Radboud University Medical Center Nijmegen

Those were the days ……

Some landmarks in the early penetration of MR in the Benelux

……a personal account.

Arend Heerschap
Arend.Heerschap@radboudumc.nl

Klaas Nicolay

Nicolay K, Kaptein R, Hellingwerf KJ, Konings WN.
31P nuclear magnetic resonance studies
of energy transduction in Rhodopseudomonas sphaeroides.
Eur J Biochem. **1981** ;116(1):191-7.

1951 Born (Stiens)
1983 PhD (Groningen)
1983 Postdoc Utrecht University (KWF)
1985 University Basel with Seelig (perfused heart)
1987 Huygens Fellowship
1991 Head in vivo NMR facility
1998 Image Science Institute Utrecht

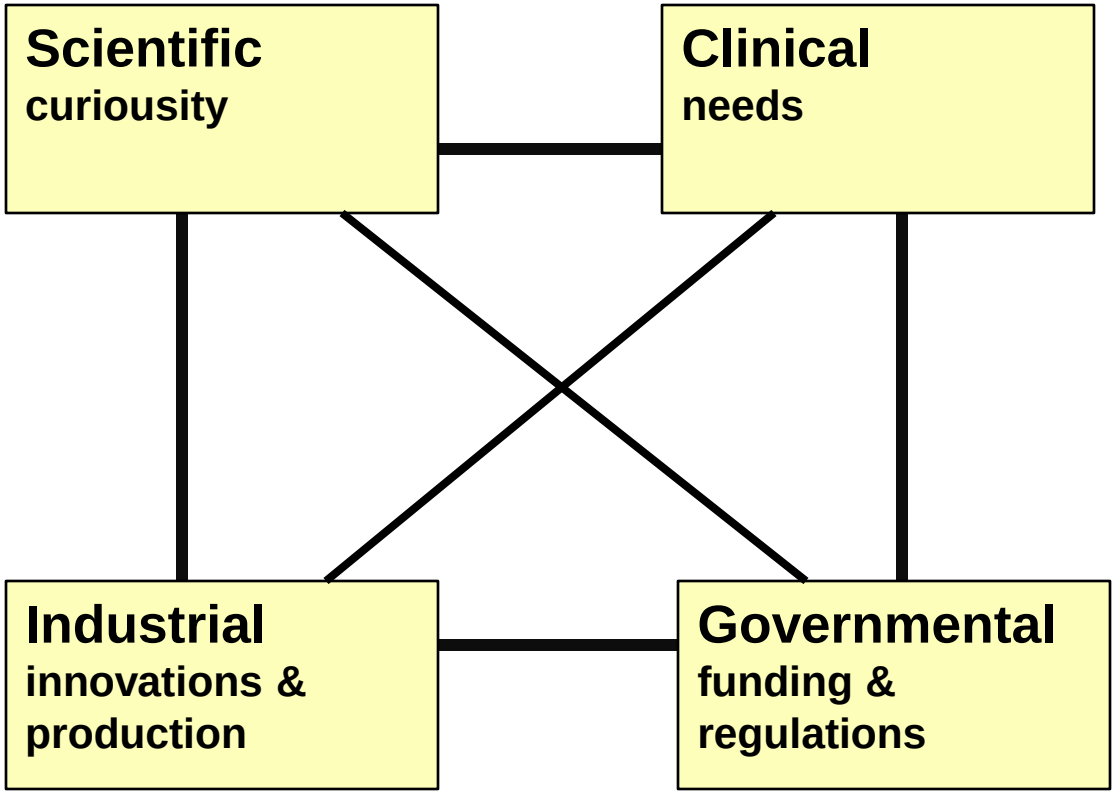
1999 Professor Biomedical NMR TU Eindhoven

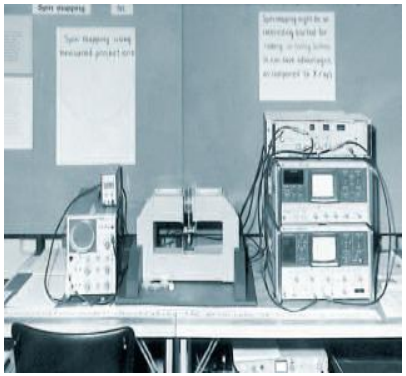
Science: molecular imaging , energy metabolism, …..

Eduction:

- Student school at the TU/e
- In vivo NMR course from ~1996

Progress in biomedical technology





This presentation:

~1975 to ~1990 …….

‘Early Benelux NMR heroes’

Cornelius J. Gorter
Universiteit Amsterdam / Leiden

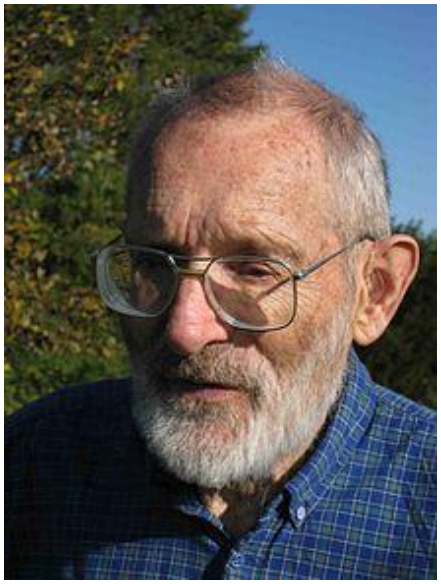
1942
First attempt NMR

Physica IX, no 6 Juni 1942

NEGATIVE RESULT OF AN ATTEMPT TO OBSERVE NUCLEAR MAGNETIC RESONANCE IN SOLIDS.

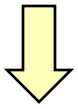
by C. J. GORTER and L. J. F. BROER

Zeeman-Laboratorium der Universiteit van Amsterdam



Jean Jeener
Universite Libre de Bruxelles (ULB)

1971
Inventor 2D NMR spectroscopy
(Lecture AMPERE Summer School,
Basko Polje, Yugoslavia)



2-3D Fourier imaging

Nobel prize

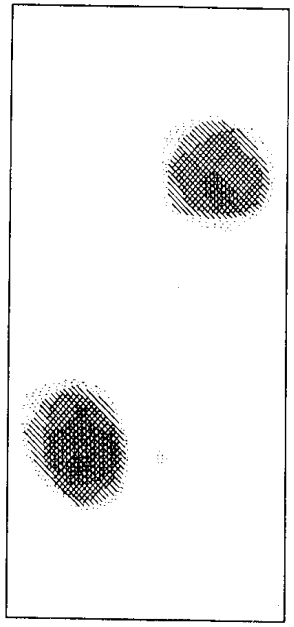
2003

Image Formation by Induced Local Interactions: Examples Employing Nuclear Magnetic Resonance

P. C. LAUTERBUR

Dep. of Chemistry, State University of New York at Stony Brook

Nature **242**, 190 - 191 (**1973**);



First MR image: 2 tubes with water

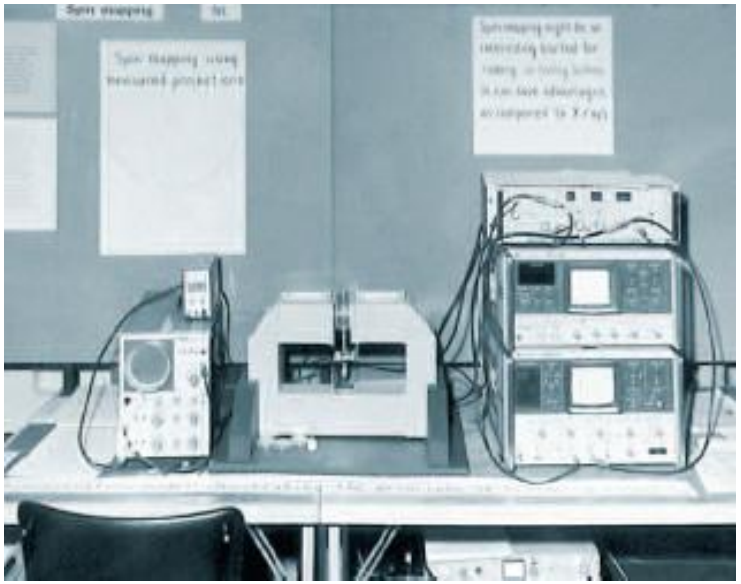
(projection reconstruction)

