THIS YEAR'S NOBEL PRIZE IN MEDICINE

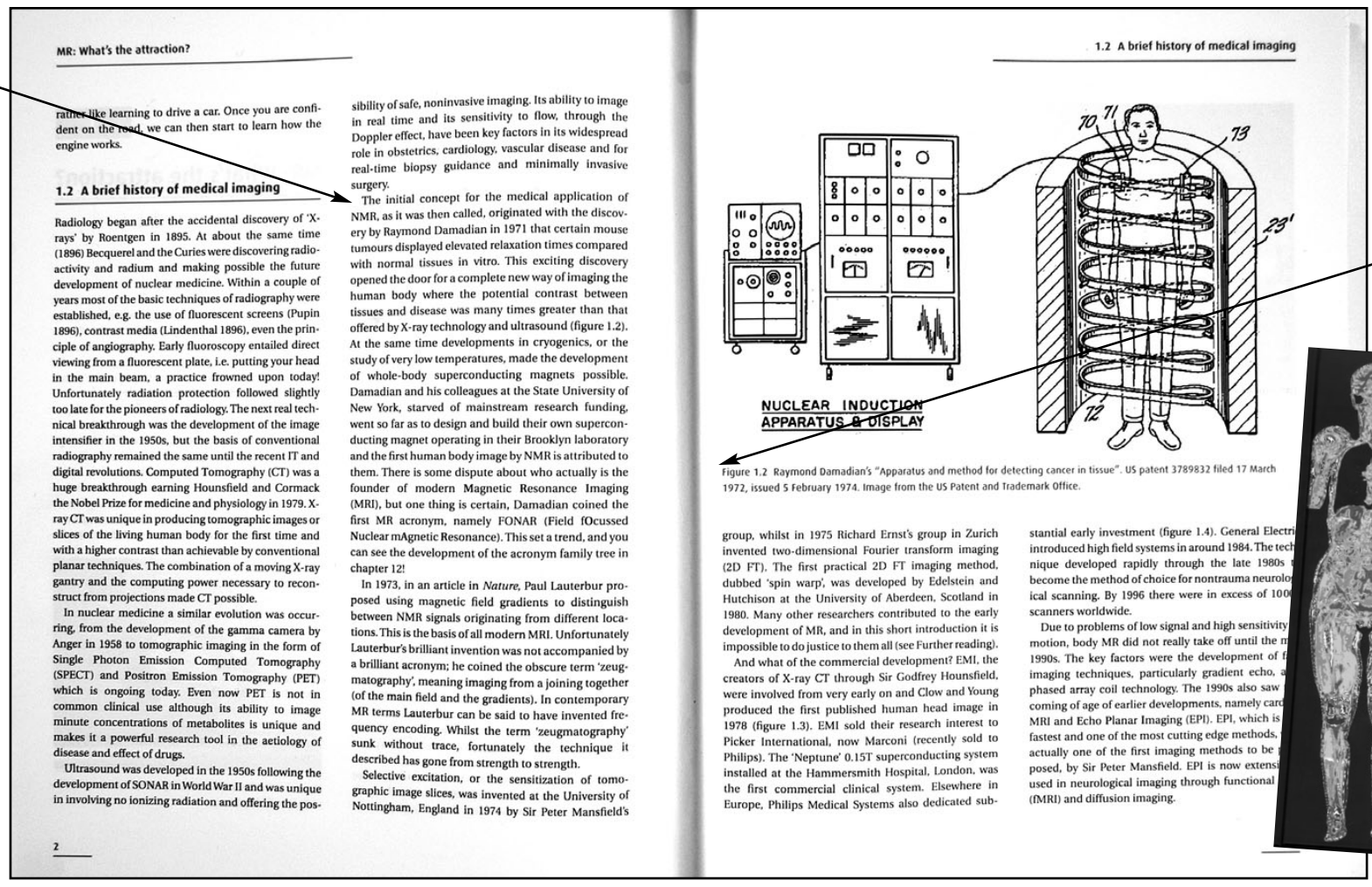
The shameful wrong that must be righted –

because the truth can be found simply by opening a medical textbook on MRI.

This is the authoritative medical textbook *MRI From Picture to Proton* (Cambridge University Press, UK, 2003).
It is an inarguably credible document. The facts presented here will either right the shameful wrong immediately or forever shame the prize.

