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Review

Nuclear magnetic resonance imaging in medicine

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SUMMARY

Using the technique of nuclear magnetic resonance (NMR, MR, MRI), the first images displaying pathology in humans were published in 1980.[1] Since then, there has been a rapid extension in the use of the technique, with an estimated 225 machines in use in the USA at the end of 1985.[2] Considerable enthusiasm has been expressed for this new imaging technique,[3] although awareness of its high cost in the present economic climate has led to reservations being expressed in other quarters.[2] The aim of this article is to give an outline of the present state of NMR, and indicate some possible future developments.

HISTORY

The phenomenon of NMR was first described simultaneously by Bloch and Purcell in 1946,[4, 5] both scientists subsequently receiving the Nobel prize for their discovery. Following their initial description, NMR signals from small samples were obtained using small bore, high field magnets. Analysis of such signals allowed identification of nuclei within the sample and also differentiation of nuclei in different chemical environments; this technique of NMR spectroscopy is now a standard method of chemical analysis of small volumes but gives no spatial information. It has, in fact, been applied in humans although the technique is still at a very early stage.[6, 7]

Use of the technique for imaging in medicine required some method of spatial localisation as well as a magnet big enough to hold a patient. Also, whilst in theory any paramagnetic atomic nucleus may be studied, the relative abundance of hydrogen nuclei (protons) compared with all other species means that they are most suited to study using NMR. The first proton NMR image was published in 1973 by Lauterbur;[8] and human *in vivo* images followed in 1977[9, 10, 11] with the first pathology demonstrated in 1980.[1]

TECHNICAL ASPECTS

Physics

Only a brief description will be given here; fuller accounts are available elsewhere.[12, 13, 14] The phenomenon of NMR depends on the fact that nuclei containing an odd number of protons or neutrons behave as tiny magnets, i.e. they have a magnetic moment. Of those present in the body, the most numerous

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are hydrogen (^{1}H), phosphorous (^{31}P), sodium (^{23}Na), carbon (^{13}C), fluorine (^{19}F) and potassium (^{39}K). The single proton nucleus of hydrogen is by far the commonest and also has the highest magnetic moment. The protons spin on their axes and, under certain conditions, when placed in a magnetic field, they can absorb and emit radiofrequency (RF) energy. This emitted energy can be detected by an appropriately tuned receiver coil and gives rise to the NMR signal.

For NMR imaging, the patient is first placed in a strong magnetic field, which is typically anything from 200 Gauss (0.02 Tesla) to 20,000 Gauss (2.0 Tesla). For comparison, the strength of the earth's magnetic field is 0.3 – 0.7 Gauss.[15] The long axis of this field is in the long axis of the patient (Fig 1) and is conventionally labelled the Z direction as shown. Protons in the body align with this field.

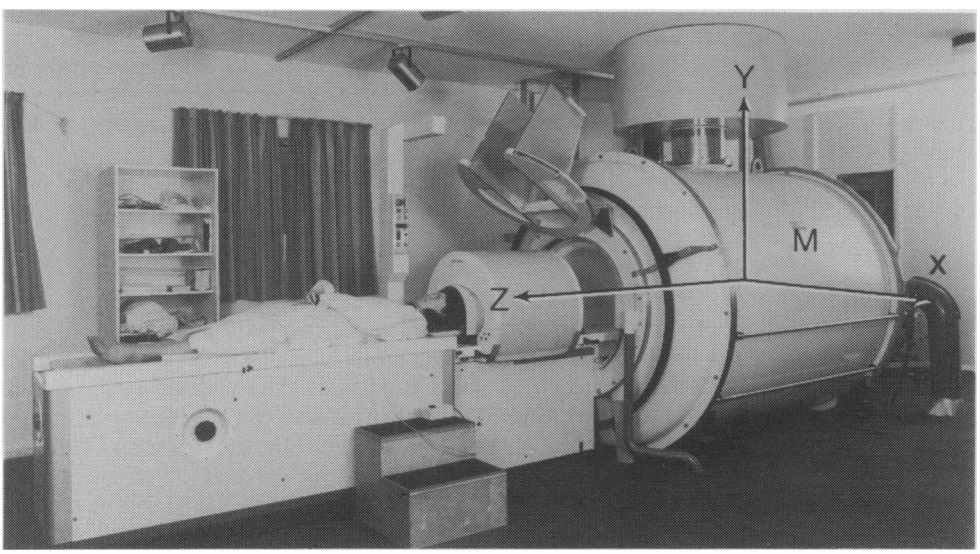

Fig 1. The NMR Scanner at the Hammersmith Hospital. Patient is in position for insertion into the circular cryomagnet (M). Relevant axes are shown (see text).