1974-1978

Rob Locher

Philips Research Laboratories

Waalre

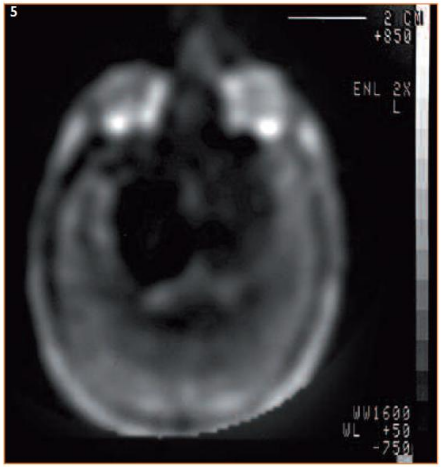


1976 Nottingham

One day NMR imaging

1978 – 1983: Proton project (Philips Research Laboratories & Medical Systems)

0.15T resistive magnet
1 m free bore

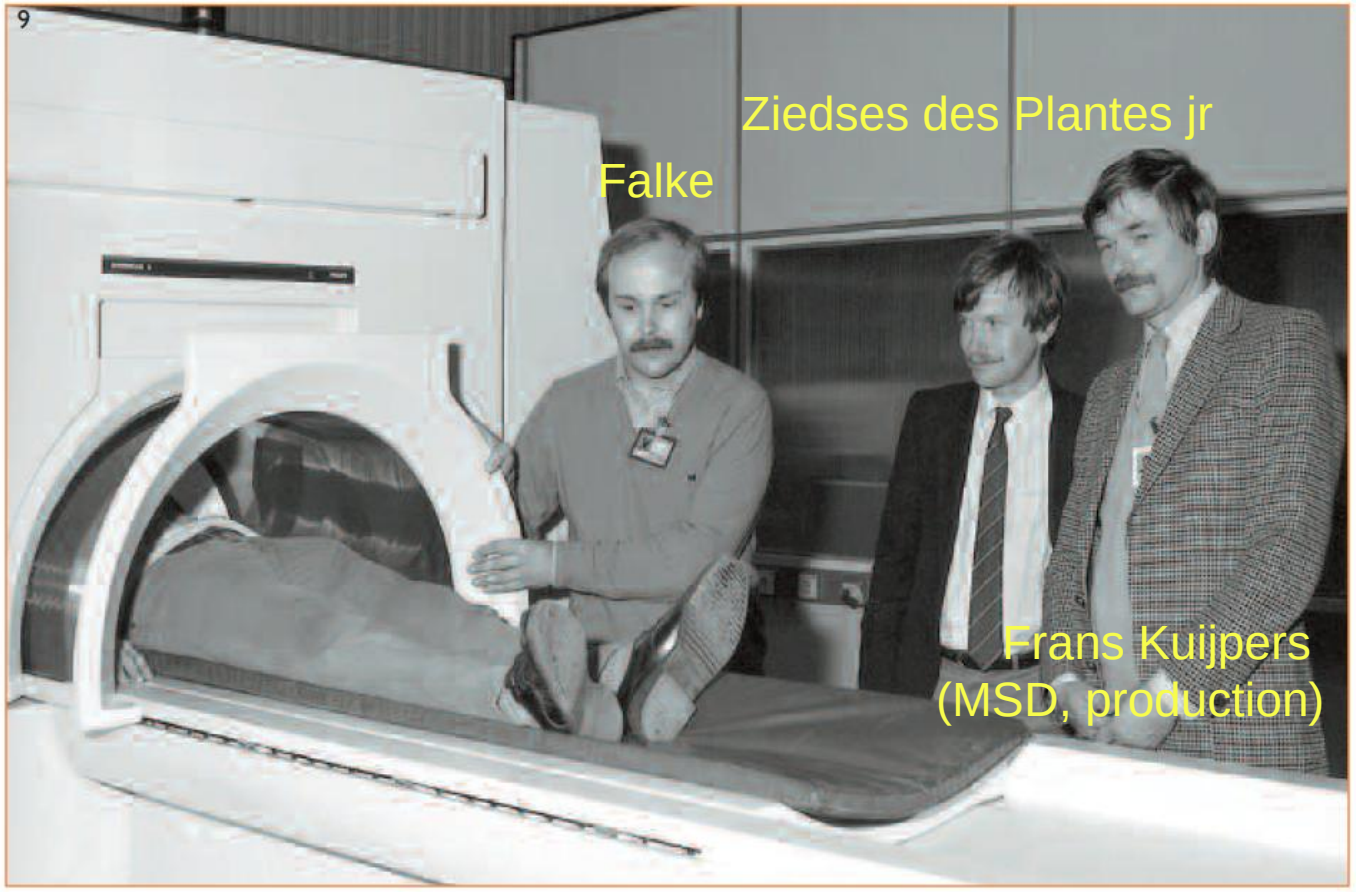


1980
First image human brain
Single slice
Acquisition: > 5 min
Reconstruction: > 15 minutes

1981
First 2D FT image

Start production and first clinical installations

1983 : Gyroscan R. Installation Leiden University
1984: Gyroscan S5 (superconductive)



~1985: major MR imaging problems are “solved”

Seminars in Nuclear Medicine, vol XV,2, 1985

Nuclear Magnetic Resonance in Oncology

David A. Turner

The application of nuclear magnetic resonance (NMR) techniques to the diagnosis of cancer was first explored by Damadian, who proposed that benign and malignant tissues could be differentiated on the basis of characteristic differences in spin-lattice and spin-spin relaxation times (T1 and T2) as determined in vitro with NMR spectrometers. Damadian's thesis was very controversial and never gained widespread acceptance. Not all investigators were able to confirm his findings. Moreover, it was improbable that NMR would ever play an important role in the diagnosis of malignancy as long as biopsy was necessary to obtain material for analysis. However, the potential usefulness of NMR in oncology

bur, who showed that NMR signals could be spatially encoded to produce images of the examined object. NMR imaging has made feasible the measurement of the T1 and T2 of lesions without biopsy. Unfortunately, initial efforts at characterizing tissues by in vivo determination of proton relaxation times have yielded disappointing results. Nonetheless, NMR imaging will be a powerful tool for evaluating patients with malignant disease because of the unique anatomic information it can provide without exposure of the patient to ionizing radiation. In vivo NMR spectroscopy of ^{31}P and other sensitive nuclei may add a new dimension to clinical and experimental oncology.

Unfortunately, initial efforts at characterizing tissues by in vivo determination of proton relaxation times have yielded disappointing results

ation times (T1 and T2, respectively) of malignant tumors, as measured in vitro with an NMR spectrometer, were longer than the T1 and T2 of normal tissues, suggesting that measurement of

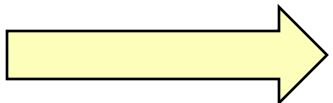
in this article.

IN VITRO NMR SPECTROSCOPY IN THE DIAGNOSIS OF CANCER

In vivo NMR spectroscopy of ^{31}P and other sensitive nuclei may add a new dimension to clinical and experimental oncology

Nuclear Medicine, Rush Medical College and Presbyterian-St Luke's Hospital, Chicago.

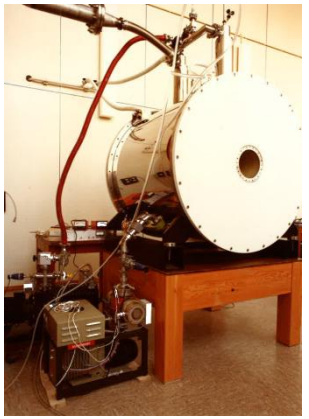
and brain of the host animals. Furthermore, the T2 values of the malignant tissues were approxi-



We need MR spectroscopy

1985 – 1990 Philips Research Laboratory
MR spectroscopy project

Ru van Stapele (group leader)
Rob Locher
Joop van Vaals
Jan den Boef
Peter van Gerwen
Tom Bergman
Arend Heerschap
Frans Verschuren /
Eric van den Boogert



MRS→ need high field

Magnet: 6.3T (Oxford Magnet Technology)
Gradients: unshielded 20 mT/m
Coils: home-built
Electronics: Nicolet components
Computer: DEC VAX 11/750

Home-built MR system
(Nat lab culture)

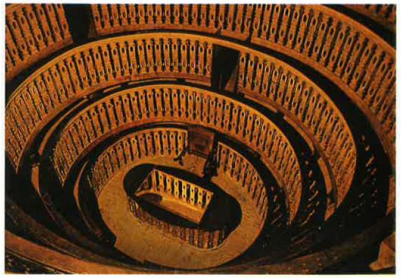
PHILIPS TECHNICAL REVIEW

VOLUME 41, 1983/84, No. 3

Proton NMR tomography

P. R. Locher

PET and NMR: !
new perspectives
in neuroimaging
and in
clinical neurochemistry
Padova (Italy)
May 15-17, 1985



