Medical Science Series

THE PHYSICS OF MEDICAL IMAGING

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CHAPTER 1

IN THE BEGINNING

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In the chapters that follow, an attempt is made to describe the physical principles underlying a number of imaging techniques that prove useful in diagnostic medicine. For brevity, we have concentrated largely on describing state-of-the-art imaging, with a view to looking to the future physical developments and applications. For the student anxious to come to grips with today's technology and perhaps about to embark on a research career, this is in a sense the most realistic approach. It does, however, lead to a false sense that the use of physics in medicine has always been much as it is today and gives no impression of the immense efforts of early workers whose labours underpin present developments. In this chapter we take a short backwards glance to the earliest days of some aspects of medical imaging.

Even a casual glance at review articles in the literature tells us that historical perspective is necessarily distorted by the prejudices of the writer. In a sense, history is best written by those who were involved in its making. During the 75th anniversary celebrations of the *British Journal of Radiology* in 1973, an anniversary issue (*Br. J. Radiol.* **46** 737–931) brought together a number of distinguished people to take stock, and although the brief was wider than to cover imaging, the impact of physics in medical imaging was a strong theme in their reviews. Since that time, of course, several new imaging modalities have burst into hospital practice and, with the excusable preoccupation with new ideas and methods, it is these which occupy most of current research effort, feature most widely in the literature and are looked to for new hope particularly in the diagnosis, staging and management of cancer and other diseases.

Against this background, what features of the landscape do we see in our retrospective glance? Within any one area of imaging, there exists a detailed and tortuous path of development, with just the strongest ideas surviving the passage of time. Numerous reviews chart these developments and are referred to in subsequent chapters. Most of us are, however, fascinated to know what was the *first* reported use of a technique or announcement of a piece of equipment, and might then be content to make the giant leap from this first report to how the situation stands today, with cavalier disregard for what lies between. So, by way of introduction, this is what we shall do here. Even so, a further difficulty arises. In a sense each variation on a theme is new and would certainly be so claimed by its originators, and yet it is not all these novelties that history requires us to remember. The passage of time acts as a filter to perform a natural selection. Perhaps what was regarded as important at its discovery has paled and some apparently unimportant announcements have blossomed beyond expectation. The organised manner in which research is required to be documented also veils the untidy methods by which it is necessarily performed. Most of the imaging modalities that are in common use were subject to a period of laboratory development and it is useful to distinguish clearly between the first reported experimental laboratory equipment and the first truly clinical implementation. Physicists might be tempted to rest content that the potential had been demonstrated in a laboratory, but were they patients they would take a different view! In most of the subjects we shall meet in later chapters, there has been (or still is!) a lengthy intermediate time between these two 'firsts'.

Wilhelm Conrad Röntgen's laboratory discovery of x-rays, when he was Professor of Physics at Wurzburg, is perhaps the only 'first' that can probably be pinned down to the time and day!—the late evening of 8 November 1895. This date was reported in *McClure's Magazine* by the journalist H J W Dam (1896): Röntgen himself never apparently stated a date. The discovery must also rank as one of the fastest ever published—submitted on 28 December 1895 and made known to the world on 5 January 1896. The prospects for x-ray diagnosis were immediately recognised. Röntgen refused, however, to enter into any commercial contract to exploit his discovery. He was of the opinion that his discovery belonged to humanity and should not be the subject of patents, licences and contracts. The result was undoubtedly the wide availability of low-cost x-ray units. A portable set in the USA cost $15 in 1896. Since it is believed that the first x-radiograph taken with clinical intent was on 13 January 1896 by two Birmingham (UK) doctors to show a needle in a woman's hand, the 'clinical first' followed the 'experimental first' with a time lapse also surely the shortest by comparison with any subsequent development. A bromide print of the image was given by Ratcliffe and Hall-Edwards to the woman, who next morning took it to the General and Queen's Hospital where the casualty surgeon J H Clayton removed the needle—the first x-ray guided operation. The single discovery of x-rays has clearly proved so important that it has already been the subject of many reviews (see e.g. Mould 1986, Brailsford 1946, Burrows 1986). It is amusing to note that many newspaper reports of the discovery were anything but enthusiastic. As equipment was readily available to the general public, there were at the time an abundant number of advertisements for x-ray sets. Mould (1986) has gathered together a plethora of these and other photographs of clinical procedures with x-rays. These are with hindsight now known to have been risky for both patient and radiologist, and many early radiation workers became casualties of their tools.