Within the bore of the magnet are transmitting and receiving RF coils; using a transmitted RF pulse of specific duration and frequency, the protons can be rotated 90° into the XY plane, and while spinning in this plane the receiver coil detects an RF signal. The strength of this signal will depend on the number of protons present (proton density, ρ). However, this signal decays rapidly; loss of coherence (phase) between the spinning protons occurs with a time constant T_2 (the spin-spin relaxation time), and the protons also return to the Z direction with a time constant T_1 (the spin-lattice relaxation time). By using different sequences of 90° and 180° pulses, the NMR signal can be made dependent to differing degrees on T_1 and T_2. A typical pulse sequence might last anything from 500msec to 2000msec and each sequence is repeated many times in order to build up the NMR image.

Selection of an anatomical slice is achieved by applying a magnetic field gradient in the Z direction so that only a 'slice' of protons responds to the transmitted RF pulse. Spatial localisation within the slice is achieved by applying X and Y gradients; image reconstruction is then carried out by computer using the

mathematical process of Fourier transformation. Flow effects can be seen on NMR because of the method of image formation. Blood which flows rapidly through the slice gives rise to no signal, because data is not retrieved from it, but slowly flowing blood may give rise to a signal ('paradoxical enhancement').[16] Quantification of flow is possible.[17]

Comparison with computed tomography (CT)

NMR sequences sensitive to T_1 and T_2 can produce images with greater soft tissue contrast than X-ray CT because of the wide range of these values for normal and pathological tissues. In CT, contrast depends on only one variable, the X-ray attenuation coefficient. However, because the relative brightness of tissues in the final NMR image may change drastically with the pulse sequence used, interpretation requires a knowledge of the physical principles involved if diagnostic information is not to be missed. Appropriate sequences must be chosen to highlight any pathology present. Transverse slices of similar thickness to X-ray CT can be obtained. However, by manipulation of the field gradients, direct sagittal and coronal images can also be obtained without moving the patient or the scanner, and oblique scans are also possible.

In CT, a single slice can be obtained in as little as two seconds, allowing breath-holding, for example in studying the chest and abdomen. In NMR, data acquisition time for a single slice is usually much longer, and may be anything up to 15 – 20 minutes for high resolution. This leads to problems with respiratory motion and patient throughput. However, it is now possible to image a number of sections simultaneously, reducing effective scanning time to levels comparable to CT.[18, 19] A method of respiratory gating without increased scan time is also available.[20]

Because of their low proton density, bone and calcium give a low signal on NMR; this is an advantage over CT in situations where artefacts from bone are a problem, for example in the posterior fossa and spine. However, bony abnormalities and calcified lesions are not well visualised with NMR. No ionising radiation is used in NMR, a major advantage especially in children and where repeated examinations are anticipated.

PRACTICAL ASPECTS

Insertion of the patient into the magnet causes claustrophobia in a small proportion of subjects. Some noise arises from the electronic gradient switching pulses but this is not usually a problem. Because of the presence of the very strong magnetic field, loose metallic objects must be excluded from the vicinity of the magnet, as must the vulnerable magnetic strip of credit cards. There is a theoretical risk of displacement of the clips used in treating intracranial aneurysms, and such patients must be excluded from study. Patients with cardiac pacemakers may also be at risk as some of these may be affected by the varying fields. No adverse effects have been demonstrated from NMR,[21] but limits on the field strength and magnitude of the varying fields and RF pulses have been set;[22] females in the first trimester of pregnancy are excluded from scanning.