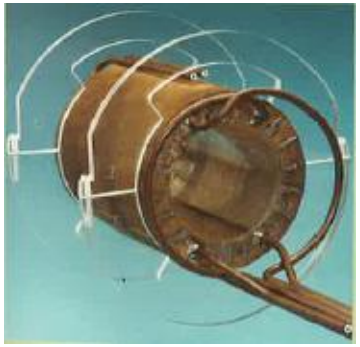
Report

Eindhoven “Animal play Lab”

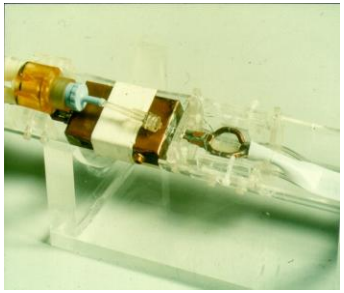
Nijmegen Animal Lab

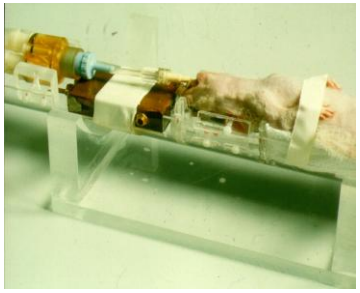
~1988

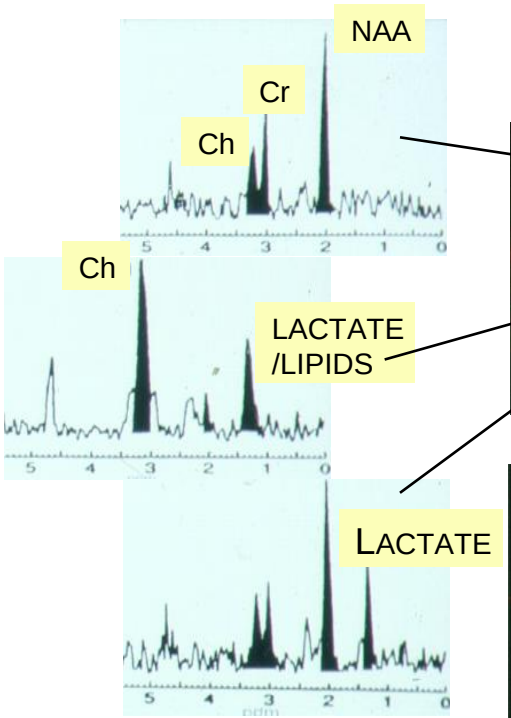
Body coil (transmit)



Surface coil (receive)

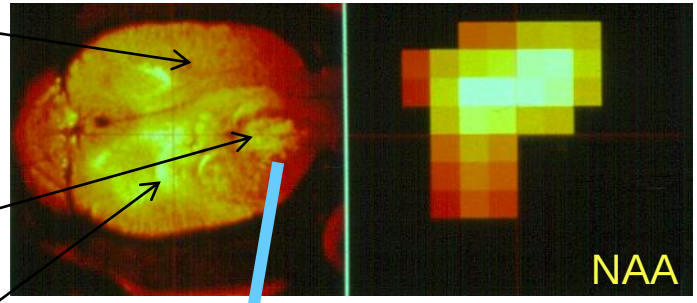


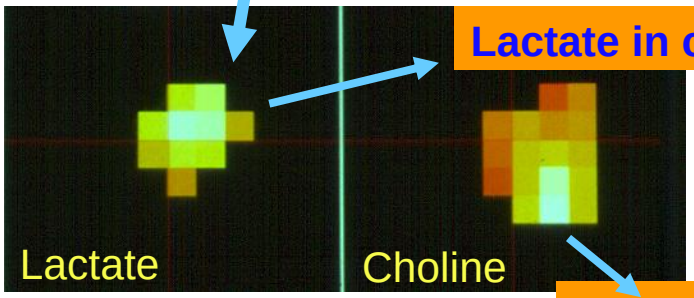




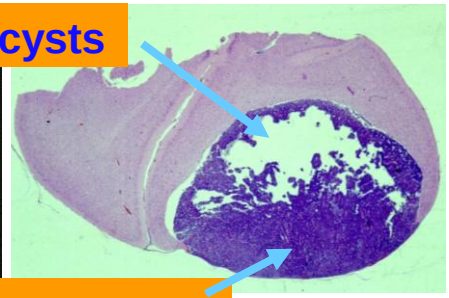
Non-invasive in vivo Localized ^{1}H Spectroscopy Of human Astrocytoma Implanted in Rat Brain

ACE localization





Lactate in cysts



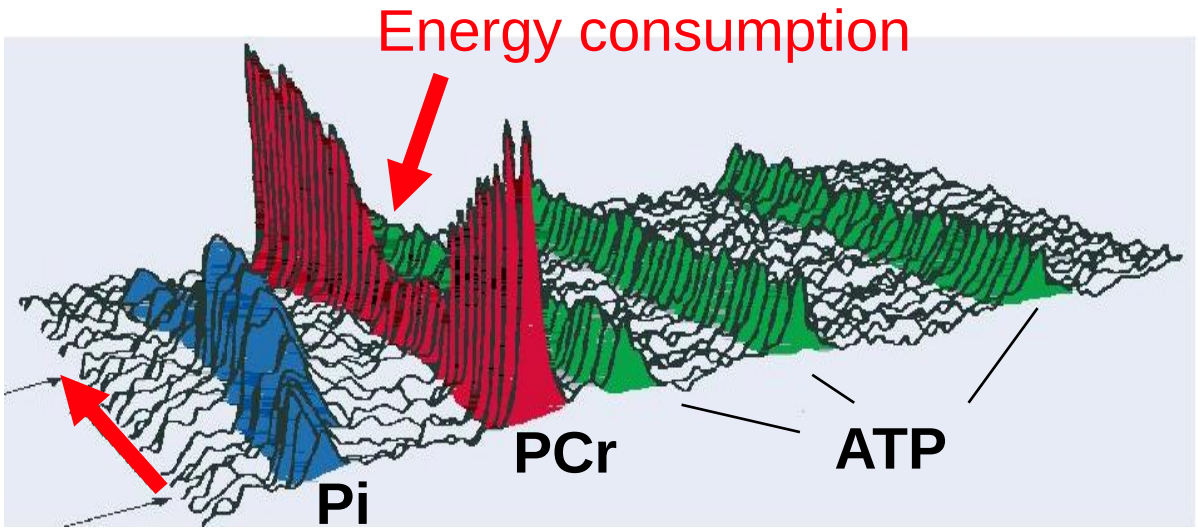
Choline in tumor

J. J. van Vaals*, A. H. Bergman, H. J. van den Boogert and A. Heerschap
Philips Research Laboratories, Bldg WAE, PO Box 80000, 5600 J A Eindhoven, The Netherlands

A. J. van der Kogel, A. C. C. Ruifrok and H. J. J. A. Bernsen
Department of Radiotherapy, University of Nijmegen, PO Box 9101, 6500 HB Nijmegen, The Netherlands

NMR IN BIOMEDICINE, VOL. 4, 125–132 (1991)

1988: First high field (6.3T) human ^{31}P MR spectroscopy



After 28 years at 7T:

Horizontal 6.3 Tesla magnet for preclinical MR Imaging

This magnet was part of pre-clinical MRI scanners at 3 research institutions: Philips Nat.Lab., TU Delft and TU/e. Every time it ushered the start of pre-clinical MRI research.
→ symbol of collaboration between academia and Philips Research.

Philips
Research

Magnet displayed at Joint Research Facility at the High Tech Campus 2012.

Tom Bergman positioning probe.
Philips Natlab. ~ 1987.

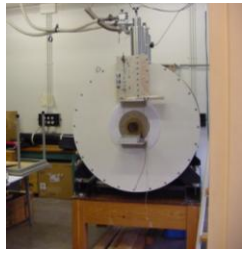
Researchers with 6.3T magnet ~1988.
From left to right:
Tom Bergman, Joop van Vaals, Jan den Boef,
Peter van Gerwen,
Eric van den Boogert.

~1983

PHILIPS NatLab

1989

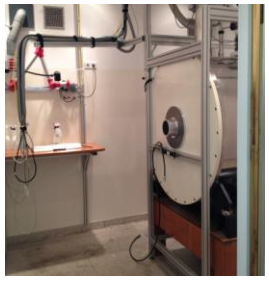
2001



MRI setup @ the TU Delft ~2000.