Step 1. Open book to page 2 and notice heading in column one: "1.2 A brief history of medical imaging." Pay particular attention to the second paragraph in column two.

This is the paragraph that begins as follows: "The initial concept for the medical application of NMR, as it was then called, originated with ***the discovery by Raymond Damadian in 1971*** that certain mouse tumours displayed elevated relaxation times compared with normal tissues in vitro. ***This exciting discovery opened the door for a complete new way of imaging the human body where the potential contrast between tissues and disease was many times greater than that offered by X-ray technology and ultrasound (figure 1.2).***



MR: What's the attraction?

rather like learning to drive a car. Once you are confident on the road, we can then start to learn how the engine works.

1.2 A brief history of medical imaging

Radiology began after the accidental discovery of 'X-rays' by Roentgen in 1895. At about the same time (1896) Becquerel and the Curies were discovering radioactivity and radium and making possible the future development of nuclear medicine. Within a couple of years most of the basic techniques of radiography were established, e.g. the use of fluorescent screens (Pupin 1896), contrast media (Lindenthal 1896), even the principle of angiography. Early fluoroscopy entailed direct viewing from a fluorescent plate, i.e. putting your head in the main beam, a practice frowned upon today! Unfortunately radiation protection followed slightly too late for the pioneers of radiology. The next real technical breakthrough was the development of the image intensifier in the 1950s, but the basis of conventional radiography remained the same until the recent IT and digital revolutions. Computed Tomography (CT) was a huge breakthrough earning Hounsfield and Cormack the Nobel Prize for medicine and physiology in 1979. X-ray CT was unique in producing tomographic images or slices of the living human body for the first time and with a higher contrast than achievable by conventional planar techniques. The combination of a moving X-ray gantry and the computing power necessary to reconstruct from projections made CT possible.

In nuclear medicine a similar evolution was occurring, from the development of the gamma camera by Anger in 1958 to tomographic imaging in the form of Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET) which is ongoing today. Even now PET is not in common clinical use although its ability to image minute concentrations of metabolites is unique and makes it a powerful research tool in the aetiology of disease and effect of drugs.

Ultrasound was developed in the 1950s following the development of SONAR in World War II and was unique in involving no ionizing radiation and offering the possibility of safe, noninvasive imaging. Its ability to image in real time and its sensitivity to flow, through the Doppler effect, have been key factors in its widespread role in obstetrics, cardiology, vascular disease and for real-time biopsy guidance and minimally invasive surgery.

The initial concept for the medical application of NMR, as it was then called, originated with the discovery by Raymond Damadian in 1971 that certain mouse tumours displayed elevated relaxation times compared with normal tissues in vitro. This exciting discovery opened the door for a complete new way of imaging the human body where the potential contrast between tissues and disease was many times greater than that offered by X-ray technology and ultrasound (figure 1.2). At the same time developments in cryogenics, or the study of very low temperatures, made the development of whole-body superconducting magnets possible. Damadian and his colleagues at the State University of New York, starved of mainstream research funding, went so far as to design and build their own superconducting magnet operating in their Brooklyn laboratory and the first human body image by NMR is attributed to them. There is some dispute about who actually is the founder of modern Magnetic Resonance Imaging (MRI), but one thing is certain, Damadian coined the first MR acronym, namely FONAR (Field fOcussed Nuclear mAgnetic Resonance). This set a trend, and you can see the development of the acronym family tree in chapter 12!

In 1973, in an article in *Nature*, Paul Lauterbur proposed using magnetic field gradients to distinguish between NMR signals originating from different locations. This is the basis of all modern MRI. Unfortunately Lauterbur's brilliant invention was not accompanied by a brilliant acronym; he coined the obscure term 'zeugmatography', meaning imaging from a joining together (of the main field and the gradients). In contemporary MR terms Lauterbur can be said to have invented frequency encoding. Whilst the term 'zeugmatography' sunk without trace, fortunately the technique it described has gone from strength to strength.

Selective excitation, or the sensitization of tomographic image slices, was invented at the University of Nottingham, England in 1974 by Sir Peter Mansfield's

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1.2 A brief history of medical imaging

Figure 1.2 Raymond Damadian's "Apparatus and method for detecting cancer in tissue". US patent 3789832 filed 17 March 1972, issued 5 February 1974. Image from the US Patent and Trademark Office.

