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Advanced MRI

Diffusion weighted imaging

Physics

In diffusion weighted pulse sequences, magnetic resonance signal is generated in proportion to the freedom with which protons are able to move. When restricted by macromolecules and cell membranes, protons move more slowly than when in aqueous solution. Diffusion weighted imaging (DWI) sequences use radiofrequency pulses and magnetic gradients to dephase protons. After a short interval, an exactly opposite pulse and gradient is applied which returns the protons into phase. Protons that have moved in the interval do not generate signal, so that DWI intensity is proportional to the amount that protons have diffused during the imaging process (Figure 1).

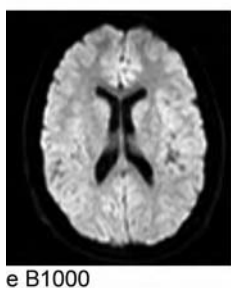
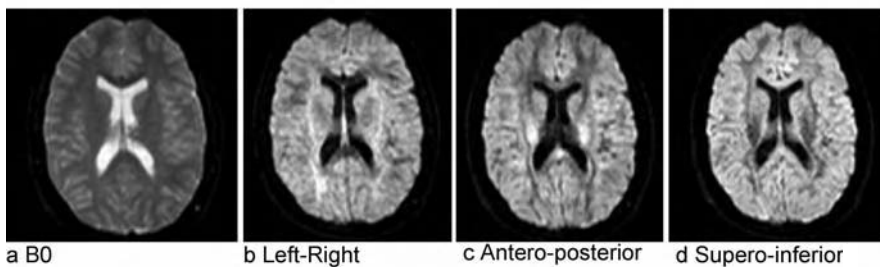
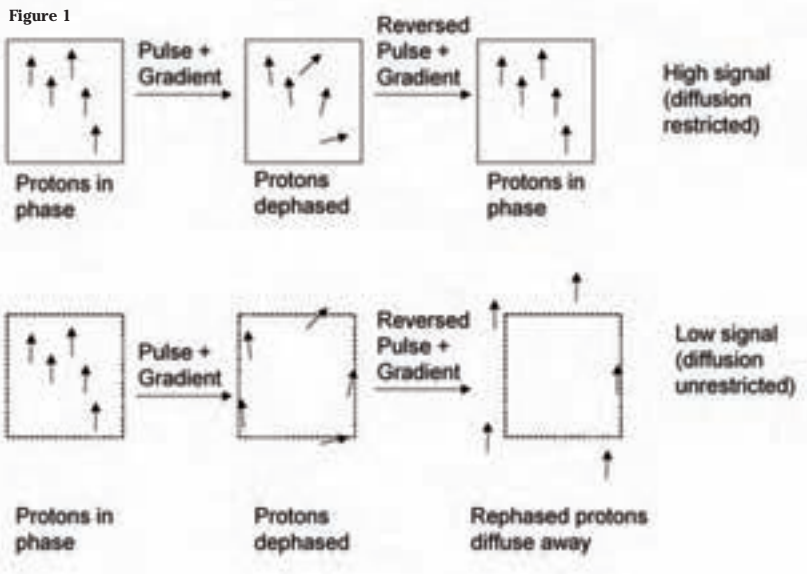


Figure 1 (top figure): Diffusion weighted imaging. The upper panel represents a region in which diffusion of protons is limited by the presence of cell membranes or intracellular organelles. The protons do not move between the dephasing and rephrasing pulses and so return high signal. The lower panel demonstrates a region with free diffusion. The protons have moved out of the region of interest between dephasing and rephrasing pulses and signal intensity is low.

Figure 2: Normal Diffusion Weighted Imaging. Images are presented as (a) B0, in which no diffusion gradients are applied and the image has T2 weighting, (b) supero-inferior diffusion gradient, (c) left-right diffusion gradient, (d) antero-posterior diffusion gradient and (e) B1000, in which signal from the 3 directions is summated which removes signal increase caused by anisotropy.

Post processing of diffusion weighted images

Raw diffusion weighted images (Figure 2) are presented as unweighted (B=0), Antero-Posterior gradient, Left-Right gradient, Supero-Inferior gradient and combined (B=1000) images.

Apparent diffusion coefficient

(ADC) maps (Figure 3) differentiate signal generated by restricted diffusion of protons from T2 effects (T2 'shine through'). ADC is a scalar quantity and does not reflect the asymmetry or direction of diffusion.

