Chapter 1

MR: What's the Attraction?

1.1 It's not Rocket Science, but I Like It

How would you impress a stranger you meet at a party with your intelligence? You might claim to be a brain surgeon or a rocket scientist. Well **M**agnetic **R**esonance (MR) is not rocket science, it's better. MR involves an amazing combination of advanced science and engineering, including the use of superconductivity, cryogenics, quantum physics, digital and computer technology – and all within the radiology department of your local hospital. MR imaging has evolved from unpromising beginnings in the 1970s to become nowadays the imaging method of choice for a large proportion of radiological examinations and the 'jewel in the crown' of medical technology. A modern MRI scanner is shown in Figure 1.1.

So what is it? It is an imaging method based principally upon sensitivity to the presence and properties of water, which makes up 70–90% of most tissues. The properties and amount of water in tissue can alter dramatically with disease and injury, which makes MR very sensitive as a diagnostic technique. MR detects subtle changes in the magnetism of the nucleus, the tiny entity that lies at the heart of the atom. This is probing deeper than X-rays, which interact with the clouds or shells of the electrons that orbit the nucleus. MR is a truly powerful modality. At its most advanced, MR can be used not just to image anatomy and pathology but to investigate organ function, to probe in vivo chemistry and even to visualize the brain thinking.

Figure 1.1 Modern superconducting MR system. Courtesy of Philips Healthcare.

In the early days, the scanners were the domain of the physicists and engineers who invented and built them, and the technique was called NMR imaging (NMR stands for nuclear magnetic resonance). The cynics may say that the technique really took off clinically when the 'N-word' was dropped. This was sensible as the term 'nuclear', although scientifically accurate, implied a connection with nuclear energy and, in the last of the Cold War years, resonated in the public's mind with the spectre of nuclear weapons.

Because of the diversity of sciences and technologies that gave birth to and continues to nurture MR, it is an extremely hard subject to learn. A lifetime is not enough to become expert in every aspect. Clinicians, technologists and scientists all struggle with the study of the subject. The result is sometimes an obscurity of understanding or a dilution of scientific truth resulting in misconceptions. This is why we have chosen to write this book. Our aim is to introduce you to MR as a tool – 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 in 1896 by Pupin, contrast media reported by Lindenthal in the same year, 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 break-through 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. **C**omputed **t**omography (CT) was a huge break-through, 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 that 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 **S**ingle **P**hoton **E**mission **C**omputed **T**omography (SPECT) and **P**ositron **E**mission **T**omography (PET), which is ongoing today. PET's clinical use is increasing, particularly in detecting metastases in oncology. Its ability to image minute concentrations of metabolites is unique and makes it a powerful research tool in the aetiology of disease and the effects 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, non-invasive 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, abdominal investigations and vascular imaging, real-time biopsy guidance and minimally invasive surgery.

As early as 1959, J. R. Singer at the University of California, Berkeley, proposed that NMR could be used as a non-invasive tool to measure in vivo blood flow. In 1971 Raymond Damadian discovered that certain mouse tumours displayed elevated relaxation times compared with normal tissues in vitro. This opened the door for a completely 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 **M**agnetic **R**esonance **I**maging (MRI), but one thing is certain: Damadian coined the first MR acronym, namely FONAR (**F**ield f**O**cused **N**uclear m**A**gnetic **R**esonance). This set a trend, and you can see the development of the acronym family tree in Chapter 4!

In 1973, in an article in *Nature*, Paul Lauterbur proposed using magnetic field gradients to distinguish

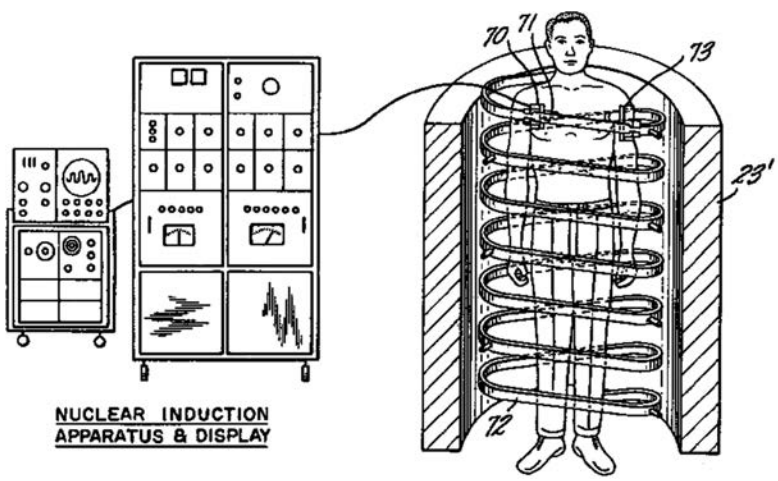

Figure 1.2 Raymond Damadian's 'Apparatus and method for detecting cancer in tissue'. US patent 3789832 filed 17 March 1972, issued 5 February 1974. Image from the US Patent and Trademark Office.

