原著

Application of T_1 data to diagnosis using the Aberdeen NMR imaging system

Hiroo Ikehira (Department of Radiology Yamanashi University School of Medicine)
Francis W. Smith (Department of Nuclear Medicine Aberdeen Royal Infirmary)

要旨

During the 2.5 years from August 1980, over 700 patients and healthy volunteers have been examined using the Nuclear Magnetic Resonance (N.M.R.) imager, designed and built at the University of Aberdeen[1~4]. The design of the system has been well described in the literature[1~4] and it is not proposed to describe it in detail here.

The experience gained in examining a large spectrum of desease in a population of patients referred for N.M.R. imaging will be discussed. Our experience has shown that N.M.R. images displayed as axial sections appear very similar to X-Ray CT images but that the T_1 data contained in them is very different. T_1 or proton spin-lattice relaxation time being a direct measure of the response of hydrogen protons to the applied radiofrequency gives unique information about the hydrogen and water within living body tissues. Information which when applied to diagnosis opens the way to the study of not only anatomy but also physiology and pathophysiology. Since the technique dose not use ionising radiation and no reports of any side effect has been reported, we believe that this is a safe imaging technique which will replace X-Ray CT and ultra-saund in many aspects of diagnosis.

1. N. M. R. method-Aberdeen

This method is as already described in the literature[1~4]. a vertical static magnetic field is used. This static field of 0.04 Tesla (400G) which is a low field compared to other systems, gives a proton N. M. R. frequency of 1.7 MHz[1,2,4]. As other reports from many trial teams show, this grade of magnetic field is very safe[9].

Three gradient magnetic fields are used[1~2]. These are Gx, Gy, Gz, Gx is a gradient along a transvers axis of the body, by this gradient we can determine the transvers position of the sampling data. Gy is a gradient along the body, it determines the slice plane and by chenging the gradient degree the slice thickness is decided. And Gz is a gradient along vertical axis it induces spinwarp in proton spin along z axis. To calculate the data of T_1, proton density, and D, set of two RF pulses are obtained. First is the 90° pulse and this gives the strength of F. I. D. (Free Induction Decay), called S_1 data, and second is the A. F. P. (Adiabatic Fast Passage), 180° pulse, and after τ seconds another 90° pulse. By this technique the S_2 data is obtained. With these two data, S_1 and S_2, these data of the T_1 time, proton density and D are calculated.

One set takes two seconds, and we need 128 sets, so it takes 256 seconds (about 4 minuits) to get one slice image. The 128×128 samples give a 256×256 display. Slice thickness is 16 mm for the body and 12mm for the head.

In this way the data of T_1, proton density and D are obtained. These data are each very useful depending on the case. Proton density images being most useful where large differences in proton density are present, such as between bone and soft tissue, and are used to demonstrate the normal bone anatomy of the skull and pelvis. The value of T_1 data will now be discussed in detail.

2. T_1 theory

It is most important to understand about T_1 theory when deciding the differencial diagnosis.

T_1 data are obtained by the method described before from S_1 and S_2 data. This relaxation time is called a spin-lattice relaxation time or longitudinal relaxation time. T_1 time is dependent on temperature, ionsolution density, solution viscosity, and strength of the static magnetic field etc. The pattern of change is different as the kind of solution. So the T_1 time of the proton indicates the strength of combination of the proton with another nucleus.

As in this description, the increase of T_1 time meens that the binding of the proton with another nucleus becomes slack. The in creased T_1 time indicates a free water increases in the tissue's water concentration, because most protons of the human body are as a hydrogen's nuclei. So when changes like these happen in the body, they change the T_1 value, so the lesion can be easily detected, and it is possible to decide the qualitative differential diagnosis, because the every normal tissue's T_1 value is in very narrow bounds. Fortunately in the N. M. R.system, the liquid matter like blood becomes a enhancemental substance, so we do not need an enhancement drug for ve-

ssel study. Also each organ has an individual T_1 value, so we can easily decide which organ it is for some kinds of organ, for example liver, spleen, kidney, gallbladder, aorta etc. If we have some knowledge about the changing of T_1 time and have enough experience about the N.M.R. clinical images, the technique of N.M.R. imaging using T_1 data would be the noninvasive best method as a qualitative image diagnosis.

