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## REVIEW

## Magnetic resonance imaging—the Aberdeen perspective on developments in the early years

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### Abstract

From the beginnings of medical imaging with radioactivity, an account is given of the development in Aberdeen of CT scanners in nuclear medicine, and their clinical value, leading to the present-day gamma-cameras. Early animal work with electron magnetic resonance is described, which developed into a programme towards nuclear magnetic resonance of water in body tissues. The 1974 NMR image of a mouse, using the nuclear medicine experience, led to a quest to build the first clinically useful whole-body MRI. The work of other teams is outlined, and the steps which led to successful diagnostic images being made with the Aberdeen machine in 1980. The welcome from the medical fraternity, and the output of the multinational medical imaging companies, has led to the present-day, worldwide use of the MRI technique.

### 1. Introduction

It is very appropriate that this review should be prepared for the 50th anniversary issue commemorating the birth of this journal, because the 25th anniversary of the birth of clinical magnetic resonance imaging (MRI) was just last August. The very first patient imaged in a whole-body magnetic resonance imager, which provided clinically useful information about his condition, was performed in Aberdeen near the end of August 1980. To commemorate that occasion, public lectures and a one-day symposium was held at King's College, Aberdeen, given by members of the original team, gathered together again from the USA, Japan, Germany, England, and Aberdeen.

I remember well the announcement, by Professor Roberts at an Hospital Physicists Association annual general meeting, that this journal was to begin, and later being Assistant Editor to Professor Rotblat with the particular remit, with my wife, to kick-start advertising in it: this helped to establish healthier finances for the journal, which, in those early days, were a struggle. Some 20 years later, the early days of MRI were a struggle also!

Many have questioned why MRI should have been pioneered in Aberdeen. There are several reasons, including the fact that the Department of Bio-Medical Physics and Bio-Engineering had pioneered the building, and clinical use of, whole-body CT scanners and gamma-cameras for nuclear medicine (SPECT), which meant that there were excellent mechanical, electronic and computing workshops with skilled personnel capable of doing that, as well as clinical staff used to the difficulties of providing a clinical service based on home-made equipment. In addition, there was a drive within the department, following early animal experiments with magnetic resonance, which indicated that there might be a potentially useful clinical imaging method using microwaves and radio-frequencies with magnetic resonance. To this end, a small team of brilliant scientists was slowly built-up, funded both locally and with research grants, knowledgeable in magnetic resonance, whose work was supplemented by MSc and PhD students from 1966 onwards.

## 2. Why did this drive towards clinical magnetic resonance imaging exist?

The author entered hospital physics, severely handicapped by deafness, in 1951, in the early days of artificial radioactive isotopes in medicine, particularly I-131, and was 'in' on the ground floor of medical imaging, forming crude images of the thyroid gland by moving a Geiger counter in steps across the neck, and drawing isocount lines (Ansell and Rotblat 1948, Mallard 1987, 1995). At Hammersmith Hospital, London, he built the first whole-body radio-isotope scanner (Mallard and Peachey 1959), which was used for thyroid, liver, pancreas, kidney and brain tumour detection and imaging (Mallard *et al* 1961a, 1961b). For the brain work, positron emission was detected from As-72, provided by the MRC cyclotron at Hammersmith: this was a forerunner for PET, when tomographic imaging later became possible. In collaboration with EKCO Ltd of Southend, the first European Anger-type gamma-camera was built with a 5 inch NaI detector and 7 photomultiplier tubes(!): very crude images of brain tumours were obtained in 20 min, about half of the time needed for the scanner, using I-131 labelled HSA (Mallard and Myers 1963).

That paper was accepted by PMB on condition that it was split into two parts—we never knew why, because they appeared adjacent in the same issue! The images from this camera were quickly digitized using two multi-channel analysers,  $x$  and  $y$ , to create the image pixels: the first digital gamma-camera image was shown at the First International Congress of Medical Physics at Harrogate in 1965 (Wilks and Mallard 1966, Mallard 1987), which was organized almost in its entirety by George Innes of St. Bartholomew's, who was the HPA President that year.

The author's PhD had been in magnetism at Nottingham, and having entered hospital physics, he hoped that magnetism could prove to be useful in medicine. In the early 1960s electron spin paramagnetic resonance (esr or epr) was contributing to the frontiers of biochemistry and pharmacology, and a method to measure the esr signals from small samples of wet, 'surviving' tissues from animals was developed (Cook and Mallard 1963). It was found, with great excitement, that tumours gave different signals from the normal tissue surrounding them—either bigger or smaller depending on the particular type of tumour (Mallard and Kent 1964, 1966). Here was the first step towards MRI—a new type of contrast, ready-made and natural, which could perhaps be 'imaged', without any injections of radioactivity. This potential new imaging technique was reported to the same congress in 1965 (Mallard and Lawn 1967, Mallard 1987). It was shown that these signals come from free-radicals (Mallard and Kent 1966) which are now known to play a part in carcinogenesis and other bodily degenerative processes.

When the author moved from London to Aberdeen in 1965, a furniture van transported the body-scanner for radio-isotopes, the gamma-camera, and the magnetic resonance spectrometers, which had all been built on research grants, to Aberdeen. Also, the research workers moved with him.

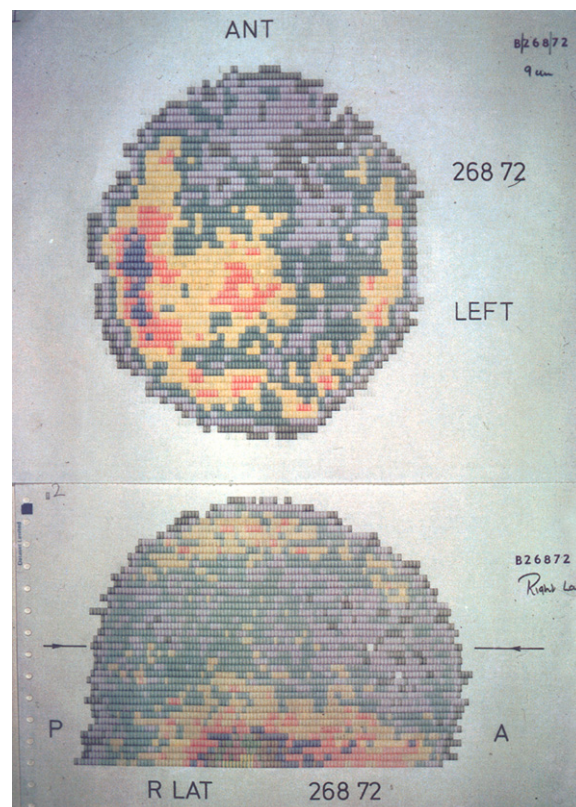
### 3. Nuclear medicine imaging in Aberdeen—1965 onwards

