

COMPUTED MEDICAL IMAGING

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BY

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In preparing this paper I realised that I would be speaking to a general audience and have therefore included a description of computed tomography (CT) and some of my early experiments that led up to the development of the new technique. I have concluded with an overall picture of the CT scene and of projected developments in both CT and other types of systems, such as Nuclear Magnetic Resonance (NMR).

Although it is barely 8 years since the first brain scanner was constructed, computed tomography is now relatively widely used and has been extensively demonstrated. At the present time this new system is operating in some 1000 hospitals throughout the world. The technique has successfully overcome many of the limitations which are inherent in conventional X-ray technology.

When we consider the capabilities of conventional X-ray methods, three main limitations become obvious. Firstly, it is impossible to display within the framework of a two-dimensional X-ray picture all the information contained in the three-dimensional scene under view. Objects situated in depth, i. e. in the third dimension, superimpose, causing confusion to the viewer.

Secondly, conventional X-rays cannot distinguish between soft tissues. In general, a radiogram differentiates only between bone and air, as in the lungs. Variations in soft tissues such as the liver and pancreas are not discernible at all and certain other organs may be rendered visible only through the use of radio-opaque dyes.

Thirdly, when conventional X-ray methods are used, it is not possible to measure in a quantitative way the separate densities of the individual substances through which the X-ray has passed. The radiogram records the *mean* absorption by all the various tissues which the X-ray has penetrated. This is of little use for quantitative measurement.

Computed tomography, on the other hand, measures the attenuation of X-ray beams passing through sections of the body from hundreds of different angles, and then, from the evidence of these measurements, a computer is able to reconstruct pictures of the body's interior.

Pictures are based on the separate examination of a series of contiguous cross sections, as though we looked at the body separated into a series of thin "slices". By doing so, we virtually obtain total three-dimensional information about the body.

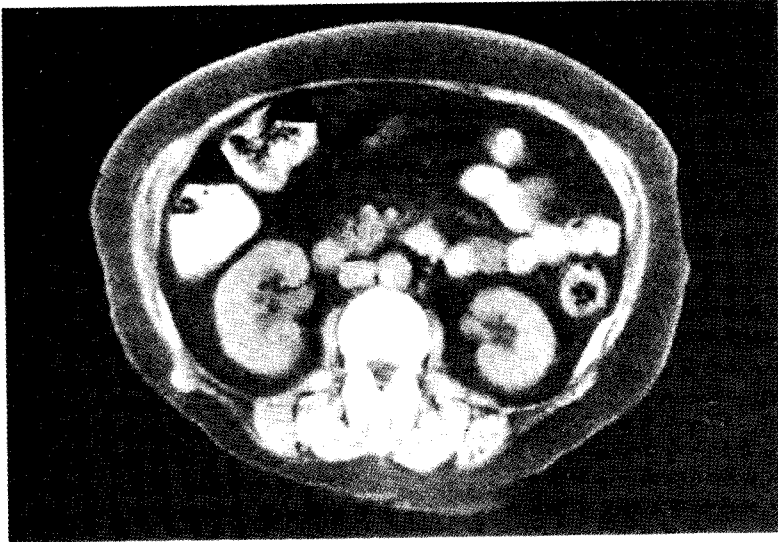


Fig. 1. CT scan taken through the kidneys

However, the technique's most important feature is its enormously greater sensitivity. It allows soft tissue such as the liver and kidneys to be clearly differentiated, which radiographs cannot do. An example is shown in Fig. 1.

It can also very accurately measure the values of X-ray absorption of tissues, thus enabling the nature of tissue to be studied.

These capabilities are of great benefit in the diagnosis of disease, but CT additionally plays a role in the field of therapy by accurately locating, for example, a tumour so indicating the areas of the body to be irradiated and by monitoring the progress of the treatment afterwards.

It may be of interest if I describe some of the early experiments that led up to the development of CT.

Some time ago I investigated the possibility that a computer might be able to reconstruct a picture from sets of very accurate X-ray measurements taken through the body at a multitude of different angles. Many hundreds of thousands of measurements would have to be taken, and reconstructing a picture from them seemed to be a mammoth task as it appeared at the time that it would require an equal number of many hundreds of thousands of simultaneous equations to be solved.

When I investigated the advantages over conventional X-ray techniques however, it became apparent that the conventional methods were not making full use of all the information the X-rays could give.

On the other hand, calculations showed that the new system used the data very efficiently and would be two orders of magnitude more sensitive than conventional X-rays. For this reason I hoped that it would be possible to distinguish between the various tissues of the body, although I could not find any literature which suggested that such X-ray absorption differences existed.

THE EARLY TEST S

I decided to do some lab experiments with gamma rays to test if the system would work. The equipment was very much improvised. A lathe bed provided the lateral scanning movement of the gamma-ray source, and sensitive detectors were placed on either side of the object to be viewed which was rotated 1° at the end of each sweep. The 28,000 measurements from the detector were digitized and automatically recorded on paper tape. After the scan had been completed this was fed into the computer and processed.

Many tests were made on this machine, and the pictures were encouraging despite the fact that the machine worked extremely slowly, taking 9 days to scan the object because of the low intensity gamma source. The pictures took 2 ½ hours to be processed on a large computer. The results of the processing were received on paper tape and these were brought to the laboratory and caused to modulate a spot of light on a cathode ray tube point by point, in front of a camera. As paper tape was used this was a slow process and it took at best two hours to produce a photograph. Clearly, nine days for a picture was too time-consuming, and the gamma source was replaced by a more powerful X-ray tube source, which reduced the scanning time to nine hours (Fig. 2). From then on, much better pictures were obtained; these were usually of blocks of perspex. A preserved specimen of a human brain was eventually provided by a local hospital museum and we produced the first picture of a brain to show grey and white matter (Fig. 3).