CLINICAL IMAGING

All the images illustrated here were obtained on the NMR imager at the Hammersmith Hospital. This is a prototype Picker 0.15 Tesla superconducting scanner operating at a radiofrequency of 6.6 MHz.

Brain

In the early days of CT, the brain was the first organ to be studied using NMR, on account of its lack of physiological motion;[1, 23, 24, 25] consequently knowledge of the appearances of brain pathology is more advanced than for the rest of the body.[26, 27, 28, 29] Advantages of NMR over CT have been identified; these relate chiefly to the increased contrast sensitivity of NMR and lack of bone artefact. The latter is especially true in the posterior fossa.[30, 31]

Multiple sclerosis was one of the first conditions in which the high contrast sensitivity of NMR was demonstrated (Fig 2).[32] In a recent study, NMR demonstrated demyelinated plaques in 85% of patients with definite MS, compared with 25% on CT.[33] Plaques are typically seen in the periventricular white matter, centrum semiovale and posterior fossa, where they are not seen with CT. They have also been demonstrated in the cervical spinal cord.[34] A variety of other diseases of grey and white matter have also been studied.[27, 29, 35, 36, 37]

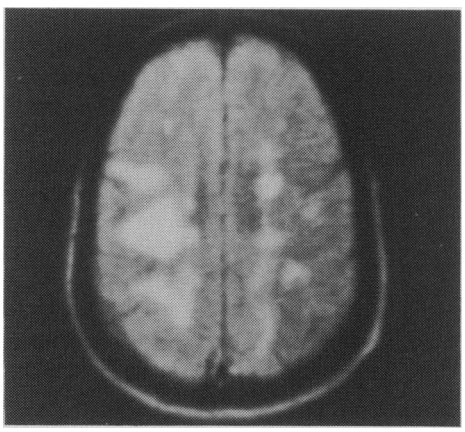

Fig 2. Transverse scan of brain in multiple sclerosis. White areas are demyelinating plaques

Cerebral tumours are well demonstrated by NMR (Fig 3),[38, 39] and the ability to provide direct sagittal and coronal studies is of value in showing their relation to other structures for planning of surgery and radiotherapy. Sagittal and coronal images of posterior fossa and brainstem lesions provide detailed information unobtainable by CT.[40, 41] In the cerebellopontine angle, the absence of bone signal may eliminate the need for CT contrast studies.[42, 43] Most tumours have an increased T_1 and T_2, but histological diagnosis on the basis of measured values has not proved possible. Benign tumours such as meningiomas may have a normal T_2 and only a moderate rise in T_1, giving rise to characteristic appearances on NMR.[44]

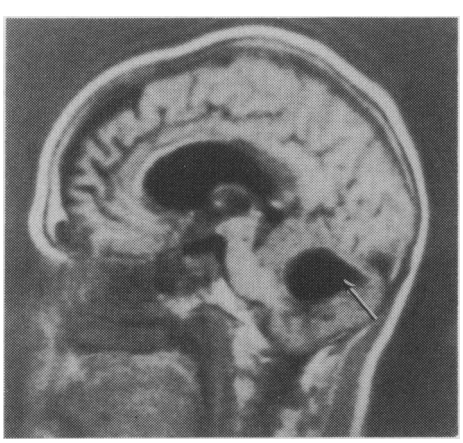

Fig 3 (a). Sagittal scan of brain. Large metastasis in cerebellum from bronchial carcinoma (arrow).

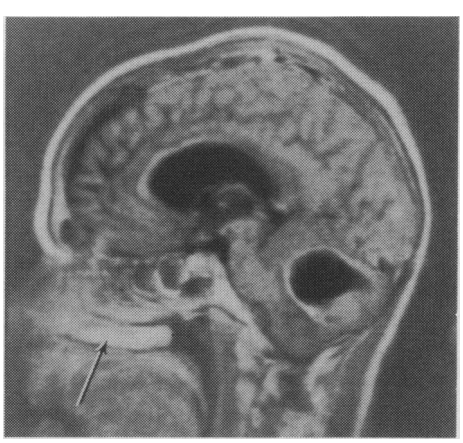

Fig 3 (b). Enhancement of tumour margin following intravenous Gd-DTPA. Note enhancement of nasal mucosa (arrow).