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.

between NMR signals originating from different locations, combining this with a form of reconstruction from projections (as used in CT). The use of gradients still forms the basis of all modern MRI as recognized by the Nobel Committee in 2003. 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. While the term 'zeugmatography' sunk without a 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 group, a contribution also recognized by the 2003 Nobel Committee, while 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. Clow and Young produced the first published human head image in 1978 (Figure 1.3). EMI sold their research interest to Picker International, which became Marconi and is now part of Philips. The 'Neptune' 0.15 T superconducting system installed at the Hammersmith Hospital, London, was the first commercial clinical system. Elsewhere in Europe, Philips also dedicated substantial early investment (Figure 1.4). General Electric introduced high-field (1.5 T) systems around 1984. The technique developed rapidly through the late 1980s to become the method of choice for non-trauma neurological scanning. By 2015 there were in excess of 35 000 scanners worldwide.

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

Figure 1.4 0.15 T resistive magnet used by Philips in the early development of MRI. Courtesy of Philips Healthcare.

'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.

The 2003 Nobel Prize for physiology or medicine was awarded to Professor Paul Lauterbur and Sir Peter Mansfield 'for their discoveries concerning magnetic resonance imaging'. Peter Mansfield left school at 15 with no qualifications, aiming to become a printer. His scientific curiosity was sparked by the V1 and V2 flying bombs and rockets that fell on London in 1944, when he was 11. After working as a scientific assistant at the Jet Propulsion Laboratory and a spell in the army, he went back to college to complete his education, eventually becoming Professor of Physics at the University of Nottingham. He was knighted in 1993.

Paul Lauterbur is said to have been inspired to use field gradients to produce an image while eating a hamburger. His seminal paper 'Image Formation by Induced Local Interactions. Examples Employing Nuclear Magnetic Resonance' (*Nature* 242, 16 March 1973) was originally rejected. Thirty years later, *Nature* placed this work in a book of the 21 most influential scientific papers of the twentieth century.

Other Nobel Laureates associated with NMR include Norman Ramsey (1989), a spectroscopy pioneer who developed the theory of the chemical shift; Isidor Rabi (1944), Ramsey's PhD mentor, 'for his resonance method for recording the magnetic properties of atomic nuclei'; and Kurt Wüthrich (2002) for his development of NMR spectroscopy for determination of the three-dimensional structure of biological macromolecules in solution.