Imaging Pulse Sequence[1,2,8]

S_1: A.F.P. (−) 90° pulse (+) signal

S_2: A.F.P. (+) 90° pulse (+) signal

τ: interval between A.F.P. and 90° pulse (sec)

T_1: Spin-lattice relaxation time (sec)

$$T_1=\frac{-\tau}{\ln\left(\frac{S_1-S_2}{2S_1}\right)}$$

3. Discussion about T_1 table of Mark-1

Table 1 is a normal tissue's T_1 table, and table 2 is a T_1 table for some desease. Each normal organ has its own T_1 value as the table 1, and the value is in very narrow bounds. For example if you compare normal liver T_1 value from table 2, the diffrentiation of T_1 value with eachother should be easily found. So you can understand clearly the usefulness of T_1 image for the differential diagnosis about these kinds of disease,that is hepatitis, cirrhosis or hepatoma or metastatic liver disease etc[5]. Nevertheless as indicated in the table the T_1 value of normal liver is very similar the T_1 value of fat tissue, the liver margin can be easily obtaind. Bacause in the liver there are many bile ducts and portal veins whose T_1 value are higher than the T_1 value of liver.

Table 1 (m sec) mean value$\pm\sigma$ n−1

Fat	139±6.8
Liver	146±9.0
Bone marrow	168±24.9
Muscle	189±12.6
Pancreas	215±19.8
Vertebra	218±24.8
Brain white matter	234±11.6
Brain gray matter	301±41.7
Spinal cord	264±29.0
Spleen	277±19.7
Kidney	324±30.6
Portal vein	356±88.3
IVC	418±79.6
Aorta	438±78.5
Bile	692±146

Table 2

Liposarcoma	150±4.0
Cirrhosis	178±8.3
Hepatitis	191±4.3
Hepatoma or metastasis	246±47.6
Pancreatitis	302±2.8
Renal cyst	800±150
Renal carcinoma	400±100

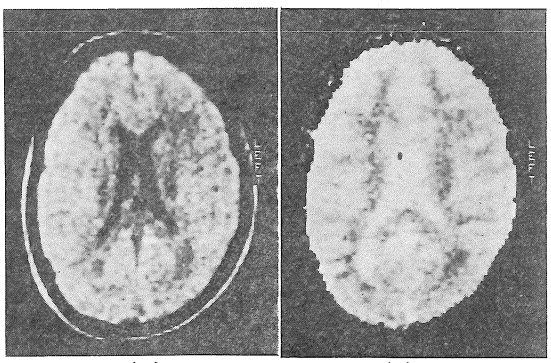
Table 3 Patients and volunteers examined from August 1980-September 1982

Healthy volunteers	120
Brain	129
Head and Neck	58
Thorax	50
Liver	153
Pancreas	41
Renal	44
Adrenal	10
Pelvis	70
Musculo-Skeletal	42
Total	717

4. The Brain

During the preliminary study of N.M.R. imaging at the Aberdeen Royal Infirmary Scotland, 717 patients and healthy volunteers have been imaged. As far as has been possible the N.M.R. imager have been compared with all other available techniques X-Ray, ultrasound, nuclear medicine and X-Ray CT. Furthermore tissue histology either by biopsy or at the time of surgical operation has been obtained.

In the examination of the most striking feature in the clarity with which the gray and white matter are differentiated. Because of the different amounts of myelin in gray and white matter so the T_1 values are different (Table 1). White matter is very clearly seen, suggesting that N.M.R. will become an ideal method for studying white matter disease (Fig. 1). A pilot study performed in our laboratory has shown a significant change in the T_1 of white matter in brains of chronic alcoholic patients undergoing treatment[10]. This leads us to believe that the study of such diseases as schizophrenia, mania etc. many benefit from N.M.R. research and a programe is currently in operation studying these psychiatric diseases.