Because the nuclear medicine imaging development work in Aberdeen from 1965 until 1980 had such a direct interaction upon the MRI programme, it is necessary to give a brief account of it here. In 1965, a radio-isotope scanning service with the scanner and gamma-camera was added to the existing Radio-isotope Clinic operated by Tom Buchanan and Alastair McIntosh. The radiologist Sandy MacDonald enthusiastically took it on clinically, and this collaboration laid the foundation of nuclear medicine as it is today, with a consultant in nuclear medicine investigating over 10 000 patients a year, with about 40 different diagnostic tests available, of which about 30 are imaging ones.

The first gamma-camera was replaced in 1967 by one of the first commercial gamma-cameras, built by the Edinburgh company Nuclear Enterprises Ltd, a company which made a big impact on the field of nuclear measurement (and ultrasound imaging) for over 40 years after World War II. It was exciting when this camera was connected online in 1968 by Dr Peter Undrill, an early computer expert, to a small computer (DEC PDP8I) and a primitive digital display system. This helped us to image the elusive pancreas more clearly, using Se-75 labelled methionine, which localizes in the pancreas and liver, and digitally subtracting an image of the liver alone, obtained with Tc-99m colloid.

The same computer and display system made it possible to pioneer single-photon emission computed tomography (SPECT or SPET) from 1967 onwards. Tomography was first carried out successfully in 1964 by Dr Dave Kuhl (Kuhl 1964) in Philadelphia, who built an analogue scanner with a translate/rotate motion of a scintillation counter (it is the author's opinion that he should have shared the Nobel Prize awarded later for CT). The Aberdeen team built the first digital CT for nuclear medicine from 1967 to 1969: it was nicknamed ASS for Aberdeen Section Scanner (Bowley *et al* 1973). This was some 5 years before the technique was applied to x-rays by Godfrey Hounsfield (Hounsfield 1973), which revolutionized x-ray diagnosis. Two opposed scintillation counters, mounted on an old Co-60 teletherapy gantry, made passes across a patient at a series of angles around the patient, all in the plane of interest. The mathematical method of reconstructing the image from the information acquired from each pass, known as back-projection, was originally described by a mathematician (Radon 1917) working in Vienna (one pictures him working in a garret there, on the meagre diet prevalent near the end of WWI!) but it was not until the digital computer, combined with digital imaging, became available, that its use was practicable.

Brain tumours seen not very positively on AP and lateral views were clearly detected and localized on the CT view (figure 1), and the addition of this view from 1971 onwards gave an improvement in brain lesion detection from 85% to 92%, halving the false negatives (Carril *et al* 1979). By 1973, much more precise radiotherapy treatment plans were being made from the scans, and another prominent use was to evolve a positive diagnosis of epilepsy in addition to the complex symptomatic tests (Choudhury *et al* 1974). At the beginning, it could not have been expected that the work of physicists in nuclear medicine—and later MRI—would lead to a step forward in the battle against mental disorders; a fulfilment of a medieval dream (figure 2). This scanner, and the improved version (Evans *et al* 1986), and the rotating gamma-camera version (Chesser and Gemmell 1982), built in Aberdeen through the mid-1970s, became the method of choice for brain tumour detection for some years. SPECT



**Figure 1.** A 1972 Tc-99m (sodium pertechnetate) brain image of a patient with a brain tumour which is very clearly perceived on the transverse section SPECT image (top), as the yellow and red region of higher counting rate near the middle of the brain, but hardly perceived on the conventional lateral view (bottom). On the SPECT view, the tumour is seen at depth in the brain, clearly separated from the high concentration of radioactivity also seen as yellow, red and black, near the periphery of the head on the right side of the patient: this is the scar tissue from surgical operation six months before to remove the primary tumour; the tumour now detected is a recurrence. On the conventional view, the scar tissue radioactivity overlaps that in the tumour, so that one cannot be sure what has been perceived. The SPECT view has made the diagnosis considerably more certain.

was therefore in regular use in Aberdeen two or three years before x-ray CT was announced in 1973, but when that did eventually arrive in Aberdeen in the early 1980s x-ray CT became the method of choice for brain lesion detection, due to the much greater detail in the images.

Professor Peter Sharp (the author's successor), with colleagues, pioneered the use of a radioactive drug (HMPAO) to image blood flow in the brain, which is used, for example, to distinguish between Alzheimer's dementia, and Huntington's chorea (Sharp *et al* 1986, Gemmell *et al* 1987).

A commercial version of ASS was produced for a few years by a small UK company (J & P Ltd of Reading), and an American company also entered the field (Cleon) (Flower *et al* 1981), but the major multinational medical imaging companies did not really take up SPECT in a big way until the rotating gamma-camera technique had been explored, and they now form the main workhorse of modern nuclear medicine imaging, producing superb images. The effort to pioneer SPECT in Aberdeen was considerable, with total 18 physicists from



**Figure 2.** A drawing from the Middle Ages which shows the fantasies (or illnesses) being radiated out from the pot-like structure into which the patient has been put. All those years ago, the conceptual relationship was predicted between the patient and modern imagers or scanners!

1967 to 1987 (part-time, of course, and not all simultaneously!), and 5 different medically qualified staff involved in the clinical interpretation and use, particularly Dr F W Smith (now Professor), the Consultant in nuclear medicine during most of that time.

The other form of tomography in nuclear medicine has also been followed in Aberdeen, with the installation in 1980 of a second-hand cyclotron (moved by the Army!) and PET at an old farm building, following a public appeal. The research carried out with this has led, amongst other things, to a valuable test for breast-tumour secondaries and their response to chemotherapy (Smith *et al* 1998, 2000), and following successful efforts by Peter Sharp, the John Mallard Scottish PET Centre was opened in 1998, in a new building with new equipment, in the Aberdeen Royal Infirmary. This has, in turn, led to a Scottish programme of PET installations to improve treatment for Scottish cancer patients.