TU Delft Delft University of Technology

2012



The 6.3 T magnet during installation in 2001 (right) and upgrade in 2005 (above) in N-laag building at TU/e.

TU/e Technische Universiteit Eindhoven University of Technology

Back to human MR ……

1980: General Electric (Paul Bottomley)

Wanted *localized human MRS* (of heart)…

> Buy highest possible B_0

Oxford 2.0T: minimum field spec 1.5T

TECHNICAL SPECIFICATION FOR NMR SUPERCONDUCTING MAGNET AND ITS POWER SUPPLY

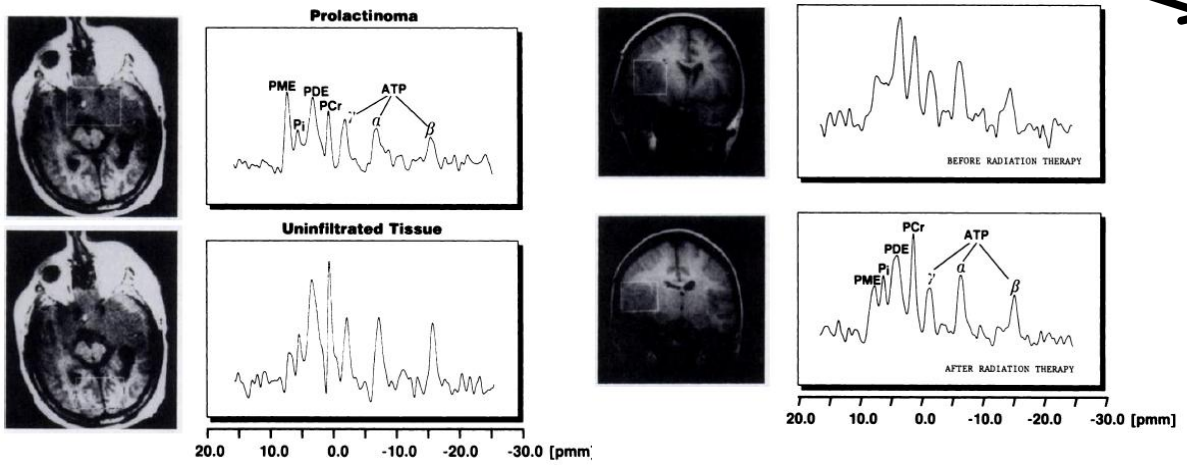
September 10, 1980

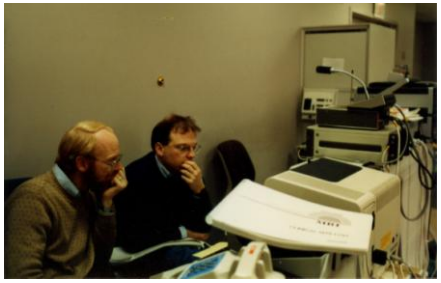
MAGNET

Maximum Field	2.0 Tesla (target); 1.5 Tesla (absolute minimum),
Inhomogeneity	0.1 ppm (in a 10 cm dsv* (max.), for fields between 0.5 and 1.5 Tesla 0.5 ppm (in a 15 cm dsv (max.), for 0.25 to 1.5 Tesla) 10 ppm (in a 30 cm dsv (max.),

Developing MR spectroscopy on a 1.5T Gyroscan

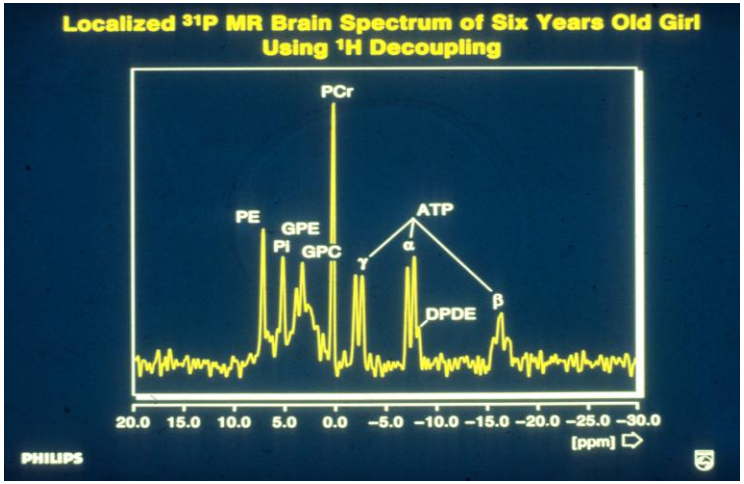
MR image-guided P-31 MR spectroscopy in the evaluation of brain tumor treatment.
Segebarth CM, Balériaux DF, Arnold DL, Luyten PR, den Hollander JA.
Radiology. **1987** Oct;165(1):215-9





Broadband proton decoupling in human ^{31}P NMR spectroscopy.
Luyten P, Bruntink G, Sloff F, Vermeulen J, van der Heijden J, den Hollander J, Heerschap A.
NMR Biomed. **1989** Apr;1(4):177-83

FIRST broadband ^{1}H decoupling humans



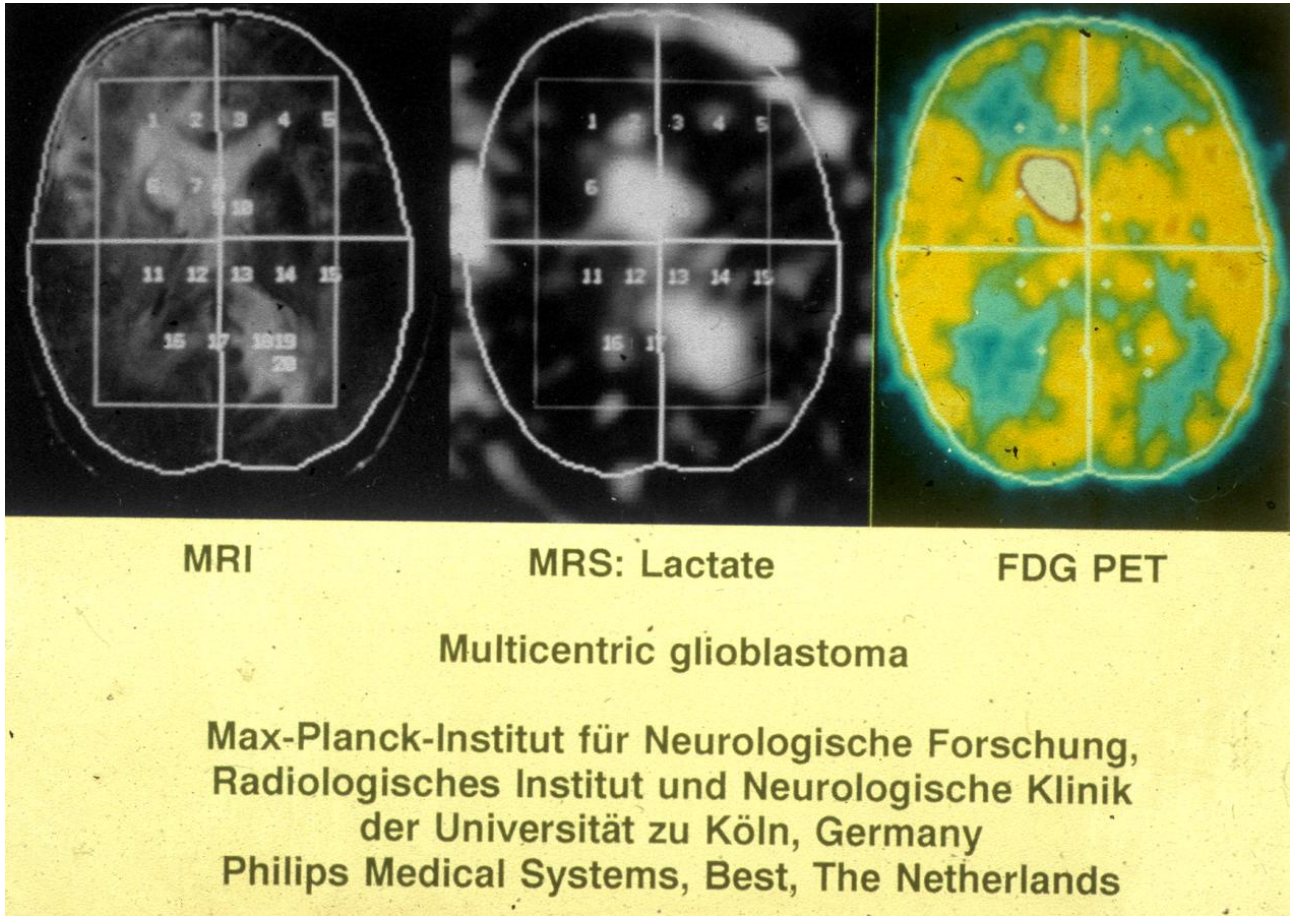
Broadband proton decoupled natural abundance ^{13}C NMR spectroscopy of humans at 1.5 T. Heerschap A, Luyten P, van der Heyden J, Oosterwaal L, den Hollander J.
NMR Biomed. **1989** Sep;2(3):124-32

Developing MR spectroscopy on a 1.5T Gyroscan

FIRST ^{1}H metabolic mapping and combination with PET

Metabolic imaging of patients with intracranial tumors: H-1 MR spectroscopic imaging and PET.