(A) (B)

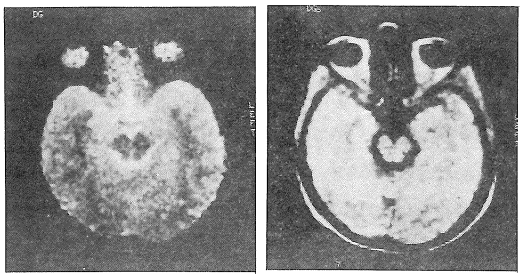
Fig. 1 A) Proton density, B) T_1 image through the cerebral cortex, gray and white matter are demonstrated in B, whilst a plaque of multiple sclerosis demyelination is seen in relation to the posterior horn of the right lateral ventricle, in both A and B.

Space occuping lesions of the cerebral cortex are clearly seen. Tumors tending to have a larger than normal T_1 than either Gray or White matter (375-425 msec.). Any surrounding oedema appearing as a very much larger T_1 (500-700 msec).

In vessel occlusion leading to cerebral infarct the area is again clearly seen. Further research into the chenging T_1 values around the periphery of infarcts is suggested as a method for further understunding cerebro vascular disease and for monitering various forms of therapy.

In multiple sclerosis the number and size of lesions is more clearly seen with N.M.R. than with X-Ray CT[11]. This is because of the superior contrast resolution obtained with N.M.R. (Fig. 1). Again larger trials are necessary to fully evaluate the role of N.M.R. in the management of this disease.

N.M.R. is superior to X-Ray CT for the demonstration of the posterior fossa. This is bacause no artifact occars from bone. It is therefore likely that it will replace CT in the investigation of cerebellar and brain stem lesions (Fig. 2). Four patients with brain stem pathology who had, had previous "normal" CT scans have been examined by N.M.R.. In are a small brain stem haemorage about 0.5 cm in diameter was demonstrated and in the other three the presence of metastatic tumor was clearly seen.



(A) (B)

Fig. 2 A) Proton density, B) T_1 image demonstrating the normal anatomy of the brain-stem and orbits.

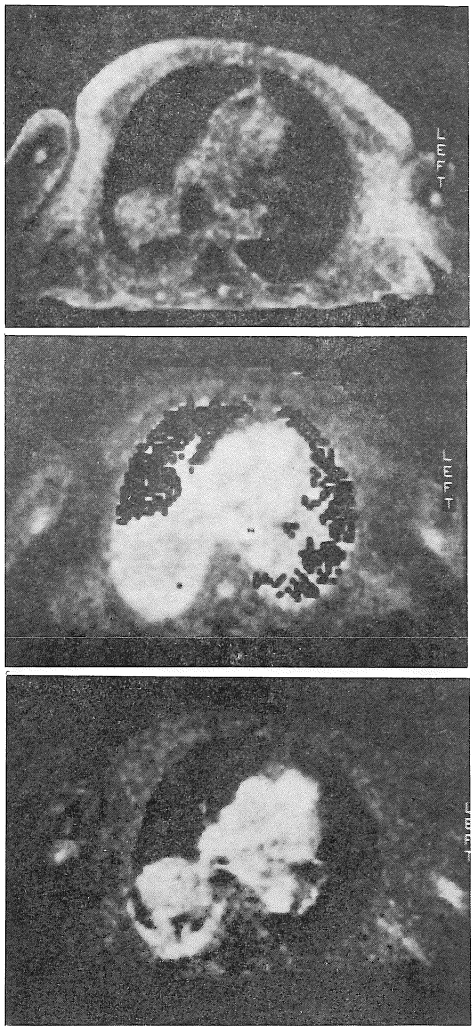
5. Head and Neck

Fifty eight patients with head or neck pathology have been examined. Twenty three were investigated for enlarged thyroid glands. By measuring T_1 it has been possible to differentiate benign goitre where the T_1 has been in the normal range 150–175 msec from hyperthyroidism where the T_1 has been in the range 190–250 msec. At the same time nodula goitre (250–400 msec) carcinoma (250–300 msec) and adenoma (225–275 msec) have been excluded. Whilst there is some overlap in the T_1 values of the different conditions, N.M.R. is able to exclude simple endocrine dysfunction and give a fairly accurate guide as to the cause of any space occuping lesion.

Thirty five patients with tumors of either tongue, tonsil, paranasal sinus, larynx or lymph nodes have been examined. In all by careful measurement of T_1 of the tumor and of any enlarged nodes the extent of the tumor and of nodal involvement has been easily achieved. In all the cases examined the N.M.R. findings were at least as good as those found an CT and in six the full extent of the tumor invasion only demonstrated by N.M.R.. All the results were our found at operation.