In cerebral infarction, increased T_1 has been visualised as early as six hours after onset.[45] Small ischaemic lesions can be seen, although their increased detection has led to difficulties in separating multiple lesion causing organic disease from lesions seen with ageing, which are also presumably ischaemic in nature.[46, 47] Intracranial haemorrhage shows a sequence of changes on NMR, with a short T_1 in the subacute stage which can allow differentiation from other pathology.[26] Subdural and extradural haematomas are well seen due to lack of signal from overlying skull.[48] Lack of signal from flowing blood is useful in demonstrating aneurysms and arteriovenous malformations.[49] A number of patients with infective conditions have been studied, and in some cases increased T_1 and T_2 lesions are seen.[27, 50]

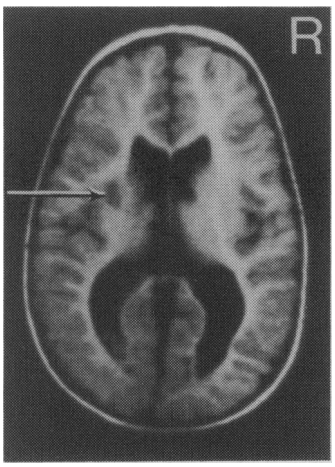

Fig 4. Transverse scan of baby at 20 months, following perinatal asphyxia. Small infarct (arrow) and delayed myelination on the left side (compare frontal lobes).

In children, a wide variety of pathology has been studied[51, 52, 53] and lack of hazard from ionising radiation is a particular advantage. In addition, NMR demonstrates the progress of normal myelination in childhood in a way impossible with any other technique. Deviations from this pattern following perinatal insults can be recognised (Fig 4).[52]

Spine

Excellent demonstration of the spinal cord and spine can be obtained using sagittal views; the cord and subarachnoid space are demonstrated without the use of contrast medium (Fig 5).[54, 55] Bone marrow in the vertebral bodies gives a high signal as does the nucleus pulposus of the intervertebral disc.[56] NMR can

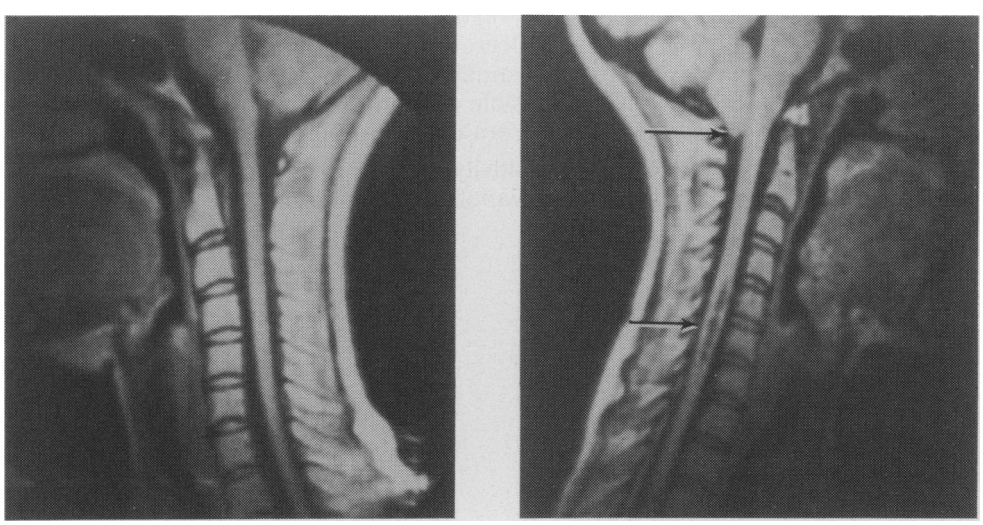

Fig 5 (a) Sagittal scan of normal cervical spine. (b) Syrinx in mid-cervical cord (lower arrow). There is also cerebellar tonsillar herniation (upper arrow) — Chiari I malformation.

