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Nuclear magnetic resonance techniques in the clinical laboratory

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Abstract - A door may be opening into what could be a treasure house of diagnostic information. For many years the resonance of protons in a magnetic field has been exploited by biochemists, who have a comprehensive range of procedures to elicit all spectral responses of which spinning nuclei are capable. These responses depend on two factors; one is the immediate intramolecular environtment of the protons and the other is the main steady magnetic field enclosing the sample. The bulk responses can be observed and measured as radiofrequency emissions.

For biochemical studies of small samples an extremely uniform magnetic field of considerable strength and a uniform sample are required to obtain the clearest information about the molecular environment of the nuclei giving the radiofrequency signals. The potential applications of proton magnetic resonance in clinical medicine are arising from the concept of using the other factor controlling the details of the responses - the precise strength of the main magnetic field - to elicit information about the spatial position of a small element of tissue in the human body. This is done by introducing small precisely controlled gradients into the magnetic field. With these gradients in one, two, or three dimensions, the protons emitting radiowaves at each exact frequency and phase and being detected and measured are restricted to a small spatial region. The region may be a plane, a line, or a point, depending on how the spatial information is to be used. Some of the methods of building an actual image from proton magnetic resonance information are based on those developed for X-ray computerised tomographic (CT) scanning.

From a combination of skills in magnetic field control, radiofrequency analysis, and image construction a potentially powerful tool for radiologists has been created. Images of normal and pathological soft tissue can give investigative and diagnostic information related to anatomy that is without comparison from any other modality (Ref. 1 & 2). Figures 1 to 6 give examples of the kinds of image obtainable and illustrate the interest and appeal that proton NMR imaging can have to radiologists and clinicians who use and are accustomed to X-ray CT, radionuclide or ultrasound tomographic images.

Figure 1 is a sagittal section of a normal head and can be compared with an illustration in an anatomy book.

Figure 2 shows a metastasis in the cerebellum.

Figure 3 is a transverse section of a normal head and the convolutions of the brain are clearly shown due to the strong contrast between white (white in the Fig.) and grey matter.

Figure 4 shows an astrocytoma surrounded by damaged and oedematous brain.

Figure 5 is a baby's head in which virtually no myelin has yet appeared and which is grossly distorted by hydrocephalus.

Figure 6 shows a shrunken liver with deposits surrounded by excess fluid in the abdominal cavity. Kidney, pancreas, muscle, spinal cord, vertebral discs, the soft tissue in bone and the heart are other organs which lend themselves to NMR imaging.

While it is clear that differentiation between tissues in NMR imaging can be very good it is based both on the level of the grey tone that each tissue shows in the image and also on general considerations such as age, site, oedema, calcification and mass effects. Thus a single number from an image is inadequate to identify and characterise fully a tissue or a pathological state in a tissue, and there is a need in radiological use for the above other general considerations. However, the NMR information can be very helpful and often better than that available for X-ray computed tomography, which is limited to distinguishing electron densities.

Tissues with identical densities, constituents, and compositions by weight may differ widely in their structure, in the way in which cellular organelles are arranged in cells and in the way in which cells are arranged in tissues. Proton NMR can distinguish such differences in structure and also differences in the proportions of water and other constituents (Ref. 3).

Figure 7 shows an image of a test object used to calibrate the NMR signals in terms of the relaxation properties of special test substances.

However, while such distinction between tissues may appear to offer the possibility of obtaining in vivo and non-invasively information about body fluids and tissues that rivals the information provided by analysis and study of samples in clinical laboratories, there are many problems to be tackled. In vivo studies can identify at best volumes of tissue no smaller than those which contain large numbers of cells and volumes of extracellular fluid and some vascular volumes. One cubic millimetre would be very good by today's technical standards. The signals detected are therefore averages over such volumes and reflect a mixture of properties from a mixture of substances themselves very complex on a microscopic scale.

Despite such formidable obstacles to specificity, there are seven NMR parameters that can be quantitated. It is possible that some combination of these parameters will provide clinically useful indices that relate uniquely and specifically both to local tissue states and to the general metabolic state of a patient which can affect all his tissues.

It is of interest to speculate on the potential influence of the above possibility on the work of clinical laboratories. There are two facets to this potential influence.

The first arises from the fact that diagnostic criteria for disease states are based substantially on laboratory reports on microscopic appearances of tissue or cell sections, on chemical analyses of blood plasma, and on other haematological, endocrinal, and bacteriological laboratory measurements. Disease states in effect are substantially defined in these laboratory terms. If it becomes possible to characterise some disease states by NMR measurements on tissue without major dependence on the anatomy shown in radiological images, then the laboratory definition and the NMR characterisation must be harmonised.

This can only be done by intensive NMR studies of tissues and fluids in the laboratory in parallel with the established laboratory procedures. The aim will be to establish empirical correlations and to gain understanding of the mechanisms underlying such correlations. This work need not be unrewarding to the laboratories since there may become available a range of new and useful NMR relaxation tests to add to the present laboratory armamentarium. Such new tests would be the second facet of the influence of NMR imaging on laboratories and could be of value even if the search for specific in vivo tissue characterisation by NMR relaxation is a partial failure.

