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PICTORIAL REVIEW

The use of diffusion weighted imaging to evaluate pathology outside the brain parenchyma in neuroimaging studies

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ABSTRACT

Diffusion-weighted imaging (DWI) has transformed the radiological assessment of a variety of cerebral pathologies, in particular acute stroke. In neuroimaging studies, DWI can also be used to evaluate pathology outside the brain parenchyma, although it is sometimes underutilized for this purpose. In this pictorial review, the principles of DWI are outlined, and 13 cases of abnormal diffusion outside the brain parenchyma are illustrated in order to show DWI as a useful sequence for the evaluation of the following recommended review areas: the dural venous sinuses, internal carotid arteries, meninges, ventricles, cavernous sinus and orbits, skull base and lymph nodes.

INTRODUCTION

Diffusion-weighted imaging (DWI) is an essential MRI sequence in stroke imaging protocols owing to its high sensitivity and specificity in the detection of hyperacute and acute infarctions. Its use is now recommended routinely in brain MRI studies,¹ as it provides useful information in regard to tumours,² cerebral infections, acute demyelination³ and a variety of neurometabolic disorders.⁴ DWI can also be used to evaluate pathology that is not within the brain parenchyma, and we present 13 cases that illustrate this.

Basic principles of diffusion-weighted imaging

Diffusion is the result of microscopic random movements of molecules known as Brownian motion. If no barriers are encountered, diffusion is said to be isotropic, indicating average displacement is the same in every direction. In brain tissues, the diffusion of water molecules is reduced by myelin and cell membranes. DWI is usually performed using an ultrafast echoplanar spin-echo T_2 weighted sequence [which includes a 90° radiofrequency (RF) pulse followed by a 180° RF pulse⁵], which is made sensitive to the movement of water molecules. This is achieved by a dephasing gradient prior

to the 180° RF pulse and a matching rephasing gradient after the 180° RF pulse.⁵ In tissues with impeded movement of water molecules, the effect of the dephasing gradient is cancelled out by the rephasing gradient, and the T_2 signal of the tissue is maintained. As a result, diffusion of water molecules causes incomplete spin rephasing and subsequent attenuation of signal. In other words, increased diffusion of water molecules corresponds to a reduction in signal intensity on diffusion-weighted (DW) images. In clinical practice, images are obtained using at least three different DW acquisitions, each obtained with a different orientation of the diffusion-sensitizing gradients. The individual acquisitions are not viewed separately but combined (most often by taking the geometric mean) to form a DW image (sometimes called an isotropic image) for diagnostic use. In each voxel, this information can be represented mathematically as the apparent diffusion coefficient (ADC). These maps are independent of the effects of T_2 shimming, and DW images are interpreted with corresponding ADC maps. The signal intensity of each voxel in DWI is inversely related to its ADC value. For example, infarcted areas with abnormal restricted diffusion lower the ADC but appear bright on the DW images.

Figure 1. An axial T_2 weighted image (a) with diffusion-weighted (DW) (b) and apparent diffusion coefficient maps (c). There is a high signal on the DW image in the superior sagittal sinus (arrow).

Conventional application of diffusion-weighted imaging for pathology in brain parenchyma

The conventional clinical applications of DWI are well described.^{2,3,6–8} DWI plays a major role in the early identification of ischaemic stroke where abnormal diffusion restriction (high signal on DW images) can be seen minutes after the onset of ischaemia.⁸ It can also help distinguish acute stroke from chronic stroke, where the ADC value is high with low DWI signal.

DWI can also be used in the evaluation of various brain infections such as cerebral abscesses where abnormal diffusion restriction is usually present centrally and in viral infections such as herpes encephalitis, which typically shows a diffuse pattern of abnormally restricted diffusion in the early stages of infection.⁶ It is also used to differentiate pyogenic brain abscesses from cystic or necrotic tumours.⁹ Other uses of DWI include identifying active plaques of demyelination,³ although these lesions are less reliably detected.

Diffusion-weighted imaging for detection of pathology outside the brain parenchyma in neuroimaging studies

In this pictorial review, we illustrate the application of DWI in the evaluation of subtle diagnoses not located within the brain parenchyma, in the following recommended review areas: the dural venous sinuses, internal carotid arteries (ICAs), meninges, ventricles, cavernous sinus and orbits, skull base and lymph nodes.

Dural venous sinuses

Dural venous sinus thrombosis is often a difficult diagnosis owing to its non-specific presentation. It is important, therefore, to maximize the chances of detecting sinus thrombosis using routine sequences. DWI may be the first sequence that indicates the diagnosis to the radiologist, especially if not suspected clinically.