Digital subtraction angiography involves the subtraction of two x-rays, precisely registered, one using contrast material, to eliminate the unwanted clutter of common structures. Historically we have a precedent. Galton (1900) wrote (in the context of photography):

> If a faint transparent positive plate is held face to face with a negative plate, they will neutralise one another and produce a uniform grey. But if the positive is a photograph of individual, A, and the negative a photograph of individual, B, then they will only cancel one another out where they are identical and a representation of their differences will appear on a grey background. Take a negative composite photograph and superimpose it on a positive portrait of one of the constituents of that composite and one should abstract the group peculiarities and leave the individuality.

We shall not attempt to document the first application of x-radiography to each separate body site, but it is worth noting (Wolfe 1974) that Salomon (1913) is reported to have made the first mammogram. Thereafter the technique was almost completely abandoned until the early 1950s.

The announcement of a machine used to perform x-ray computed tomography (CT) in a clinical environment, by Hounsfield at the 1972 British Institute of Radiology annual conference, has been described as the greatest step forward in radiology since Röntgen's discovery. The relevant abstract (Ambrose and Hounsfield 1972) together with the announcement entitled 'X ray diagnosis peers inside the brain' in the *New Scientist* (27 April 1972) can be regarded as the foundation of clinical x-ray CT. The classic papers that subsequently appeared (Hounsfield 1973, Ambrose and Hounsfield 1973) left the scientific community in no doubt as to the importance of this discovery. Hounsfield shared the 1979 Nobel Prize for Physiology and Medicine with Cormack. The Nobel lectures (Hounsfield 1980, Cormack 1980) were delivered on 8 December 1979 in Stockholm. It was made quite clear, however, by Hounsfield that he never claimed to have 'invented CT'. The importance of what was announced in 1972 was the first practical realisation of the technique, which led to the explosion of clinical interest in the subsequent years. Who really did 'invent CT' has been much debated since. The original concept is usually credited to Radon (1917), whilst Oldendorf (1961) is often quoted as having published the first laboratory x-ray CT images of a 'head' phantom. What Oldendorf actually did was to rotate a head phantom (comprising a bed of nails) on a gramophone turntable and provide simultaneous translation by having an HO-gauge railway track on the turntable and the phantom on a flat truck, which was pulled slowly through a beam of x-rays falling on a detector. He showed how the internal structures in the phantom gave rise under such conditions to characteristic signals in the projections as the centre of rotation traversed the phantom relative to the fixed beam and detector. He was well aware of the medical implications of his experiment, but he did not actually generate a CT image. In his paper he referred to the work of Cassen and also Howry, who appear elsewhere in this chapter in another context. It is certainly not difficult to find papers throughout the 1960s describing the potential of reconstruction tomography in medicine, suggesting methods and testing them by both simulation and experiment. Cormack in particular was performing laboratory experiments in CT in 1963 (Cormack 1980). It is perhaps less well known that a CT scanner was built in Russia in 1958. Korenblyum *et al* (1958) published the mathematics of reconstruction from projections together with experimental details and wrote: ‘At the present time at Kiev Polytechnic Institute, we are constructing the first experimental apparatus for getting X-ray images of thin sections by the scheme described in this article’. This was an analogue reconstruction method, based on a television detector and a fan-beam source of x-rays. Earlier reports from Russia have also been found (e.g. Tetel’Baum 1957).