Fractional anisotropy, FA (Figure 4) is a tool for quantifying the extent to which diffusion is restricted asymmetrically (anisotropically). At the time that workers were investigating DWI in stroke, it was observed that the sig-

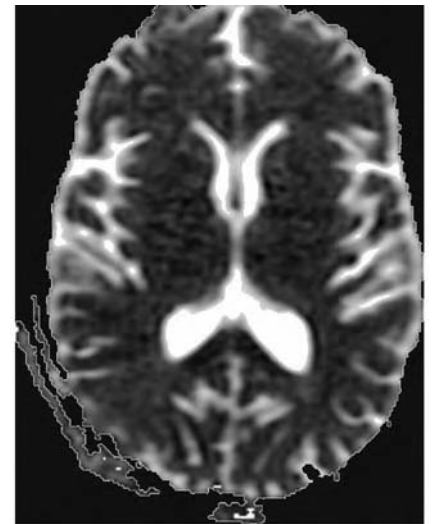


Figure 3: Normal Apparent Diffusion Coefficient (ADC) map. Values of apparent diffusion coefficient can be calculated from the diffusion and T2 weighted data according to the equation:

$$ADC = -1/b \ln (DW \text{ image} / T2W \text{ image})$$

If DW values are equivalent to T2 values, the ADC is 0, thus T2 effects are minimised. The contrast between normal grey and white matter is not marked, but areas of abnormal diffusion are shown with good contrast (see Fig 6).

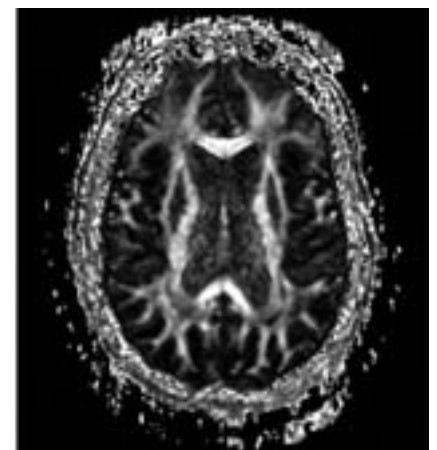


Figure 4: Normal Fractional Anisotropy map. There is marked difference in intensity between grey and white matter, reflecting the organised, parallel axons in white matter. The corpus callosum is of particularly high intensity.

nal obtained depended on the direction in which the diffusion imaging gradient was applied. This is because axons tend to be arranged in parallel tracks and cell membranes/ myelin allow proton diffusion along axons but not across the myelin sheath.

FA varies from 0 (spherical pattern of diffusion=perfectly isotropic) to 1 (diffusion restricted to a single linear direction=perfectly anisotropic). Heavily myelinated structures such as the corpus callosum have a high FA (0.90), unmyelinated regions such as cortex have a low FA (<0.20) and water has an FA of 0. Note that FA is a scalar quantity and does not take account of the direction in which diffusion is occurring, only the extent to which diffusion is asymmetric.

FA can be used to map normal fibre tracts and is a sensitive method for detecting abnormal white matter. White matter pathology affects myelination and reduction in FA can be detected before signal change can be seen on other sequences such as T2 weighted imaging.

Diffusion Tensor Imaging, DTI (Figure 5) combines diffusivity with the direction in which diffusion is restricted to give a parameter that has magnitude and direction (a tensor). By applying sufficient diffusion gradients (a minimum of 6 directions as well as an unweighted, b=0 image) a map of the direction of axons throughout the brain can be obtained. This anatomical data is useful in surgical planning so that important white matter tracts close to tumours can be avoided.

Clinical applications of DWI

Stroke (Figure 6): The first clinical application that was found for DWI was in the field of stroke imaging. Restriction of proton movement in acutely ischaemic tissue occurs because of failure of membrane pumps

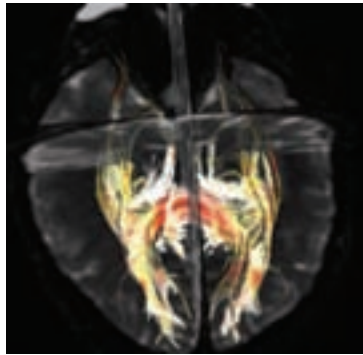


Figure 5: Tractography using tensor imaging. Tensor imaging provides the direction of maximal diffusion for each voxel. The likely path of axons can be tracked by analysing these directions resulting in a colour coded map. Heavily myelinated regions such as corpus callosum and visual pathways are the most readily mapped using this method.

and consequent neuronal swelling. This results in an increase in the ratio of intracellular to extracellular space. Proton diffusion is restricted in the intracellular space because of protein content, intracellular organelles and lipid membranes. It has been shown that tissue which shows restricted diffusion has suffered irreversible damage and will not recover even if perfusion is restored, making DWI a useful discriminator of patients who will benefit from thrombolytic and other acute interventions.