The case in Figure 1 is of a patient who presented with headaches and papilloedema. Whilst the diagnosis of superior sagittal sinus thrombosis was appreciable on routine sequences, acute sinus thrombosis was readily detected on DWI shown as increased signal in the dural venous sinus. The high signal on the dark background in DWI appears more striking when compared with T_2 weighted imaging (Figure 1). The high signal of intraluminal thrombi on the high b -value images may be due to diffusion restriction relative to the surrounding venous blood and cerebrospinal fluid and also due to T_2 shinerthrough.¹⁰ In acute thrombus, the high erythrocyte content of the thrombus may lead to restricted diffusion.¹¹ As the thrombus is cleared of dead erythrocytes, there is a slight increase of water diffusion that reaches a maximum ADC value between 7 and 14 days.¹¹ In the later stages, a collagen-rich scar can lead to decreased diffusivity of water and a lower ADC value. Thus, low ADC values could represent either acute or chronic thrombus.¹¹ In one study, 41% of patients with venous sinus thrombosis had corresponding reduced ADC values. It has been suggested that

Figure 2. Axial MR head images at the level of the superior cervical segment of the internal carotid arteries (ICAs) just below the skull base. The T_2 weighted image (a) demonstrates a thin high signal rim around the signal void of the right ICA lumen (encircled). This correlates with high signal on diffusion-weighted imaging (encircled) (b) and low signal on the apparent diffusion coefficient map (encircled) (c) consistent with diffusion restriction from an intramural haematoma.

Figure 3. Corresponding axial images of an unenhanced CT head (a) and CT angiogram (b) at the level of the occipital condyles. These were performed 4 days prior to the MRI head of the patient in Figure 2. They demonstrate an expanded right internal carotid artery with intramural thrombus narrowing the vessel lumen (encircled).

the duration of symptoms is longer and complete recanalization is less frequent in patients with restricted diffusion in the thrombus.¹⁰ Early haematoma, however, can sometimes appear hypointense on high b -value images, probably owing to increased susceptibility artefact from concentrated intracellular methaemoglobin.^{12,13} This susceptibility artefact is thought to dissipate with lysis of red blood cells, when the methaemoglobin disperses uniformly through the haematoma.

Internal carotid arteries

ICA dissection is a significant cause of stroke in patients who are young and middle aged. ICA dissection occurs more often in the cervical segment than in the intracranial segment. Most commonly, ICA dissection occurs in the distal cervical ICA just below the skull base, and so it is possible to detect the dissection by assessing the few caudal slices of the axial MRI head. An acute intramural haematoma is often shown as a T_1 hyperintense

crescentic often eccentric region adjacent to the vessel lumen/flow void.¹⁴ Dedicated dissection protocols include axial T_1 with fat saturation to suppress adjacent fat and make the T_1 hyperintense thrombus more conspicuous.¹⁴ The cross-section of the vessel is often expanded by the intramural haematoma, and the vessel lumen may or may not be narrowed.¹⁴ However, routine MRI brain does not always include an axial T_1 , as in our case. For the patient in Figure 2a, the thin rim of T_2 hyperintense intramural haematoma narrowing the right ICA lumen could go undetected but is immediately evident on review of the corresponding DW image (Figure 2b). An unenhanced CT brain performed 4 days earlier also shows intramural haematoma expanding the right ICA just below the skull base, and the dissection is confirmed on CT angiography (Figure 3a,b).

Meninges

Small meningiomas can be more conspicuous on DWI than on other unenhanced MRI sequences (Figures 4–6). In Figure 4,

Figure 4. Axial T_2 weighted (a) and diffusion-weighted (b) images with an apparent diffusion coefficient map (c) showing a small meningioma posterior to the callosal splenium (arrow). The image (d) shows the same calcified meningioma on a subsequent CT brain.

Figure 5. Axial T_2 weighted fluid-attenuated inversion-recovery (a) and diffusion-weighted (b) images with an apparent diffusion coefficient map (c) showing a left petrous ridge meningioma (encircled areas).

a small meningioma is seen posterior to the splenium of the corpus callosum and is shown to be calcified on CT (Figure 4d). Figure 5 shows a left petrous ridge meningioma that increased in size on follow-up imaging, and Figure 6 shows a small sphenoid wing meningioma that could easily be missed on other sequences.

Small meningiomas like these can often be missed on other sequences if post-contrast imaging is not performed. Their high cellularity often makes them more conspicuous on DWI, which can be advantageous in the incidental detection of small meningiomas.

Another important pathology involving the meninges is empyemas, which may be subdural or extradural. Purulent material appears bright on DW images with corresponding low ADC values reflecting low diffusivity in a similar fashion to brain abscesses. Subdural empyemas are an important diagnosis not to be missed, as the infection can spread to the adjacent brain and cortical veins with subsequent infarction. They most commonly develop as a complication of sinusitis or mastoiditis or as a consequence of meningitis. MRI can detect small subdural collections that are not readily seen on CT, and DWI can be used as an adjunct to contrast-enhanced imaging to confirm their presence when they can be easily overlooked (Figure 7). A complex mixture of proteins, inflammatory cells, cellular debris and bacteria in high-viscosity

pus lead to diffusion restriction¹⁵ and therefore high signal on DWI.