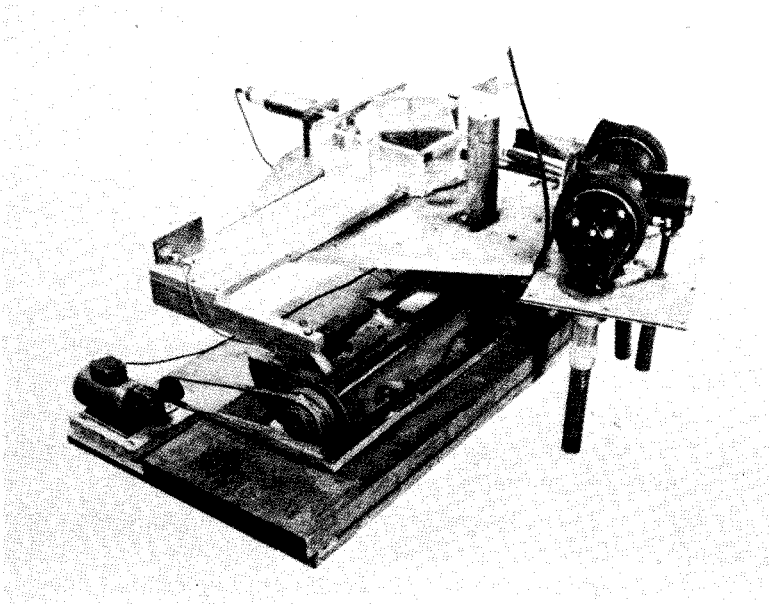


Fig. 2. Laboratory machine, showing X-ray tube and detector traversing along a lathe bed across a human brain. At the end of the stroke the brain would be rotated 1° and the traverse would be repeated.

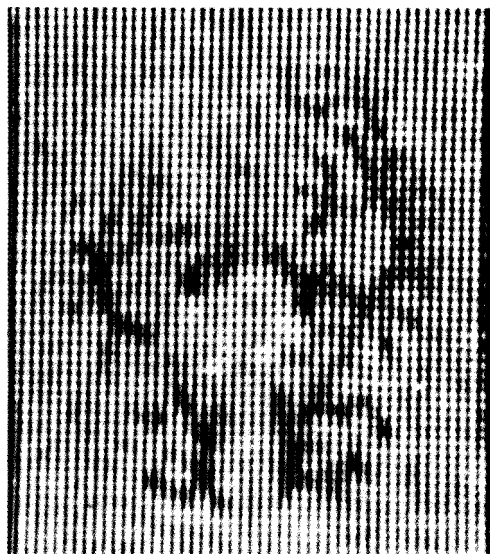


Fig. 3. Picture of the first brain scanned on Laboratory machine Fig. 2.

Disappointingly, further analyses revealed that the formalin used to preserve the specimen had enhanced the readings, and had produced exaggerated results. Fresh bullock's brains were therefore used to cross-check the experiments, and although the variations in tissue density were less pronounced, it was confirmed that a large amount of anatomic detail could be seen. In parallel, tests were carried out on sections through pigs

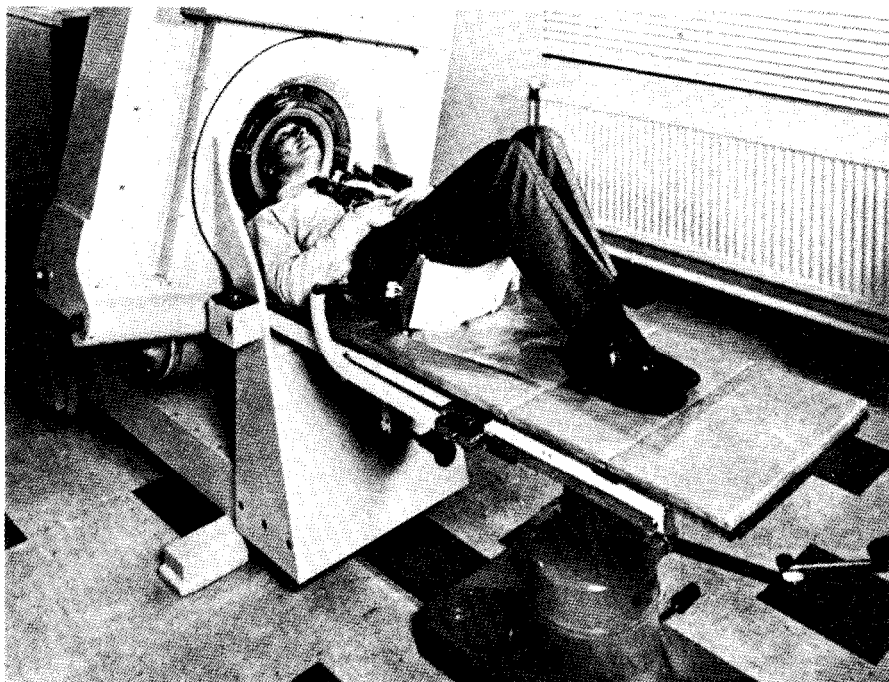


Fig. 4. First clinical prototype brain scanner installed at Atkinson Morley's Hospital, London.

in the area of the kidneys, and this work also produced most encouraging results. Although the speed had been increased to one picture per day, we had a little trouble with the specimen decaying while the picture was being taken, so producing gas bubbles, which increased in size as the scanning proceeded.

At this point in time, we found that we could see brain and body tissues clearly but we were still very worried as to whether tumours would show up at all. Unless it could do this, the machine would be of very little use. To test this, we had to build a much faster and more sophisticated machine that would scan the brains of living patients in a hospital (Fig. 4).

In 1972 the first patient was scanned by this machine. She was a woman who had a suspected brain lesion, and the picture showed clearly in detail a dark circular cyst in the brain (Fig. 5). From this moment on, as more patients were being scanned, it became evident that the machine was going to be sensitive enough to distinguish the difference between normal and diseased tissue.



Fig. 5. First clinical picture obtained from prototype machine.

Applying the principles to scanning the body seemed to be the next logical step, a larger and faster scanner was designed capable of taking high resolution pictures of the body in 18 seconds. Fig. 1 is a typical picture taken by this machine.

Since then, there has been a tendency to construct more complicated machines with a scan time of 3 seconds or less (Fig. 6).