Luyten PR[1], Marien AJ, Heindel W, van Gerwen PH, Herholz K, den Hollander JA, Friedmann G, Heiss WD. Radiology **1990** Sep;176(3):791-9.

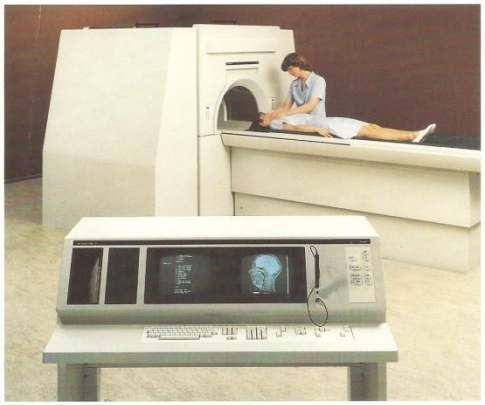


NMR flyer ~1987

The Philips GYROSCAN is a family of diagnostic imaging systems, based on the principle of Nuclear Magnetic Resonance (NMR). Unlike systems based on the use of X-rays or radioactive isotopes, the GYROSCAN uses no ionizing radiation: the images are derived from radio signals emitted by tissues in the body in response to a rapidly alternating electro-magnetic field.

Mit der Baureihe GYROSCAN bietet Philips Systeme für die NMR-Tomographie (NMR = Nuclear Magnetic Resonance oder Kernspinresonanz). Anders als beim Röntgen und bei nuklearmedizinischen Verfahren wird hierbei nicht mit ionisierender Strahlung gearbeitet.

Le nom de GYROSCAN a été donné à une gamme de systèmes d'imagerie médicale conçus par PHILIPS et fondés sur le principe de la Résonnance Magnétique Nucléaire (R.M.N.).



NMR imaging shows no adverse biological effects and is consequently gaining acceptance as a safe and non invasive technique for visualizing internal structures, particularly soft tissues.

At present, NMR imaging is based on the detection of hydrogen atoms and their behaviour in body tissues, providing valuable information on the morphology and chemical composition of soft tissue.
Good results have been achieved in the detection of brain oedema, and the study of pathological processes such as necrosis, ischaemia and various types of neoplasm and degenerative disease.
The GYROSCAN family includes the 'S5' and 'R', two members dedicated to proton imaging with the most powerful member of the family, the 'S15', giving additional possibilities to observe specific metabolic processes by looking at other elements, such as P^{31}, Na^{23} and F^{19}.

Das Verfahren beruht auf der Wechselwirkung von Atomkernen des Körpergewebes mit Hochfrequenzstrahlung in einem starken Magnetfeld.

Die NMR-Tomographie wird zunehmend als sichere, nicht invasive Methode zur Darstellung von Weichteilen betrachtet. Hinweise auf schädliche Nebenwirkungen gibt es bisher nicht.

Gegenwärtig wird die NMR-Tomographie vorzugsweise zur Darstellung der Dichteverteilung und des Verhaltens von Wasserstoffatomen in Körpergeweben eingesetzt. Sie bietet morphologische [illegible] Gewe[illegible] der Er[illegible] ebenso beim Studium von Nekrosen, Ischämien und anderen neoplastischen oder degenerativen Prozessen.
Die Systeme GYROSCAN R und GYROSCAN S 5 sind für die Messung an Wasserstoffatomen konstruiert, während sich das leistungsfähigste System GYROSCAN S 15 auch für die Messung an anderen Atomkernen (P^{31}, Na^{23} und F^{19}) und damit zur Untersuchung von Stoffwechselprozessen eignet.

Contrairement aux appareils basés sur l'utilisation des Rayon X ou d'isotopes radioactifs, les GYROSCAN n'utilisent aucune radiation ionisante: les images sont obtenues à partir des signaux de radio fréquence émis par les tissus humains soumis à une variation rapide alternative du champ électromagnétique. L'imagerie R.M.N. n'a aucun effet biologique et est par conséquent une méthode diagnostique sûre et non invasive pour la visualisation des structurers internes, particulièrement des tissus moux.
Actuellement, l'imagerie R.M.N. est fondée sur la détection des atomes d'hydrogène [illegible] de leur [illegible] tissus moux; d'excellents résultats ont été obtenus dans la détection d'oedèmes cérébraux et l'étude de processus pathologiques tels que les nécroses, ischémies, et différents types de tissus néoplasmiques ou dégénérescents.
La gamme GYROSCAN comprend le 'S 5' et le 'R', deux appareils destinés à l'imagerie protonique, ainsi que le 'S15', permettant également l'étude des processus métaboliques spécifiques en observant d'autres éléments tels que le phosphore (P^{31}), le sodium (Na^{23}) et le fluor (F^{19}).

PHILIPS

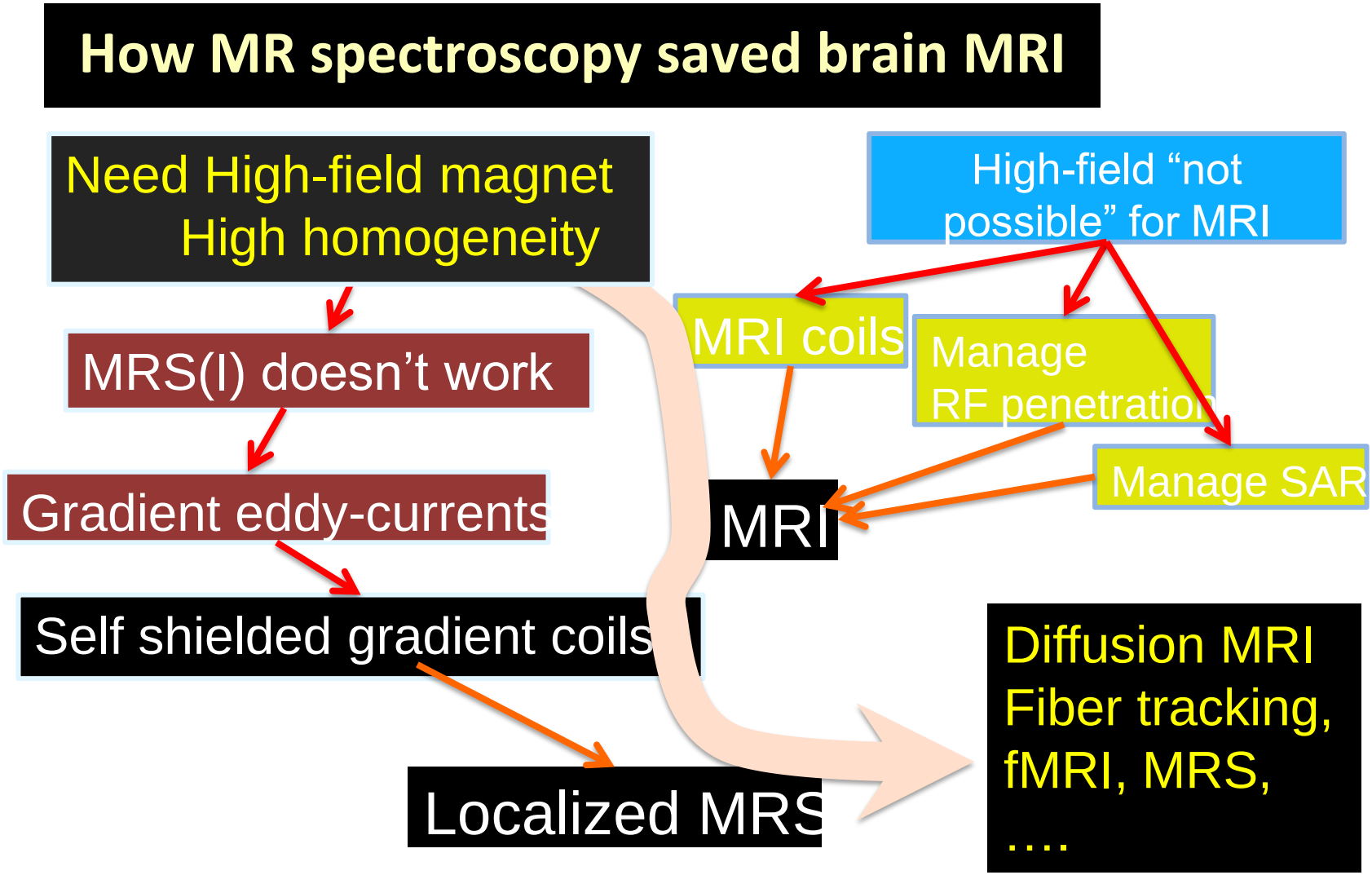
PHILIPS Medical Systems

The GYROSCAN family includes the 'S5' and 'R', two members dedicated to proton imaging with the most powerful member of the family, the 'S15', giving additional possibilities to observe specific metabolic processes by looking at other elements, such as P^{31}, Na^{23} and F^{19}.