#### 4. Magnetic resonance imaging (MRI)—the beginning years 1965–1974

In parallel with the nuclear medicine SPECT and PET work, the author's quest towards imaging with magnetic resonance quietly continued. It was boosted when two post-docs—Jim Hutchison (MR physicist from St. Andrews) and Meg Foster (biologist)—were recruited to the MR group; they became husband and wife. They played a vital role, and throughout the development in Aberdeen, a biological programme to understand the resonance signals went hand-in-hand with the physics and technological development of the imager (Foster 1984). The electron MR work on animal samples continued (Mallard and Kent 1966), and a spectrometer was built to try to obtain electron MR signals from mice (Hutchison and Mallard 1971), but the electromagnetic frequency necessary was too much absorbed in soft tissues, and was also scattered too excessively to be useful in a human (Mallard and Whittingham 1968). A further difficulty is that these signals originate from free radicals in the tissues, which are of low concentrations. (It is to be noted here that the goal of imaging free radicals in the body continues to be pursued in Aberdeen by Professor David Lurie, using a double resonance technique known as PEDRI (Lurie *et al* 1990, 1992).)

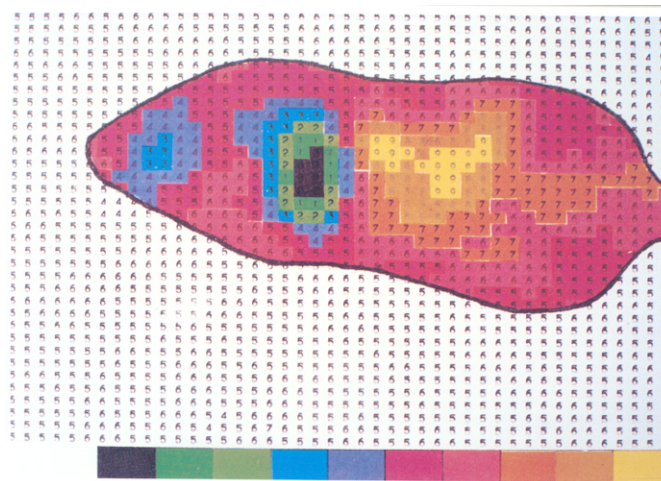


In the early 1970s we switched from electron to nuclear magnetic resonance, in particular to that of the hydrogen protons in water. This decision was driven by Damadian's measurements of the parameter T1 (spin-lattice relaxation time) of water in tissue samples (Damadian 1971), not unlike our own early tissue sample work. For this proton NMR, the lower electromagnetic frequency necessary has much less absorption and scatter, which, together with much lower magnetic fields and the much higher concentration of water protons, made it a much more practicable possibility for human imaging, than electron magnetic resonance. We immediately set out to confirm Damadian's results, and although we did find that malignant tumour samples had a longer T1 than normal tissues they were less than he had found. The differences were about 10%, and appeared to be related to the water content of the tissues (Gordon 1974, Ross and Gordon 1981), and the extent to which it is bound to proteins (see Hutchison (1976)). Dr Foster measured the T1 of 39 rabbit body tissues and fluids, and found that the T1 of rabbit liver was about 1/10th that of pure water, which is 3.5 s at 24 MHz, with the spleen being 60% longer, and white brain tissue was about 40% shorter than grey brain (Ling *et al* (1980); a very important Letter in PMB). Thus NMR imaging, displaying the T1 of water protons, might distinguish between the various body organs and between grey and white brain, not possible hitherto by external imaging; as well as possibly differentiating tumours from their surrounding tissues, and displaying inflammation since it would have a long T1 approaching that of pure water. Meg Foster had fun drawing a prediction of what a rabbit T1 image might look like, and even a human sectional image, based on the rabbit tissue values(!), was drawn (Mallard *et al* 1979, 1980); it turned out to be surprisingly accurate!

In 1973, Paul Lauterbur in the USA made the key proposal of how to form an NMR image (Lauterbur 1973): in addition to the standing magnetic field required to create the magnetic resonance within a sample, a magnetic field gradient is also applied, which increases linearly with position across the standing field. This codes the frequency of the resonance in the sample linearly with position across the standing field, giving one-dimensional localization. By applying this gradient at different angles across the sample, and obtaining the resonance frequency spectrum at each angle, the sample can be localized within a two-dimensional image by computed tomography. In Aberdeen we were already to the fore in computed tomography with our SPECT imagers, with all the computer programmes to hand, so Dr Hutchison and the team quickly put together a Watson-type permanent magnet and magnetic field gradient system to try it out. This led in March 1974 to the first ever NMR image of a whole mouse displaying T1 (figure 3) (Hutchison *et al* 1974). The mouse was outlined by proton concentration signals, and the liver and brain were localized within it by the average T1 values through the thickness of the animal which had been measured, from point to point. The exposure needed to build up the image was about an hour, during which the animal had to be completely still, so immediately beforehand its neck had been broken. To our astonishment, we saw also on the image, the long T1 values of the inflammation surrounding the fracture. The very first image had shown a sort of pathology! At the invitation of Professor Raymond Andrew at Nottingham University, this image was shown there at an annual academic physics conference in April 1974.

## 5. MRI milestones on the road to clinically useful images 1974–1980

For a brand-new imaging technique to prove its worth clinically, the author's radio-isotope imager experience had shown that it must be able to image any part of the body: also, the mouse image had shown that it must display T1 as well as proton content. We thus set out to build a whole-body NMR imager which could display T1 in addition to signal intensities. The magnet needed to image a body trunk was very large, and a uniformity of the field strength



**Figure 3.** The first-ever NMR image of a mouse displaying relaxation time information. The outline of the mouse, which was newly dead and had a broken neck, is shown by NMR intensity signals (related to the concentrations of protons in each pixel of the image). The liver and brain were localized within it by the yellow and blue regions which display the longer values of the average T1 throughout the thickness of the animal. Excitingly, the long T1 of the oedema around the broken neck was imaged as the very black area. The very first image had shown an abnormality. It was also the first-ever quantitative T1 image.

of  $1$  in  $10^4$  was vital so that the image did not suffer from large non-uniformities. Permanent magnets and iron-cored electromagnets were considered but, at that time, a potential weight of 6 tonnes was thought to be unacceptable for typical hospital floors: also the eddy-current problems were unknown, and so we therefore adopted an air-cooled electromagnet. A vertical standing field, at  $90^\circ$  to the radio-frequency and the supine patient, gave a favourable  $\sqrt{2}$  gain in signal/noise, but to achieve adequate cooling and the necessary uniformity, we dare not go above 0.04 T (Mallard *et al* 1979, 1980). The magnet was built for us, as its very first one-off imaging magnet, by Oxford Instruments Ltd, and to pay for it, and to build by ourselves the radio-frequency and the three gradient coils ( $x$ ,  $y$ ,  $z$ ), and all the electronics necessary, we needed about £30 000. Although this sum sounds modest today, it took 18 months to obtain this research grant from the MRC (the author has been told by one of the referees that he had not recommended that the grant be given, because his calculations had shown that it would not work!).