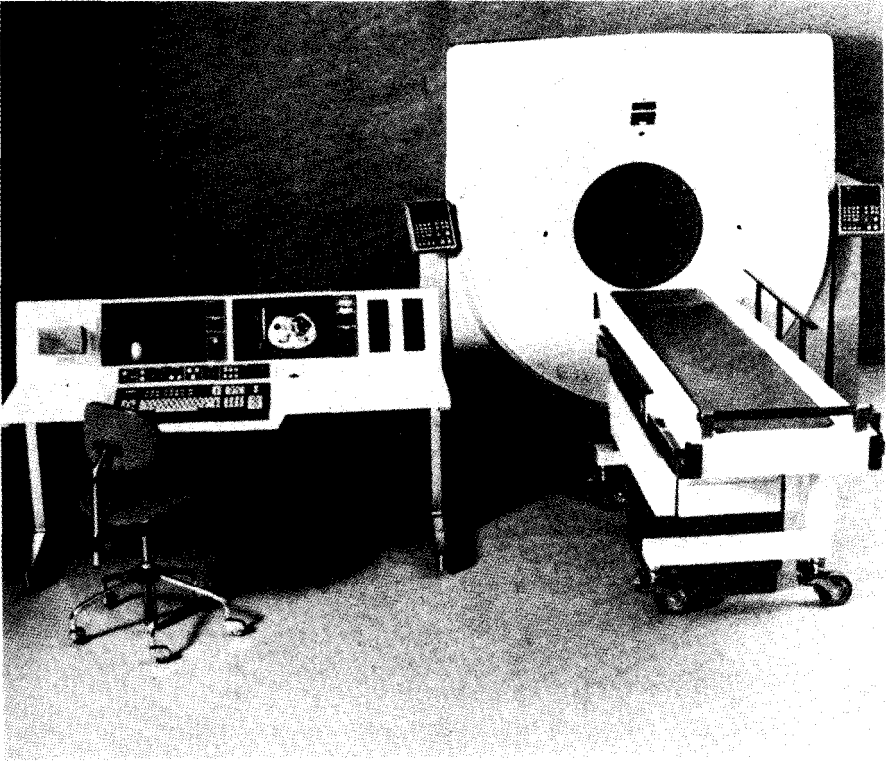


Fig. 6. A machine capable of scanning at a rate of 3 sec/picture.

PRINCIPLES OF THE TECHNIQUE

There are three types of CT machine currently in use (Fig. 7). Basically all three systems use different methods of scanning the patient but end up by taking approximately the same pattern of readings, namely sets of readings across the patient either as parallel sets or into the form of a fan. These are taken at a multitude of different angles (Fig. 8).

The system shown in Fig. 7a, translates across the body, each detector taking parallel sets of readings, at the same time as it rotates around the body. It could have 30 detectors and take 18 seconds to scan a picture.

In the second system (Fig. 7b) the sets of readings taken are in the form of a fan. It does not translate across the body but only rotates around it. This system usually has approximately 300-500 detectors but is faster and can take a picture in three seconds. The detectors in this picture have to be accurately stabilised.

In the third system (Fig. 7c) the detectors are assembled in a fixed circle and only the X-ray tube sweeps around the body, taking a fan of readings as it does so. This system requires 700- 1000 detectors and it also

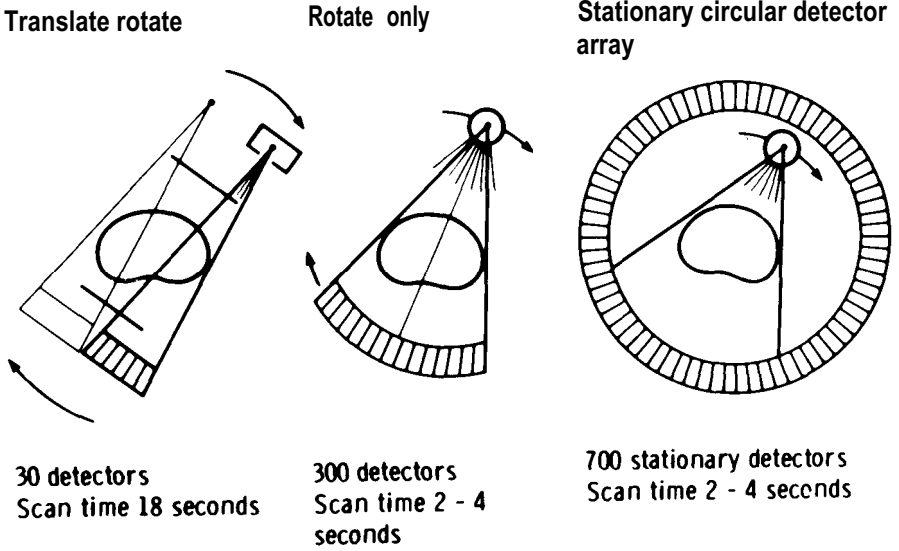


Fig. 7. Three different methods of scanning the patient.

takes a picture in three seconds. It is not necessary to stabilise detectors in this case.

The whole effect of this motion is to take approximately one million accurate absorption measurements through the body in the form of a number of sweeps across (or projections through) the body. These are taken at all angles through the slice, thus providing us with an enormous amount of information about the composition of the slice (Fig. 8). The

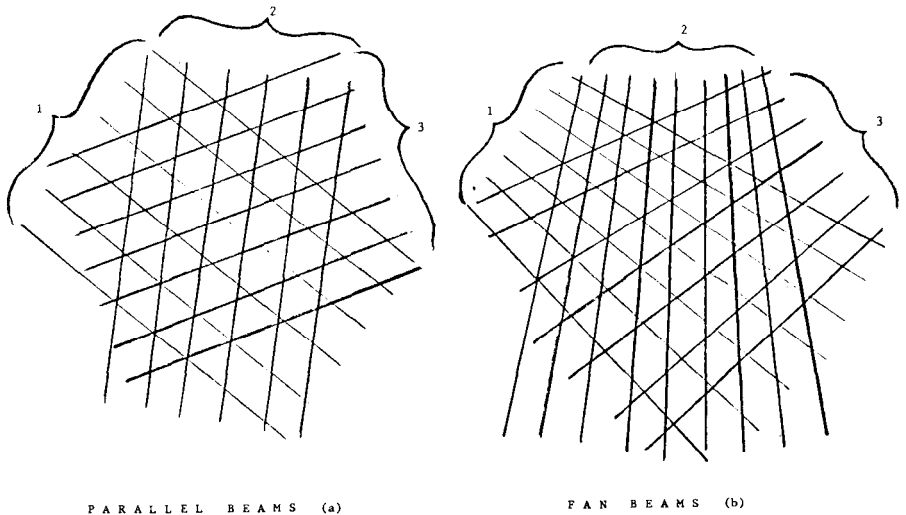


Fig. 8. Illustrating two arrangements of beams for scanning the patient. Usually there are more than 500 readings taken in one scan across the patient and the angles between scans advance approx. $1/3^\circ$.

readings from the detectors are fed into a computer which derives the absorption of the material in the path of the X-ray beam.

$$\text{Absorption} = \log \frac{\text{Intensity X-rays}}{\text{Detector reading}}$$

The absorption coefficients of the various substances within each square millimetre of the slice can be reconstructed from the readings (i.e. from approximately 1000 back projections each of some 500 readings). They can be displayed as grey tones on a picture or printed out to an accuracy of approx. 1/4 % with respect to water.