6. Thorax

The most obvious advantage to N.M.R.



(A)

(B)

(C)

Fig. 3 A) Proton density, B) T_1. C) D images of a large bronchogenic carcinoma in the pulmonary vein and cardiac chambers are clearly seen in B and C without the use of any additional contrast media.

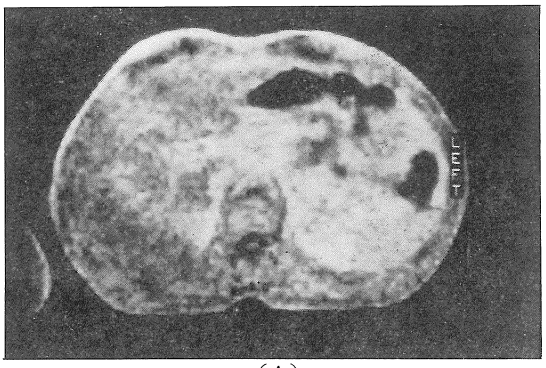
imaging in the chest is the ability to visualize the major blood vessels and cardiac chambers without the addition of any contrast agent (fig. 3).

Despite cardiac and respiratory movement the heart and major vessels are clearly seen. Similarly pneumonic consolidation, pulmonary embolic and pleural effusions are easily demonstrated. Small pulmonary tumors less than 1 cm in diameter are not seen, presumably due to respiratory motion but large pulmonary tumors are clearly seen. Preliminary comparison with X-Ray CT indicates that N. M. R. is more sensitive in the demonstration of hilar and mediastinal tumor and that its full extent can be seen using N. M. R..

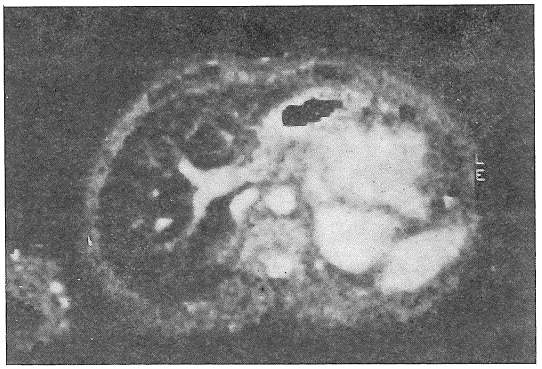
7. Liver

Table 4 outlines the breadth of pathology examined in the liver during this preliminar study. The normal liver has a T_1 which falls in the narrow rainge 130-155 msec (Fig. 4). When infiltrated with fat or a paramagnetic substance such as iron or copper the T_1 is shorter than 130 msec but when infiltrated with inflammatory cells, such as in cirrhosis or hepatitis the T_1 falls between 160 and 200 msec. Tumors, both primary and secondary malignant areas have T_1 values in the range 200-300 msec, whilst there is overlap in the T_1 values of all malignant tumors, their shape, size and position make them easy to differentiate from cirrhosis(Fig. 1). Benign tumors such as hemangioma are easily diagnosed by measurment of their T_1 which is the same as that of blood[12].

In the investigation of jaundice, N.M.R. will cleary demonstrate the presence or absence



(A)



(B)

Fig. 4 A) Proton density, B) T_1 image of the normal upper abdomen. The major structures are clearly seen in both images.

of dilated bile ducts. By simple measurement of T_1 dilated bile ducts can be differentiated from the portal vein (Table 1). The cause of obstruction in obstructive jundice is clearly demonstrated if the cause is a tumor either pancreatic, hepatic or nodal but as yet no biliary calculus has been domonstrated on N. M. R., T_1 or proton density images. In cases of cholecystitis, the gallbladder may be enlarged and is surrounded by a halo of larger T_1 due to the presence of oedema and inflammation. The larger the T_1 the more inflammation present[13].

