NUCLEAR MAGNETIC RESONANCE IMAGING

a report by the

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A report by the National Health Technology Advisory Panel on the introduction of NMR Imaging in Australia.

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Introduction

Nuclear Magnetic Resonance imaging (NMRI) is an emerging diagnostic technique with the potential to complement, provide alternatives to or in some cases supersede other imaging methods such as computed tomography (CT) and ultrasound (US). This report summarises aspects of the technique considered by the National Health Technology Advisory Panel (NHTAP) and makes recommendations on its introduction in Australia with particular regard to the need for thorough evaluation of its cost effectiveness.

NMRI is used to produce pictures of the body which superficially resemble those given by CT. The technique is particularly appropriate for imaging soft tissue, and high quality pictures of the brain have been produced at a number of centres. There is also the prospect of clinically useful NMR imaging of other organs.

In addition to its imaging capabilities, NMR can produce useful biochemical information. However, routine clinical application of this potential is probably some way off and has not been considered by the Panel.

Principles of the Technique

An NMR scanning unit is essentially based on a powerful magnet which surrounds the patient and produces a strong and homogeneous field, subsidiary coils which modify the field in a precise manner and which transmit and receive radio frequency (RF) signals and a computer which controls the scanning sequence and handles image reconstruction and presentation.

Construction of an image with the technique depends on the detection and computer manipulation of RF signals emanating from atomic nuclei in the part of the body under investigation. Such signals are generated by changes in the magnetic and RF fields applied to the body. Radioactivity and other ionising radiation is not involved. The physics of the NMRI process is complex and applications and methods of operation are evolving rapidly.

The information obtainable from NMRI can be varied by using different scanning sequences to alter the way in which magnetic fields and RF radiation are applied to the body. In addition to obtaining images which are maps of proton density, use can be made of the ways that nuclei which have been perturbed by an RF field emit radiation as they return to equilibrium. These processes are associated with relaxation times referred to as T_1 and T_2. By varying the T_1 and T_2 dependence of the imaging process, images can be produced with a range of diagnostically useful data, as the relaxation times are dependent on gross chemical characteristics such as state of hydration, fat content and presence of paramagnetic substances.

Equipment Required

A number of different machines have been developed incorporating many variations in sequencing patterns and image reconstruction. Present machines use either resistive electromagnets or superconducting magnets to provide the powerful field required for NMR imaging. It is uncertain at this stage which type of magnet will predominate.

Resistive magnets are cheaper but require considerable quantities of electricity and cooling water. Adequate image quality has been produced but is inferior to that obtainable with machines based on superconducting magnets. For most applications, work with resistive magnets is limited to images based on hydrogen nuclei within the body. Installation is possibly easier and less expensive than with superconducting systems, but the Panel notes that serviceability and reliability of the cooling water systems might present significant problems for this type of unit. Good quality water would be essential for operation of a resistive magnet system and there would be a need for a stand-by chiller.

Units based on superconducting magnets are more expensive but possibly have lower running costs. Electricity consumption is much less than for resistive magnets but expenditure is required on liquid nitrogen and helium. The higher field strengths possible with superconducting magnets give a potential for improved image quality and use for nuclei other than hydrogen. These units could have a longer life than resistive systems but would be more expensive to install and might produce higher stray magnetic fields. Difficulties with stray fields and magnetic homogeneity should decrease as shielded superconducting systems become available.

The image reconstruction components in NMRI machines bear a resemblance to those used in CT scanners. Work on image quality and scanning sequences is still evolving and development of magnets and other instrument components is proceeding rapidly. There is a strong possibility that present units will be superseded by new technical developments over the next few years and this might be particularly true of superconducting units.

