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A short history of magnetic resonance imaging

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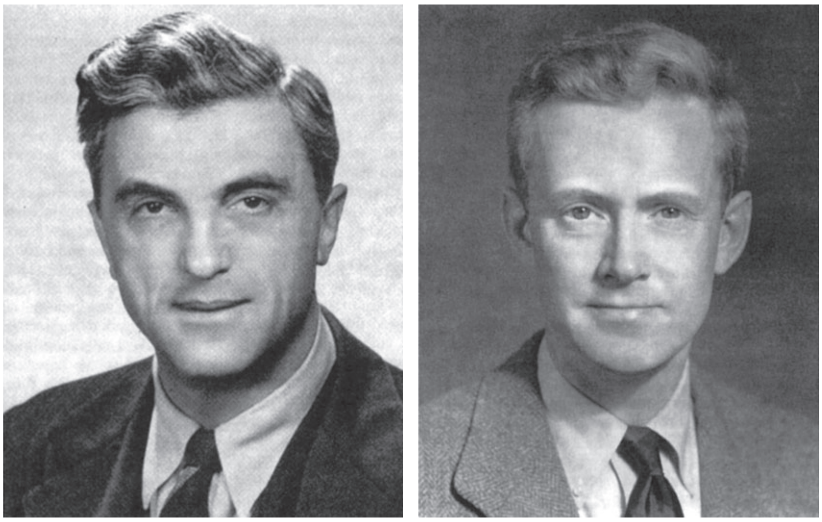

Figure 1. Left: Felix Bloch (1905–1983); right: Edward M. Purcell (1912–1997).

In 1946, two scientists in the United States, independently of each other, described a physicochemical phenomenon that was based upon the magnetic properties of certain nuclei in the periodic system. This was "nuclear magnetic resonance", for short "NMR". The two scientists, Felix Bloch and Edward M. Purcell, see Figure 1, were awarded the Nobel Prize in Physics in 1952.

Purcell worked at the Massachusetts Institute of Technology, MIT, and later joined the faculty of Harvard University. Bloch, a Swiss national, taught at the University of Leipzig until 1933; he then moved to the United States and joined the faculty of Stanford University at Palo Alto in 1934. In 1962 he became the first director of CERN in Geneva. Bloch was a protagonist for the interaction between Europe and the United States. NMR and magnetic resonance imaging (MRI) would not exist without this interaction.

Bloch and Purcell were not the only scientists working in the field. Already in 1924, Wolfgang Pauli suggested the possibility of an intrinsic nuclear spin. The year after, George Eugene Uhlenbeck and Samuel A. Goudsmit introduced the concept of the spinning electron. Two years later Pauli and Charles Galton Darwin developed a theoretical framework for grafting the concept of electron spin into the new quantum mechanics developed the year before by Edwin Schrödinger and Werner Heisenberg.

This development continued in the 1930s. After their initial pace-making work at the University of Frankfurt's Institute for Theoretical Physics, Otto Stern and Walther Gerlach in 1933 were able to measure the effect of the nuclear spin by deflection of a beam of hydrogen molecules. During the early 1930s, Isidor Isaac Rabi's laboratory at Columbia University in New York became a major centre for related studies.

Rabi's research was successful, but only the visit by Cornelis Jacobus Gorter from the Netherlands in September 1937 finally showed how to measure the nuclear magnetic moment. Gorter had tried similar experiments and failed. Rabi accepted and realised Gorter's suggestions concerning his experiments, changed them, and was able to observe resonance experimentally. This led to the publication (in *Physical Review*) of "A New Method of Measuring Nuclear Magnetic Moment" in 1938. Gorter first used the term "nuclear magnetic resonance" in a publication, which appeared in the war-torn Netherlands in 1942, attributing the coining of the phrase to Rabi.

Electron spin resonance was discovered at Kazan University by Yevgeni K. Zavoisky towards the end of the war. Zavoisky had first attempted to detect NMR in 1941, but like Gorter he had failed.

After the final breakthrough by Bloch and Purcell, NMR developed across a wide range of applications. Hardly any of them were medical, although *in vivo* NMR already had been performed since the early 1950s. In 1955/1956, Erik Odeblad and Gunnar Lindström from Stockholm published their first NMR studies of living cells and excised animal tissue, including relaxation time measurements. Odeblad continued working on tissues throughout the 1950s and 1960s. He is the major early contributor to NMR in medicine.