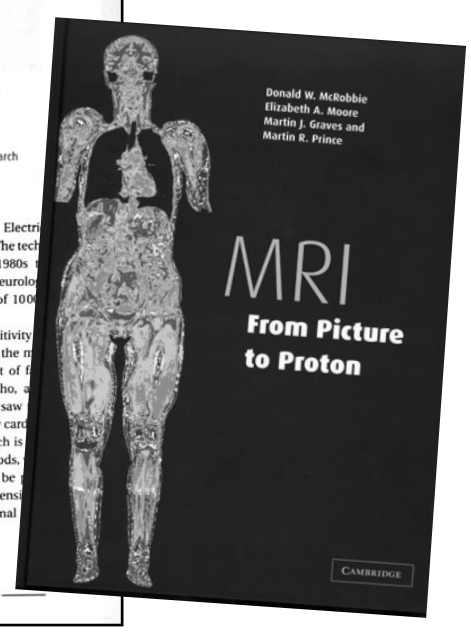
group, whilst in 1975 Richard Ernst's group in Zurich invented two-dimensional Fourier transform imaging (2D FT). The first practical 2D FT imaging method, dubbed 'spin warp', was developed by Edelstein and Hutchison at the University of Aberdeen, Scotland in 1980. Many other researchers contributed to the early development of MR, and in this short introduction it is impossible to do justice to them all (see Further reading).

And what of the commercial development? EMI, the creators of X-ray CT through Sir Godfrey Hounsfield, were involved from very early on and Clow and Young produced the first published human head image in 1978 (figure 1.3). EMI sold their research interest to Picker International, now Marconi (recently sold to Philips). The 'Neptune' 0.15T superconducting system installed at the Hammersmith Hospital, London, was the first commercial clinical system. Elsewhere in Europe, Philips Medical Systems also dedicated substantial early investment (figure 1.4). General Electri
introduced high field systems in around 1984. The tech
nique developed rapidly through the late 1980s
become the method of choice for nontrauma neurolo
ical scanning. By 1996 there were in excess of 100
scanners worldwide.

Due to problems of low signal and high sensitivity
motion, body MR did not really take off until the m
1990s. The key factors were the development of f
imaging techniques, particularly gradient echo,
phased array coil technology. The 1990s also saw
coming of age of earlier developments, namely card
MRI and Echo Planar Imaging (EPI). EPI, which is
fastest and one of the most cutting edge methods,
actually one of the first imaging methods to be
posed, by Sir Peter Mansfield. EPI is now extensi
used in neurological imaging through functional
(fMRI) and diffusion imaging.

Step 2. Go to page 3. Look at figure 1.2. Note caption:

"Figure 1.2 Raymond Damadian's 'Apparatus and method for detecting cancer in tissue.' US patent 3789832 filed 17 March 1972, issued February 1974. Image from the US Patent and Trademark Office."



Step 3. Turn to page 4, column two. Follow arrow and read important passage.

"So what were NMR researchers doing between the forties and the seventies – that's a long time in cultural and scientific terms. The answer: they were doing chemistry, including Lauterbur, a professor of chemistry at the same institution as Damadian. NMR developed into a laboratory spectroscopic technique capable of examining the molecular structure of compounds, ***until Damadian's ground-breaking discovery in 1971."***

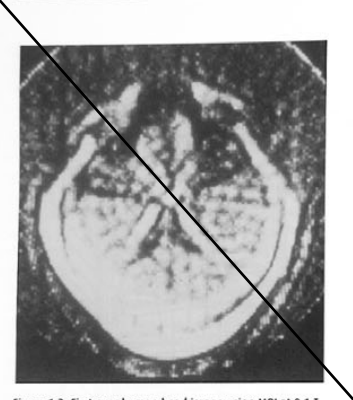


Figure 1.3 First ever human head image using MRI at 0.1 T from EMI Central Research Laboratories. For this image CT type "back projection" was used. Courtesy of Ian Young.

Figure 1.4 Walker 0.1 T resistive magnet used by Philips in the early development of MRI. Courtesy of Philips Medical Systems.

