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DIFFUSION WEIGHTED MR IMAGING OF THE BRAIN: REVIEW OF CLINICAL APPLICATIONS

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ABSTRACT

Diffusion is referred to as random microscopic motion of water molecules; Diffusion Weighted Imaging (DWI) is based on the measurement of Brownian motion of molecules. It is now a well-established technique implemented as a part of routine protocol of the brain magnetic resonance imaging. Diffusion weighted magnetic resonance imaging is a very sensitive technique for the detection of many brain pathologies. It is critical in the evaluation of stroke patients. It is also valuable in the evaluation and investigation of a wide variety of other diseases of brain such as infections, neoplastic lesions, demyelinating diseases, encephalopathies, eclampsia, leukodystrophies, vasculitis, hemorrhage and trauma. This paper reviews the current applications of diffusion weighted magnetic resonance imaging in different pathologies of the brain.

Key Words: Brain Imaging, Magnetic Resonance Imaging, Diffusion Weighted Magnetic Resonance Imaging

INTRODUCTION

Diffusion Weighted Magnetic Resonance Imaging is one of the most rapidly evolving techniques in the MRI examinations and is critical in the evaluation of diverse brain pathologies. It has found its primary role in the central nervous system. The purpose of this paper is to review and to consider the current applications and clinical role of Diffusion-Weighted MRI in diagnosing brain pathologies.

Diffusion Weighted Imaging (DWI) is a well-established technique in which contrast within the image is produced by the random microscopic motion of water molecules within the tissues. Diffusion weighted MR imaging is obtained with a high field (1.5-Tesla) echo-planar imaging technology. The imaging time ranges from a few seconds to 2 minutes. DWI consists of a diffusion weighted image and an Apparent Diffusion Coefficient (ADC) maps 1. DW-MRI is performed with different b values to obtain maps of ADC values. There is a change in ADC value according to pathophysiologic states of the tissue, and it can be calculated by measuring the change in signal intensities by using different b values in a series of diffusion weighted magnetic resonance images. At higher b values, DWI producing T2 shine through effect. So all DWI should be correlated with ADC maps. Lesions with diffusion restriction appear bright on DWI and dark on ADC maps [2]. Diffusion Weighted Magnetic Resonance Imaging is very sensitive for the detection of many brain pathologies especially acute ischemic stroke. They are expressed as changes in MRI signal intensity on DWI or as variations in the ADC of water [3]. DWI is also increasingly used in the investigation of other brain diseases including hemorrhage, trauma, abscess, neoplastic lesions, infections, demyelinating diseases, encephalopathies, leukodystrophies, vasculitis, and vasculopathies [4]. DWI has been applied for differentiation between residual or recurrent tumors and post radiation or post-surgical changes in the brain.

Diffusion Weighted Magnetic Resonance Imaging can differentiate cytotoxic from vasogenic edema. Cytotoxic edema is characterized by restricted diffusion. On ADC images cytotoxic edema caused by ischemia is always hypointense and vasogenic edema is hyperintense. Vasogenic edema is characterized by elevated diffusion. Vasogenic edema is hypo to slightly

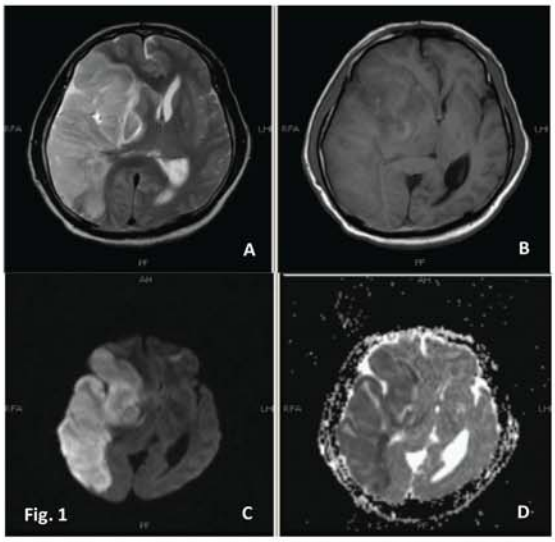

Figure 1 (A to D): Acute ischemic infarction; T2 (A), T1 (B) DW (C) and ADC (D) images shows a large diffusion restricted area in right middle cerebral artery territory showing high signals on DWI and low on ADC representing acute ischemic infarction.

hyperintense in DWI [5]. As a result DW MR imaging has vital role in the diagnosis of acute brain infarction and in the differentiation of acute infarction from other brain pathologies.

False Negative Diffusion Weighted Images lesions have been reported for deep grey matter or lacunar brain stem infarcts [6]. False Positive Diffusion Weighted Images lesions with restricted diffusion can be seen in tumor and in cerebral abscess. Differentiation in such cases can usually be made on the basis of routine T1, T2 weighted and post contrast images [5].