… and all early 1.5T MR instruments had Na^{+} options

Results combined MRS efforts for after 1990:

- Ahead with MRS(I)
- Drive for MRI developments (Patents)



Technical University Delft

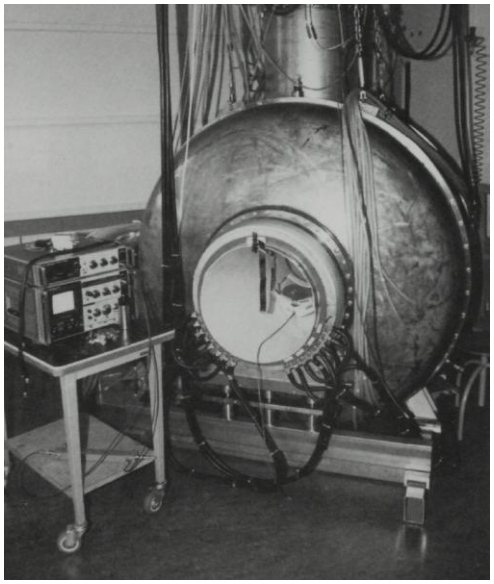
Applied Physics Department: MR and Low temperature groups

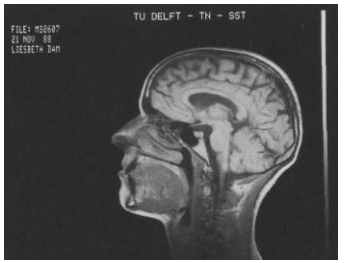
~1980 - 1988

A 1.5 T superconducting magnet with closed cooling system for spin-imaging: an outline

K Pieterman and H Postma

Cryogenics, February 1984, pages 59 to 62.





JOURNAL OF MAGNETIC RESONANCE **95**, 396–404 (1991)

A Single-Shot Localization Pulse Sequence Suited for Coils with Inhomogeneous RF Fields Using Adiabatic Slice-Selective RF Pulses

J. SLOTBOOM, A. F. MEHLKOPF, AND W. M. M. J. BOVÉE

Department of Applied Physics, Delft University of Technology, P.O. Box 5046, 2600 GA Delft, The Netherlands

THE LASER sequence !

First quadrature coil

Van Stekelenburg

2D Approach to Quantitation of Inversion-Recovery Data

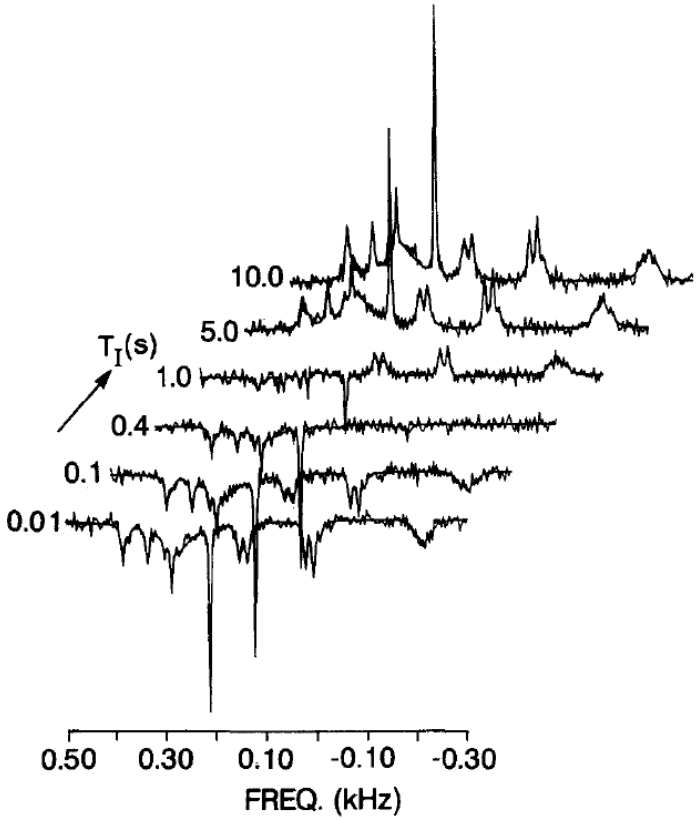
D. VAN ORMONDT AND R. DE BEER

Applied Physics Department, Delft University of Technology, The Netherlands

A. J. H. MARIËN, J. A. DEN HOLLANDER, P. R. LUYTEN, AND J. W. A. H. VERMEULEN

Philips Medical Systems, Best, The Netherlands

JOURNAL OF MAGNETIC RESONANCE **88,** 652–659 (1990)



2D time domain model function

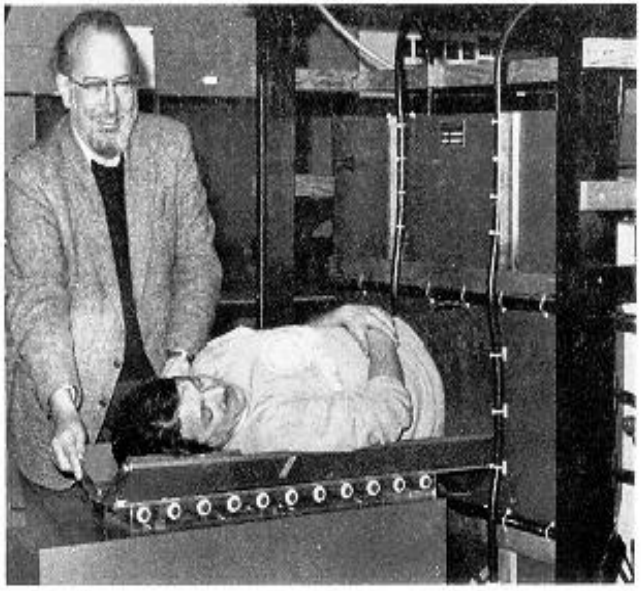
Decanniere C., **Van Hecke P**., Chen H., **Van Huffel S.,** Van der Voort C., **Van Ormondt D**.,
Comparison of model function fitting algorithms for the quantification of strongly overlapping peaks in 31P NMR spectra",
Proc. of the Society of Magnetic Resonance in Medicine, Twelfth Annual Scientific Meeting, New York, Aug. **1993,** 972 p.,

Decanniere C., **Van Hecke P.,** Vanstapel F., Chen H., **Van Huffel S.,** Van der Voort C., Van Tongeren B., **Van Ormondt D.**,
Evaluation of signal processing methods for the quantification of strongly overlapping peaks in 31P NMR spectra",
Journal of Magnetic Resonance B, vol. 105, **1994**, pp. 31-37..

→ jMRUI for MRS postprocessing

1981-1982

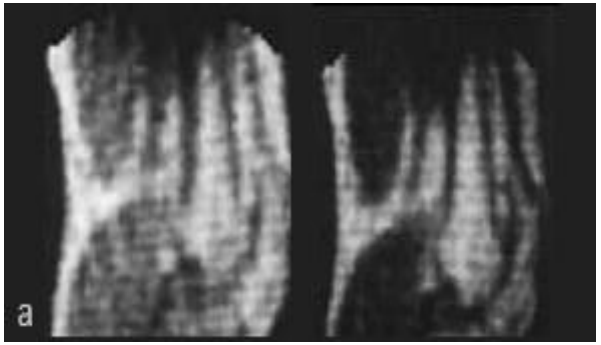
Dr. Paul C. Lauterbur demonstrates the test model of the Nuclear Magnetic Resonance. Participating in the test is Dr. Robert Muller from Belgium's University of Mons who is spending the year working with Dr. Lauterbur.