Originally the method of picture reconstruction, I like to think, was attained by common-sense practical steps. Most of the available mathematical methods at the time were of an idealised nature and rather impractical.

FACTORS WHICH GOVERN THE IMPROVED SENSITIVITY OF THE SYSTEM

Many will be aware of the conventional tomogram which also images a slice through the body. This is achieved by blurring the image of the material on the picture either side of the slice, by moving both the X-ray tube and photographic plate in opposite directions while the picture is being taken.

If one makes a comparison of CT with conventional tomography (Fig. 9a) it is clear that in the latter only a short path of the beam (1/10th of its length AR) passes through the slice to be viewed, collecting useful information. The other 9/10ths of the beam pass through material on either side of the slice, collecting unwanted information which will produce artefacts on the picture. Referring to Fig. 9b in computed tomography, the X-ray beam passes along the full length of the plane of the slice via its edges, and thus the measurements taken by it was 100 % relevant to that slice and that slice alone. They are not affected by the materials lying on either side of the section. The material inside the CT slice is seen as a mesh of variables, which is intersected by all the beam paths at a multitude of different angles (Fig. 10). As the absorption measured by each beam path is the sum of all the mesh squares it passes through, the solution of the mesh variables is possible. If the X-ray beam is confined to the slice and there are no external variables, the entire information potential of the X-ray beam is therefore used to the full.

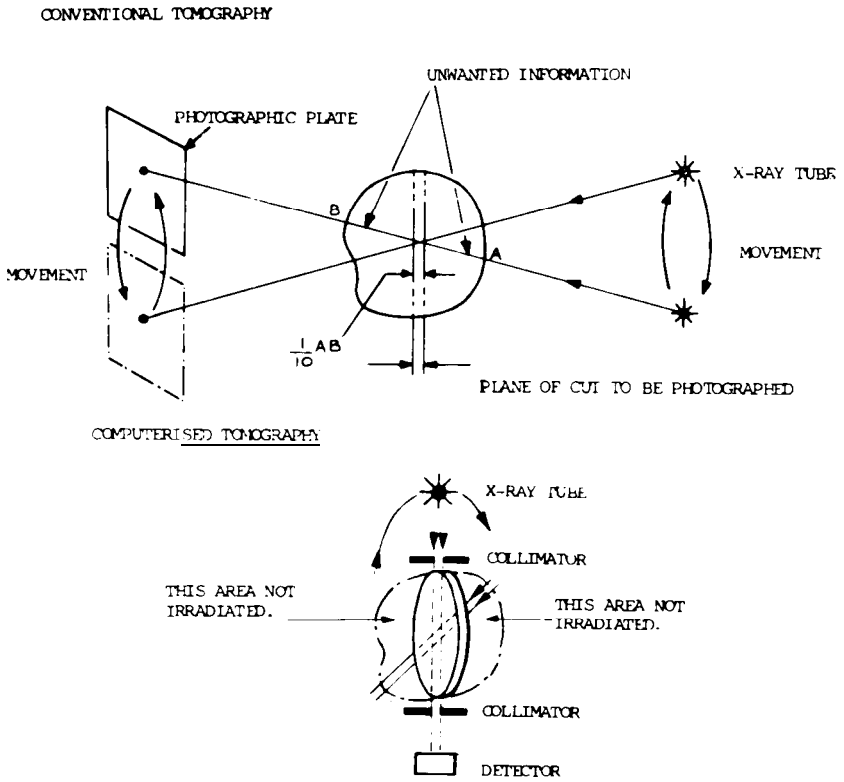


Fig. 9. Illustrating the improved efficiency of information collection when conventional tomography and CT are compared.

Note that in the case of CT the X-ray beam passes through only the material required to be viewed.

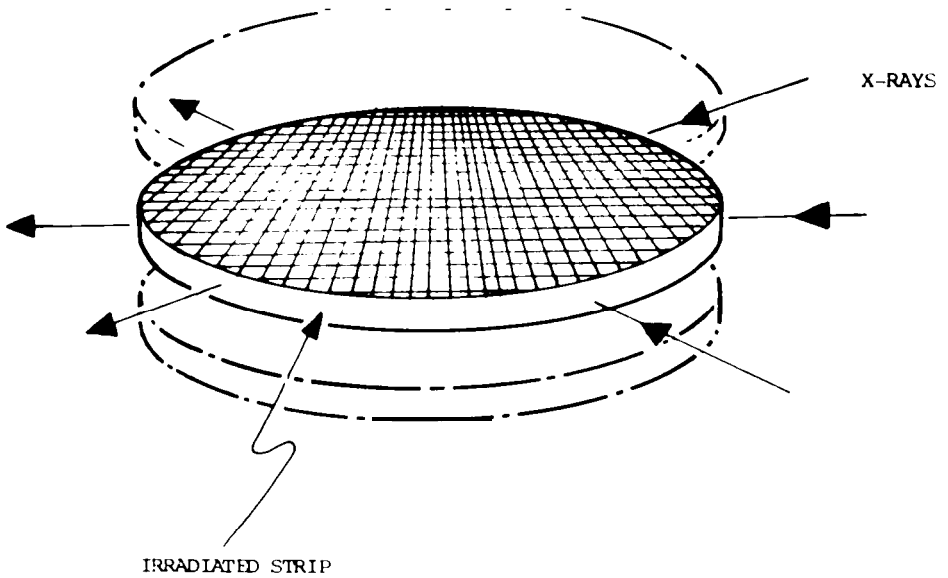


Fig. 10. Showing that the paths of the X-rays are confined to the slice and pass in a straight line through the imaginary elements of the mesh.

ACCURACY

The scale shown (Fig. 11) demonstrates the accuracy to which the absorption values can be ascertained on the picture. It shows the whole range of the machine, from air (-1000) at the bottom of the scale, to bone at the top of the scale, covering some 1 000 levels of absorption either side of water, which has been chosen to be zero at the centre. (This is done for convenience, as the absorption of water is close to that of tissue). To obtain readings which relate to true absorption, 1000 must be added to these readings, making air zero, and water would then be + 1000.

The range of tones between black and white seen on the picture can be restricted to a very small part of the scale. This "window" can be raised or lowered according to the absorption value of the material we wish to compare: for example, it must be raised to see the tissue of the heart or lowered to see detail within the air of the lung. The sensitivity can be increased by reducing the "window" width, where the absorption difference between the liver and other organs can be more clearly differentiated.