DIFFUSION WEIGHTED IMAGING IN STROKE

Diffusion-Weighted Magnetic Resonance Imaging is extremely sensitive in diagnosing ischemic changes in acute stroke patients. It is better than routine MRI in detecting early ischemic lesions. Within minutes after onset of early cerebral ischemia, cytotoxic edema which is caused by accumulation of intracellular water causes restriction of microscopic proton diffusion. Acute ischemic stroke can be detected with DWI within minutes after symptoms onset [7]. It is associated with decreased water diffusion and can be reflected as bright areas of signal hyperintensity in DWI, or as dark areas of signal hypointensity in ADC maps [8] (Figure 1). The signal intensity increases during the first week after onset of symptoms and remain hyperintense for up to 72 days [9], and decreases thereafter. The ADC values decreases rapidly after symptoms onset and then increase from dark to bright 7-10 days later [10]. Other advantage of DWI is the differentiation between acute and chronic ischemic lesions [11]. Chronic ischemic lesion can be detected as elevated diffusion and appear hypo, iso or hyperintense on DWI and hyperintense on ADC maps 2.

For infarction imaged within 6 hours of ischemic stroke onset, reported sensitivities are 38% to 45% for CT scan and 18% to 46% for conventional MR imaging. Diffusion weighted imaging has shown to be highly sensitive (88-100 %) and specific (86-100%) in the detection of hyperacute and acute infarction [12].

In 2002, a large study by Mullins ME et al, of 691 patients admitted to the emergency department with suspected acute stroke found that diffusion weighted imaging had an accuracy of 97% in identifying ischemic lesions, whereas conventional MR imaging (T1-weighted and T2-weighted) showed an accuracy of about 64% [13].

DIFFUSION WEIGHTED IMAGING IN INTRACRANIAL HEMORRHAGE

Hyperacute and late subacute hemorrhage are characterized by hyperintensity on DWI. The ADC values are decreased (Figure 2) in hyperacute stage and increased in late subacute stage [14].

CENTRAL NERVOUS SYSTEM INFECTIONS

DWI provides additional information in the assessment of CNS infections.

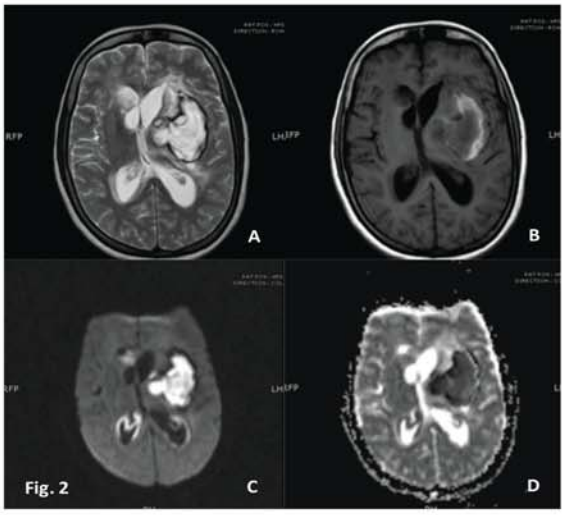

Figure 2 (A to D): Intracerebral Hemorrhage; A large intracerebral hematoma in left basal ganglia region showing intraventricular extension. T2 (A), T1 (B), DW (C) and ADC (D) images showing a diffusion restricted hematoma. The intraventricular component is better appreciated on DWI and ADC images.

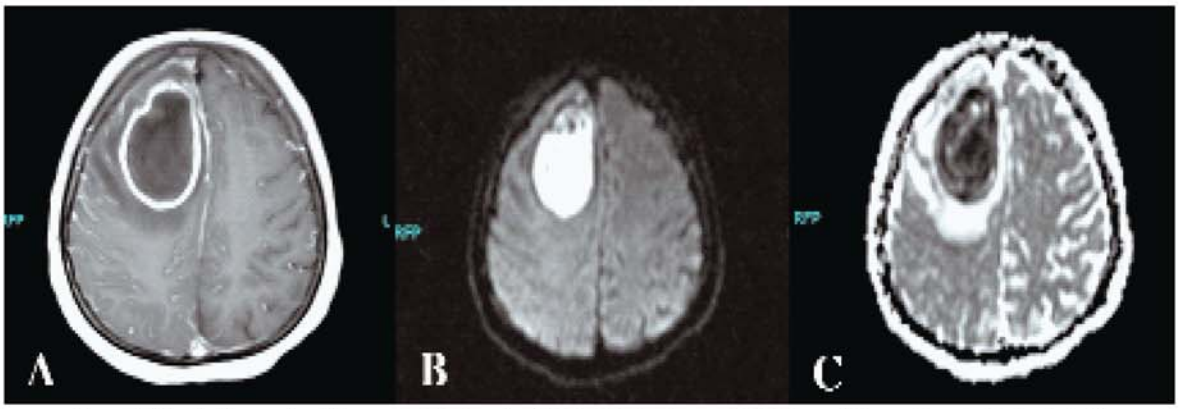

Figure 3 (A to C): Intracerebral Abscess; (A. Axial contrast T1; B. Diffusion image; C. ADC image): Ring enhancing lesion in right frontal lobe showing diffusion restriction infective abscess on aspiration.