It soon became clear that the CT method was far too slow for clinical imaging: with the short magnetic resonance signals, pulse-sequence methods, analogous to those used in laboratory NMR spectroscopy, needed to be used (Hutchison 1976, 1979). Dr Hutchison introduced the inversion-recovery pulse sequence to provide T1-weighted images and approximate T1 values (Sutherland and Hutchison 1978). It became necessary to increase the number of people working on the many problems of designing and building the machine, and a second research grant had to be obtained, which led to a young go-getting American, Bill Edelstein, joining us from the University of Glasgow. The team was now 7 strong, including the PhD students.

Whilst our whole-body machine was being evolved—far too slowly!—other teams were making progress towards MRI, spurred on by the mouse image, so the author has been told. There were three teams in the Physics Department of the University of Nottingham: one led by



the late Professor Raymond Andrew, who was the Head of the Department, and who produced the first image of a wrist in 1977 and an arm in 1979 (Hinshaw *et al* 1979, Andrew 1980). The author believes that his contribution to the early days of MRI has not been fully recognized, since his enthusiasm and knowledge of magnetic resonance fostered not only his own team, but the creation of the two other teams there. One was led by Professor Peter Mansfield (now Sir); who showed how to select the spins from a slice and patented the method of selectively exciting and defining the slice across a sample in 1974 (Garraway *et al* 1974); obtained images of a finger in 1974 and a cross section of an abdomen in 1978 (Mansfield *et al* 1978), and who then concentrated on echo-planar fast pulse sequences (Mansfield *et al* 1980), for which many believe that he shared the Nobel Prize with Lauterbur in 2003—importantly, this led later to more rapid clinical imaging. The third team at Nottingham was one led by the late Bill Moore, who built a whole-body imager in the early 1980s (Moore and Holland 1980).

There was also a team led by Ian Young at GEC Wembley, London, who first imaged a human head in 1978 (Young and Clow 1978). Dr Young is an Aberdonian, and was awarded an Honorary DSc by Aberdeen University in 1992 for his work in MRI. There was also Raymond Damadian's team in New York, who produced the first human thorax section in 1977 (Damadian 1980).

Although all of these images, acquired by various different methods, were of considerable scientific and laboratory interest, they were really not of sufficient clarity and detail for the rigours of diagnostic clinical work. There were times from 1974 to 1980 that we wondered whether we had made a mistake by jumping in at the deep end, and striving to build a whole-body imager capable of imaging T1 as well as proton density, since all these other teams seemed to be leading the way. In the end, however, it proved to be absolutely right!

All the UK teams were brought together in November 1978 at the HQ of the Institution of Electrical Engineers, London, for a symposium on NMR Imaging. They all presented what images they had, but Aberdeen could only show pictures of our machine (figure 4) and the predictive T1 image of a man that we hoped to achieve (Mallard *et al* 1979). We all came together again in March 1979 for the Royal Society Discussion on Nuclear Magnetic Resonance of Intact Biological Systems. Both Lauterbur and Damadian made presentations (Lauterbur 1980, Damadian 1980) as well as the UK teams. By this time we had made real progress and images were shown of ourselves of recognizable shape, and identifiable organs, but many were badly spoiled by interfering artefacts due to body movements such as heart beats (figure 5), which made them of little use for clinical purposes (Mallard *et al* 1980). At that time we were using a line-by-line subtraction method, in which the spins were reversed in each line and subtracted.

These movement artefacts were not removed until the spring of 1980, when the first of the two-dimensional Fourier transforms was introduced (Edelstein *et al* (1980); an important Letter in PMB, Hutchison *et al* (1980), Johnson *et al* (1982)), nicknamed 'spin-warp' (the proton-spin columns resemble the warp threads of cloth, and, of course, Star Trek!). This gave, for the first time, an accurate distribution of the resonance signals in the two dimensions of the plane across the patient, allowing for body movements. Also, an interleaved set of gradient and radio-frequency pulses gave us both a proton density image and a T1-weighted image, with approximate T1 values for each pixel.

Spin-warp was the real breakthrough for MRI. Realistic images of ourselves showed startling anatomic detail of soft tissues, and this period from spring to summer of 1980 also allayed fears of short-term damage from the various fields applied to the body. The first patient, from Dr F W Smith, was imaged in late August 1980 (figure 6), and showed the primary Ca. oesophagus, numerous liver secondaries, and a metastasis in the spine, not suspected before

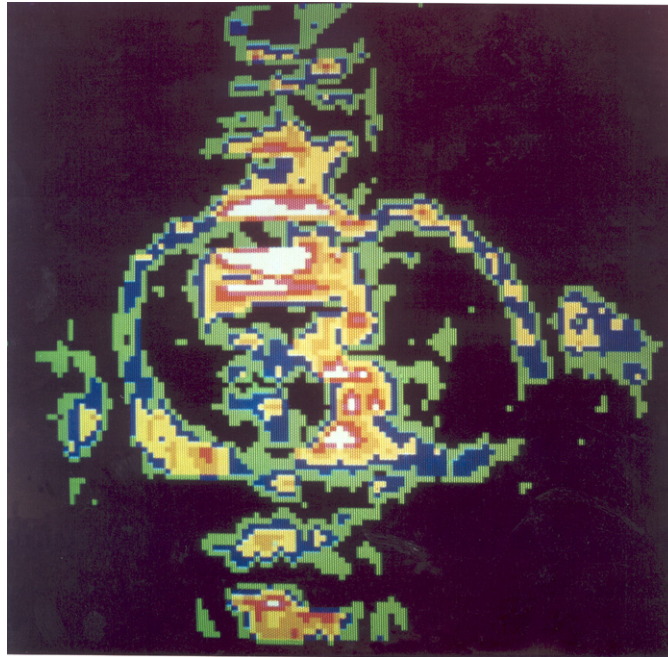


**Figure 4.** The Aberdeen NMR Mark I machine as it was in 1979. Dr J M S Hutchison lying in the position of the patient, inside the four horizontal coils (black) of the main electromagnet which provides the standing magnetic field of 0.04 T (400 G). The circular coils wound around the cylindrical tube in which the patient lies are pulsed with radio-frequency current to excite the protons in the patient: the same coils receive the signals radiated back. The coils which localize the signals from left to right, and from back to front of the patient, are also wound on this cylindrical tube. The coils which select the plane of the patient to be imaged are the rectangular white ones above and below the patient.