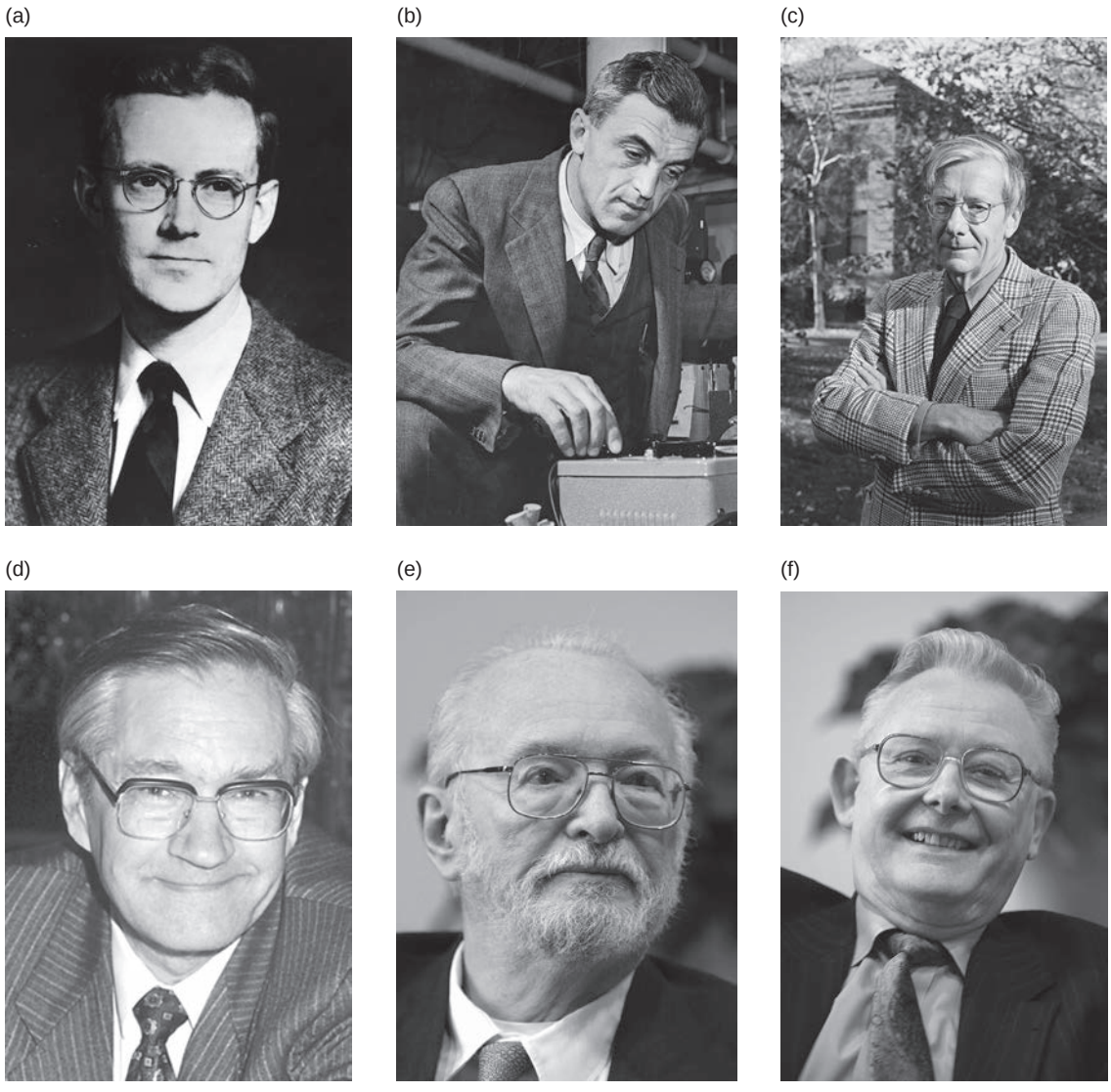

Figure 1.5 Nobel prize-winners in NMR: (a) Purcell 1912–1997, (b) Bloch 1901–1999, (c) Bloembergen b. 1920, (d) Ernst b. 1933, (e) Lauterbur 1929–2007 and (f) Mansfield b. 1933–2017. Images courtesy of Ullstein Bild/Getty Images; Bettman/Getty Images; Ira Wyman/Getty Images; the Nobel Museum; and Sven Nackstrand/Getty Images (x2) respectively.

Due to problems of low signal and high sensitivity to motion, body MR did not really take off until the 1990s. The key factors were the development of fast imaging techniques, particularly gradient echo, and phased array coil technology. The 1990s also saw the coming of age of earlier developments, namely cardiac MRI and **E**cho **P**lanar **I**maging (EPI). EPI, which is the fastest and one of the most cutting-edge methods, was actually one of the first imaging methods to be proposed, by Sir Peter Mansfield. EPI is now extensively used in neurological imaging through functional **MRI** (fMRI) and diffusion imaging.

MR development has since then exploded into new innovations and clinical applications explored throughout this book, some of which are illustrated in Figure 1.6.

1.3 How to Use this Book

Everyone starts MRI with the same basic problem: it's like nothing else they've learned 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