The history of the detection of gamma-ray photons emitted from the body after injection of a radionuclide is a fascinating mix of contemporary detector physics and the development of radiopharmaceuticals. Detection techniques are almost as old as the discovery of radioactivity itself. The Crookes’ spinthariscope (1903), the Wilson cloud chamber (1895), the gold-leaf electroscope and the Geiger counter (1929) were all used to detect, although not image, radiation. Artificial radionuclides did not arrive until Lawrence invented the cyclotron in 1931. Interestingly $^{99}Tc^{m}$ was first produced in the 37 inch cyclotron at Berkeley in 1938. Following the first experimental nuclear reactor in 1942, several reactors, notably at Oak Ridge and at the Brookhaven National Laboratory, produced medically useful radionuclides. Nuclear medicine’s modern era began with the announcement in the 14 June 1946 issue of *Science* that radioactive isotopes were available for public distribution (Myers and Wagner 1975). A famous one-sentence letter from Sir J D Cockcroft at the Ministry of Supply, AERE, Harwell, to Sir E Mellenby at the MRC, dated 25 November 1946, said: ‘I have now heard that the supply of radioactive isotopes to the UK by the US Atomic Energy Project is approved’. In September 1947, UK hospitals were receiving the first shipments from the GLEEP (graphite low-energy experimental pile) reactor at AERE, Harwell, Europe’s first nuclear reactor (N G Trott, private communication).

Mallard and Trott (1979) have reviewed the development in the UK of what is today known as nuclear medicine. The *imaging* of radiopharmaceuticals was a logical extension of counting techniques for detecting ionising radiation, which go back to the invention of the Geiger–Müller tube in 1929. The development of Geiger–Müller counting was largely laboratory-based even in the early 1940s (notably in the UK at the National Physical Laboratory), and commercial detectors did not appear until after the Second World War (McAlister 1973). It was not, however, until 1948 that the first point-by-point image (of a thyroid gland) was constructed by Ansell and Rotblat (1948), which might be regarded as the first clinical nuclear medicine scan. The advantages of employing automatic scanning were recognised by several early workers. Cassen *et al* (1950) developed a scintillation (inorganic calcium tungstate) detector and wrote of their desire to mount it in an automatic scanning gantry, which they later achieved (Cassen *et al* 1951). Cassen *et al*'s paper appeared in August 1951, whilst in July 1951 Mayneord *et al* (1951a,b) introduced an automatic gamma-ray scanner based on a Geiger detector. Mayneord *et al* (1955) reported an improved scanner, which used a coincident pair of scintillators and storage tube display.

The concept of the gamma camera might be credited to Copeland and Benjamin (1949), who used a photographic plate in a pinhole camera. Their invention was made in the context of replacing autoradiographs, and long exposure times of the order of days were required. It is interesting to note that they came to criticise their own instrument's usefulness because 'many of the tracers used in biological work have little gamma activity', a situation rather different from what we know today! Anger (1952) first announced an electronic gamma camera with a crystal acting as an image intensifier for a film (also with a pinhole collimator), which used a sodium iodide crystal of size $2 \times 4 \times \frac{5}{16}$ inch^3. This was regarded as a large crystal at the time. The first electronic gamma camera with multiple photomultiplier tubes (PMT) was reported in 1957 (Anger 1957, 1958). It had a 4 inch diameter crystal of thickness 0.25 inch and just seven 1.5 inch diameter photomultiplier tubes. Commercial cameras followed soon afterwards, amongst the first in the UK being the prototype Ekco Electronics camera evaluated by Mallard and Myers (1963a,b) at London's Hammersmith Hospital. In 1968 Anger (1968) was also the first to report how a gamma camera could be used in a rectilinear scanning mode to perform multiplane longitudinal tomography. The new machine made redundant the need to perform several rectilinear scans with different focal-length collimators on single or double detectors.