Let us now consider to what accuracy one can ascertain the absorption values of CT pictures. The clarity of the picture (Fig. 1), and hence the accuracy to which one can measure absorption values, is impaired by a

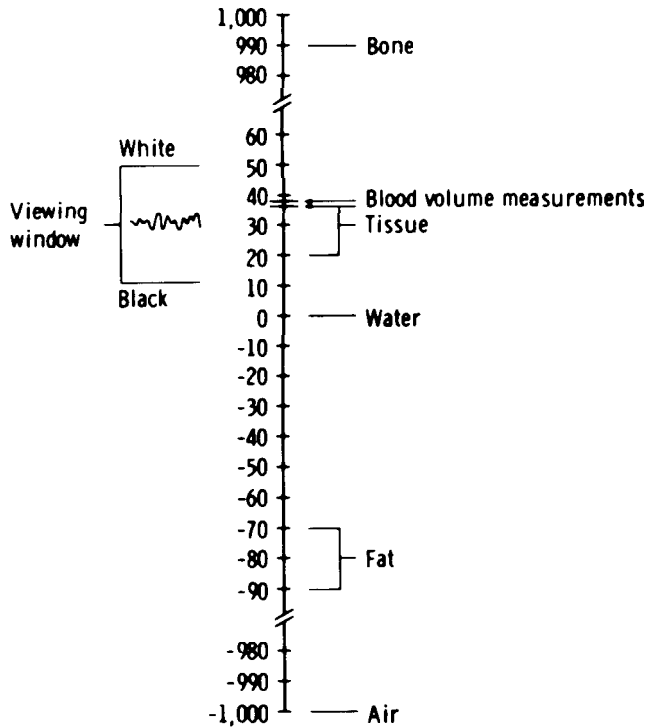


Fig. 11. Demonstrating the accuracy to which absorption values can be ascertained on the CT picture.

mottled appearance (or grain) which unfortunately is fundamental to the system. It is caused by there being a limited number of photons arriving at the detectors after penetrating the body. This results in a statistical spread between readings and is a situation that must be accepted. A typical spread would be a standard deviation of 1/2 % on tissue. (Displayed on a 320x320 matrix).

Present CT methods use very nearly all the available photon information that can be extracted from the X-ray beam, and we must therefore deduce that there is little room for further improvement in grain reduction. However, for industrial uses there are no X-ray dose constraints to be considered. The improvements to picture grain would be proportional to dose for a particular picture resolution.

THE RELATIONSHIP BETWEEN RESOLUTION AND PICTURE NOISE (OR GRAIN)

The study of picture noise reveals a rather important fact. The picture noise concentrates mainly at the high frequencies, there being very little noise at the lower frequencies. In other words, if we reduce the resolution of the picture by filtering out the higher frequency components, the remaining low frequencies will then be very small in amplitude, enabling the sensitivity of the machine to be increased without undue noise appearing on the picture. There is therefore a "trade off" between noise and resolution.

$$\text{Noise} \propto (\text{resolution})^{3/2}$$

During the development of the whole-body CT scanner, it became clear that the availability of an accurate cross-sectional picture of the body, the CT "slice", would have an important effect on the precision and implementation of radiotherapy treatment planning. For many years had existed an imbalance in the degree of precision of various aspects of the chain of events which make up a course of treatment by radiation therapy. For example, the linear accelerator, now regarded as the preferred treatment equipment for radical radiotherapy, can deliver X-ray beams with a precision of approximately ± 1.00 mm in terms of spatial "aiming". It can also achieve accuracies of the order of 1% in most of the other essential parameters of its operation. CT provides us with accurate measurements for aligning these beams.

In the past, radiation treatment planning has been a very lengthy procedure. Now with the aid of CT therapy planning computer programs, we can position the therapy beams automatically with precision in a few minutes. The system is linked to a CT diagnostic display console and a colour display monitor which shows the radiation isodose distributions overlaid on the basic CT scan itself (Fig. 12). The scan is used as the "patient input" to the system and areas of interest such as tumour, bone, lung or sensitive organs are outlined by an interactive light-pen.

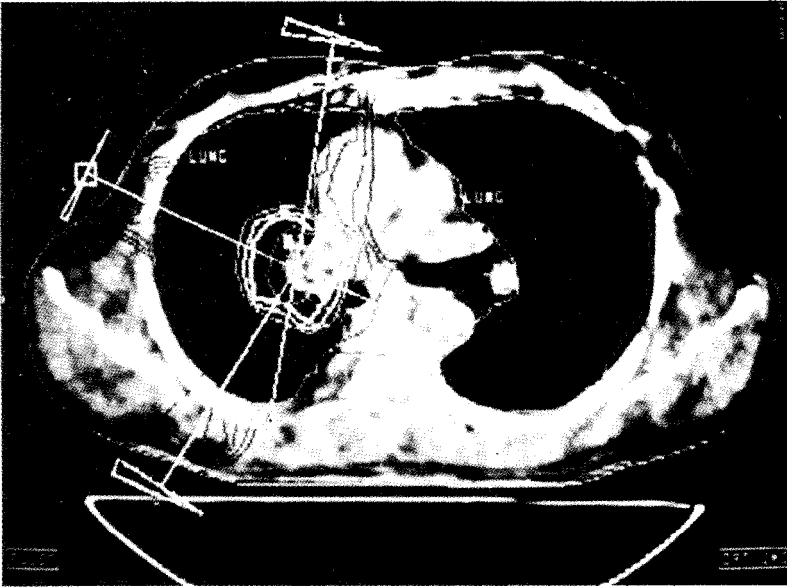


Fig. 12. Computer calculated isodose contours for therapy treatment.

Radiation beams and their computed isodose contours appear as overlays on the colour screen, and the lines of dose level are given different colours to aid the assessment of the plan.

The system uses the CT density numbers for the calculation of the effect of inhomogeneities in the path of radiation beams, although the absorption coefficients have to be corrected for the X-ray energy to be used in the actual treatment.

After areas to be irradiated and those to be avoided (such as the spine) have been outlined by means of a light pen, the position of the beam (shown Fig. 12 as T-shaped lines) can either be rotated around the tumour by means of the same light pen or the optimum position of the beams can be chosen automatically by program. This takes into account the CT numbers on the picture, the size and position of the tumour and the areas outlined by the operator which needs to be avoided. It automatically adjusts position and strength of the beams in order to choose the optimum contour of irradiation across the body.