Oleg Jardetzky and colleagues, at the Stanford University Medical Center, performed sodium NMR studies in blood, plasma and red blood cells in 1956. T_1 and T_2 relaxation time measurements of living frog skeletal muscle were published

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by Bratton and colleagues in 1965. In the 1960s and 1970s a very large amount of work was published on relaxation, diffusion and chemical exchange of water in cells and tissues of all sorts. In 1967, Ligon at Oklahoma State University reported the measurement of NMR relaxation of water in the arms of living human subjects. In 1968, Jackson and Langham of the University of California, Los Alamos Scientific Laboratory, Los Alamos, New Mexico, published the first NMR signals from a living animal.

In the late 1960s, Jim Hutchison at the University of Aberdeen in Scotland began working with magnetic resonance on *in vivo* electron spin resonance studies in mice. Hazlewood from Baylor College of Medicine, Houston, Texas, added to the work on relaxation time measurements by studying developing muscle tissue. Cooke and Wien from the University of California at San Francisco and Stanford University worked on similar topics. Hansen from the Procter and Gamble Company, Cincinnati, Ohio, added NMR studies of brain tissue. Others joined in this kind of research, among the better known being the research groups of Raymond Damadian at Downstate Medical Center in Brooklyn and Donald P. Hollis at Johns Hopkins University in Baltimore. Damadian's group measured T_1 and T_2 relaxation times of excised normal and cancerous rat tissue and stated that tumorous tissue had longer relaxation times than normal tissue. Hollis and his collaborators achieved similar results, but were more balanced and scientifically critical in their postulations and deductions. Damadian wrongly thought that he had discovered the ultimate technology to detect cancer and, in 1972, filed a patent claim for an *Apparatus and Method for Detecting Cancer in Tissue*. The patent included the idea but no description of a method or technique of using NMR to scan, but not to image, the human body. In February 1973 Abe and his colleagues at the University Hokkaido in Sapporo applied for a patent on a targeted NMR scanner. They published this technique in 1974.

Actual *in vivo* NMR spectroscopy took off in Oxford from 1974, with the group of Rex E. Richards and George K. Radda. Among others, David Hoult and David G. Gadian belonged to this group.

Figure 2. Paul C. Lauterbur (1929–2007).

Spatial encoding

In September 1971, Paul Lauterbur (see Figure 2) of the State University of New York at Stony Brook had the idea of applying magnetic field gradients in all three dimensions and a back-projection (= projection–reconstruction) technique to create NMR images. He published the first images of two tubes of water in March 1973 in the journal *Nature*. This was followed later in the year by the picture of a living animal, a clam, and in 1974 by the image of the thoracic cavity of a mouse. Lauterbur called his imaging method zeugmatography, a term which was later replaced by (N)MR imaging.

Field gradients had been used before. They are an essential feature of the study of molecular diffusion in liquids by the spin-echo method developed by Erwin L. Hahn in 1950; his group at Berkeley used a gradient approach also to create a storage memory. In 1951, Roger Gabillard from Lille in France had imposed one-dimensional gradients on samples. Carr and Purcell described the use of gradients in the determination of diffusion in 1954.

However, Lauterbur's idea revolutionised NMR because it opened the field to imaging. Many of today's innovations were thought of and developed in his laboratory in the late 1970s and 1980s. When he presented his approach to NMR imaging at the International Society of Magnetic Resonance (ISMAR) meeting in January 1974 in Bombay, Raymond Andrew, William Moore and Waldo Hinshaw from the University of Nottingham, UK, were in the audience and took note. As a result, Hinshaw developed his own approach to MR imaging with their sensitive point method.

In April 1974, Lauterbur gave a talk at a conference in Raleigh, North Carolina. This conference was attended by Richard Ernst from Zurich, who realised that instead of Lauterbur's back-projection one could use switched magnetic field gradients in the time domain. This led to the 1975 publication, *NMR Fourier Zeugmatography* by Anil Kumar, Dieter Welti and Richard Ernst, and to the basic reconstruction method for MR imaging today.

A second NMR group in Nottingham also got involved in MR imaging. Its leader, Peter Mansfield, worked on studies of solid periodic objects, such as crystals. At a Colloque Ampère conference in Cracow in September 1973, Mansfield and his collaborator Peter K. Grannell presented a one-dimensional interferogram to a resolution of better than 1 mm. This, however, cannot be considered an MR image. However, one year later, Alan Garroway and Mansfield filed a patent and published a paper on image formation by NMR. By 1975, Mansfield and Andrew A. Maudsley proposed a line technique, which, in 1977, led to the first image of *in vivo* human anatomy, a cross-section through a finger. In 1978, Mansfield presented his first image through the abdomen.