Single-photon emission computed tomography (SPECT) stands in relation to planar Anger camera imaging as x-ray CT stands to planar x-radiology. Its importance in diagnostic nuclear medicine is now clearly established. Who invented SPECT and when? Once again, the honours are disputable, largely because what was suspected to be possible did not become a clinical reality for some while. It is also possible to identify several 'firsts' since SPECT has been achieved in several widely different ways. Kuhl and Edwards (1963) published the first laboratory single-photon emission tomography (SPET) (note: no 'C') images based on a rotate–translate arrangement and collimated crystal detectors. What we would now call a transverse section tomogram was generated entirely by analogue means without the need for a computer. The angular increment for rotation was a coarse 15°. Kuhl and Edwards (1964) published a photograph of the first SPET scanner (which was also capable of other scanning modes such as rectilinear and cylindrical scanning) and, in their explanation of how the analogue image is built up on film, provided what is possibly the first description of windowed tomography by which potentially overbright values were 'top-cut'. They also refined the image formation method to produce an image on paper tape whose contrast could be adjusted *a posteriori*. One of the first tomographic images visualised a malignant astrocytoma using an intravenous injection of chlormerodrin ^{197}Hg. Interestingly, in an addendum to the 1964 paper, they wrote: 'we have had good results with technetium 99m in pertechnetate form for brain scanning since March 1964'. This represents one of the earliest reports of the use of this isotope, which was to have such an important impact thereafter. The technetium generator was one of the first 'radioactive cows' and was conceived at the Brookhaven National Laboratory by Green, Tucker and Richards around the mid-1950s, being first reported in 1958 (see Ketchum 1986, Tucker *et al* 1958, Tucker 1960, Richards *et al* 1982), although the original identification of technetium as an impurity in the aluminium oxide generator of ^{132}I was reportedly made by a customer for one such generator. Generators were also available in the UK from AERE in the 1950s, supplied by G B Cook, and were in use at the Royal Cancer Hospital (N G Trott, private communication).

Anger himself showed how SPECT could be achieved with a gamma camera as early as 1967, rotating the patient in a chair in front of the stationary camera and coupling the line of scintillation corresponding to a single slice at each orientation to an optical camera (Anger *et al* 1967). Tumours were satisfactorily delineated and the technique was established, but it was far from today's clinical situation. These results were reported on 23 June 1967 at the 14th Annual Meeting of the Society of Nuclear Medicine in Seattle. In 1971 Muehllehner and Wetzel (1971) produced some laboratory images by computer, but the lack of a clinical SPECT system based on a rotating camera was still being lamented as late as 1977 when Jaszczak *et al* (1977) and Keyes *et al* (1977) were reporting clinical results obtained with a home-made camera gantry. The first commercial gamma-camera-based SPECT systems appeared in 1978 and at much the same time single-slice high-resolution SPECT systems were also marketed (Stoddart and Stoddart 1979). Almost a decade earlier, however, SPECT tomograms had been obtained in the clinic by Bowley *et al* (1973) using the Mark 1 Aberdeen Section Scanner, whose principles were largely similar to those of Kuhl and Edwards' laboratory scanner. We see, therefore, that with regard to SPECT imaging there was no clear date separating the impossible from the possible.

Logically complementing imaging with single photons is the detection of the annihilation gammas from positron emitters in order to form images of the distribution of a positron-labelled radiopharmaceutical in the body. The technology to achieve positron emission tomography (PET) is now established commercially but the market is small, although a number of specialist centres have been conducting clinical PET since the early 1960s. Perhaps it is surprising, therefore, to find that the technique of counting gammas from positron annihilation was discussed as early as 1951 by Wrenn *et al* (1951). They were able to take data from a source of ^{64}Cu in a fixed brain enclosed within its skull using thallium-activated sodium iodide detectors. Images as such were not presented, but certainly by 1953 simple scanning arrangements had been engineered for the creation of images. Brownell and Sweet (1953) showed the *in vivo* imaging of a recurrent tumour using ^{74}As. In this paper they write: 'we have been working independently on this [i.e. PET imaging] problem for a period of approximately two years'. It would be reasonable then to assign the beginnings of PET imaging to the year 1951.

The discovery of the phenomenon of nuclear magnetic resonance (NMR) was announced simultaneously and independently in 1946 by groups headed by Bloch and by Purcell, who shared a Nobel Prize. Thereafter, there was a steady development of NMR spectroscopy in chemistry, biology and medicine. NMR imaging followed much later and several 'firsts' are worth recording. In a letter to *Nature* in 1973, Lauterbur (1973) published the first NMR image of a heterogeneous object comprising two tubes of water, but the date of publication is preceded by a patent filed in 1972 by Damadian (1972), who proposed without detail that the body might be scanned for clinical purposes by NMR. The first human image of a live finger was reported by Mansfield and Maudsley (1976) and there followed the first NMR image of a hand (Andrew *et al* 1977) and of a thorax (Damadian *et al* 1977) in 1977. An article in the *New Scientist* in 1978 amusingly entitled 'Britain's brains produce first NMR scans' (Clow and Young 1978) was the first NMR image produced by a truly planar technique. In the same year, the first abdominal NMR scan was reported by Mansfield *et al* (1978). This (1978) was also the year in which the first commercial NMR scanner became available, and the first demonstration of abnormal human pathology was reported in 1980 by Hawkes *et al* (1980). The beginnings of NMR imaging clearly require the specification of a large number of 'firsts'!