Fig. 13 shows a series of pictures demonstrating the regression of a seminoma (a very radio-sensitive tumour). The radiation is applied at a low level while the tumour is large, but as the lesion regresses the smaller area is taken advantage of and larger doses are then applied. In this particular case the tumour was completely removed by accurate intense radiation.

These are, however, early days in the applications of CT to radiotherapy planning. It remains to be seen whether the increase in precision really results in a better five-year survival rate. In the opinion of many leading oncologists, evidence already points to such improvements, but it will be the next five years which provide the answers to these questions.

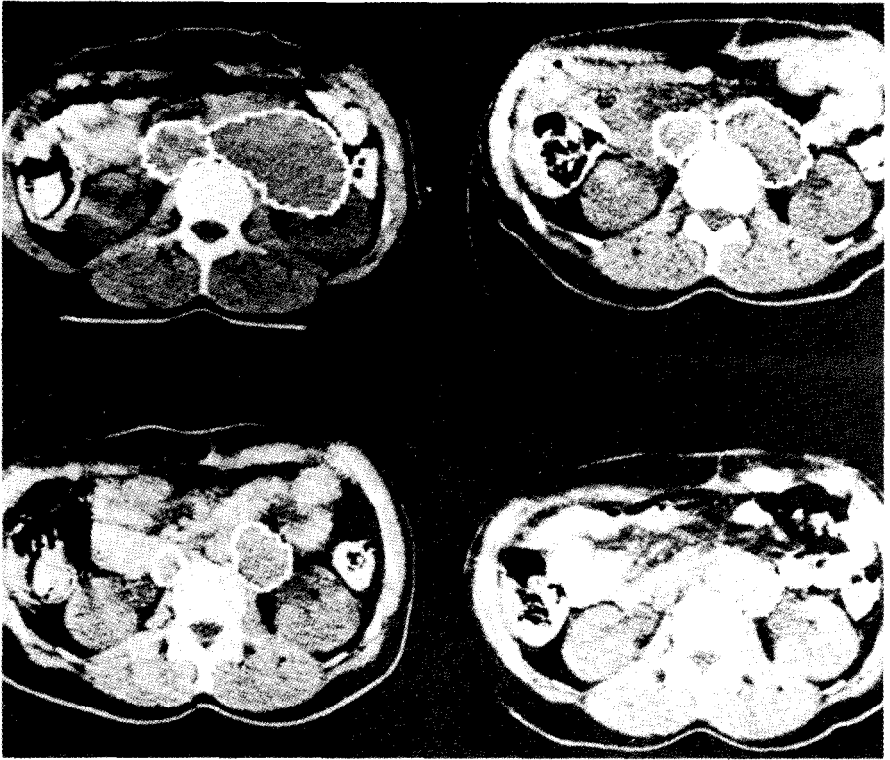


Fig. 13. Demonstrating the regression of a seminoma after four stages of therapy treatment.

WHAT IMPROVEMENTS SHOULD WE EXPECT TO SEE IN THE FUTURE?

Various attempts have been made to achieve useful pictures of the heart.

The time available for taking a picture of the heart is obviously longer than one heart beat. Some experiments were conducted some time ago using conventional CT machines but in which the traverse of the detectors was synchronised to the heart beat via an electro-cardiograph, passing over the heart in diastole (when the heart movement is at a minimum). Fig. 14 shows a picture from the experiment.

The heart chambers can be discerned by a little intravenous injected contrast media.

Another approach is being made at the Mayo clinic, Rochester, America, where a large machine is being constructed with 27 X-ray tubes designed to fire sequentially. It is hoped to take a sequence of pictures in a fraction of a second during one heart beat. However, the complexity and cost may rule out such a machine being used world-wide.

A further promising field may be the detection of the coronary arteries. It may be possible to detect these under special conditions of scanning.

Fig. 15 is an example of present high resolution CT scans of the skull using contrast media. It is more than likely that machines in the future will

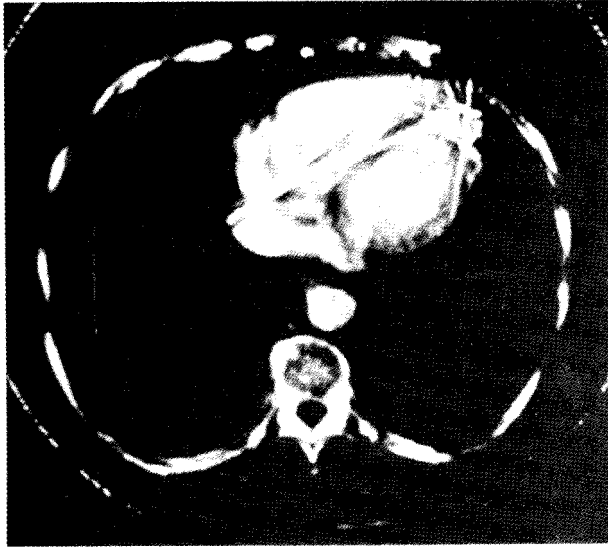


Fig. 14. Scanning of the heart with **detectors** synchronised to the heart-beat passing over the heart in diastole. (The line artefacts are streaks caused by the wire of a pace-maker).

be designed to provide considerably higher resolution than shown in this picture. Such machines would take up many of the present uses of conventional radiography but would do the job considerably better. They would have the added bonus of having more sensitive detectors than does film.

As all the information on the body is stored in three dimensions, it is possible therefore to display the object at any angle; this allows it to be examined by rotating it around on the screen. The views seen around the organ to be examined may reveal information that hitherto could have been missed, when it was viewed normally in one fixed plane, normal to the axis of the body.



Fig. 15 Higher resolution picture of the base of the skull.

NMR IMAGING

So far, it has been demonstrated that a picture can be reconstructed from X-ray sweeps forming sets of line integrals taken through the body at a multitude of different angles.

However, there are methods other than those using X-rays which are capable of measuring tissue variation, such as the use of protons, neutrons or nuclear magnetic resonance. These can be caused to generate sets of measurements of line integrals at different angles across the body, and in a similar manner a picture can be reconstructed from them.

Fig. 16 shows what is believed to be the first picture taken of a human head using Nuclear Magnetic Resonance. It was taken in 1978 by a team led by Dr. Hugh Clow and Dr. Ian Young of EMI Central Research Laboratories, England. Since then considerable improvements have been made to both head and body pictures and progress is continuing.

