=M_0 + \Delta M\ e^{-t/T_1}$

Static Field

t

T_2 – Contrast (Transverse Relaxation T_2, T_2^*)



Decay of transverse magnetization

(dephasing, loss of coherence)

=> T_2 relaxation is tissue dependent

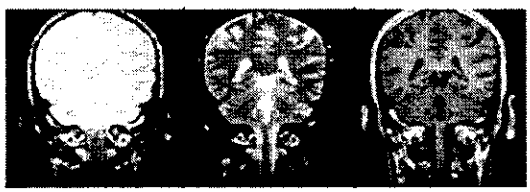
M

t

Static Field

$M(t)=M(0)\ e^{-t/T_2}$

Standard Contrasts in Cranial MRI



Proton-Density | T_2-weighted | T_1-weighted

TR/TE: 2500/30ms | *TR/TE: 2500/80ms* | *TR/TE: 400/15ms*

MRI: Contrast Mechanisms

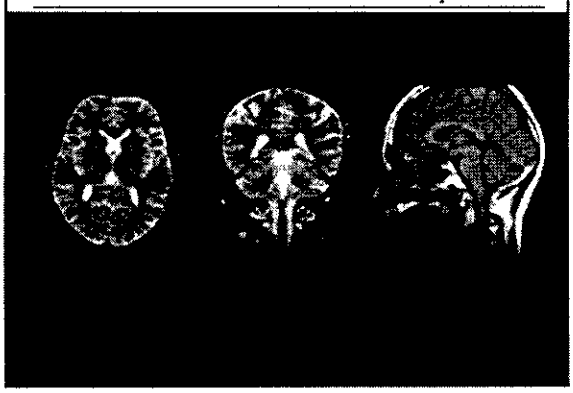
❑ inherent

- T1
- T2
- T2* (susceptibility)
- Diffusion (DWI, ADC, orientation)
- Perfusion /Flow
- Magnetization transfer (MM / water)
- Bulk motion
- Chemical shift (chemical analysis by spectroscopy)

❑ induced

- Contrast agents (Gd, Fe, ...)
- Endogenous contrast agents (deoxy-myoglobin, deoxy-hemoglobin- ⇒MRI)
- Hyperpolarized gas (^{3}He, Xe ⇒ Lung)
- Dynamic MRI (joints)

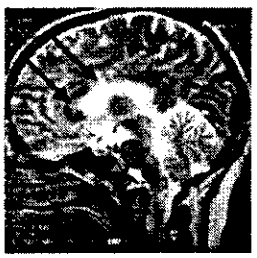
MRI: Routine Clinical Techniques



Multiple Sclerosis (MS)

typical MS lesions in white matter (Corpus Callosum)

Retrobulbar Neuritis (often 1st signs of MS)