Installation

Most NMR machines used to date emit significant stray magnetic radiation and the homogeneity of their magnetic fields is influenced by metallic objects in their immediate vicinity. This imposes constraints on the installation of such units and could necessitate construction of special suites in which steel structures were excluded or at a suitable distance from the magnet. The stray magnetic field also has implications for the positioning of other diagnostic equipment and for mobile ferromagnetic ancilliary equipment which must be excluded from the immediate vicinity of the magnet. In addition, fluorescent lighting and dimmers should not be used in the magnet room. Because of the size of the magnet, access of the machine to the room must be considered when preparing the site. The weight of most imaging units is between 2 and 7 tonnes.

Some resistive systems are now being marketed which are claimed to give very low stray magnetic fields and not be significantly influenced by external structures. Machines of this sort incorporate iron shielding to effectively isolate the magnet from its surroundings. Such units could be attractive from the point of view of installation convenience but there would still be constraints because of the weight, which with the iron shielding is as much as 7 tonnes.

Suitable air conditioning for the scanner and ancilliary equipment would be essential and should be regarded as a non-trivial requirement.

Capital Costs

Current prices for superconducting systems are of the order of $M1.6 with recent resistive units somewhat cheaper at around $M1.2-1.4. All machines are manufactured overseas and freight, handling and installation costs would have to be added to these prices. Construction of new accommodation to house a machine would further increase costs, and site costs of about $M0.6 could be anticipated.

Running Costs

Resistive systems would probably require $10-15 000 per year to meet power costs. For superconducting systems power costs would be much less but there would be expenditure on cryogens which could be as high as $15 000 per year. This estimate could, however, decrease substantially with the development of more efficient systems. Maintenance costs might be between 6-10% of capital costs per annum and would include standard checks of electronic components (similar to CT scanners) and overhaul of cooling systems. Proper maintenance of cooling water supplies to resistive magnets would be essential. Total recurrent costs, including salaries of operating staff, could be of the order of $M0.3 per annum.

Reliability

The reliability of NMRI units is not yet known but both the concept of NMR and the computer facilities are based on well known technologies. Suitable reliability will depend on the availability of a stable electricity supply. As there are no moving parts on NMR machines there should be relatively little potential for mechanical failure. Possible obsolescence could be deferred by up-dating various components over a number of years. Life times might be of the order of 10 years for resistive magnets and rather longer for superconducting systems. Essentially, all machines in current use are research instruments which require great care to maintain optimum image quality. More dependable instrumentation can be expected to become available in a few years.

Performance Parameters

Instrument performance is advancing very rapidly. While the imaging process in NMRI is intrinsically slower than in CT, there have been significant reductions in the time taken to produce an image, so that total examination time for patients could be of the same order as CT. Recent developments include a T_2 imaging facility capable of making a projection in 16 milliseconds, and suitable quality three dimensional images should be obtainable in minutes. Use of different scanning modes on the same patient would of course increase imaging time. Currently marketed machines can produce three dimensional images in 20-60 minutes for examinations which require only one type of scan.

Image quality of the technique depends on the strength of magnetic field available. The resolution obtainable is comparable to that from CT when soft tissue is being imaged. CT may retain resolution advantages for other types of tissue. Further improvement in performance is probable and NMR has advantages over CT in that resolution is the same in all planes and artefacts due to bone and air are not present. Movement of the patient during imaging degrades the picture quality but this is seen as an overall loss in resolution rather than as blurring or a shadow.

Good contrast resolution is obtainable with both resistive and superconducting systems. Spatial resolution is not at present as good as with CT, but could improve. Conditions for optimum imaging have yet to be defined.

Most work has been done so far on imaging based on signals from protons, which will become the initial focus for clinical application. Images from other nuclei may be feasible for clinical use, particularly at the higher field strengths available with superconducting magnets. There is interest in the possibility of obtaining phosphorous images (based on ^{31}P) but clinical application is some way off. Use of non-imaged ^{31}P - based information, in the form of spectral data from regions of the body of interest, has been described by several centres, and has prospects of eventually being diagnostically useful. Other atoms which might be used in future to produce images are sodium (^{23}Na), fluorine (^{19}F) and carbon (^{13}C). Sodium images of the heart have been obtained in animals and ^{19}F might be used to image the cardiovascular system with suitable fluorine - containing compounds as tracers. Imaging with ^{13}C will have to await major development in technology.