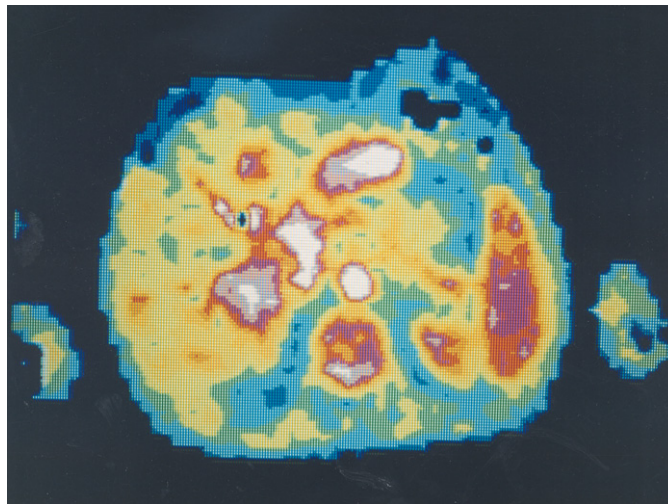
in that patient (Mallard *et al* 1980, Smith *et al* 1981), which was subsequently confirmed by a nuclear medicine bone scan. These images were first shown publicly the following week at an IAEA conference in Heidelberg.

## 6. The early days of clinical MRI

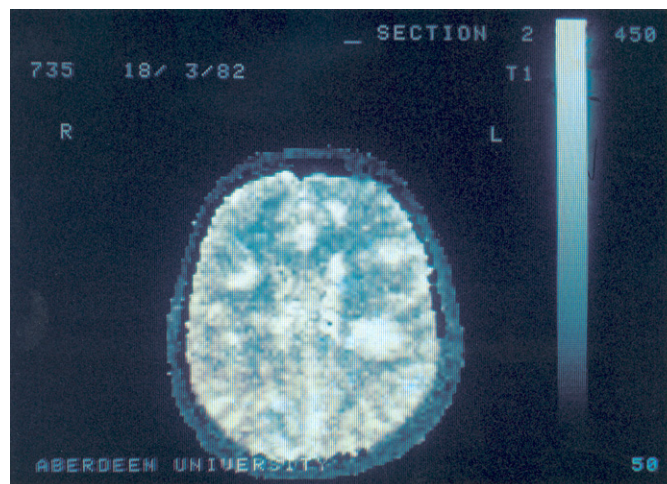
The prototype machine, in a research laboratory in a building on the hospital campus but separate from it, was quickly in use to investigate patients, who were selected and cared for by Dr F W Smith, the Consultant in nuclear medicine, who explored its clinical potential. Patient facilities had to be created, which meant that the store of Cleaning materials for the Medical School had to be moved elsewhere! Patients had to be pushed over in wheelchairs from the hospital, and because the hospital porters would not have insurance cover, we all took turns in doing this—there is a photograph of a patient being pushed through the snow by Dr Smith. Very quickly MRI was found to be diagnostically useful for many things,



**Figure 5.** A 1979 image across the chest of a volunteer in the Aberdeen NMR imager before the spin-warp breakthrough. The outline of the body and some internal structures are recognizable, but the image is of no use clinically, because of the huge interfering artefact caused by the heart movements.



**Figure 6.** The world-first clinically useful MRI image. The abdominal transverse image shows massive secondary malignant deposits (white) of very long T1 ( $T1 > 500$  ms), in the liver, which also shows a very swollen outline ( $T1 = 140$  ms). Also seen is the spleen, and the splenic artery; the cross section of the aorta is the white circle, and the spine (in section) shows the cerebrospinal fluid. Also a secondary malignant deposit is seen in the spine which was not suspected hitherto, which has a longer T1 shown by higher red and blue colours: it was subsequently confirmed by nuclear medicine scans. The arms at the side of the body are also seen.



**Figure 7.** An early image of a section across the head of a patient with multiple sclerosis. The disease removes the fatty-like (low T1) myelin sheath from the nervous tissue, so that where there is disease, the T1 is higher and those areas are seen as whiter blobs in the image. MRI is now the method of choice for diagnosing multiple sclerosis and other functional cerebral pathologies.

including multiple sclerosis (figure 7), for which it is now the method of choice. It gave superb contrast between different soft tissues, and unlike x-rays or radioactivity, it is very unlikely to cause any long-term hazard, because the quantum energy of the radiation used is 9 orders of magnitude lower. Over 900 patients were imaged with this prototype over the next 2 or 3 years, and many papers were published of world-first clinical explorations which blazed the trail of the applications for which MRI is now the established practice (Smith *et al* (1981) give a selection, Mallard (1984/1986)). There was much excitement in medical circles, some going over the top and likening the breakthrough to the discovery of x-rays in 1895! There was an absolutely frenetic period of national and international invited presentations all over the world and one became used to living out of one's briefcase. Editors welcomed our papers. All this work was taking place in a typical hospital physics department, providing all the services to all the hospitals throughout the region, which are its bread and butter, as well as teaching radiologists and major MSc courses. No wonder some of our papers took a long time to get written-up!

The multinational medical imaging companies had been taking much interest in the work in Aberdeen: Johnson and Johnson (owners of Technicare) made a most valuable gift of the up-to-the-minute computer and display system on which we were displaying our images from 1979 onwards. All of these major companies crashed in, pouring in megabucks to develop prototype machines as quickly as possible, and the UK teams lost important members of their teams to them. We lost Edelstein to GE in New York, and all our know-how went with him within months of the breakthrough.