T_2-weighted MRI

T_1-weighted CE MRI

Astrocytoma: CT vs. MRI

CT

No detectable lesion

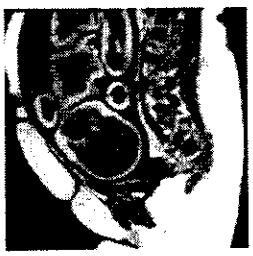
T_1-weighted MRI

prominent lesion in brainstem

3-year old boy with behavioural changes, tumor inoperable

Fetal MRI in Utero

Coronal view w.r.t. Mother



Sagittal View w.r.t. Mother

Cardiovascular Magnetic Resonance Imaging at the IBT Zurich

Sebastian Kozerke, Klaas P. Pruessmann, P. Boesiger

Institute for Biomedical Engineering, ETH Zurich, Switzerland

Standard Views

short axis view

long axis view

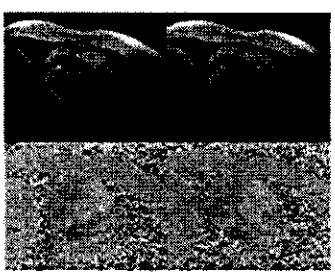
axial view

valve

Real-Time Imaging

Moving slice imaging

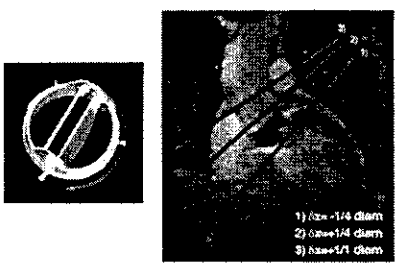
Normal aortic heart valve



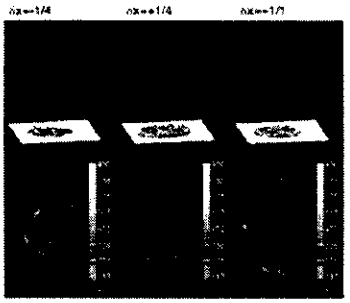
Moving slice imaging Static slice (conventional)

Aortic regurgitation

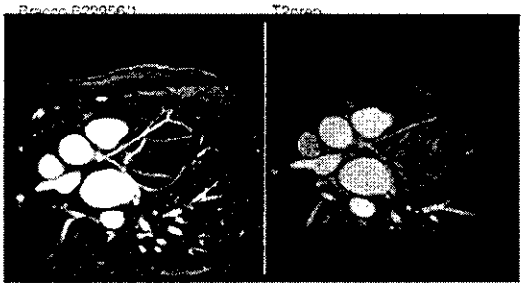
Heart valve prostheses



Blood velocity/shear rate

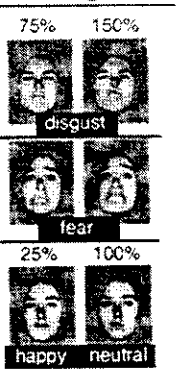


Blood pool contrast agent



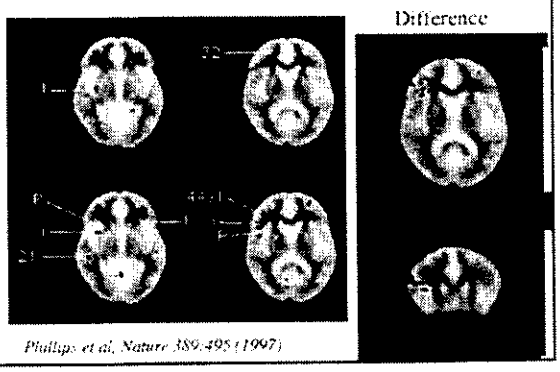
Functional MRI: Principles

Activation upon Perception of Disgust



Phillips et al, Nature 389:495 (1997)

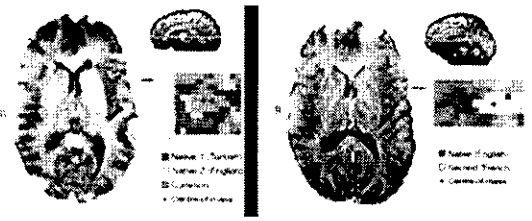
Activation upon Perception of Disgust



Phillips et al, Nature 389:495 (1997)

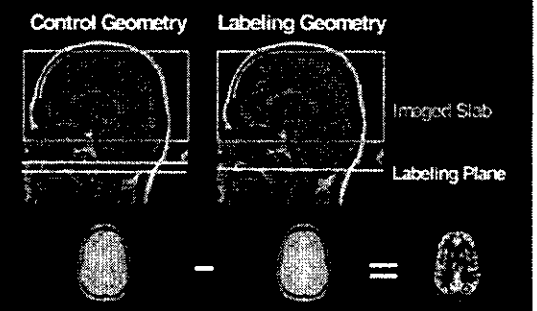
Late vs. Early Second Language

Early-learned 2nd language Late-learned 2nd language



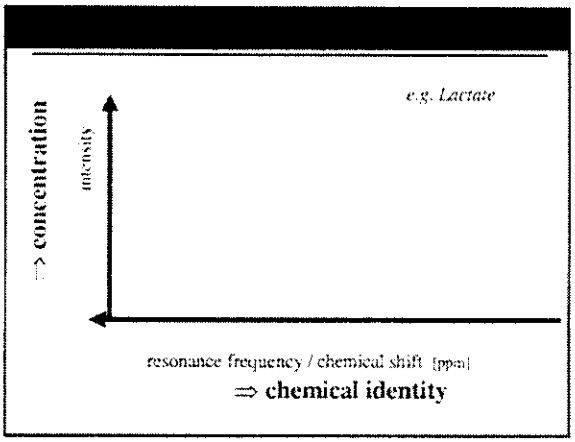
Kim et al. Distinct cortical areas associated with native and second languages. Nature 388:171 (1997)