Clinical Indications

NMR imaging has already been shown to be very appropriate for soft tissue, especially brain, and appears to be also of major use in imaging the spine, cardiovascular system and possibly the abdomen.

Compared with other imaging techniques NMRI appears to offer advantages in the diagnosis of a number of conditions. Present indications are that NMRI is comparable with CT in most areas of neuroradiological diagnosis and better in some areas. There seems to be consensus that it will probably supersede CT scanning for most indications over the next decade. However replacement of CT units by NMRI over the next 5 years is not seen as significant and shold not be a factor in current assessment of diagnostic imaging requirements. NMRI imaging is unlikely to completely supersede other diagnostic imaging techniques and will be complementary to other methods. Its exact role in diagnosis is still not clear and further extensive assessment is required.

NMRI has been shown to be capable of demonstrating abnormalities in brain resulting from a wide range of disease states. Image quality achieved in recent work has been very good, and comparable with CT. Some abnormalities seen with NMRI could not be detected by CT and tissue characterisation using the T_1 and T_2 modes may have a wider diagnostic application than attenuation values have had with CT.

Useful images of the heart have been obtained, with gating methods being used to compensate for heart movement. These methods generate artefacts which might produce diagnostic confusion. Some workers suggest that NMRI can already compete with US in producing static images of cardiac characters. Recently, real time NMRI images of the beating heart in children has been demonstrated. There also is a potential for using contrast agents to study conditions such as perfusion defects. NMRI images are sensitive to blood flow and could provide information on tissue function and metabolism.

Malignant tumours and other abnormalities have been demonstrated in liver, kidney, pancreas and forearms. However, in some instances, lesions detected by CT and US could not be seen with NMRI. Apparent failures of NMRI to detect some abnormalities might be overcome as more is learned of the use of different scanning sequences.

NMRI could prove to be more sensitive to disease states than other technologies and provide very accurate tissue characterisation. For example NMRI might eventually be used to detect a tumour and assess its histology, biochemical characteristics and potential for therapeutic control through drugs or radiation. The technique is potentially not merely a method of producing an image but also a means of obtaining two and three dimensional projections of physicochemical and biochemical information. However, the Panel considers that it will be some time before the biochemical monitoring potential of NMRI will find useful clinical application.

At this stage the accuracy of NMRI has not been established and detailed protocols for its use in diagnosis will need to be developed.

Training and Staff Requirements

Because of the complexity of the information potentially available from NMRI, extensive research on the optimum use of the technique will be required and training will need to be more extensive than is the case with radiological methods. Effective use of an NMRI unit will require the full time services of a clinician trained in radiological procedures, a physicist or other scientist familiar with NMR and other imaging methods, technicians to operate the instrument and a nurse. There will also need to be access to expertise in data processing, biochemistry and possibly electrical engineering. Addition of a full time data processing expert to the team might be appropriate in the initial stages of operation.

Safety Considerations

No adverse reactions due to NMR imaging procedures have been reported so far in any patients or volunteers studied by the technique. Potential hazards include the possibility of damage to excitable tissue through electrical currents induced by changing magnetic fields, heating of prostheses and alteration of pathological states such as infarcts through thermal effects of RF radiation.

Results of exposure of animals and bacteria to NMR imaging conditions and stronger magnetic fields have been negative with regard to induction of mutagenic, biochemical and cytological effects.

The U.K. National Radiological Protection Board has cautioned that there is insufficient information on relevant radiation biology to allow a definite statement of risks or safe conditions. It is recommended that the guidelines for exposure to clinical NMRI, published by the Board, should be adopted for any work of this nature in Australia. As long term effects of magnetic radiation are unknown, any patients tested in Australia should be followed up.

Certain categories of patients should be excluded from NMR examination. These include patients with uncontrolled seizures or vomiting, cardiac pacemakers, epilepsy, inability to remain supine, acute claustrophobia and possibly persons with large prostheses.