It is believed that after x-radiology the use of ultrasound in medical diagnosis is the second most frequent investigative imaging technique. The earliest attempts to make use of ultrasound date from the late 1930s, but these mimicked the transmission method of x-rays and cannot really be recorded as the beginnings of ultrasound imaging as we know it today. Ultrasonic imaging based on the pulse–echo principle, which is also the basis of radar, became possible after the development of fast electronic pulse technology during the Second World War. The use of ultrasound to detect internal defects in metal structures preceded its use in medicine and was embodied in a patent taken out by Firestone in 1940. The first two-dimensional ultrasound scan was obtained using a simple sector scanner and showed echo patterns from a myoblastoma of the leg in a living subject (Wild and Reid 1952). This paper was received for publication on 25 October 1951. Prior to this, ultrasonic echo traces from human tissue had been demonstrated as early as 1950 by Wild (1950), but two-dimensional images had not been constructed. Very shortly afterwards, on 2 June 1952, Howry and Bliss (1952) published the results of their work, which had been in progress since 1947, and their paper included a two-dimensional image of a human wrist. Wild and Reid (1957) went on to develop the first two-dimensional ultrasound scanner and used it to image the structure of the breast and rectum. It was not until 1958 that the prototype of the first commercial two-dimensional ultrasonic scanner was described by Donald *et al* (1958) as a development of a one-dimensional industrial flaw detector made by Kelvin and Hughes. This machine was used to carry out the first investigations of the pregnant abdomen (Donald and Brown 1961). For a more detailed history of ultrasonic imaging, one might consult Hill (1973), White (1976) and Wild (1978). A number of other groups were actively investigating the use of ultrasound in medicine in the early 1950s, including Leksell in Sweden and a group led by Mayneord in what was then the Royal Cancer Hospital in London (now the Royal Marsden Hospital). Wild visited the Royal Cancer Hospital in 1954 and concluded that the group were quite familiar with the high-amplitude echo from the cerebral midline and the connection between its displacement and cerebral disease, which has subsequently become the basis of cerebral encephalography. The early UK work was documented only in the Annual Reports of the British Empire Cancer Campaign but may have provided a basis for the subsequent work of Donald's group in obstetrics.

In the following chapters we shall encounter the attempts that have been made to image a wide variety of different physical properties of biological tissue. Some of these are the bases of well established diagnostic techniques whose origins have been mentioned above. Other imaging methods are less widely applied or are still to reach the clinic. Some are still subject to controversy over their usefulness. For example, we shall find that diaphanography (the measurement of the light transmission of tissue) is receiving renewed interest of late for early diagnosis of breast disease. Commercially available equipment appeared for the first time in the late 1970s and yet Cutler (1929) reported the first attempts at transillumination some 50 years earlier in New York. Perhaps in contrast to the time lapse between the discovery and clinical use of x-rays, this ranks as the longest delay! Thermometric methods for showing the pattern of breast disease were first reported by Lloyd-Williams *et al* (1961). The use of xeroradiographic techniques for mammography were pioneered in the late 1960s and early 1970s when the image quality of the electrostatic technique became comparable with film imaging and the usefulness of the extra information offered was appreciated (Boag 1973). The first medical xeroradiographic image (of a hand) was, however, published in 1907 by Righi (1907), and was reproduced by Kossel (1967). (Righi had been working on the method since 1896.) The process was patented in 1937 by Carlson. This long delay was largely due to the inadequacies of the recording process, which were to be dramatically improved by the development of the Xerox copying process in the 1940s and 1950s. In 1955 Roach and Hilleboe (1955) described their feelings that xeroradiography was a logical replacement for film radiography particularly for mobile work. Their paper begins with an extraordinary justification for the work, namely the preservation of the lives of US casualties in the aftermath of a nuclear attack. They wrote:

In the event of the explosion of an atomic bomb over one of the major cities in the United States, the number of casualties produced and requiring emergency medical care would be tremendous. . . . xeroradiography offers a simple, safe and inexpensive medium for the recording of rontgen images. No darkrooms or solutions of any type are needed. No lead lined storage vaults are required and there is no film deterioration problem. No transport of large supplies is involved.