Table 4 Patients studied with suspected liver disease

Normal	23
Hepatoma	4
Cholangio carcinoma	3
Metastatic tumor	40
Liposarcoma	2
Carcinoid	1
Haemangioma	2
Cystic tumor	2
Cirrhosis	24
Hepatitis	5
Jaundice	29
Other	18
Total	153

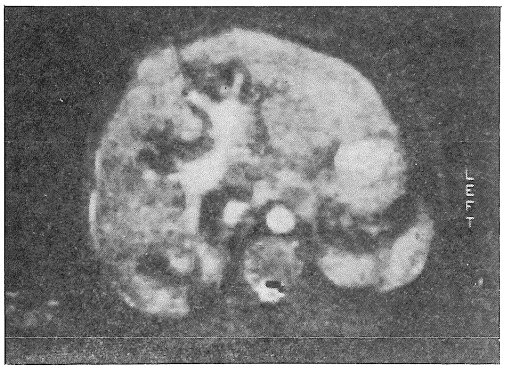


Fig. 5 T_1 image of a liver infiltrated with secondary tumor from a primary carcinoma of colon.

Six patients with hepatic metastases have been imaged or a number of occasions during their treatment with chemotherapy, changes in the T_1 of the tumors has been noted, the significance of which is not yet fully understood and more work is being performed in this area.

8. Pancreas

The normal pancreas is not always clearly visualized, but when inflammated as in pancreatitis it appears as an organ of large T_1 (Table 2). Tumors of the pancreas bacause of their larger than normal T_1 are clearly demonstrated[7]. The relationship of the pancreas to the duodenum, superior mesenteric artery and renal veins is well known. Since all there structures are clearly demonstrated on T_1 images the location of the normal pancreas is never in doubt.

9. Genito-urinary tract

The kidneys because of their characteristic T_1 are clearly seen (Table 1, Fig. 6). The renal pelvis when filled with urine is similarly well seen bacause of the long T_1 of urine which is much larger than that clearly visualized as would be expected. Differentiation of tumor from cyst being accomplished by T_1 measurement (Table 2, Fig. 7). Preliminary reports have demonstrated the use of N.M.R. in the demonstration of a wide range of renal pathologies[6,14] in both normally situated kidneys

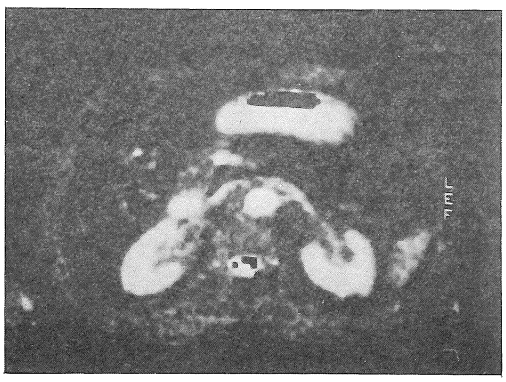


Fig. 6 T_1 image of a normal abdomen at the level of the renal arteries, demonstrating the kidneys, renal arteries, stamach and duodenum.

and renal transplants.

Two cases of acute tubular necrosis have been studied. In both the kidneys were enlarged, swollen and had a T_1 in excess of 450 msec. Since no contrast medium was required to make the diagnosis and to differentiate renal from post renal, renal failure and no ionising radiation was used we believe that N.M.R. is the method of choice for the investigation of acute renal failure.

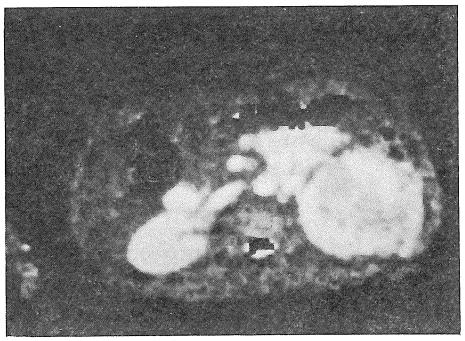
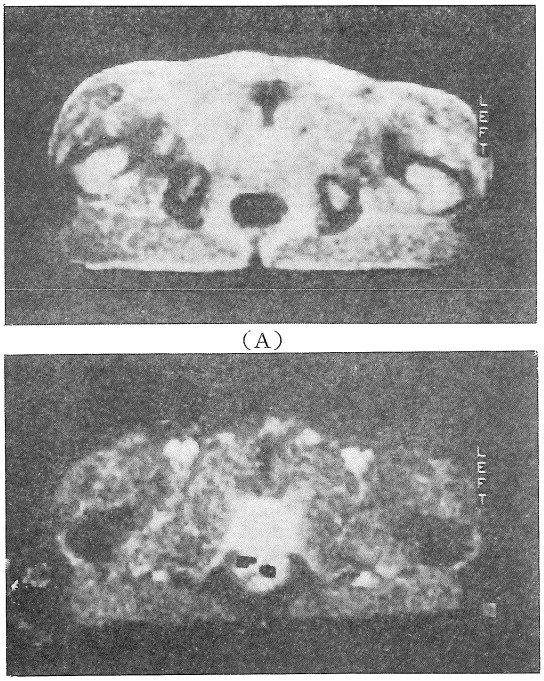