The principle of NMR Spectroscopy was well known in the 1960's and was first suggested for imaging by Lauterbur in 1973. It is a new and quite different form of imaging, in which the radio frequencies emitted by the hydrogen nucleus can be measured after they have been excited in a particular way by radio frequency. The nucleus of special interest is the proton of water molecules within the body.

I would now like to compare the merits of CT with those of NMR. Before doing this I must first describe the principles on which NMR operates.

When hydrogen protons are placed in a magnetic field they will precess (or "wobble") around the field direction just as a spinning top precesses around its vertical gravitational field. This precession occurs at a definite frequency, known as the Larmor frequency, and is proportional to the magnetic field intensity.

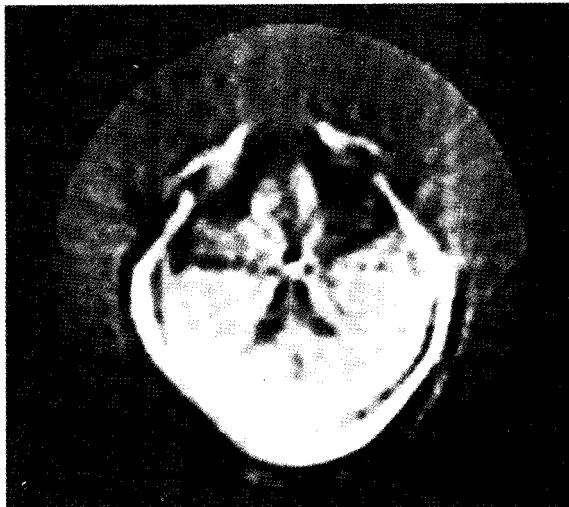


Fig. 16. Picture taken in 1978 of the human head using Nuclear Magnetic Resonance.

The usual NMR procedure for imaging is to apply a strong magnetic field along the body to be studied. (Figs. 17a & 17b). After a short period of time, the nuclei will align with their magnetic movements along the field. A radio frequency tuned to the precession frequency of the hydrogen nucleus is then applied at right angles to the main field by means of a set of coils at the side of the body (Fig. 17c). This causes some of the hydrogen nuclei to precess—all keeping in step. After the radio frequency field has been switched off, the nuclei will continue to precess in phase, generating a similar radio frequency which can be picked up in receiver coils placed at the side of the body (Fig. 17d); these signals detect the water content of the body. It will take some time for the precession to die away, as the nuclei

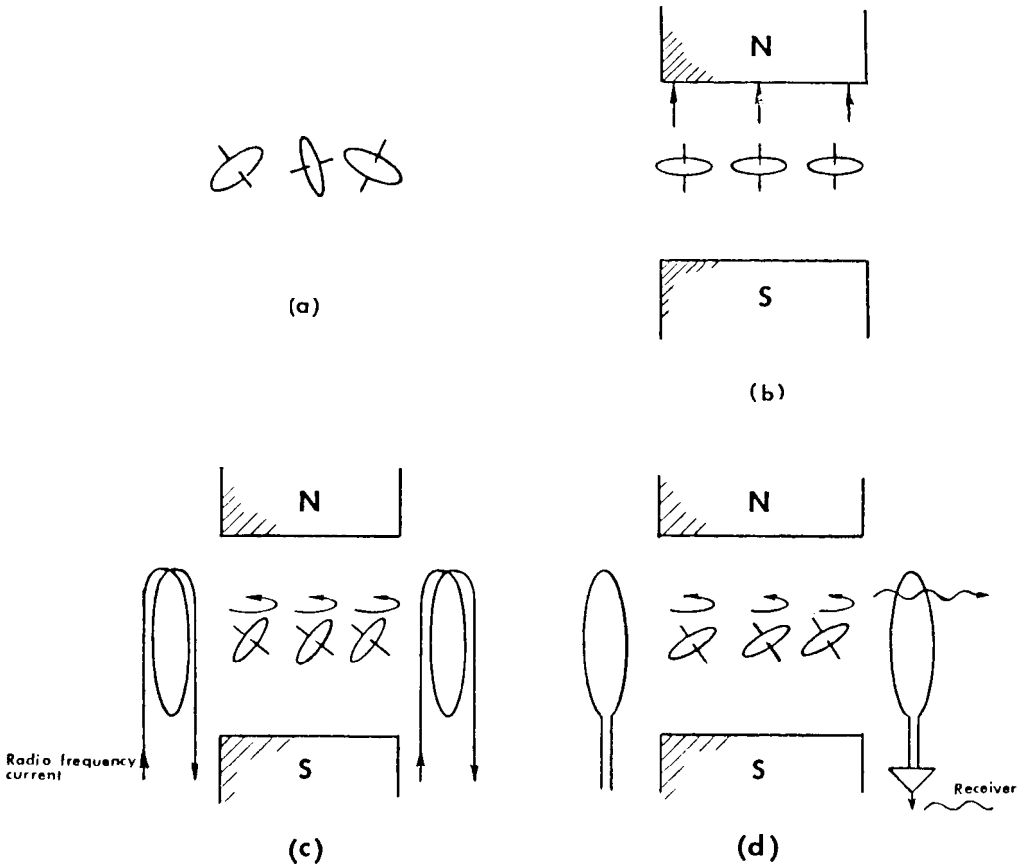


Fig. 17 a) Representation of nucleus without magnetic field applied.
 b) Nucleus with field applied.
 c) Radio frequency field applied.
 d) Radio frequency switched off – receiver on.

again realign themselves with the magnetic field. The measurement of this time is important as it gives some information about the nature of the tissue under investigation. It approximates to an exponential decay of the order of "tenths of a second". (It is known as T_1 or the spin lattice relaxation time).

METHOD OF PRODUCING AN NMR PICTURE

The procedures above refer only to a method of tissue detection. In order to produce a picture which maps the difference of tissue within the body it is necessary to independently measure small volumes of material across it. In NMR imaging this is done by applying a small magnetic field gradient across the body in addition to the main uniform field. The frequency of the nuclei, being dependent upon the magnetic field, will resonate at different frequencies across the body according to the magnitude of the field gradient present (Fig. 18). In one method of NMR imaging, the frequencies received in the coil can be separated (by Fourier analysis) and the whole spectrum of frequencies will represent a series of line integrals across the body, each frequency representing the amount of hydrogen nuclei resonating along that particular line. As a comparison with CT this is equivalent to one X-ray sweep across the body at a particular angle.

A number of "sweeps" can be repeated at different angles by rotating the gradient field, and sufficient data can be built up to reconstruct a picture in similar way to that in which a CT picture is constructed.