Ventricles

Pyogenic ventriculitis is important to recognize early, as it often presents in an indolent manner but can lead to meningitis and often be lethal. This 60-year-old patient had a cerebral abscess in the frontal deep white matter, which subsequently ruptured into the ventricular system (Figure 8). The purulent material in the trigonal lateral ventricle could be overlooked using the T_2 weighted image, whereas the abnormal diffusion restriction in the DW image is much more striking in appearance (Figure 8). A small amount of pus in the ventricles can often be missed on other sequences, but as described above the diffusion restriction of pus makes it more striking in appearances on DWI.

Cavernous sinus and orbits

An idiopathic inflammatory process involving the cavernous sinus and orbital apex led to the diagnosis of Tolosa–Hunt syndrome in a patient with painful ophthalmoplegia. Gadolinium-enhanced MRI is currently the modality of choice for evaluation, but Figure 9c,d highlights that restricted diffusion can delineate the extent of disease just as well. There was almost complete resolution of this abnormality after steroid treatment (Figure 9e,f).

Figure 6. Axial T_2 weighted fluid-attenuated inversion-recovery (a) and diffusion-weighted images (b) with an apparent diffusion coefficient map (c) showing a right greater wing of sphenoid meningioma (encircled areas).

Figure 7. An axial T_2 weighted image (a): a small high signal intensity crescentic collection overlies the left lateral temporal convexity (arrow). This corresponds to a more conspicuous area of high signal on the diffusion-weighted (DW) image (b) and low signal on the apparent diffusion coefficient map (c) in keeping with a subdural empyema (arrows). High signal intensity on the DW image in the left transverse sinus is from a thrombus (circled areas), which can be easily overlooked on the T_2 image.

Infiltration by inflammatory cells can lead to mild diffusion restriction which together with T_2 shine-through can make regions of inflammation more conspicuous on DWI. In Tolosa–Hunt syndrome, infiltration of the cavernous sinus and superior orbital fissure with plasma cells and lymphocytes may lead to increased signal on the high b -value images.¹⁶ As illustrated in Figure 9, DWI is able to delineate the extent of the lesion and monitor for response to therapy.

Figure 10 is a case of an 80-year-old patient who presented with loss of visual acuity in the right eye. Imaging revealed a large skull base tumour pathologically diagnosed as a diffuse large B-cell lymphoma. DWI was able to show tumour invasion of the orbital apex on the initial non-contrast imaging, which may be overlooked on the fluid-attenuated inversion-recovery sequence, as demonstrated in Figure 10. The high cellularity of the tumour allows for better contrast on the high b -value DW images than on other unenhanced sequences.

Skull base

Bony metastases most often occur in patients with metastatic breast, lung or prostate malignancy, and from various haematological malignancies. Abnormal diffusion restriction

reflects the increased cellularity of the infiltrated bone marrow.¹⁷

The skull base is a review area where metastases are often missed. The cases in Figures 11 and 12 are of two different patients with prostate cancer who had bony metastases in the skull base that were best appreciated on DWI. These findings were subtler on other sequences. Highlighting the extent of disease can help guide radiotherapy to these areas.

MRI findings of another case (Figure 13) suggested leukemic infiltration of the skull base, which was best appreciated on DWI where the mandibular condyles and skull base including the jugular tubercles showed abnormal diffusion restriction (Figure 13b). The diffusion abnormalities resolved on repeat imaging following treatment (Figure 13d,e).

It is important for the radiologist to be aware of the potential presence of malignant bony infiltration on brain imaging. Studies have showed a skull metastasis incidence rate of 23% in patients with breast, lung or prostate malignancy, and the skull may be the only site of metastasis in up to 11.6% of patients.¹⁸ The detection of malignant bony infiltration can be

Figure 8. Axial images at the level of the occipital horns of the lateral ventricles. T_2 weighted (a) T_1 post-contrast images (b) fail to definitively illustrate the abnormality. The diffusion-weighted image (c) with an apparent diffusion coefficient map (d) shows the abnormal diffusion restriction in the trigonal left lateral ventricle (arrow) consistent with ventriculitis.