Hills *et al* (1955) were already comparing xeroradiography and screen–film radiography.

Imaging the electrical impedance of the body is a very new technique whose description in Chapter 10 also serves for its history. The first *in vivo* cross-sectional clinical images were recorded early in the 1980s and to date there is no commercially available equipment for applied potential tomography.

In figure 1.1 some of these firsts have been plotted on a non-linear

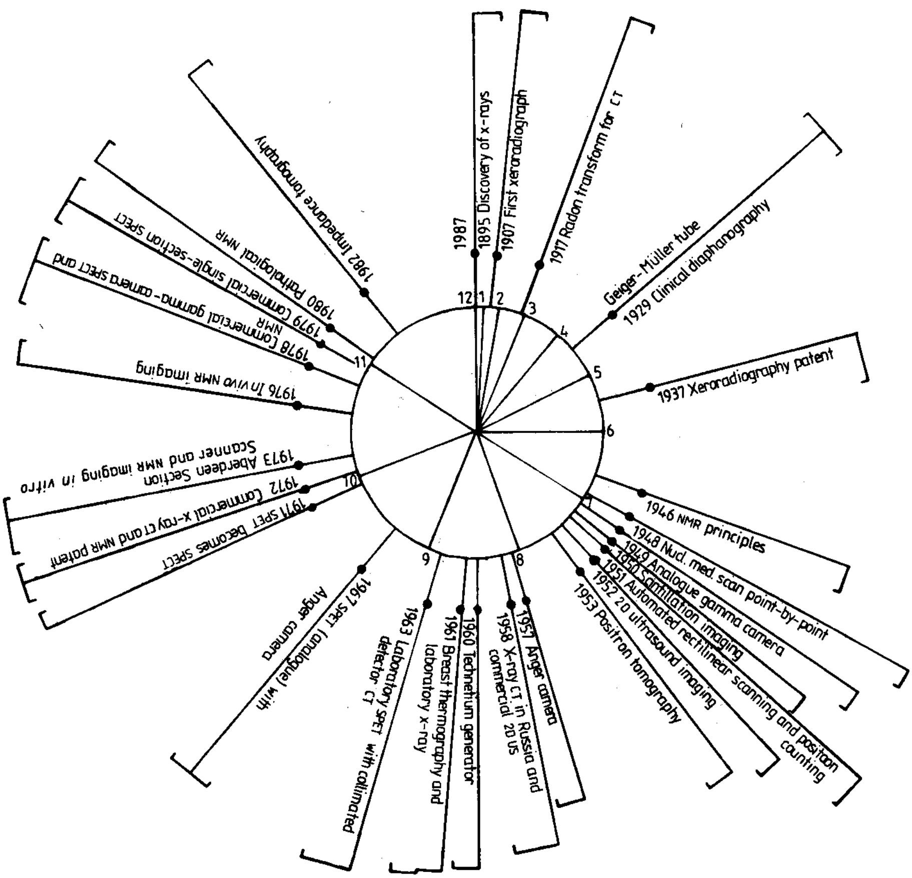

Figure 1.1 Non-linear clock of important 'firsts'.

clock. The period between 1895 and 1987 has been divided up such that the 92 years correspond to 12 h. The 'hour hand' sweeps the fraction of 360°, which is the square of the fraction of the 92 year period elapsed since 1895.

In the introduction it was tentatively suggested that the period between the mid-1940s and the present may have 'completed the set' of all physical probes to which the patient is semi-opaque and which are therefore available as the basis of imaging modalities. This is graphically illustrated in the figure by the crowding of events in the latter half of the timespan. With this brief historical scene setting, let us proceed to examine the physical basis of imaging.

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