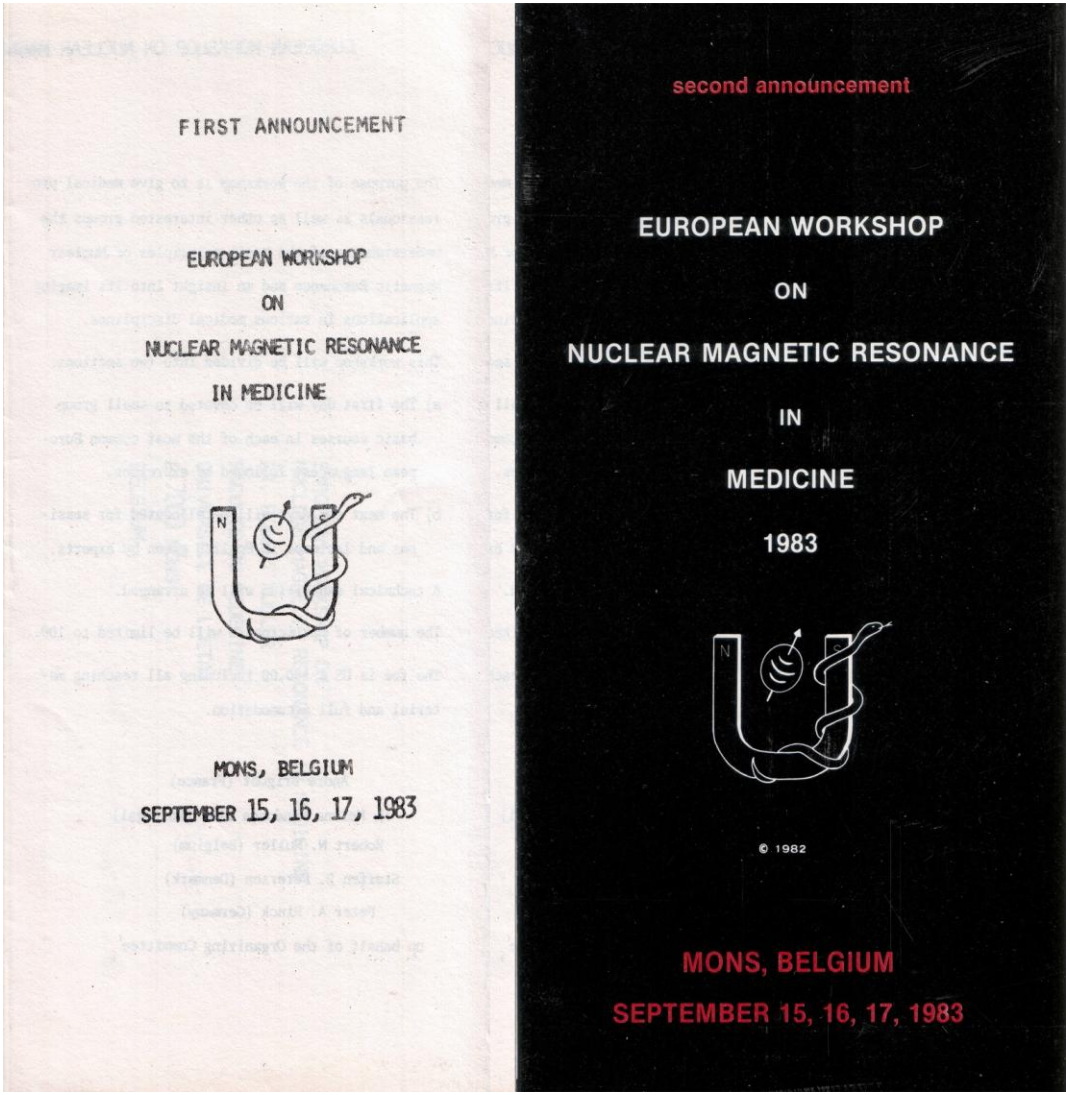
Robert Muller

Mons University

Muller RN, Marsh MJ, Bernardo ML, Lauterbur PC.
True 3-D imaging of limbs by NMR zeugmatography with off-resonance irradiation.
Eur J Radiol **1983**; 3: 286-290.



1983 First European *in vivo* NMR workshop



FIRST ANNOUNCEMENT

EUROPEAN WORKSHOP
ON
NUCLEAR MAGNETIC RESONANCE
IN MEDICINE

MONS, BELGIUM
SEPTEMBER 15, 16, 17, 1983

second announcement

EUROPEAN WORKSHOP
ON
NUCLEAR MAGNETIC RESONANCE
IN
MEDICINE
1983

© 1982

MONS, BELGIUM
SEPTEMBER 15, 16, 17, 1983

ESMRMB 1985

president 1988

First installations clinical MR in Belgium

1983 – 1985, 2 Technicare 0.15 T resistive magnet machines in private clinics in
- Charleroi (prof M. Collard)
- Middelheim (prof A. Lowenthal)

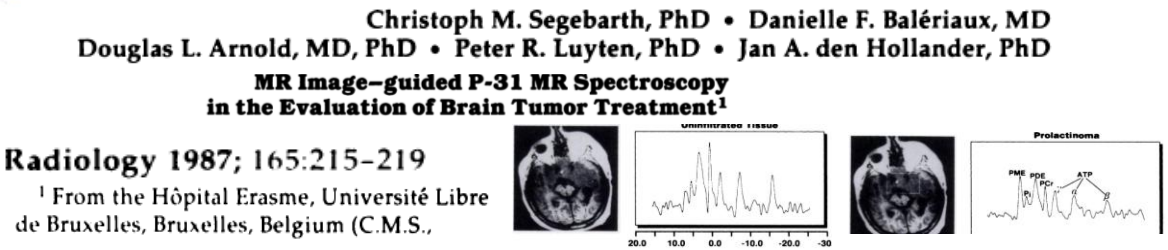
Appel B, Muller RN, Collard M, Moens E, Mortelmans L, Martin J, Lowenthal A.
NMR approach of the periventricular white matter. *Arch Int Physiol Biochim* **1985** 93(5):19
Abstract: From a series of 117 neurological patients presenting a pathological periventricular white matter signal on NMR, ……,on their localization in the brain, and on the calculated apparent T2 (T2**) values achieved with the single multi-echos technique …

- Installations "illegal", i.e. before governmental regulations w.r.t. MR acquirement (~beds)

1987 – 1989, regulations and governmental funding of 0.5 - 1.5T machines
- UZ Gent, VU Brussels, KU Leuven, CHU Liège (Siemens)
- UC Louvain, UL Bruxelles (Philips)

Balériaux D, Deroover N, Hermanus N, **Segebarth C**.
Diagn. Imaging Clin Med **MRI of the spine.**
1986;55(1-2):66. ***On 0.5T Philips Gyroscan***

Former PhD student Jean Jeener



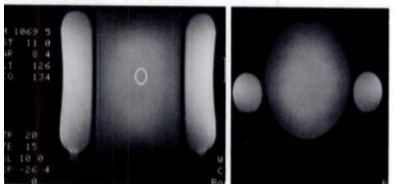
Christoph M. Segebarth, PhD • Danielle F. Balériaux, MD
Douglas L. Arnold, MD, PhD • Peter R. Luyten, PhD • Jan A. den Hollander, PhD

MR Image–guided P-31 MR Spectroscopy in the Evaluation of Brain Tumor Treatment[1]

Radiology 1987; 165:215–219

[1] From the Hôpital Erasme, Université Libre de Bruxelles, Bruxelles, Belgium (C.M.S.,

Van Hecke PE, Marchal GJ, Baert AL
Use of shielding to prevent folding in MR imaging.
Radiology. 1988 May;167(2):557-8.



University of Leuven

Achten R, Demeirleir K, Van Cauteren M, Osteaux M.
In vivo magnetic resonance spectroscopy of muscle metabolism.
J Belge Radiol. 1988;71(2):255-7.