Our prototype was so busy with patients that we could not work on it enough to continue its improvement: it soon became clear that we needed to build another machine. But no one was prepared to fund it—not even MRC, who had been the main grant-giver so far. Following an invited lecture which the author gave in Maebashi, Japan, in November 1980, many Japanese companies wanted to work with us, but it was only Asahi Chemical of Tokyo who were prepared to pay the £283k for us to build the second machine (Mark II) in return for the know-how.



The contract was negotiated with the help of the then NRDC (National Research Development Corporation—the Government forerunner of the BTG (British Technology Group)). Mark II was built in part of the department's classroom, with Asahi engineers in attendance, and was installed in the Aberdeen Royal Infirmary at the end of 1982 (Redpath *et al* 1987), in a newly built room provided by the Grampian Health Board. In the interest of speed, it was of the same configuration, using a similar electromagnet but at twice the field strength of 0.08 T: it gave much improved images, and over the next ten years imaged over 9000 patients. It was not dismantled until 1993, when it was replaced with a commercial machine of 0.5 T in a new suite of rooms.

Fortunately, with the help of the BTG, the patents had been taken out properly, even though at this time it was not really fashionable in academic circles. The royalty sharing agreement with BTG has brought £17.2m to the University of Aberdeen. It is worth recording here that the major multinational companies began to produce and sell their MRI machines from 1983 onwards, and the author believes that in the beginning, they did not pay royalties: it was not until the BTG took the biggest one to court and won (costing £1.25m it is said) that royalties began to be paid.

By mid-1981, it was clear that MRI was here to stay, and by then the author had received requests to build machines for others, notably from the Edinburgh radiologist Professor Jonathan Best. To satisfy this, and also in an attempt to try to keep some of the manufacturing and employment in Scotland, the author set up a small company—M & D Technology Ltd. It took so long to obtain the approval of the University and to obtain the finance (£1.5m) from four institutions, that it was not functioning until early 1982, the year in which it is said that IGE spent \$112m on MRI development. As well as being undercapitalized, the NHS did not buy like the USA and Japanese hospitals, so it was beaten down eventually by the superior models now coming on-stream from the multinationals (with superconducting magnets and at over £1.5m each). However, all three machines that were sold served well for over a decade, and the one built for Edinburgh is now in the Scottish National Museum, and the one for St. Bartholomew's is in the Science Museum, London. The third machine, installed on the first floor of a house in Geneva, initially suffered from magnetic field interference problems from the tramline electric power return cable in the vicinity! The worst feature of M & D's collapse was the break-up of a magnificent team of 30 physicists, engineers and technical staff. The Japanese story was completely different, Asahi selling 145 almost identical Aberdeen-type MRI machines mainly in Japan! Is there a message for Britain here?

## 7. MRI with superconducting magnets

Ian Young made the next major stride forward by installing at Hammersmith Hospital in 1981, a machine with a superconducting magnet (the first one from Oxford Instruments) providing a horizontal field of 0.15 T. This gave much better stability, and due to the higher field strength, more detailed images, more akin to x-radiographs. The competing multinationals quickly adopted them, in spite of their great expense, and, certainly in the early days, there were major problems of liquid helium refills, fears of quenching and the necessity of limiting access to the machines. By 1984, fields of up to 0.5 T became available (Mallard 1984/1986), and there were many hundred imagers in use in the USA, Japan and Germany; whilst the UK, which had developed MRI, had barely 10! Ironically, this meant that papers from Aberdeen were now being rejected by Editors as being 'not state-of-the-art'. In the hands of clinical teams worldwide, MRI was applied to a vast range of clinical problems, and readers of this journal will be familiar with its impact upon modern medicine. New consolidations of its diagnostic value,



and new applications, are the subject matter of many national and international conferences and journals.

Machines with magnetic field strengths of up to 1.5 T are now becoming commonplace, providing fantastic detail in the images. 3.0 T machines are becoming generally available in teaching hospitals, and 7.0 T imagers are presently being installed as research tools. A machine for heads at 9.4 T is under development (Vaughan *et al* 2005). In addition to diagnostic work, numerous pulse sequences are now in use which exploit a wide range of different natural contrasts, such as diffusion, for example, and tremendous strides are being made into research studies of natural body processes and functions, ageing being one.

There are now a few hundred machines in the UK and it is estimated that worldwide there are now about 25 000 machines carrying out about 60m investigations each year, all still using some of the methods evolved in Aberdeen.

## 8. Epilogue

It is perhaps not out of place here to mention the Nobel Prize awarded for MRI in 2003 to Paul Lauterbur and Sir Peter Mansfield, about which there was some tremendously publicized and unseemly controversy. The limitation to three persons for such an award, which is perhaps an outdated one, and which was not in Nobel's original Will, has frequently led to the omission of worthy names in the past. It is relevant to remember that the Royal Society awarded its Wellcome Prize and Gold Medal for MRI in 1984 to four UK physicists. If, in imagination, the Nobel limitation were removed, then the author would name seven people for the creation of clinical MRI.

Magnetism has been fascinating for centuries: although it was most likely first known by the Chinese, in the Middle Ages it was Peter the Pilgrim, a military engineer for the King of Sicily, who first studied it, and published *Epistola di Magnete* in 1269—one of the first scientific works. He had seen his soldiers amuse themselves by throwing 'spoons' on to a board to foretell their future—a forerunner of dice. Some of these 'spoons' were lodestone, one of the five sacred stones, and they tended to fall facing the same direction. Magnetism was not studied again until Robert Norman, a compass maker, reported the dip of a lodestone (in the earth's field) in 'The New Attractive' in 1591. Shortly afterwards, William Gilbert, physician to Queen Elizabeth I, published his widely acclaimed 'De Magnete' in 1600 and also reported the extension of the attractive principle to amber, which was the first essay into electricity. This led on to electromagnetism, and ultimately to MRI. How pleased Gilbert would be to see magnetism come back to medicine! On the way came the towering genii of Helmholtz, Michael Faraday, and Aberdeen's own Professor of Natural Philosophy from 1856–1859, James Clerk Maxwell. It seems natural that Aberdeen University, founded in 1495 in the Middle Ages, should be where the team that from 1965 onwards made MRI really work well for the benefit of mankind, were from.