In 1977, Hinshaw, Paul Bottomley and Neil Holland succeeded with an image of the wrist. Human thoracic and abdominal images followed, and by 1978, Hugh Clow and Ian R. Young, working at the British company EMI, reported the first transverse NMR image through a human head. Two years later, William Moore and colleagues presented the first coronal and sagittal images through a human head.

In the research group of John Mallard at the University of Aberdeen, Jim Hutchison, Bill Edelstein and colleagues developed the spin-warp technique. They published a first image through the body of a mouse in 1974. Margaret Foster contributed much to this work.

Some of the pioneers had performed quite impressive research in the United States; among them was Robert N. Muller (see Figure 3), who, in 1982, described off-resonance imaging, a technique known today as "magnetisation-transfer" imaging. Rinck *et al.* described, while at the State University of New York at Stony Brook, the first fluorine lung images.

Paul C. Lauterbur received the Nobel Prize in Medicine or Physiology in 2003 for the invention of magnetic resonance imaging. Peter Mansfield shared the Nobel Prize for his further development of MRI.

In the 1980s, Continental Europe started to contribute intensively to MR imaging. Rapid imaging originated in European laboratories. Jürgen Hennig, together with A. Nauerth and Hartmut Friedburg, from the University of Freiburg introduced RARE (rapid acquisition with relaxation enhancement) imaging in 1986. This technique is probably better known under the commercial names of fast or turbo spin-echo.

At about the same time, FLASH (fast low angle shot) appeared, opening the way to similar gradient-echo sequences. This sequence was developed at the Max-Planck-Institute, Göttingen, by Axel Haase, Jens Frahm, Dieter Matthaei, Wolfgang Hänicke and Dietmar K. Merboldt. FLASH was very rapidly adopted commercially. Hennig's RARE was slower, and echo-planar imaging (EPI)—for technical reasons—took even more time. Echo-planar imaging had been proposed by Mansfield's group in 1977, and the first crude images were shown by Mansfield and Ian Pykett in the same year. Roger Ordidge presented the first movie in 1981. Its breakthrough came with manifold improvements in many aspects of the associated methodology and instrumentation—from gradient power supply and gradient coil design to pulse sequence development, presented by Pykett and Rzedzian in 1987.

Figure 3. Early magnetic resonance imaging experiment at Paul C. Lauterbur's Laboratory in Stony Brook, NY, around 1981: left Peter A. Rinck, right Robert N. Muller.

Clinical applications

At about this time, MR imaging started being clinically evaluated. One of the most admirable research groups worked at Hammersmith Hospital in London. The head of the group was Robert E. Steiner, but Ian R. Young and Graeme M. Bydder were the moving forces. Among others, Frank H. Doyle and Jacqueline M. Pennock supplemented this group.

Early clinical imaging was extremely difficult, time-consuming and often disappointing. Spin-echo imaging, for instance, was a bigger step than many imagine. Today it is taken for granted, but it has helped immensely to enable MR imaging to become a routine technique.

Early MR images were mainly based upon proton-density differences, later upon differences in T_1 weighting. By 1982–1983, the Hammersmith and Wiesbaden groups pointed out that long heavily T_2-weighted SE (spin-echo) sequences were better at highlighting pathology. It took some years until this was generally accepted, mostly because many companies claimed that long TE (echo times) was neither possible nor necessary.

The input and impact of European scientists to MRI has been enormous, even though, at some stage of their career, many European scientists contemplate emigration to the USA. Some become trans-Atlantic travellers, and some even stay for good; others return, while there is hardly any movement in the other direction. The historical reasons were different prior to and after the Second World War. Before the war, plain survival for many depended on emigration, or it was at least guided by political necessity. After the war, research facilities in the United States were more attractive than those in Europe because the academic system in the USA was more flexible than the university structures in Europe—and dollars were plentiful for research and for personal income!

Yet, the majority of novel developments in MR imaging originated at European research sites. Hardware, software, new imaging techniques and accessories such as contrast agents were all advanced in Europe, not only at academic facilities, but also because some of the major commercial players in the field are European.

References

An extensive list of primary and secondary references can be found at the European Magnetic Resonance Foundation web site at: http://emrf.org/New Site/FAQs/FAQs History of MRI page05.htm