The early history of NMR

'Nuclear Induction', as it was first described, was discovered in 1945, soon after the close of World War II, by Bloch and independently by Purcell and Pound. It is said that the development of radio communications in the war effort, to which Purcell had contributed scientifically, was one of the factors underpinning this important scientific discovery. Another important factor, as in the development of atomic physics, was the expulsion or fleeing of European physicists from the Nazi regime, an exodus that included Bloch and Bloembergen. What did these MR pioneers discover? That you can detect a signal (a voltage in a coil) when you place a sample in a magnetic field and irradiate it with radiofrequency (RF) energy of a certain frequency, the resonant or Larmor frequency. The signal is produced by the interaction of the sample nuclei with the magnetic field. The spin echo was 'stumbled upon' by Hahn in 1949. He discovered that you could get a repeat of the NMR signal at a delayed time by adding a second burst of RF energy. That's all you need to know for now. So what were NMR researchers doing between the forties and the seventies – that's a long time in cultural and scientific terms. The answer: they were doing chemistry, including Lauterbur, a professor of chemistry at the same institution as Damadian. NMR developed into a laboratory spectroscopic technique capable of examining the molecular structure of compounds, until Damadian's ground-breaking discovery in 1971.

1.3 How to use this book

Everyone starts MRI with the same basic problem: it's like nothing else they've learnt in the past. All that knowledge you have about radioactive isotopes and film-screen combinations is useless to you now. Where do you start? Most MRI books start at the beginning (a very good place to start, according to the song), and introduce protons, net magnetization, precession and the Larmor equation all in the first three pages. We think

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1.3 How to use this book

The spin doctors: Nobel Laureates' roll-call (figure 1.5)

In 1952 Edward Purcell (Harvard) and Felix Bloch (Stanford) jointly received the Nobel Prize for physics 'for their development of new methods for nuclear magnetic precision measurements and discoveries in connection therewith'. Of Purcell's discovery, the *Boston Herald* reported that 'it wouldn't revolutionize industry or help the housewife'. Purcell himself stated that 'we are dealing not merely with a new tool but a new subject which I have simply called nuclear magnetism. If you will think of the history of ordinary magnetism, the electronic kind, you will remember that it has been rich in difficult and provocative problems and full of surprises.' It seems that the *Boston Herald* misjudged the importance of NMR!

Bloch, a Swiss-born Jew and friend of quantum physicist Werner Heisenberg, quit his post in Leipzig in 1933 in disgust at the Nazi's expulsion of German Jews (as a Swiss citizen, Bloch himself was exempt). Bloch's subsequent career at Stanford was crammed with major contributions to physics and he has been called 'the father of solid state physics'.

Nicolaas Bloembergen, a Dutch citizen, was forced to hide from the Nazis for the duration of the War, reputedly living on boiled tulip bulbs, until becoming Purcell's first graduate student at Harvard two months after the discovery of NMR. With Purcell and Robert Pound he developed the theory of NMR relaxation, known now by their initials BPP. In 1981 he won a Nobel Prize for his work in laser spectroscopy.

In 1991 Richard Ernst joined the MRI Nobel Laureates 'for his contributions to the development of the methodology of high resolution nuclear magnetic resonance spectroscopy'. You could say Richard Ernst achieved the same trick twice: by his novel applications of 2D FT in both spectroscopy and imaging.

Other Nobel Laureates associated with NMR include Norman Ramsay (1989), a spectroscopy pioneer who developed the theory of the chemical shift, and Isidor Rabi (1944), Ramsey's PhD mentor, 'for his resonance method for recording the magnetic properties of atomic nuclei'.

Figure 1.5 Nobel prize-winners in NMR: (a) Purcell 1912–1997, (b) Bloch 1901–1999, (c) Bloembergen b. 1920 and (d) Ernst b. 1933. Courtesy of the Nobel Museum.

that are produced, which is much more useful if you're already working in the MR unit. After all, you don't expect to understand how the internal combustion engine works before you learn to drive.

The book is divided into two parts. In part A you will find everything you need to know about the basics of MRI, but presented in reverse order. We start with things you can touch and look at: the equipment you find in an MR unit and what the images look like, using terms like 'T_1-weighted' simply as labels. Later on we talk about how the images are produced and finally we cover the underlying physics. By that stage you will be able to link these rather difficult concepts back to things which matter – the images.