Until further work has been done on potential hazards, pregnant women should be excluded and NMRI should not be made available for surveys of symptomless patients. Resuscitation and patient monitoring protocols would need to be developed for use by operators of NMRI equipment.

Hazards associated with attraction of mobile ferromagnetic objects need to be overcome by suitable operating practices, including removal of all mobile iron-containing objects from the clothing of patients and persons operating the apparatus.

Conclusions

The Panel, from the information available to it, is of the opinion that NMRI has the potential to make a major contribution to diagnostic imaging services. Results already obtained in imaging soft tissue, especially brain, are impressive, and it is likely that the technique will come to be of value in diagnosis involving other organs. The Panel also notes the extent and complexity of the physicochemical and biochemical information available through NMRI and its possible future clinical application to nuclei other than protons. Several submissions to the Panel included the opinion that NMRI would eventually supersede CT for many or most applications.

Rapid progress is being made in the development of NMRI instrumentation, and while it may be possible to update existing machines, it is probable that the present equipment will be overtaken within a few years by units with greater reliability, flexibility, resolution and accuracy. Installation constraints and costs for many existing machines are significant and need to be considered in relation to the useful lifetime of the present instrumentation and the desirability of locating NMR scanners close to other diagnostic procedures so that comparative studies can be readily carried out.

The very active research programs in progress at a number of centres have shown the potential of NMRI but clinical indications are still difficult to define. There is no standardisation of image between different machines and the operating conditions for optimum imaging quality (field strength, pulse sequence, pulse routines and data processing) have not yet been established. Further extensive research is needed to determine the accuracy of NMRI in diagnosis, and to evolve suitable approaches for making optimum use of the variety of data that can be produced.

The place of NMRI in diagnosis has not yet been established, and a great deal of further work is required on development of the imaging apparatus, its clinical application and its relationship to other diagnostic techniques. It is not apparent that there is at present an identifiable benefit in terms of patient outcome.

It seems clear that NMRI is not an appropriate technique, at present, for application by individual clinicians. Considerable training will be required to enable users of the technique to become proficient. The Panel agrees with the view expressed in several submissions that NMRI units must be operated by a full time team, including a radiologist and a scientist, which should have ready access to other necessary expertise.

These considerations of available instrumentation and its possible obsolescence, limited knowledge of the application of the technique, need for training, and operation of the equipment by a team need to be taken into account when assessing how NMRI might be introduced into Australia. With capital costs of the order of $M1.6 per unit and running costs of perhaps $M0.2 per annum (excluding salaries) diagnosis by NMRI will be expensive, and general introduction of the technique in Australia cannot be justified at present.

Widespread proliferation of NMRI units, as has occurred with CT machines, must be avoided at least until suitable information on clinical benefit has been obtained. In view of the experimental nature of the technique in its present state, and the difficulty in defining a standard service, the Panel is of the opinion that NMRI diagnosis should not attract medical benefits payments at the present time.

However, the Panel considers that it would be appropriate for planning to commence on making NMRI available in Australia, on a restricted basis, so that its future role in diagnostic services in this country can be properly evaluated and expertise with the technique acquired before any widespread introduction is considered.

The Panel agrees with suggestions made in several submissions regarding the siting of the first NMRI units and notes that there will be a need to obtain data from a large number of patients using appropriate protocols. The volume of work required to establish the place of NMR imaging in Australia suggests that more than one unit might be necessary. The Panel also notes that a lead time of about 18 months would be required, if a decision was taken at the present time, before an NMR scanner could be installed and brought into operation.

Recommendations

The Panel recommends that:

1. A two stage program should be undertaken to introduce NMRI scanners at public sector institutions with the first coming into operation at a suitable centre during 1984/85.

   Depending on the extent of evidence of clinical benefit which emerges in the interim, either one or two additional scanners should be acquired and installed at other centres during 1985/86.