Perfusion MRI by Continuous Arterial Spin Labeling



Alsop and Detre, Radiology 208:410-16 (1998)

Courtesy of P. van Zijl



Finish up

MRI vs. MRS

With MRI you depict

WATER

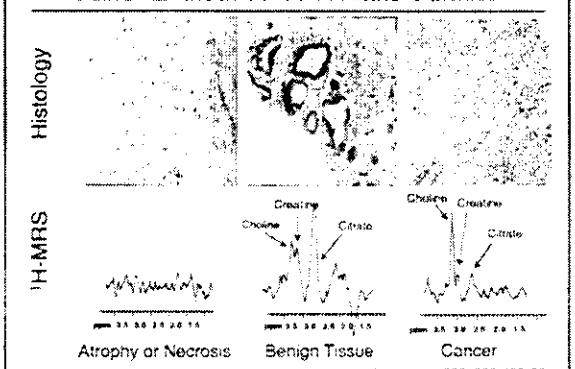
and

Fat

With MRS you determine

Water, Intra- and extracellular Lipids, Acetate, Alanine, Aspartate, Choline, N-acetylaspartate, Creatine, myo-Inositol, Ethanol, Lactate, Glutamate, Phosphorylcholine, Glycerophosphorylcholine, Ketone Bodies, γ-Aminobutyrate, Glucose, Glutamine, Glycine, scyllo-Inositol, Macromolecules, N-Acetylaspartylglutamate, O-Phosphorethanolamine, Taurine, Threonine, Glycogen, Carnosine, Carnitine, Acetylcarnitine, Phenylalanine, Succinate, Phosphocreatine, Adenosinetriphosphate, pH, NAD, 2,3-Diphosphoglycerol, Deoxymyoglobin, Deoxyhemoglobin, Citrate, Betaine, Propanediol, Homocarnosine, Glutathione

MRS: Evaluation of Prostate Tumors



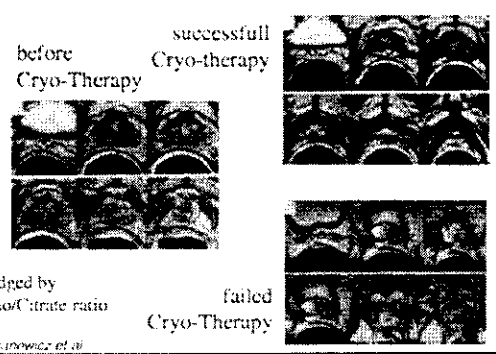
Kurhanewicz et al, Radiology, 1996, 200 489-96

Finish up

MRS: Therapy Control for Prostate Tumors

before Cryo-Therapy

successfull Cryo-therapy



Judged by Cho/Citrate ratio

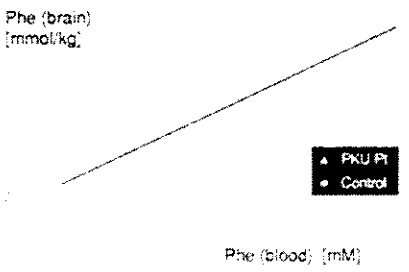
failed Cryo-Therapy

Kurhanewicz et al

MRS: Therapy Management in Phenylketonuria

Do we have to measure phenylalanine (Phe) in brain by ^{1}H-MRS for dietary control?

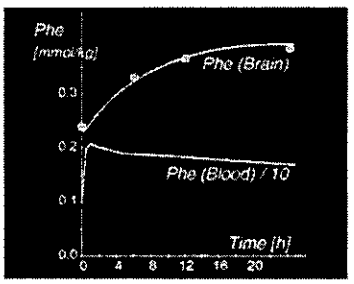
NO, blood Phe reflects brain Phe!