Part B contains more advanced topics, such as cardiac MR and spectroscopy, in no particular order. You don't have to work right through part A before you read these chapters, we just couldn't fit them neatly into the reverse order!

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Step 4. Look at page 5, right column. See pictures of Nobel Laureates. Notice that none are medical doctors.

Ask yourself, What about the medical applications of NMR (original name for MRI)? Why aren't any of them credited for that? Who should be? Recall that Raymond Damadian, M.D., studied NMR way back in 1963 when he was a postgraduate fellow at Harvard, and he studied under none other than Edward Purcell, Ph. D., the first laureate named in the book for the development of NMR. Say to yourself, No wonder Raymond Damadian, M.D., began to think about the medical applications of NMR way before anyone else.

When presented with such widely recognized historical evidence, most people might well wonder why Raymond Damadian, M.D., who has been nominated for the Nobel Prize for the MRI for many years, was not selected to receive it. In fact, since three people can be named for the award but only two were, the Nobel Committee for Physiology or Medicine actually made the calculated decision to exclude him. How is such a disgraceful act possible?

The blistering truth is, the insider club of NMR chemists and physicists just can't seem to accept the rather logical reality that a medical doctor made the discovery in their field that, in Alfred Nobel's words, has "conferred the greatest benefit on mankind." It's time for them to realize that the attempt to reserve the MRI prize for themselves only makes it scornfully meaningless for their own distinction and irrelevant to history.

Step 5. Insist that Raymond Damadian be included in this year's Nobel Prize for Medicine, which claims to honor "discoveries concerning magnetic resonance imaging."

THE SIMPLE TRUTH IS, RAYMOND DAMADIAN:

- Made the original tissue discoveries on which all MRI machines are based (T1 and T2 relaxation times)
- Devised the first workable 3D method to scan the human body
- Built the first scanner by hand with two of his postdoctoral fellows
- Achieved the first MR scan (image) of the living human body
- Successfully patented the MRI
- Started the company Fonar to advance the MRI
- Introduced the first MRI that went into the service of patients
- When his patent was challenged by GE, had it affirmed by the High Court on U.S. Patents and the U.S. Supreme Court, Chief Justice William H. Rehnquist presiding. The Court found "insubstantial differences" between the method of Dr. Damadian's patent and the method all modern MRI's use to produce an image
- Invented the first open MRI, the first mobile MRI, and now the first Stand-Up™MRI

Raymond Damadian is unequivocally the founder of modern magnetic resonance scanning. The two winners simply improved the way the scanning is done.

COMPARE THE ACHIEVEMENTS OF THE TWO WINNERS

The men who have been chosen to receive the Nobel Prize for the MRI did nothing more, or less, than invent improved ways to image the tissue signals discovered by Dr. Damadian, which the medical textbook notes is the "...exciting discovery [that] opened the door for a complete new way of imaging the human body..."

The NMR chemist Paul Lauterbur, Ph.D., only began to think about medical imaging after witnessing Damadian's tissue experiments, which were repeated for him by others when he was the chief executive at the same company Dr. Damadian had conducted them. Right afterward, in fact, when he went out to dinner, he got the idea to apply the magnetic gradient to image the tissue signals![1] (The magnetic gradient was invented by Gabillard in the 1950's. It came as standard equipment on all NMR machines to help the scientist even out the signal from the inert compounds he was popping into an opening less than 2 inches wide.)

Lauterbur credited Dr. Damadian's March 1971 *Science* paper (in which Dr. Damadian described his "ground-breaking" signal discoveries) in his private but witnessed notebook when he wrote down his idea, but he failed to credit Damadian in his first published paper and over many years. This is called citation plagiarism and is a scientific disgrace.

The NMR physicist Peter Mansfield, Ph.D., only began to think about imaging after Damadian's work on tissues was brought to his attention. Then his team improved the way the magnetic gradient made an MRI image. In Mansfield's own words, "I think Damadian's work had some influence on everyone."[1]

ONLY DAMADIAN'S DISCOVERY IS STILL IN USE ON EVERY MRI

The landmark cancer-signal discovery and the signal differences of healthy tissues that Dr. Damadian discovered continue to drive every MRI machine in the world. Meanwhile, the contributions of the two winners were surpassed and replaced by the spin warp technique invented in 1980 by a group at Aberdeen University.