therefore directly demonstrate cord abnormalities such as syringomyelia, in which the cystic cavity gives a low signal;[57] associated cerebellar tonsillar herniation can be assessed at the same time.[58] Tumours,[59] arteriovenous malformations,[60] demyelinating plaques and other abnormalities have been demonstrated.[54, 55] Disc herniation can be recognised with NMR.[61] In addition, loss of the normal signal from the nucleus pulposus may be an early signal of disc degeneration.[55, 62]

Musculoskeletal

Whilst cortical bone and calcium give a low signal on NMR, the technique has proved useful in defining the extent of bone tumours, especially within the marrow (Fig 6).[62, 63, 64] Direct coronal and sagittal scans can reveal the longitudinal extent of the tumour, which is of particular importance in planning surgery. NMR has also demonstrated marrow abnormality in leukaemia[65] and in the early stages of avascular necrosis, and may be useful in other joint disease.[62]

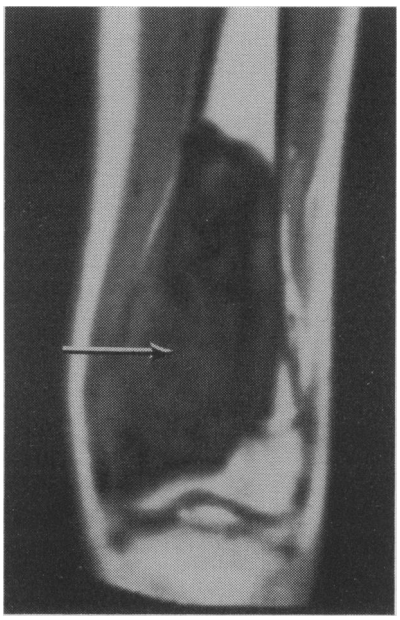

Fig 6. A coronal scan in a child with osteosarcoma of the lower femur (arrow). The tumour has broken through the epiphyseal plate inferiorly.

Abdomen

NMR imaging of the abdomen is hampered by respiratory artefact, although adequate images can be obtained. Respiratory gating[20] and special pulse sequences[66] can reduce this problem. In the liver, hepatic vessels can be identified without the use of contrast medium, and differentiation from bile ducts is possible (Fig 7a).[67, 68] This is valuable in assessing the spread of hepatocellular carcinoma prior to resection.[69] Initial studies indicated that most liver disease increased T_1 and that it might be possible to differentiate them on this basis;[70] however, this has not been confirmed.[67, 71] One possible exception is cavernous haemangioma, whose long T_2 may allow distinction from other tumours.[72, 73]

In focal liver disease, NMR has a sensitivity comparable with CT (Fig 7b).[74, 75, 76] In diffuse disease, changes are more variable. Cirrhosis may increase T_1, while in

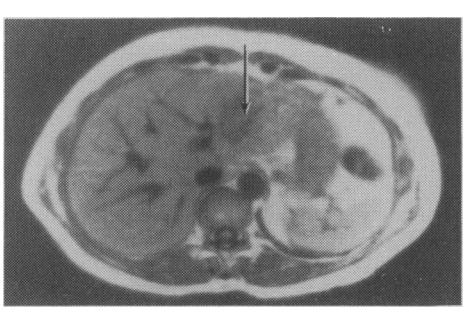

Fig 7 (a). Transverse scan of abdomen showing liver metastasis with area of low signal from calcification (arrow). Note low signal from vessels.

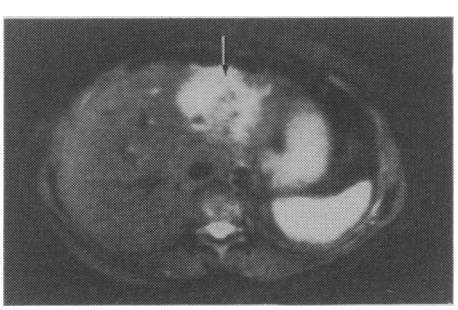

Fig 7 (b). Different pulse sequence highlights tumour (arrow).