## References

- Andrew E R 1980 NMR imaging of intact biological systems *Phil. Trans. R. Soc. B* **289** 471–81  
Ansell G and Rotblat J 1948 Radioactive iodine as a diagnostic aid for intrathoracic goitre *Br. J. Radiol.* **21** 552–8  
Bowley A R, Taylor C G, Causer D A, Barber D C, Keyes W I, Undrill P E, Corfield J R and Mallard J R 1973 A radioisotope scanner for rectilinear, arc, transverse and longitudinal section scanning (ASS—the Aberdeen Section Scanner) *Br. J. Radiol.* **46** 262–71  
Carril J M, MacDonald A F, Dendy P D, Keyes W I, Undrill P E and Mallard J R 1979 Cranial scintigraphy: value of adding emission computed tomographic sections to conventional pertechnetate images (512 cases) *J. Nucl. Med.* **20** 1117–23

- Chesser R and Gemmell H H 1982 The interfacing of a gamma camera to a DEC gamma-11 data processing system for single photon emission tomography *Phys. Med. Biol.* **27** 437–41
- Choudhury A R, Keyes W I and MacDonald A F 1974 Cerebral scanning, including transverse section technique in the investigation of symptomatic epilepsy *Hans Berger Centenary Symposium on Epilepsy (Edinburgh, 1973)* ed C Harris and J Maudsley (London: Churchill and Livingstone) pp 243–9
- Cook P D and Mallard J R 1963 An electron spin resonance cavity for the detection of free radicals in the presence of water *Nature* **198** 145–7
- Damadian R 1971 Tumor detection by nuclear magnetic resonance *Science* **171** 1151–3
- Damadian R 1980 Field focussing NMR (FONAR) and the formation of chemical images in man *Phil. Trans. R. Soc. B* **289** 489–500
- Edelstein W A *et al* 1980 Spin-warp NMR imaging and application to human whole-body imaging *Phys. Med. Biol.* **25** 751–6
- Evans N T S *et al* 1986 The Aberdeen Mark II single photon emission tomographic scanner: specification and some clinical applications *Phys. Med. Biol.* **31** 65–78
- Flower M A, Rowe R W, Webb S and Keyes W I 1981 *Phys. Med. Biol.* **26** 671–91
- Foster M A 1984 *Magnetic Resonance in Medicine and Biology* (Oxford: Pergamon)
- Foster M A and Hutchison J M S 1989 *NMR Imaging* (Oxford: IRL)
- Garraway A N, Grannell P K and Mansfield P 1974 Image formation in NMR by a selective irradiative process *J. Phys. C: Solid State Phys.* **7** L457–L462
- Gemmell H G *et al* 1987 Differential diagnosis in dementia using the cerebral blood flow agent <sup>99m</sup>Tc HM-PAO: a SPECT study *J. Comput. Assist. Tomogr.* **11** 398–402
- Gordon R E 1974 Proton NMR relaxation time measurements in some biological tissues *PhD Thesis* University of Aberdeen Scotland 74
- Hinshaw W S *et al* 1979 An *in vivo* study of the fore-arm and hand by thin section NMR imaging *Br. J. Radiol.* **52** 36–41
- Hounsfield G 1973 Computerized transverse axial scanning (Tomography). Ft. 1. Description of system *Br. J. Radiol.* **46** 1016–22 and Ambrose J and Hounsfield G 1973 Pt. 2 Clinical applications *Br. J. Radiol.* **46** 1023–31
- Hutchison J M S 1976 Imaging by nuclear magnetic resonance *Proc. 7th. L H Gray Memorial Conf. (Leeds)* (Chichester: Wiley) pp 135–41
- Hutchison J M S 1979 Imaging by nuclear magnetic resonance *Medical Imaging Techniques (IEE Medical Electronic Monographs)* ed B W Watson (London: Peter Peregrinus) pp 79–93
- Hutchison J M S, Edelstein W A and Johnson G 1980 A whole-body NMR imaging machine *J. Phys. E: Sci. Instrum.* **13** 947–55
- Hutchison J M S, Edelstein W A, Johnson G, Redpath T and Mallard J R 1980 *UK Patent* 2079946A
- Hutchison J M S and Mallard J R 1971 Electron spin resonance spectrometry on the whole mouse *in-vivo*: a 100 MHz spectrometer *J. Phys. E: Sci. Instrum.* **4** 237–9
- Hutchison J M S, Mallard J R and Goll G C 1974 *In-vivo* imaging of body structures using proton resonance *Proc. 18th. Ampere Conf. (Nottingham)* ed P S Allen, E R Andrew and C A Bates (Nottingham: University of Nottingham) pp 283–84
- Johnson G, Hutchison J M S and Eastwood L M 1982 Instrumentation for NMR spin-warp imaging *J. Phys. E: Sci. Instrum.* **15** 74–9
- Kuhl D E 1964 A cylindrical radioisotope scanner for cylindrical and section scanning *Medical Radioisotope Scanning I* (Vienna: IAEA) pp 273–89
- Lauterbur P C 1973 Image formation by induced local interactions: examples employing nuclear magnetic resonance *Nature* **242** 190–1
- Lauterbur P C 1980 Progress in NMR zeugmatographic imaging *Phil. Trans. R. Soc. B* **289** 483–87
- Ling C R, Foster M A and Hutchison J M S 1980 Comparison of NMR water proton T1 relaxation times of rabbit tissues at 24 MHz and 2.5 MHz *Phys. Med. Biol.* **25** 748–51
- Lurie D J, Nicholson I, Foster M A and Mallard J R 1990 Free radicals imaged *in-vivo* in the rat by using proton-electron double resonance imaging (PEDRI) *Phil. Trans. R. Soc. A* **333** 453–6
- Lurie D J, Nicholson I, McLay I and Mallard J R 1992 *Appl. Magn. Reson.* **3** 917
- Mallard J R 1967 Medical physics—what is it? Hybrid Tea—numerically scanning clockwise *Abn. Univ. Rev.* **42** 12–29
- Mallard J R 1984/1986 Nuclear magnetic resonance imaging in medicine: medical and biological applications and problems *The Wellcome Foundation Prize Lecture, Proc. R. Soc. B* **226** 391–419
- Mallard J R 1987 Some call it laziness: I call it deep thought (with apologies to Garfield) *Hevesy Memorial Lecture (1985), Nucl. Med. Commun.* **8** 691–710
- Mallard J R 1995 *Medical Physics* (Bristol: Institute of Physics) chapter 25, pp 1855–1941 (*Twentieth Century Physics* vol 3)