WHY HAS IT TAKEN NEARLY 20 YEARS TO MAKE THE AWARD FOR THE MRI?

Given the overwhelming evidence of Dr. Damadian's priority, why on earth has it taken 20 years or so to figure out who to award the Nobel Prize for MRI? And how on earth was the decision made to exclude Dr. Damadian, even given the evident risk of unprecedented disgrace to the Nobel Prize?

The insider clubhouse of NMR chemists and physicists have been determined to limit the award to their own kind. Paul Lauterbur himself has said repeatedly that he would not accept the prize if Dr. Damadian were named. His cronies decided to let him have his way – regardless of the risks to their own credibility and to the prize!

A FLAGRANT VIOLATION OF ALFRED NOBEL'S WILL

This year's decision to exclude Raymond Damadian is also a flagrant violation of Alfred Nobel's will. He specified very clearly in his will that he wished the award in physiology or medicine to recognize only "discovery." He does not allow for an "invention" or "improvement," as he does in physics and chemistry. The Commitee carefully calculated the wording of their reasons for awarding the prize to avoid the appearance of a violation of the will. Yet, as you can see by the language in the textbook that referes to the contributions of the two winners, "invention" is clearly the only thing being honored this year.

It is the fiduciary responsibility of the trustees of the prize to award it according to Nobel's last will and testament. It's not only ethically correct. It's the law.

THREE WINNERS CAN BE NAMED, BUT TIMES IS RUNNING OUT

The prize ceremony is scheduled for the evening of December 10th.

We urge that the Nobel Committee for Physiology or Medicine and the Nobel Assembly, to which the Committee made the outrageous recommendation to exclude Dr. Damadian, rescue the prize from a night of irremediable disgrace.

It is way past time for the disgraceful stonewalling in Stockholm to stop.

There is still time for those who know the wrong that has been done to step forward to reclaim the prize for the truthful commendation of scientific achievement. Such an unprecedented and courageous action will in no way reduce the credibility of the prize. It is, in fact, the only way to redeem it.

We urge you now to transform the Nobel Prize ceremony into a celebration worthy of the distinction it claims. Should you persist without an emendation of the wrongheaded decision that has led to the impending catastrophe, the damage to the prestige of the Nobel Prize will be far more calamitous than the unwarranted damage to Raymond Damadian.

After all, he has been in the history books for over 30 years as the inventor of MRI. Your only credible role is to recognize, with unimpeachable exactitude, the history of scientific achievement. It is not, nor can it ever be, a scandalous attempt to rewrite it.

At this time, we urge all right-minded readers to join us in our efforts to right this shameful wrong.

ABOUT THE MEDICAL TEXTBOOK *MRI FROM PICTURE TO PROTON*

It was published in 2003 by Cambridge University Press, in the UK.

QUOTE FROM THE BOOK

"*MRI from Picture to Proton* presents the basics of MR practice and theory as the practitioner first meets them.... *MRI from Picture to Proton* is an essential text for the student of MR whatever their background: medical, technical or scientific."

ABOUT THE AUTHORS

Ronald W. McRobbie is the Head of Radiological and MR Physics in the Radiological Sciences Unit, the Hammersmith Hospitals NHS Trust and Senior Lecturer in Imaging at Imperial College London.

Elizabeth A. Moore was Principal Medical Physicist at the National Hospital for Neurology and Neurosurgery (London), and is now working as MR Clinical Scientist for Philips Medical Systems Australasia.

Martin J. Graves is Principal Clinical Scientist in the Department of Radiology at the University of Cambridge and Addenbrooke's NHS Trust.

Martin R. Prince is Professor of Radiology at Weil Medical College of Cornell University and Chief of MRI at New York Hospital.

Paid for by The Friends of Raymond Damadian
Contact DanielCulver@aol.com or call him at 631-694-2929.

Write to: The Nobel Committee for Physiology or Medicine, Nobel Forum, Box 270 SE – 171 77 Stockholm, Sweden **E-mail to:** secr@mednobel.ki.se **Or call:** 011-46-8-585-823-44 • 011-46-8-662-64-31 • 011-46-8-51-77-45-00

All facts are public record. Documentation may be found at www.fonar.com.

1. *A Machine Called Indomitable,* by Sonny Kleinfield, Times Books, Inc., 1985.