MRS: BBB Kinetics in Phenylketonuria

Can we measure the blood-brain-barrier kinetics for PHE with ^{1}H-MRS?

YES, but exact model up to debate!



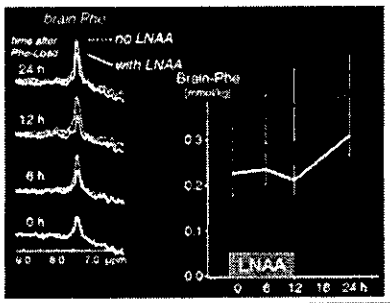
Phe dynamics after oral Phe load in PKU patients

Kreis, Ernst et al.

MRS: BBB Kinetics in Phenylketonuria

Can we block the blood-brain-barrier uptake of PHE and observe this with ^{1}H-MRS?

YES and YES !



Phe uptake blocked by saturation of carrier by other amino acids (LNAA: Large Neutral Amino Acids)

Pietz et al. J. Clin. Invest. 103 1169 (1999)

MRI of Thin Air

... but surely you can't image air !

No, not thick air,

but if we add hyperpolerized gas,

... !

Hyperpolarized ^{129}Xe Imaging

^{129}Xe

MRI of the lung

^{1}H

Mugler et al. MRI and MRS using hyperpolarized ^{129}Xe Gas: Preliminary results Magn Reson Med 37 809 (1997)

MRI of Gene Expression

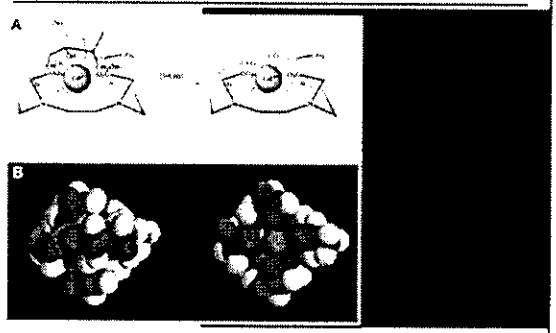
... but surely MRI is no good for molecular imaging !

No, not right away,

but if we use special contrast agents,

... !

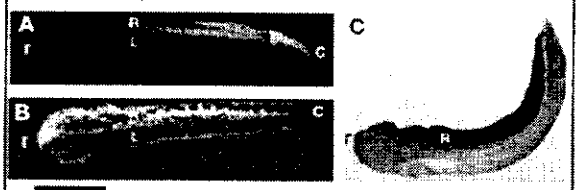
Contrast Agent for MRI of Gene Expression



In vivo visualization of gene expression using MRI
Angelique Y. Louie *et al.* Nature Biotechnology 18, 321 - 325 (2000)

MRI of Gene Expression

fluorescence image — **single living *X. laevis* embryo**



MRI with CA activated where marker gene expressed

light microscopy after staining

Marker gene expressed on R of animal mainly due to early cell injection

In vivo visualization of gene expression using MRI
Angelique Y. Louie *et al.* Nature Biotechnology 18, 321 - 325 (2000)

Why I couldn't cover it all ..

Interventional MRI

MRS Tumor Diagnosis

Diffusion-weighted MRI

Spectroscopic Imaging

Fast Imaging

Ultra-high Field MR (4-9T)

NMR for body fluids

Phased array coils SENSE

MEDLINE-search: magnetic resonance (text) + human (MESH) + (imaging (text) || spectroscopy (text))

Take Home Message

- ***MR inherently is an insensitive technique***
- ***MR has huge success in medicine due to***

NON-INVASIVENESS

and

tremendeous ***VERSATILITY***

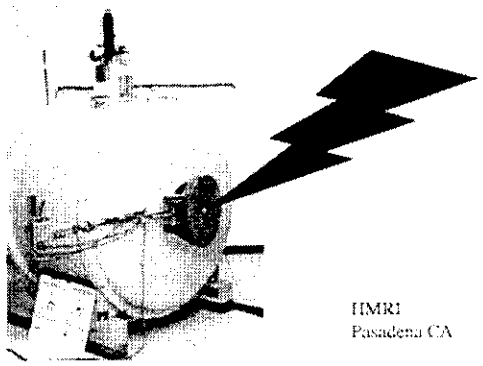
Acknowledgement

Many Thanks for slides and movies obtained from:

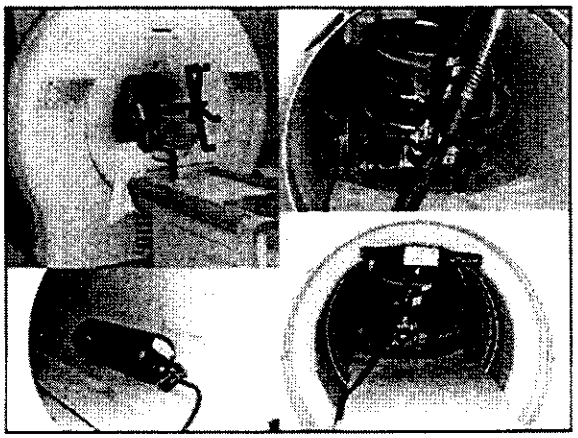
- Chris Boesch,
  Dept. Clinical Research, University Berne
- Sebastian Kozerke, Peter Boesiger,
  IBZ, ETH & University Zurich
- Peter Van Zijl,
  Johns Hopkins University, Baltimore, USA
- Chris Ozdoba,
  Neuroradiology, University Hospital Berne
- Russell Jacobs,
  Caltech, Pasadena USA http://www.mma.caltech.edu

X.laevis

Dangers of MRI



IIMRI
Pasadena CA



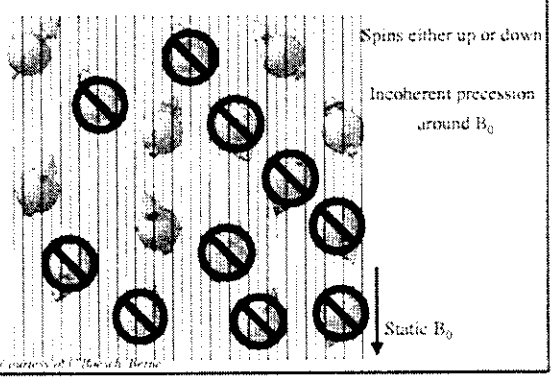
Arbitrary Slice Orientations in MRI

axial coronal sagittal

Why I can't cover all of it ..

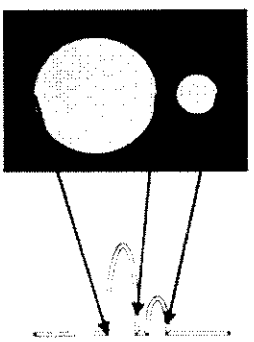
MEDLINE-search: magnetic resonance (text) + human (MESH) + (imaging (text) || spectroscopy (text))

Nuclei (spins) with external B field



Frequency Encoding by Projections 2

Magnetic field

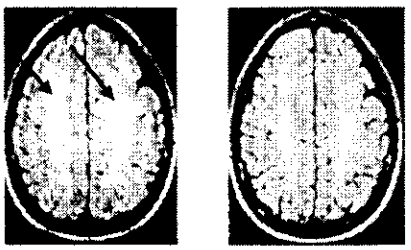


Spatially varying magnetic field
=> Resonance frequency depends on spatial position

Resonance frequency => projection

Leukoencephalopathy

Diffusion-weighted-MRI in acute leukoencephalopathy following inhalation of a single dose of heroin (Chasing the dragon)



After 5 days

After 2 months

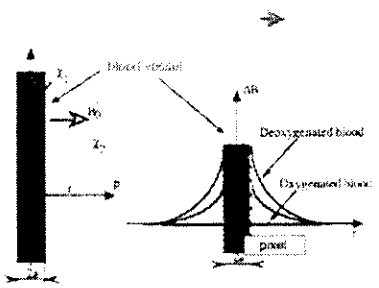
Vella, Lovblad et al. University Hospital Berne

Blood pool contrast agent

Bracco B22956/1

T2prep

Functional MRI: BOLD Effect



Coronary sinus flow