Abscess (Figure 7): Conventional sequences cannot always distinguish a cystic tumour from an abscess. Diffusion weighted imaging can be helpful when an abscess is a possibility.

CJD (Figure 8): DWI helps confirm the diagnosis of Creutzfeldt-Jakob disease (CJD). In sporadic CJD, there is restricted diffusion in the cortex and basal ganglia. In new variant CJD, there is signal change in the posterior thalami (pulvinar sign).

Epidermoid (Figure 11): These masses arise from congenital remnants of cutaneous ectoderm within the cranial cavity. They contain keratin which returns high signal intensity on DWI which helps to distinguish them from similar appearing lesions such as arachnoid cysts.

Functional MRI

Physics

Functional MRI (fMRI) generates contrast on images on the basis of different oxygen levels and is also known as BOLD (Blood Oxygen Level Dependent) imaging. As regions of the brain become active, their demand for blood supply increases and surrounding vessels dilate resulting in a local increase in oxyhaemoglobin levels. This causes a small reduction in intensity on T2 weighted images which is detected by the MRI equipment. Acquisitions are made before and after a specific task which may be:

- Sensory - visual (lights, faces, scenes etc)
- auditory (voice, sound)
- somatosensory (cutaneous stimulation)
- Motor - finger, toe movement
- Cognitive - recall, arithmetic, word finding

The images viewed are statistical maps showing areas with significantly reduced signal after the task. These areas are shown in colour on an anatomical image of the subject's brain.

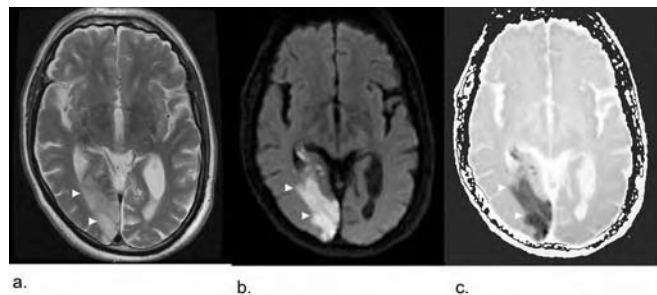


Figure 6: Acute infarct. (a) T2 weighted image (FSE, TR=6080 msec, TE=102 msec, slice=6 mm) and (b) Diffusion weighted image (EPI, TR=6000 msec, TE=69 msec, slice=5 mm) show increased intensity in occipital cortex and underlying white matter (arrow heads). This represents a combination of ischaemic oedema and alteration in diffusion signal intensity thought to be caused by failure of membrane pumps and cell swelling. (c) ADC map shows decreased ADC (reduced intensity) in areas of infarction (arrow heads)

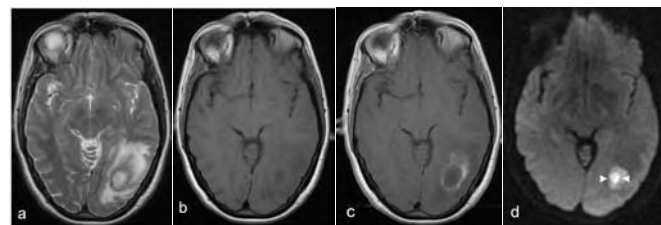


Figure 7: Bacterial abscess. (a) T2 weighted image (FSE, TR=6220 msec, TE=107 msec, slice=6 mm), (b) T1 weighted image (SE, TR=520 msec, TE=15 msec, slice=6 mm) and (c) T1 weighted image with Gd-DTPA (SE, TR=520 msec, TE=15 msec, slice=6 mm) show a ring enhancing mass in the left occipito-temporal region with surrounding oedema. These appearances could represent tumour or abscess. (d) Diffusion weighted image (EPI, TR=10000 msec, TE=89 msec, slice=5 mm) shows high signal in the centre of the lesion (arrow heads). This implies proteinaceous cellular content and is suggestive of abscess rather than tumour.