haemochromatosis T_1 may be reduced: this has been ascribed to the paramagnetic properties of iron (see *Contrast agents,* below). However, in Wilson disease and primary biliary cirrhosis T_1 has been increased, presumably due to the cirrhosis associated with the copper deposition.[67] Fatty change has not been well visualised on NMR, although specialised sequences may show it.[76] In portal hypertension, portal vein flow has been assessed.[77]

In the kidney, NMR gives good distinction between cortex and medulla and can visualise Gerota's fascia, the adrenal glands and the renal vessels.[78] Loss of cortico-medullary differentiation has been seen in glomerulonephritis, renal failure, renal artery stenosis and transplant rejection.[78, 79] NMR can distinguish solid masses from cysts,[80] and has identified extension of hypernephroma into the renal vein and vena cava.[80, 81] The place of NMR in renal, adrenal and pancreatic disease remains to be established.[82]

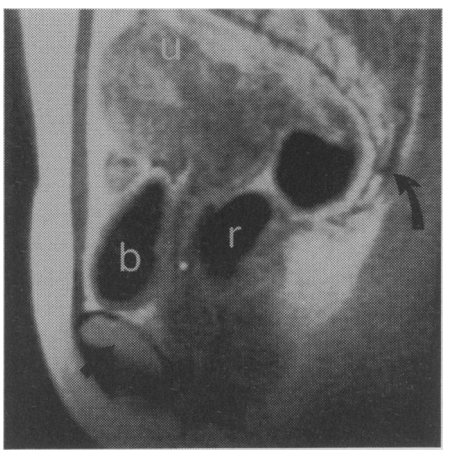

Fig 8. Sagittal scan of normal pelvis. b = bladder, r = rectum, u = uterine wall. Short arrow = pubic symphisis, curved arrow = tip of sacrum.

Pelvis

Lack of respiratory motion makes the pelvis more suited to NMR scanning, and direct coronal and sagittal images are especially valuable in assessing the cervix and uterus and conditions of the bladder base (Fig 8).[83, 84, 85] NMR has shown promise in the distinction of bladder carcinoma from other conditions and in staging the tumour although the problems are encountered as on CT in staging nodal involvement.[86, 87] In the male, the prostate, seminal vesicles and ductus deferens can be demonstrated.[85] Prostatic enlargement is well seen on sagittal studies, although initial enthusiasm for the specificity of the findings in prostatic disease has not been confirmed.[88]

In the female, myometrium and endometrium can be distinguished and cyclical endometrial changes have been seen.[83] The cervix contains a band of low signal intensity and the ovaries are also seen. Benign and malignant gynaecological conditions have been studied, although more experience is required; NMR may have a role in staging of malignancy. The pregnant uterus in the second and third trimester has been studied and also a number of first trimester pregnancies scheduled for termination. Real-time ultrasound has obvious benefits; it is safe, inexpensive and not limited by fetal motion. Nevertheless, some possible advantages of NMR have been identified. The cervix and internal os are well visualised and their relationship to the placenta evaluated. Bladder distension is not necessary, and this may be an advantage over ultrasound in diagnosis of cervical incompetence.[89] The fetus is best seen in the last trimester when movement is least,[90, 91] and the demonstration of fetal fat by NMR may be of value in assessing intra-uterine growth retardation.[92]

Thorax

Mediastinal structures are well seen on NMR, vascular structures giving no signal due to flowing blood within them.[93] This is a major advantage over CT, which

requires intravenous contrast for vessel delineation. Difficulties arise in CT in distinguishing large benign lymph nodes from those involved by metastatic tumour, but NMR encounters the same difficulties[94, 95] and lack of visualisation of calcification of benign nodes is a disadvantage. NMR may be able to improve differentiation of central tumour from distally collapsed or consolidated lung.[96] Vascular structures are well delineated and a variety of lesions have been demonstrated, including aortic aneurysm, atheroma and dissection.[97, 98]

