Special Lecture 2

Nuclear Magnetic Resonance Imaging and its Bio-Medical Applications—Past, Present and Future

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This paper reviews the work of the NMR group of this Department since 1972 which, in addition to the authors, included R. E. Gordon until 1974 (now at Oxford Instruments Ltd.) and R. Sutherland until 1978 (now at Culham Laboratory, Abingdon).

Nuclear Magnetic Resonance imaging at present is concerned with the protons which are the nuclei of hydrogen atoms, which are part of the molecules of water (and fat) distributed in tissues of the body. The technique can display the spatial distribution of proton concentration, and that of proton spin-lattice relaxation time, T_1. The theory and methodology has been reviewed[1] and the Aberdeen programme for the development of a whole-body NMR tomographic imager and the accompanying laboratory programme to investigate T_1 values of tissues has been described[2,3]. Details of the more recent instrumentation and imaging technique can be found elsewhere[4,5], a brief description of the principle only being given here.

Hydrogen protons spin about an axis and behave like a very small bar magnet. When placed in a magnetic field the proton magnetic axis precesses around the field direction at a frequency (the Larmor frequency) proportional to the applied magnetic field strength. If irradiated with a pulse of electromagnetic radiation of this frequency, energy is absorbed such that the proton can be made to flip over through 180° or 90°. After a 90° pulse, the protons fall back, re-radiating their surplus energy at the same frequency which can be detected as a signal. If two tubes of water are placed in a magnetic field gradient, after a 90° pulse, the frequency of the signal from the tube in the lower magnetic field is lower than that from the tube in the higher field, so that the position of the water is identified from the frequency. The amplitude of each signal is related to the amount of water in each tube, and the rate of fall of the signal after a 180° pulse is a measure of Tl, which for pure water is about 3 sec. but for tissues is much shorter and is believed to be related to the binding of the water to proteins in the tissue.

The first method suggested for NMR imaging was based on applying the field gradient at a series of directions around the sample and using computed tomography[6]. During the Aberdeen programme, an image of a whole mouse was obtained by this method in 1974[7].

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The whole-body imaging machine built in Aberdeen* is based on a four coil, air-cored electromagnet, providing a magnetic field of 0.04 Tesla. The patient lies with this field in the PA direction. The resulting Larmor frequency for the hydrogen protons of water is 1.7 MHz. A lateral cross section of spins across the patient is selected by a 90° pulse and a field gradient applied along the head to toe direction. During the read-out period, a field gradient is applied across the patient and 64 signals derived, each resulting from a PA column of spins through the patient. Information in the PA direction is obtained by applying a series of 64 field gradients in the PA direction, and utilizing the phase of each signal as well as its amplitude. The image reconstruction is by digital two-dimensional Fourier analysis. T_1 information is obtained by applying a 180° pulse, 200 m.sec. before the main pulse sequence already described. 128 electrical signals are obtained, each one taking 1 sec.: an entire section takes just over two minutes, from which a complete section of proton concentration, and one of T_1 is displayed.

For the Aberdeen machine, the sections have a Gaussian profile with thickness (equivalent rectangular width) of 18.5 mm. Each imaging element is 7.5 mm. wide, 7.5 mm. high and 18.5 mm. thick, comprising a volume of 1 cm^3. In each imaging element the uncertainty in proton density is about 2.5% (for muscle) and in T_1 is about 3.5% at 200 ms. with some worsening as T_1 departs from that optimum value.

T_1 in a region depends essentially upon the relative proportions of free and bound water for the tissue in that region, tissues with more free water having longer relaxation times[8]. T_1 values for rabbit tissues at 2.5 MHz range from 141 m.sec. for liver to 463 m.sec[9]. for testis with the body fluids, bile and blood serum, being much higher at over 800 m.sec. This threefold range of values for soft tissues is much greater than the range of water content values, which are from 69% for skin to 83% for grey brain tissue.

There is much evidence to suggest that animal malignant tumours show a longer T_1 than the equivalent normal tissues (see [3]). There is also interesting evidence of T_1 changes in rat muscle surrounding implanted tumour[10] and changes of spleen T_1 when rats are fed with hepatic carcinogen[11].

To evaluate the system, ten healthy volunteers have been examined. Sections from the head, thorax and abdomen, including the pelvis, and the thighs have been obtained. No adverse effect was experienced by any of the volunteers either during or after the examination. Images of the head have been obtained which show the cerebral cortex, pineal gland, choroid plexes, sagittal sinus, cerebellum, fourth ventricle, brain stem, paranasal sinuses, orbits, eyes and ocular muscles. Thorax sections have demonstrated the major blood vessels, such as the left pulmonary artery and descending aorta, right and left ventricles of the heart and lungs, best seen in T_1 images, whilst chest wall and breast tissue are best seen on proton density images. Abdominal sections have again shown major blood vessels. Liver, spleen and kidneys are best seen in T_1 images, whilst stomach and colon are seen in both T_1 and proton density images, whilst lumbar muscles and vertebral canal are seen well in proton density images. We were not able to demonstrate the pancreas in any of the volunteers. In the pelvis, the descending colon, rectum and bladder are seen, as are the testes in the male.

* The subject of Patents held by the U.K. National Research Development Corporation, P.O. Box 236, Kingsgate House, 66–74 Victoria Street, London, SW1 E 6SL.

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We believe our equipment provides a potentially useful diagnostic imaging system which should provide valuable information in the investigation and diagnosis of a large number of conditions. It does not use ionizing radiation, and there is no evidence of objective or subjective, short or medium term effects arising from the radiofrequencies, or magnetic fields and their gradients, at the levels used[12]. It appears, therefore, to be a safe, non-invasive, technique. In addition, images are formed of the distribution in any transverse section across the body, which display either the concentration of water (protons) in each pixel, or the spin-lattice relaxation time, T_1, of those water protons.

Thus, two completely new imaging parameters can now be used to characterize normal and diseased tissue for investigation and diagnosis. Whilst it will be used to provide information on those conditions which can also be studied by other imaging techniques, this new procedure may provide further information not yet readily available: for example, it is theoretically possible that it may differentiate fibrous benign tumours from malignant ones in the breast. It also seems very likely that it may provide useful clinical information on conditions which have not, so far, yielded to these other techniques, for example, inflammatory or oedematous states. One example is that it may be useful in differentiating the pleural effusion of cardiac failure from that of infection.

As a beginning of the exploration of its possible role in malignant disease, we are presently studying a number of patients who have primary carcinoma with evidence to suggest the presence of either hepatic or pulmonary metastases. The seven patients examined so far include the imaging of:

1) (a) primary oesophageal carcinoma,
   (b) hepatic metastases
   (c) small bilateral pleural effusions.
2) and 3). T_1 of satisfactory kidney transplant lower than that of less satisfactory one.
4) (a) Cerebellar metastasis (from primary carcinoma rectum)
   (b) Sinusitis
5) Primary cholangiocarcinoma
6) (a) inflamed gall bladder
   (b) ? blocked bile duct
   (c) osteoarthritis of R hip
7) (a) primary carcinoma rectum
   (b) hepatic metastases

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