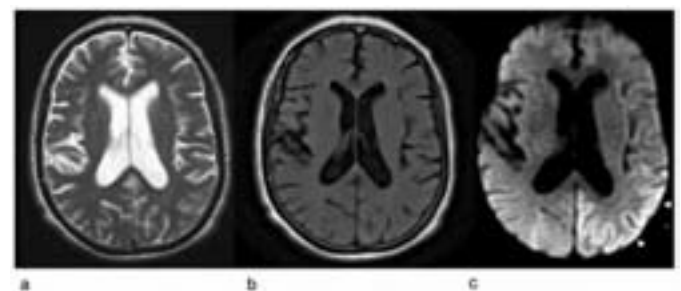


Figure 8: Sporadic Creutzfeldt-Jakob Disease (CJD). (a) T2 weighted image (FSE, TR=6000 msec, TE=106 msec, slice=6 mm) and (b) FLAIR image (FSE, TR=8002 msec, TE=166 msec, slice=6 mm) show mildly prominent ventricles but no other abnormality. (c) Diffusion weighted imaging (EPI, TR=10000 msec, TE=83 msec, B=1000, slice=5 mm) demonstrates cortical high signal intensity in a non-vascular distribution (arrow heads). This is suggestive of sporadic CJD.

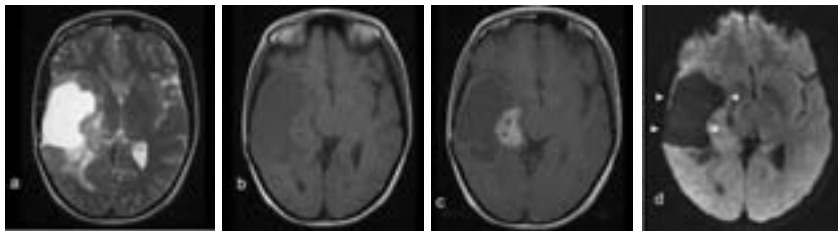


Figure 9: Astrocytoma Grade 3
 (a) T2 weighted image (FSE, TR=4000 msec, TE=100 msec, slice=6 mm),
 (b) T1 weighted image (SE, TR=2525 msec, TE=12 msec, slice=6 mm) and
 (c) T1 weighted image with Gd-DTPA (SE, TR=2525 msec, TE=12 msec,
 slice=6 mm) show a cystic mass in the right temporal lobe with an
 enhancing mural nodule
 (d) Diffusion weighted image (EPI, TR=10000 msec, TE=89 msec, slice=5
 mm) shows low signal (unrestricted diffusion) in the cystic part of the
 mass (arrow heads). This suggests tumour rather than abscess.

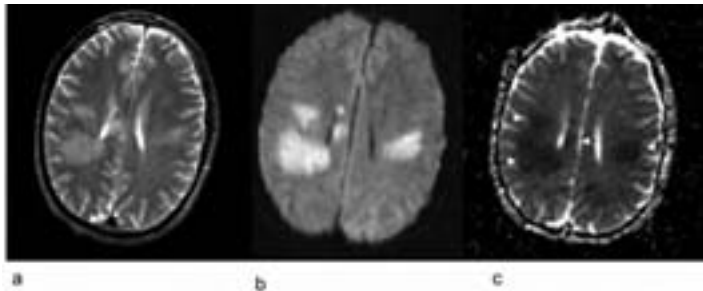


Figure 10: Acute Disseminated Encephalomyelitis (ADEM)
 (a) T2 weighted image (FSE, TR=4000 msec, TE=101 msec, slice=5 mm) and (b) Diffusion Weighted image
 (EPI, TR=6000 msec, TE=98 msec, slice=5 mm) shows multiple high intensity lesions in cerebral white
 matter in keeping with demyelination. c) ADC map demonstrates the presence of restricted diffusion
 rather than T2 'shine through' (arrow heads).

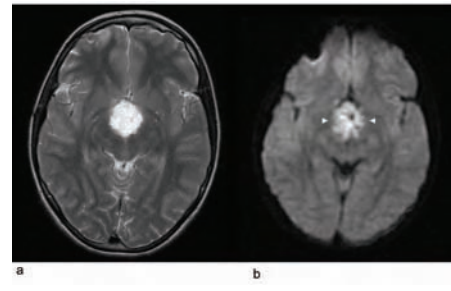


Figure 11: Epidermoid
 (a) T2 (FSE, TR=3000 msec, TE=105 msec, slice=6 mm) and (b) Diffusion weighted (EPI,
 TR=10000 msec, TE=111 msec, slice=6 mm) show high intensity in a suprasellar epidermoid
 (arrow heads). These are characteristically high intensity on DWI in contrast to arachnoid
 cysts which are usually low intensity.

Clinical applications

Although primarily a research tool, fMRI can be useful for surgical planning:

- to localise memory function in children undergoing temporal lobe resection for seizures.
- to minimise post-operative deficits in cases where brain tumours are close to neurologically eloquent areas of cortex (Figure 12).