Thus, although spectroscopic NMR has revolutionised chemistry and biochemistry over the past decades without having much direct effect on clinical chemistry, relaxation proton NMR may find a major role in clinical laboratory practice.

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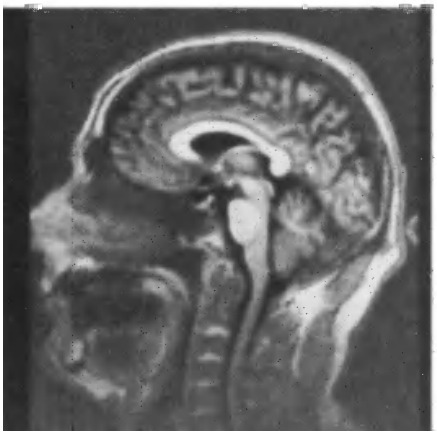

Fig. 1. Normal head (sagittal section)

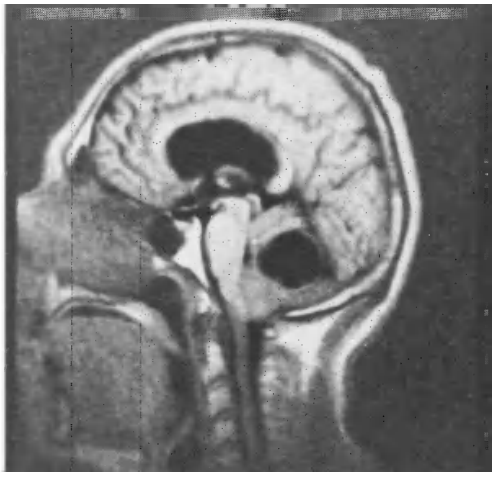

Fig. 2. Cerebellar metastasis

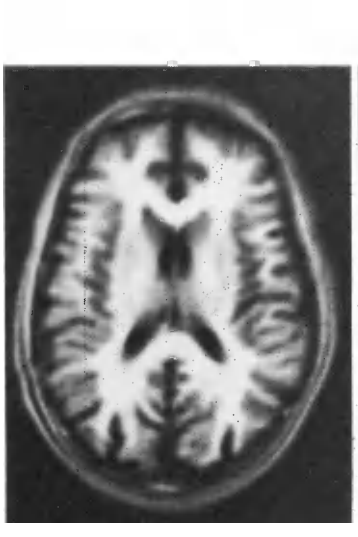

Fig. 3. Normal head (transverse section)

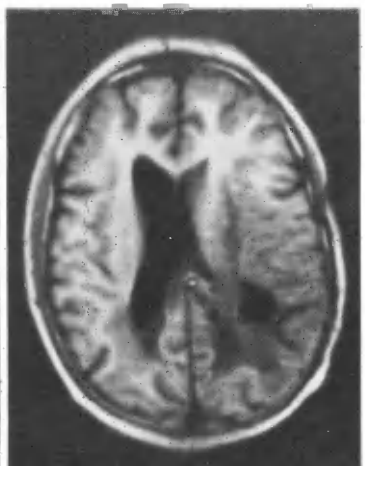

Fig. 4. Astrocytoma

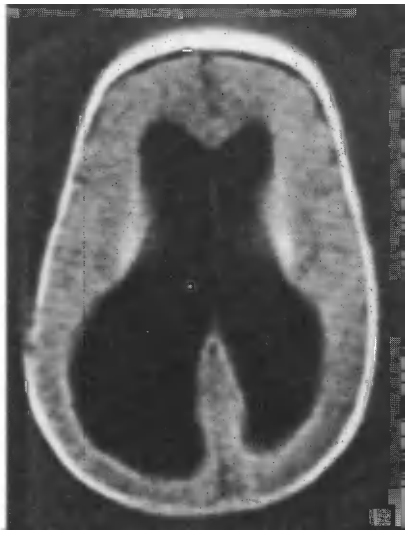

Fig. 5. Hydrocephalic infant

Fig. 6. Diseased liver

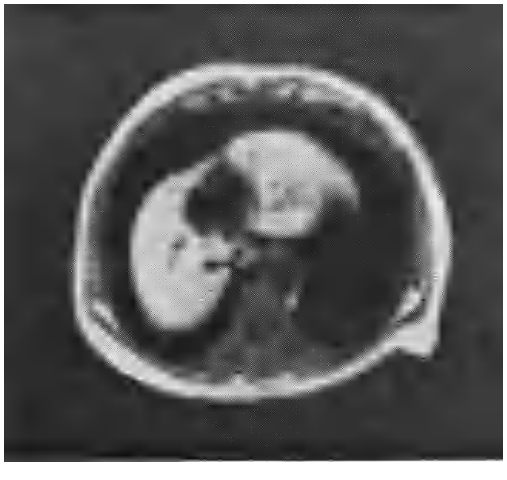

Fig. 7. Image of test object for calibrating NMR images