University of Gent

Carlier PG, Grandjean J, Michel P, D'Orio V, Rorive GL.
Arterial metabolism as studied in vitro by NMR: preliminary results in normotensive and hypertensive aortas.
Arch Int Physiol Biochim. **1985** Dec;93(5):107-18

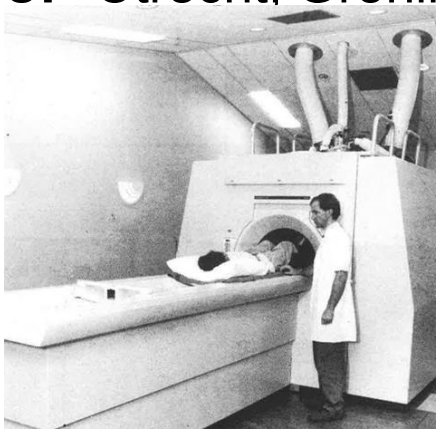
University of Liege

1991 – 1992, Installation first MRI in Luxembourg (CHL), GE 1.5T

First installations clinical MR in the Netherlands

1983 – 1984 Leiden: 0.15T Philips Gyroscan R (van Voorthuisen)
1983 – 1985 Amsterdam VU: 0.6T Technicare (Valk),
1985 – 1987 Utrecht, Groningen, Leiden 0.5 – 1.5 T Philips

} Funding under regulation by law (art 18)



Utrecht : Gyroscan S15 with visitor J Barentsz

1989: Local chair (I)SMRM Amsterdam

The Netherlands' initial experience with NMR imaging.
Falke TH, Ziedses des Plantes BG Jr, **van Voorthuisen AE**.
Diagn Imaging Clin Med. **1984**;53(1):43

Abstract. A survey is provided of the first clinical results of NMR scanning with an experimental 0.14-Tesla resistive magnet system at Philips Medical Systems at Eindhoven. Between 1981 and 1983, 173 NMR examinations were performed on 43 healthy volunteers and 130 patients.

Contrast enhanced magnetic resonance imaging of the brain using gadolinium-DTPA
Valk J, *de Slegte RG, Crezee FC, Hazenberg GJ, Thjaha SI, Nauta JJ.*
Acta Radiol. ***1987*** *28(6):659-65*

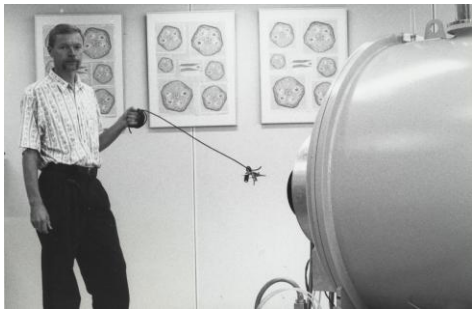
1987 – 1990 Regulations relieved → funding for 6 more installations …..

The role of MR imaging in carcinoma of the urinary bladder.
Barentsz JO, **Ruijs** SH, Strijk SP. AJR Am J Roentgenol. **1993**;160(5):937

About 1990, need for installation of dedicated animal MR facilities
→ high field (> 4T), horizontal wide-bore (mouse, rats, …)

1991

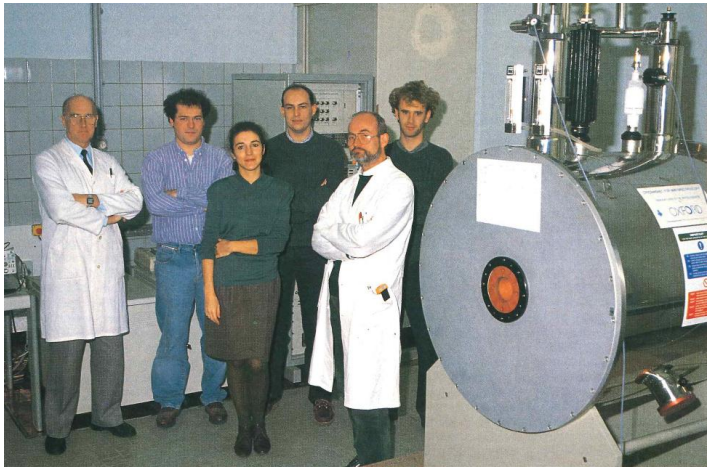
- Dutch in vivo NMR facility, Bijvoet Center, Utrecht
- Klaas Nicolay
- 4.7T SISCO



[1]H-NMR imaging of fimbria fornix lesions in the rat brain. Dijkhuizen RM, Muller HJ, Tamminga KS, van Doremalen HA, Spruijt BM, **Nicolay K**. Brain Topogr. **1992**;5(2):147-51

1994

- Bio-imaging Lab, RUCA , Antwerpen.
- Annemie van der Linden
- **First** 7T MR system (SMIS).
- ~ 1991 a 1.9T Biospec (Domisse)

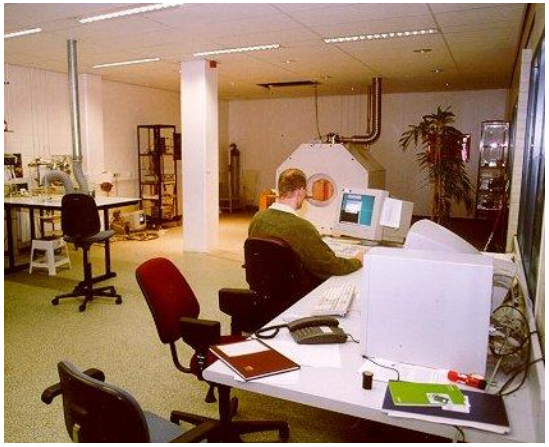


In vivo noninvasive determination of abnormal water diffusion in the rat brain studied in an animal model
for multiple sclerosis by diffusion-weighted NMR imaging.
Verhoye MR, Gravenmade EJ, Raman ER, Van Reempts J, Van der Linden A
Magn Reson Imaging **1996**;14(5):521-32.

About 1990, need for installation dedicated animal MR facilities
→ high field (> 4T), horizontal wide-bore

1997

- Biomedical MR facilty Nijmegen
- Arend Heerschap
- 7T MR system (SMIS)
- 1991 ~ vertical 4.7T

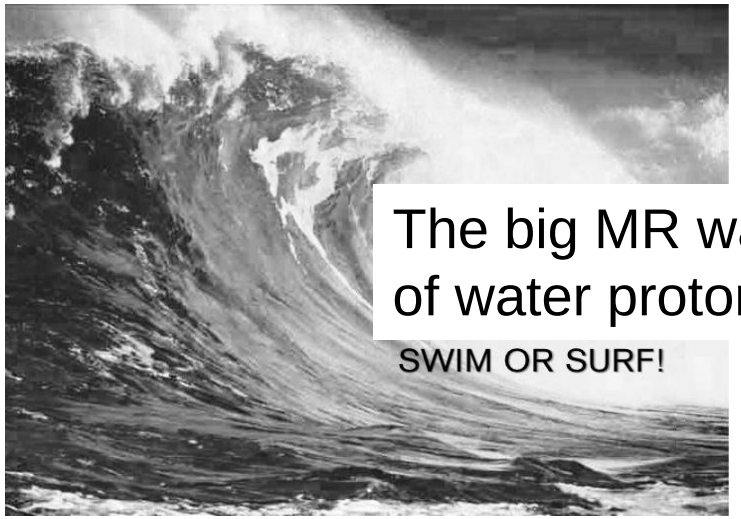


Effects of **high energy shock waves** on tumor blood flow and metabolism: $^{31}P/^{1}H/^{2}H$ NMR resonance study. Smits G, Cornel E, van de Boogert E, Oosterhof G, Debruyne F, Schalken J, Heerschap A. NMR Biomed. **1994**;7:319

2015

- In vivo imaging facilty. Luxembourg Institute of Health
- Olivier Keunen
- 7T MR system (MR solutions)

- In the 20+ years after 1995 …….



The big MR wave of water protons

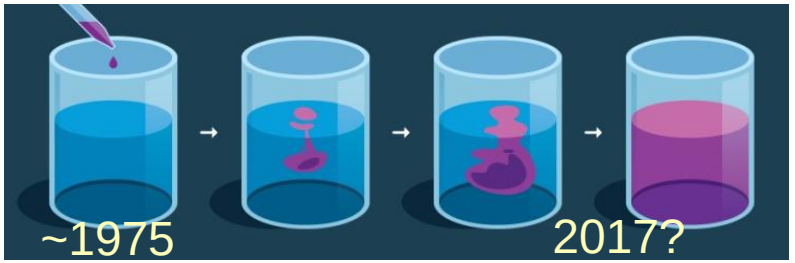
- ISMRM Benelux 2016:

In 40 years:

from  to >300 “MR researchers”

- Magnetic resonance in biomedicine,
  …. more versatile and powerful than initially though of….

- Developments biomedical MR:
  → a multi-dimensional diffusion proces in a vast space



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Pierre Carlier
Ruud de Boer
Jeanine Prompers
Christoph Segebarth
Olivier Keunen
Klaas Nicolay
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Biomedical MR group 2015/2016