Magnetic resonance spectroscopy (MRS)

Physics

Spectroscopic signals are obtained from hydrogen nuclei in organic molecules. The technique relies on subtle alteration ('shift') of the resonant frequencies of hydrogen nuclei because of the effect of adjacent nuclei and electrons in the molecule. Spectra are presented as plots of amplitude against parts per million shift in resonant frequency. Principal metabolites detectable on clinical MRS are:

N-Acetyl Aspartate (NAA) – is a marker for neurones and is decreased in conditions that cause axonal or neuronal cell loss. There are a few metabolic conditions in which too much NAA is produced (eg Canavan disease)

Creatine (Cr) – is a marker of the intracellular energy stores and is relatively constant in most disease processes. Other metabolites may be compared to the Cr peak.

Choline (Cho) – is a marker of cell turnover since it is an important constituent of cell membranes. Rapidly dividing tumours, particularly those with small cells (high surface area to volume) contain choline peaks.

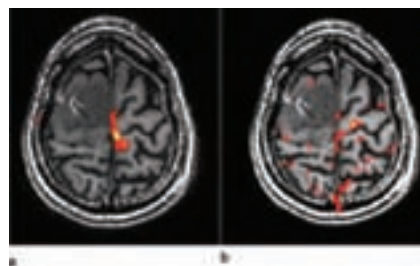


Figure 12: Functional MRI. Pre-operative study for planning of right superior frontal tumour resection. The patient has been given the task of toe movement. a) Axial image, patient moving right toe. There is activation in the medial left precentral gyrus. b) Axial image, patient moving left toe. Activation is more diffuse and bilateral with some activity seen on the periphery of the right frontal tumour.

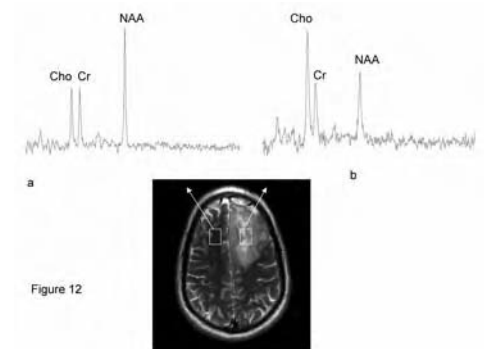


Figure 13: Spectroscopy. Grade III glioma.
 a) Control. The NAA peak at 2.0 ppm is approximately twice the amplitude of the Choline and Creatine peaks.
 b) Tumour. The NAA peak is reduced and the Choline peak is greater in amplitude compared to Creatine.

clues about the grade of a glioma, although not accurately enough to avoid biopsy in most cases.

Alzheimer's disease (Figure 14) – Myo inositol is a breakdown product of myelin and is seen in Alzheimer's disease more commonly than in other forms of dementia. It may also be seen in malignant tumours.

Stroke (Figure 14) – The striking feature in stroke is loss of NAA. Choline may be raised in this condition. Ischemic penumbra shows relatively normal spectra. Spectroscopy is not widely used in stroke imaging because of the relatively long time an acquisition requires.

Metabolic diseases (Figure 14) – Some leukodystrophies (e.g. Canavan disease, adrenoleukodystrophy) can be diagnosed and the effect of treatment can be assessed using MRS. ♦

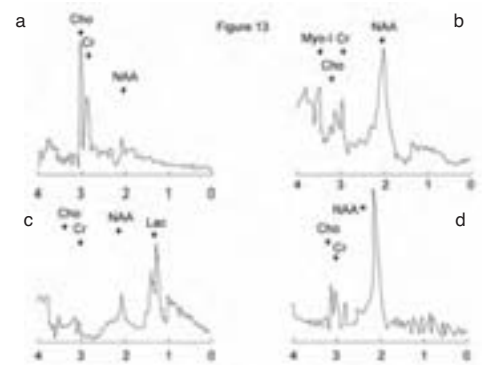


Figure 14: Spectroscopy.
 (a) High grade glioma. The Choline peak is increased and NAA is barely detectable. In some high grade tumours, lactate may be present although not in this case. (b) Alzheimer's disease. The most striking feature in this spectrum is the presence of myo-inositol. In later stages of the disease, NAA is reduced. (c) Infarct. There is reduction of Choline, Creatine and NAA with a prominent lactate peak. Some infarcts may show increased Choline. (d) Canavan disease. There is a raised NAA peak and this finding is almost pathognomic for this condition.