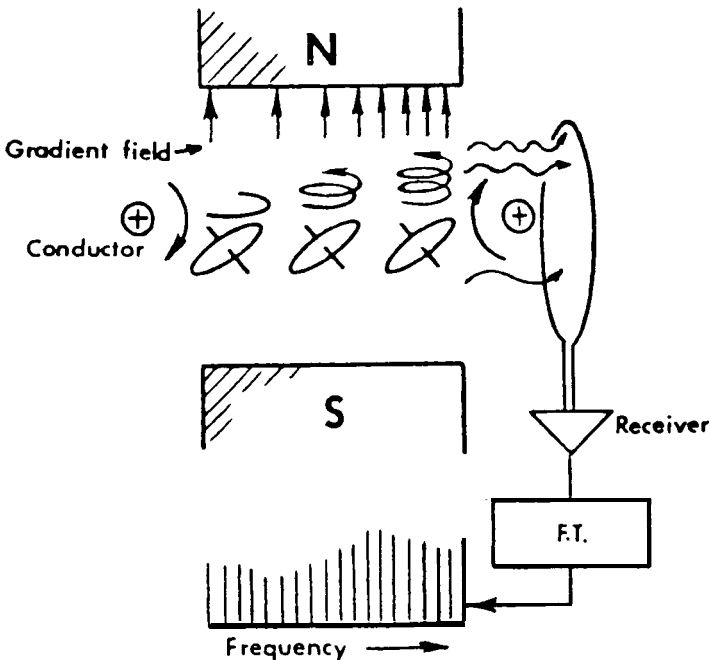


Fig. 18. Field gradient applied.

COMPARISONS OF NMR WITH CT

It is early to predict with certainty the levels of accuracy of a future NMR system, but one could speculate in the following way to illustrate its possible advantages.

Fig. 19a illustrates approximately the number of levels about "noise" one would expect CT to be able to discriminate in tissue when an average scan is taken.

It detects mainly one variable - density. It also detects a minor one - atomic number, which relies upon the photo-electric effect for separation. The discrimination of iodine from tissue by subtraction of two pictures at different X-ray energies is the most used example.

In comparison, Fig. 19b shows the variables one would expect to detect in NMR. It may be possible to separate more than one decay time (the figure indicates that these may be three). If the sensitivity above noise is such that it is possible to select three levels in each of the three decay variables, there should be 27 possible permutations to characterise the tissue to be displayed as against the nine levels of tissue discrimination usually displayed on CT picture (Fig. 19a). This illustrates the major advantage of NMR but is only speculative.

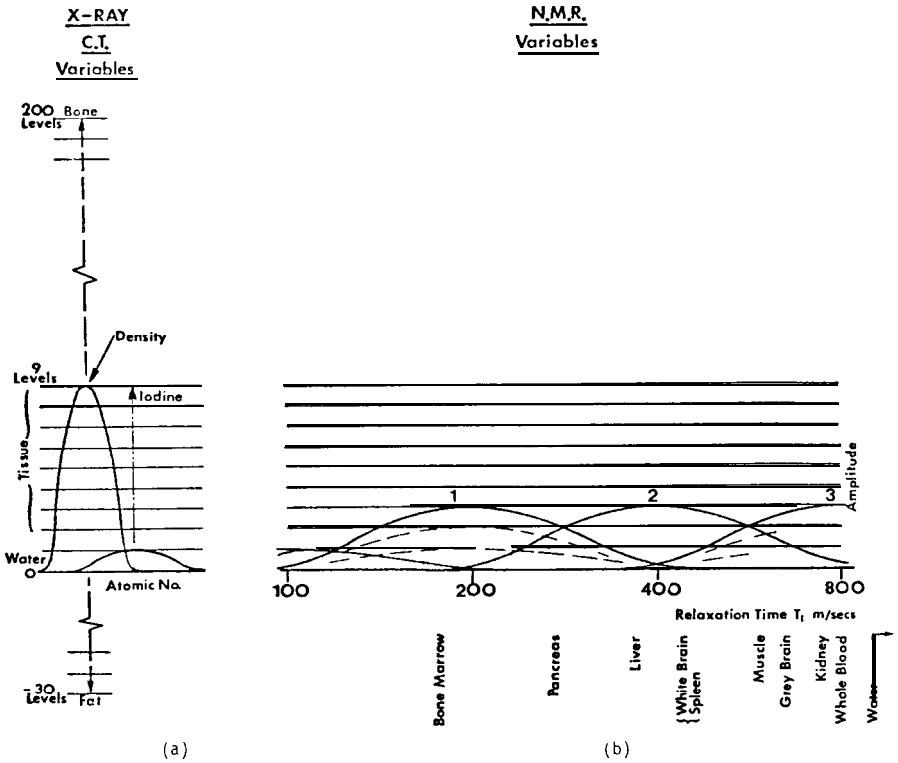


Fig. 19. Comparison between CT and NMR - showing the variables one would expect to find in tissue in both systems.

However, CT has other advantages:

Fat in CT is very easily discriminated with respect to tissue (over 30 levels). For comparison, it is poorly discriminated in NMR.

So far there are indications that the picture resolution on CT is considerably better than in NMR, and a picture can be scanned in a considerably shorter time (2 to 3 sets.). With NMR it is usual to scan the patient over at least a minute or more to collect sufficient data for good tissue discrimination. It must be remembered that each NMR, T_1 measurement is very time consuming, as long relaxation times (tenths of a second) need to be measured, and a few hundred sets of these readings are required to reconstruct one picture. On the other hand, as far as is known, NMR is non-invasive and the long periods of scanning time that the patient may be subjected to should do him no harm.

However, a systems design of NMR has not yet stabilised. There still exist many different avenues which may in the future reveal improvements in both speed and sensitivity.

Despite the fact that it is not yet clearly known what the parameters are that it is measuring, it is felt that NMR has great possibilities for indicating more about the chemistry of the tissue being selected. It is a technique which could image water concentration, its impurities and its binding to macro-molecules in or between the cells of the body. It remains to be seen how this extra information can help diagnoses.

Work on NMR is still in its early stages and has a long way to go. At the present time, the two techniques of CT and NMR should perhaps be seen not as potential competitors but rather as complementary techniques that can exist side by side; NMR providing us with information on the chemical composition of the tissue, and CT providing us with a means of visualising its position and shape.

May I thank all those at EM1 Research Laboratories who have helped me so much in the past in my work - especially Steven Bates who worked on some of the early experiments.

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