Figure 9. (a) The T_1 weighted image, (b) T_1 weighted image with contrast, (c) diffusion-weighted (DW) image and (d) apparent diffusion coefficient (ADC) map show an abnormal soft tissue in the right cavernous sinus extending forwards to reach the orbital apex in a patient with Tolosa-Hunt syndrome. It is intermediate signal on the T_1 weighted image, enhances with gadolinium and demonstrates restricted diffusion (arrows). (e) DW and (f) ADC images show almost complete resolution of the abnormality after treatment with steroids. The initial and the follow-up images (e, f) were acquired on different MRI scanners, which accounts for the slight difference in appearance of the DW images.

facilitated by DWI because of its sensitivity to bone marrow cell density, the relative proportion of fat and marrow cells, water content and bone marrow perfusion.¹⁹ Increasing bone

marrow cellularity leads to increased signal on the high b -value images. This high signal on a dark background immediately draws attention to potentially abnormal skeletal

Figure 10. An axial T_2 fluid-attenuated inversion-recovery image (a), a diffusion-weighted (DW) image (b) and an apparent diffusion coefficient map (c) showing tumour invasion of the orbital apex (encircled areas) in a patient with diffuse large B-cell lymphoma presenting with loss of visual acuity in the right eye. The tumour invasion in this is best appreciated on the DW images.

Figure 11. Axial slices of the skull base at the level of the nasopharynx of a patient with prostate cancer: the T_2 weighted image (a) less readily identifies the metastases, but the diffusion-weighted image (b) and apparent diffusion coefficient map (c) demonstrate restricted diffusion and the presence of metastases in the mandibles (arrows) and occipital condyles (dashed arrow). Mild restricted diffusion in the parotid glands is a normal phenomenon.

regions. The relationship with ADC is, however, more complex, as ADC values tend to increase with increasing cellularity initially until most marrow fat cells are displaced by tumour cells.²⁰ Diffuse bony infiltration (Figure 13) can sometimes be difficult to differentiate from hypercellular marrow, particularly in children, but it can be very useful to assess response to treatment, as illustrated in Figure 13d,e. In general, lytic bone metastases are better visualized than purely sclerotic lesions owing to the lower water and cellular content of sclerotic lesions.

Lymph nodes

Lymph nodes can be difficult to assess using conventional imaging techniques. Their high cellular density, however, makes them more conspicuous on DWI. In the case of Figure 14, the patient developed sudden onset of transient blindness affecting both eyes. MRI brain showed evidence of cerebral small vessel disease and an incidental finding of marked abnormal restricted diffusion in several occipital, cervical and parotid nodes bilaterally. A subsequent fine needle

aspiration of one of these nodes revealed a low-grade non-Hodgkin's B lymphocytic lymphoma.

Lymph nodes are traditionally characterized based on features such as their size, shape morphology and distribution. DWI can be very useful in the identification of lymph nodes, particularly in the context of malignancy, as their high cellularity makes them easily visible. It is important to note, however, that normal lymph nodes also demonstrate diffusion restriction. Studies investigating the role of DWI in various pelvic and head and neck malignancies have shown lower ADC values in malignant lymph nodes compared with benign nodes,^{21,22} although a definite cut-off value has not been established. Extending the use of DWI as a modality for the evaluation of nodal status may increase the accuracy of staging.

CONCLUSION

The use of DWI is now recommended routinely in most brain MRI studies. However, it is often underutilized to evaluate

Figure 12. Axial T_1 weighted (a), T_2 weighted (b) and diffusion-weighted (DW) images (c) with an apparent diffusion coefficient map (d): there is a high signal on the DW image in the right jugular tubercle (arrow) consistent with a bony metastasis in a patient with prostate cancer. This is detectable as low signal on T_1 but "stands out" on DW image. A small focus of high signal in the right cerebellum in (b) is from T_2 shine through.

Figure 13. Axial T_1 weighted (a) and diffusion-weighted (DW) images (b) with an apparent diffusion coefficient map (c) showing abnormal diffusion restriction of the heads of the mandibular condyles and skull base including the jugular tubercles (arrows) suggestive of leukemic infiltration. A DW image 1 month following treatment shows resolution of the diffusion abnormality (d, e).

pathology outside the brain parenchyma. DWI is one of the quickest MRI sequences to obtain, which can be used in the diagnosis, characterization and follow-up of a variety of pathologies outside the brain parenchyma. Some important diagnoses, such as dural sinus thrombosis, empyema and ventriculitis can potentially be overlooked on other sequences

but are more conspicuous on DWI, as they “stand out” against a dark background on the high b -value images. Some lesions, for example small meningiomas and certain inflammatory lesions, can be well delineated on DWI without the need for contrast. Further studies to better characterize such lesions on DWI could significantly reduce total scan times.

Figure 14. Axial T_2 weighted (a) and diffusion-weighted images (b) with an apparent diffusion coefficient map (c) at the level of the occipital condyles show abnormal diffusion restriction of an occipital lymph node (arrow). Fine needle aspiration revealed non-Hodgkin's lymphoma.

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