Gating data acquisition to the R-wave of the ECG gives good images of the heart (Fig 9).[99, 100] Details of cardiac muscle, chambers, valves and papillary muscles can be seen.[100] By varying the data acquisition delay after the R wave, a series of pictures of the slice can be built up in different phases of the cardiac cycle; by 'looping' these together a cine-type moving image of cardiac motion can be obtained. Orientation of the slice to the ventricular axes may allow assessment of ventricular volumes and function.[101] However, this is time-consuming, and multi-section and volume acquisition techniques are being developed. Echo-planar imaging can produce true real-time rapid images but resolution is, as yet, poor.[102] Following successful animal studies, acute infarcts in man have been successfully imaged as areas of increased T_1.[103, 104] Subacute and old infarcts appear as areas of thinned myocardium, and aneurysms and mural thrombus have been demonstrated.[99] Congenital disorders have also been studied.[105]

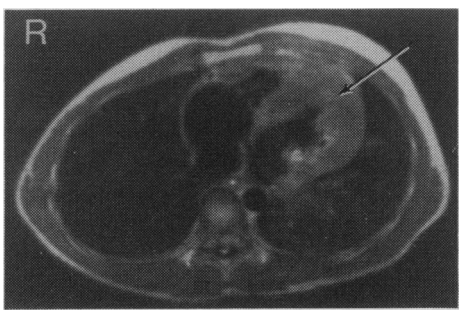

Fig 9. Transverse scan of thorax (ECG gated). Marked thickening of left ventricle in a patient with hypertrophic obstructive cardiomyopathy (arrow).

NMR images of the breast demonstrate normal ductal structures within the fatty stroma of the breast and can differentiate duct dysplasia, cysts and fibroadenoma from malignant lesions.[106] However, lack of visualisation of calcification, an important mammographic sign, is a disadvantage. NMR has obvious advantages as a possible alternative safe screening technique.

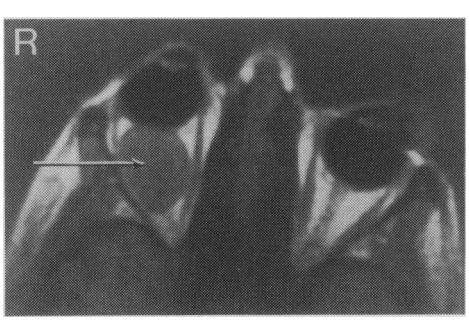

Fig 10. Surface coil study of orbits: right cavernous haemangioma (arrow).

OTHER TECHNIQUES

Surface coils

By placing a copper receiver coil close to the part being imaged, the NMR signal quality can be improved allowing increased resolution. This is of particular interest in small structures such as the orbit (Fig 10),[107] and may also be used in the inner ear, breast, spine and limbs.[108] The principle can, in fact, be extended to larger organs and, at the Hammersmith Hospital, surface coils are used for all examinations including the pelvis, abdomen, chest and brain.[109] Surface coils are now offered by most NMR manufacturers.

Contrast agents

To date, the most widely used contrast agent has been the intravenous agent gadolinium (Gd^{3+}) chelated to diethylenetriamine penta-acetic acid (DTPA). This is a paramagnetic ion which exerts local magnetic effects and reduces T_1 and T_2, thus altering or 'enhancing' the appearance of the tissue in the final image (Fig 3b). It behaves similarly to iodinated X-ray contrast media in not crossing the normal blood-brain-barrier and is excreted unchanged by the kidneys. Gd-DTPA improves differentiation between cerebral tumours and surrounding oedema[110,111] and may also improve detection of metastases.[111] Improved visualisation of spinal cord tumours has also been seen.[112] Enhancement has been observed in tumours of the liver[113] and kidney.[79]

CONCLUSION

NMR has already established itself as the imaging method of choice in several neurological conditions, while clinical experience is accumulating rapidly for the rest of the body. Study of phosphorous and of other spectra from human subjects *in vivo* has already identified some metabolic disorders, for example of muscle metabolism, although research is still at an early stage and the problem of spatial localisation with spectroscopy remains to be solved. This would be of great interest in, for example, monitoring the metabolism of tumours. Imaging using other nuclei such as sodium has also been achieved.

NMR is more costly than CT, and this together with doubts about its true role has led to a slower rate of diffusion than occurred following the invention of CT.[2] It will most likely prove to have a complementary role to CT rather than replacing it, and with increasing experience there is no doubt that NMR will find an established place as an imaging technique.

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