Fig. 7 T_1 image demonstrating a carcinoma in the lower pole of left kidney.

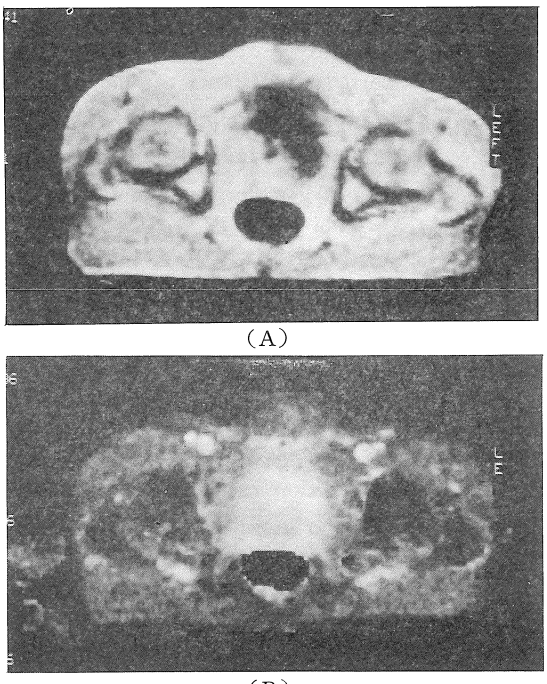
In the lower urinary tract tumors of the bladder are easily staged. Extension of the tumor through the bladder wall are more easily seen on N.M.R. T_1 images than on X-Ray CT. An ongoing study is evaluating the role of N.M.R. in demonstrating lymphatic spread from bladder tumors, also from the female repro-



(A)

(B)

Fig. 8



(A)

(B)

Fig. 9

Fig. 8 and 9 A) Proton density, B) T_1 images of a male pelvis. Proton density images show normal bone anatomy clearly. T_1 images show large carcinoma of the prostate extending up into the bladder.

ductive tract and the prostate in men.

Images of the pelvis made using proton density data give a very clear display of both the bone anatomy and the bladder when filled with urine (Fig. 8, 9). The T_1 images give the vascular anatomy and are used to assess the pelvic organs. The normal prostate and the benignly hypertrophied prostate have T_1 values between 240–290 msec, whilst carcinoma has T_1 values between 300–400 msec. Folse positives for carcinoma unfortunately occur in patients with prostatitis.

10. Musculo skeletal

Originally it was believed that N.M.R. would be of little value in the study of bone. However experience is showing that by the use of both proton density images to show the bone cortex and the T_1 images to demonstrate changes from normal, a large amount of information about bone can be obtained (Fig. 8, 9).

Metastases in bone cause an irregularity in the appearance of bone on proton density images and a significant lengthening of T_1. Unfortunately the appearances and T_1 measurements in osteomyelitis and metastatic disease are similar, so no distinction between the two may be made. Never the less the potential of N.M.R. in examining bone is clearly present.

Six patients with rheumatoid arthritis effecting the knee joints have been studied. Each was imaged before and after treatment with an intra articular steroid analogue. In all than a significantly long T_1 of the joint synovium was seen prior to treatment, 48 hours after treatment the anti-inflammatory drug had reduced the T_1 of the treated joint by over 75 %. Thus demonstrating visually the response to treatment, opening the way to further study of different medicines in different organ systems. Indicating that N.M.R. may prove to be a safe method for the monitoring of a wide range of treatments.