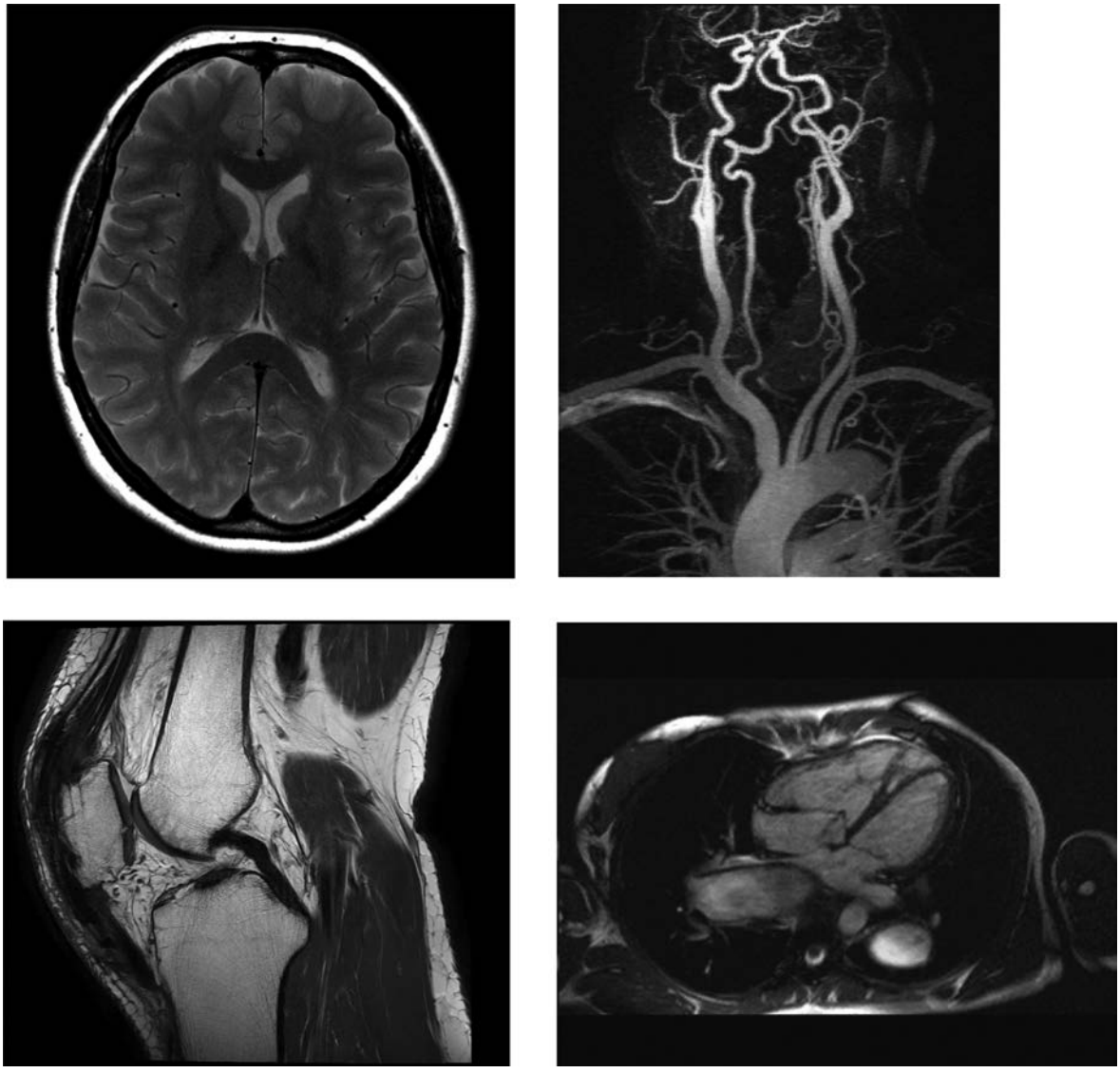

Figure 1.6 Diverse clinical applications of MRI.

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 there is another way: starting at the end with the images 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 I 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 II contains more advanced topics, such as cardiac MR and spectroscopy, in no particular order. You don't have to work right through Part I before you read these chapters; we just couldn't fit them neatly into the reverse order!

In all the chapters you will find the most basic information in the main text. Clinical boxes, shaded green, provide the clinical context as you go along. Yellow boxes are about trying things for yourself: simple (and not-so-simple) imaging experiments to run on your own scanner. Advanced boxes, shaded in blue, deal with various topics in more detail and are placed at appropriate places throughout the text.

If you're completely new to MR, we suggest you read straight through Part I, skipping all the advanced boxes. When you need to understand something a bit better, re-read the chapter, this time taking in some of the boxes. And when you're ready for more advanced subjects like spectroscopy or fMRI, head over to Part II. The topics can seem to jump around a bit by splitting them up this way, but we think it is a good compromise, which allows us to include enough information for everyone, whether you are a new radiographer hoping to make a good impression in your new job, a radiologist interested in improving diagnostic image quality or a physicist studying for a postgraduate degree.

Further Reading

Christie DA and Tansey EM (eds) (1996) *Making the Human Body Transparent: The Impact of Nuclear Magnetic Resonance and Magnetic Resonance Imaging*. London: Wellcome Institute for the History of Medicine. Available from: www.histmodbiomed.org/witsem/vol2 [accessed 8 January 2015].

Dawson M Joan (2013) *Paul Lauterbur and the Invention of MRI*. Cambridge, MA: MIT Press.

Mansfield P (2013) *The Long Road to Stockholm: The Story of Magnetic Resonance Imaging – An Autobiography*. Oxford: Oxford University Press.