- Mallard J R *et al* 1979 Imaging by nuclear magnetic resonance and its bio-medical implications *J. Biomed. Eng.* **1** 153–60
- Mallard J R *et al* 1980 Medical imaging by nuclear magnetic resonance—a review of the Aberdeen physical and biological programme *Medical Radionuclide Imaging* (Vienna: IAEA) pp 117–44
- Mallard J R, Fowler J F and Sutton M 1961a Brain tumour detection using radioactive arsenic *Br. J. Radiol.* **34** 562–8
- See also, Mallard J R, Fowler J F and Sutton M 1961b *Proc. 3rd. Int. Conf. Med. Electronics* pp 513–6
- Mallard J R *et al* 1980 *In-vivo* NMR imaging in medicine: the Aberdeen approach, both physical and biological *Phil. Trans. R. Soc. B* **289** 519–33
- Mallard J R and Kent M 1964 Differences observed between electron spin resonance signals from surviving tumour tissues and from their corresponding normal tissues *Nature* **204** 1192
- Mallard J R and Kent M 1966 Electron spin resonance in surviving rat tissues *Nature* **210** 588–91
- Mallard J R and Lawn D G 1967 Dielectric absorption of microwaves in human tissues *Nature* **213** 28–30
- Mallard J R and Myers M J 1963 The performance and clinical applications of a gamma camera for the visualization of radioactive isotopes *in vivo* *Phys. Med. Biol.* **8** 165–92
- Mallard J R and Peachey C J 1959 Quantitative automatic body scanner for the localization of radioisotopes *in-vivo* *Br. J. Radiol.* **32** 652–7
- See also, Mallard J R and Peachey C J 1960 *Proc. 3rd. Int. Conf. Med. Electronics (London) (Int. Fed. Med. Biol. Eng.)* (London: Peter Peregrinus) pp 511–2
- Mallard J R and Whittingham A 1968 Dielectric absorption of microwaves in human tissues *Nature* **218** 366–7
- Mansfield P *et al* 1980 Human whole body imaging and detection of breast tumours by NMR *Phil. Trans. R. Soc. B* **289** 503–10
- Mansfield P, Pykett I L, Morris P G and Coupland R E 1978 *Br. J. Radiol.* **51** 921–22
- Moore W S and Holland G N 1980 Experimental considerations in implementing a whole body multiple sensitive point nuclear magnetic resonance imaging system *Phil. Trans. R. Soc. B* **289** 511–8
- Radon J 1917 Über die bestimmung von functionen durch ihre integralwerte langs gewisser mannigfaltigkeiten *Berl. Verh. Sachs. Akad. Wiss. Math.-Phys. Kl. Lpz.* **69** 262
- Redpath T W *et al* 1987 A low field imager for clinical use *J. Phys. E: Sci. Instrum.* **20** 1228–34
- Ross K F A and Gordon R E 1981 Water in malignant tissue measured by cell refractometry and nuclear magnetic resonance *J. Microsc.* **128** 7–21
- Sharp P F *et al* 1986 Technetium 99m HM-PAO stereoisomers as potential agents for imaging regional cerebral blood flow: human volunteer studies *J. Nucl. Med.* **27** 171–7
- Smith F W *et al* 1981 Clinical application of nuclear magnetic resonance *Lancet* **I** (10 Jan) 78–9
- See also, Smith F W *et al* 1981 *Br. Med. J.* **282** 510–2
- Smith F W, Mallard J R, Reid A and Hutchison J M S 1981 Nuclear magnetic resonance imaging in liver disease *Lancet* **I** 963–66
- Pollet J E, Smith F W, Mallard J R, Ah-See A K and Reid A 1981 Whole-body nuclear magnetic resonance imaging in medicine: the first report of its use in surgical practice *Br. J. Surg.* **68** 493–4
- Besson J *et al* 1981 NMR observations in alcoholic cerebral disorder and the role of vasopressin *Lancet* **II** 923–24
- Smith F W *et al* 1982 Nuclear magnetic resonance imaging of the pancreas *Radiology* **54** 724–26
- Steyn J R and Smith F W 1982 Nuclear magnetic imaging of the prostate *Br. J. Urol.* **54** 726–28
- Smith F W 1983 The potential role of NMR imaging in paediatric practice *Paediat. Radiology* **13** 141–7
- Smith F W 1983 *J. Cereb. Blood flow Metab.* 263–9
- Smith F W *et al* 1984 NMR imaging in human pregnancy—A preliminary report *Magn. Res. Imaging* **2** 57–64
- Smith I C *et al* 1998 Gamma emission imaging in the management of breast cancer *Eur. J. Surg. Oncol.* **24** 320–29
- Smith I C *et al* 2000 Positron emission tomography using 18F1-fluorodeoxy-D-glucose to predict the pathologic response of breast cancer to primary chemotherapy *J. Clin. Oncol.* **18** 1676–88
- Sutherland R J and Hutchison J M S 1978 Three-dimensional NMR imaging using selective excitation *J. Phys. E: Sci. Instrum.* **11** 79–83
- Vaughan T *et al* 2005 Highest field human imaging *Present Status and Future Trends of Ultra-High Magnetic Field MRI* (Tokyo: NIRS) pp 48–52
- Wilks R J and Mallard J R 1966 A small gamma camera—improvements in the resolution, a setting-up procedure and a digital print-out *Int. J. Appl. Radiat. Isot.* **17** 113–9
- Young I R and Clow H 1978 NMR imaging *New Sci.* (11 Nov) 588

## Biography



**John R Mallard** began Medical Physics in 1951 at the Liverpool Radium Institute and was at Hammersmith Hospital, London 1953–1964. After one year at St. Thomas's Hospital Medical School, London, he occupied the first Chair of Medical Physics in Scotland at the University of Aberdeen. He was Head of the Joint University and NHS Department of Bio-Medical Physics and Bio-Engineering until 1992. In both London and Aberdeen, he created and led teams of physicists, engineers, technicians and students who built the equipment and used it, to pioneer nuclear medicine imaging, and MR imaging.