A similar observation has been made when muscle has been studied at rest and then after 10 minuites of severe exercise. The quadriceps muscles of a volunteer (F. W. Smith) were imaged before and after numering up and down stairs for 10 minuites. The T_1 at rest was in the range 180–185 msec, whilst that after exercise was 210–215 msec. Whether thus rise in T_1 was due to increased blood flow, capillary permeability or to a build up of lactic acid is not clear. What is clear is that N.M.R. imaging provides a safe method for visualising physiological changes and will provide a method for physiologic investigation.

11. Discussion

In the study of over 700 patients and volunteers no reaction or side effect from the magnetic field, changing electro-magnetic gradients or radio frequency pulse has been observed, especially no cardiac arrhythmia or epileptic fit has been precipitated. The only patients excluded from the study have been those who had cardiac pacemakers *in-situ*. In all the causes examined N.M.R. was found to be at least as sensitive as the best other diagnosis test and in most it provided more information than any other one investigation. Because of the unique native of the T_1 information gained, we believe that when more is understood

about the meaning of T_1 than large advances in both diagnosis and in the monitoring of treatment will be possible using N. M. R. imaging.

The work described in this paper was performed on a very simple prototype imager. As the technique is further developed both in Japan and in Europe, resolution will improve and the technique will become even more accurate. We believe that in radiological terms we are at the same stage as radiology was in the 1890s, shortly after Roentgen's discovery of X-Rays. The next 10 years may well see a revolution in diagnostic imaging lead by N. M. R..

References

1) Edelstein WA, Hutchison JMS, Johnson G, Redpath T: Spin-warp NMR imaging and applications to whole body imaging. Phys. Med. Biol. 1980; 25: 751-756
2) Hatchison JMS, Edelstein WA, Johnson G: A whole-body NMR imaging machine. J. Phys. E. Sci. Instrum. 1980; 13: 947-955
3) Smith FW, Mallard JR: Whole body nuclear magnetic resonance tomographic imaging. J. Med. Imagings. 1982; 2, special issue: 1-23
4) Endo M: Recent trends on NMR imaging in U. K. and U. S. A.. J. NMR Med. 1981; 1, 1: 34-39
5) Smith FW, Mallard JR, Reid A, Hutchison JM: Nuclear magnetic resonance tomographic imaging in liver disease. Lancet 1981; 8227: 963-966
6) Smith FW, Hutchison JMS, Mallard JR: Renal cyst or tumor differentiation by whole body nuclear magnetic resonance imaging. Diag. Imaging 1981; 50, 2: 61-65
7) Smith FW, Reid A, Hutchison JMS, Mallard JR: Nuclear magnetic resonance imaging of the pancreas. Radiology 1982; 142: 677-680
8) Redpath T: Calibration of the Aberdeen NMR image for proton spin-lattice relaxation time measurements in vivo. Phys. Med. Biol. 1982; 27, 8: 1057-1065
9) Nakagawa M: Magnetism and medicine. J. NMR Med. 1982; 1, 1: 79-85
10) Besson JAO, Glen AIA, Foreman EI, Mac Donald A, Smith FW, Hutchison JMS, Mallard JR, Ashcroft GW: Nuclear magnetic resonance observation in alcoholic cerebral disorder and the role of vasopressin. Lancet 1981; 2: 923-924
11) Young IR, Hall AS, Pallis CA, Legg NJ, Bydder GA, Steiner RE: Nuclear magnetic resonance imaging of the brain in multiple sclerosis. Lancet 1981; 2: 1063-1066
12) Smith FW, Mallard JR, Hutchison JMS, Reid A, Johnson G, Redpath TW, Selbie RD: Clinical application of N. M. R.. Lancet 1981; 1: 78-79
13) Pollet JE, Smith FW, Mallard Jr, Ah-See AK, Reid A: Whole body N. M. R. imaging: the first report of its use in surgical practice. Br. J. Surg. 1981; 68: 493-494
14) Smith FW, Reid A, Mallard JR, Hutchison JMS, Power DA, Catto GRD: Nuclear magnetic resonance tomographic imaging in renal disease. Diag. Imag. 1982; 51: 209-213