2. The program should be implemented in the following sequence:

   (a) Invite applications from manufacturing industry and institutions interested in operating the NMR centres;

   (b) Select site, evaluate and select equipment, using experts and representatives from the organisation housing the first centre;

   (c) Plan siting requirements in association with the selected NMRI manufacturer;

   (d) Carry out site work;

   (e) Begin selection process for second stage of the program;

   (f) Install first instrument and commence operation;

   (g) Commence site works for second (and third) NMR centres;

   (h) Install and operate second and third units.

   Recent developments in NMRI would need to be taken into account throughout the acquisition program and reflected in decisions taken on equipment and evaluation protocols.

3. Because of the need to obtain significant numbers of patients for investigation by the technique and to compare NMRI with other imaging methods, the NMR centres should be established at sites within major teaching hospitals and in close proximity to other diagnostic technologies.

4. Selection of the sites and of NMR instrumentation should be made by a technical committee under the auspices of the Panel. The committee should have sufficient expertise to assess relative merits of different instruments and should include a physicist, a nominee of the Royal Australasian College of Radiologists, a nominee of the Commonwealth Department of Health and a member of the Panel.

   The Panel considers that involvement of the Ultrasonics Institute in the work of the committee may be appropriate. After a site has been chosen, the committee should also include representation from the organisation which will operate the scanner. The manufacturer of the scanner selected should be involved in planning site preparation.

5. The committee should have an on-going monitoring function, once the NMR centres commence operation, in co-ordinating development of evaluation protocols to assess the clinical benefits and economic implications of the technique. Economic assessment should include the use of cost-effectiveness analysis.

   Persons with appropriate expertise should be co-opted, as necessary, to assist in carrying out this function and to provide health services research input on a project basis. The committee should report to the Minister, through the Panel, with its findings being given wide publicity.

6. Funding for the NMR centres should be on a project basis through a Government grant to include operating costs for two years.

   For each unit, this would imply expenditure of $M3.0, at current prices, made up of $M1.6 capital costs, $M0.6 site preparation and $M0.8 for operating costs, salaries and overheads for the two year period.

   The Panel considers that these substantial costs should be viewed in the context of the greater expenditure which could result through uncontrolled introduction of NMRI.

7. Each NMR unit should be serviced full time by a radiologist, a scientist with knowledge in NMR, and appropriate technical and clerical support. Clerical support on site will be essential to deal with patient records and other documentation

and to provide proper liaison with the technical committee. There should also be access to a person with expertise in data processing.

8. The centres should act as the national focus for clinical and economic evaluation of NMRI and provide suitable training experience for persons with an interest in using the technique at a later stage, including radiologists, physicists, electronic engineers and technicians.

   Work performed by the centres should be directed towards establishing the place of NMRI in clinical diagnosis in comparison with other imaging modalities, probably in association with existing Departments of Radiology. It would seem appropriate for a link to be established with an overseas centre of excellence in NMR imaging so that data on clinical applications can be exchanged.

9. The Panel notes and agrees with the suggestions in submissions that development of data processing techniques for NMRI should be undertaken in Australia. Some of this work might be undertaken at the NMRI centres, with additional inputs from other institutions.

10. All patients and volunteers tested by NMRI at the centres should be followed up over a number of years to assist in long term assessment of the safety and accuracy of the technique. Such follow up would require the active support of Commonwealth and State Health Authorities.

11. Medical benefits for NMR diagnosis should not be available at the present time pending evaluation of the technology over 2-3 years. This limitation should not continue, however, if overwhelming evidence of clinical benefit becomes available in the meantime.

The Panel considers that introduction of NMRI into Australia as recommended above would provide an excellent opportunity to obtain a thorough assessment of this expensive health technology under well controlled conditions. It is suggested that it would be appropriate for the NHTAP to continue to monitor the progress of NMRI development internationally and in due course co-ordinate an assessment of the Australian experience with a view of defining the conditions for any wider introduction on NMRI in this country.

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