ABSCESSES

Diffusion weighted imaging is helpful in differentiating between brain abscesses and necrotic and cystic neoplasms on MRI. Brain abscesses show hyperintensity on DW image with reduced ADC values. The restricted diffusion is due to the high viscosity of proteinaceous fluid and hypercellularity of pus [15] (Figure 3). Cystic and necrotic tumors show hypointense signal on DWI with an increased ADC (Figure 4).

GRANULOMAS

Tuberculomas and metastases both can manifest as solitary or multiple ring enhancing intra axial lesions, and are difficult to differentiate by conventional magnetic resonance imaging, the use of diffusion and perfusion magnetic resonance imaging would make differentiation of these lesions.

Generally DWI show hyperintense signal and low ADC values in inflammatory granulomas [15] (Figure 5).

In 2010 a study by Chatterjee et al, showed that lesions showed different perfusion characteristics depending on whether they were due to tuberculosis or metastasis. The mean regional cerebral blood volume ratio between the lesion periphery and normal white matter was inferior to one for tubercular lesions and greater than five for metastases. However, ADC values were similar [16].

HERPES SIMPLEX ENCEPHALITIS

Herpes Simplex Viral Encephalitis has predilection for medial temporal lobes, insular cortex and infero-lateral frontal lobes with characteristic sparing of lentiform nucleus [17].

DW image in Herpes Encephalitis lesions are characterized by marked hyperintensity in the lesion with usually decreased ADC values representing cytotoxic edema.

MENINGITIS

DWI may show pathologic changes of meningitis that vary with phase and severity of infection. In acute meningitis generally extra-axial fluid collection is seen. Subdural and epidural empyemas show hyperintense signal on DWI and hypointense signal on apparent diffusion coefficient map. In vascular complications diffusion weighted imaging has higher sensitivity than conventional MRI for small cortical or deep white matter infarcts [18].

INTRACRANIAL NEOPLASTIC LESIONS:

Diffusion-weighted imaging can increase both the sensitivity and specificity of MR imaging in the evaluation of brain tumors. DWI and ADC map show variable signal intensity in characterizing brain neoplasms. High grade tumors or tumors with higher cellularity, for example high grade gliomas, lymphomas, malignant meningioma, epidermoid and primitive neuroectodermal tumors show increased signal on the DW image and reduction in ADC values [15]. Low grade tumors or tumors with low cellularity, for example low grade gliomas have higher ADC values because of low cellularity [19]. In the evaluation of cystic tumors diffusion weighted imaging show low signal and on ADC sequence show high signal.

ARACHNOID CYST AND EPIDERMOID CYST

DW image can effectively differentiate an Arachnoid

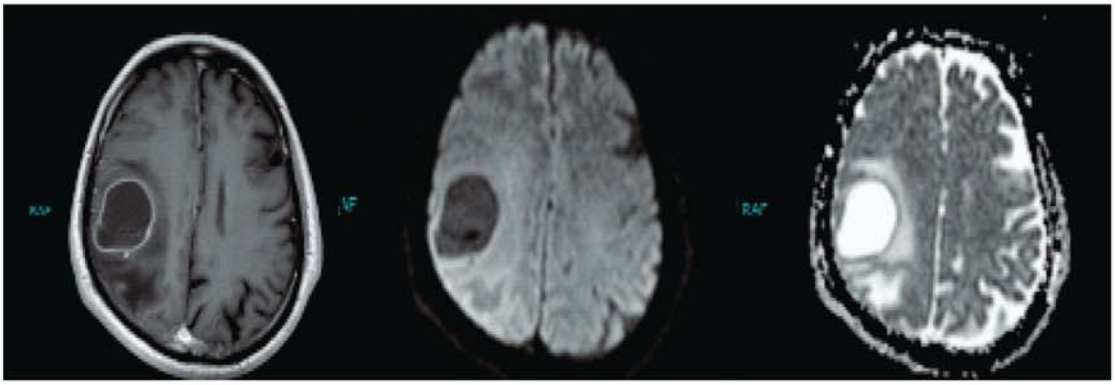

Figure 4 (A to C): Cystic Astrocytoma); (A. Axial Contrast T1; B. Diffusion Image; C. ADC image): Ring enhancing lesion in right parietal lobe without diffusion restriction turned out to be astrocytoma on biopsy.

Cyst from Epidermoid Cyst. Both show similar signal characteristic of CSF density on T1 and T2 weighted images. Epidermoid cyst show hyperintense signal compared with CSF and brain tissue on DW image and its ADC values are similar to those of the gray matter and lower than those of CSF [20] (Figure 6). Arachnoid Cyst appears similar to CSF on DW and ADC images 2.

METASTASIS

On DWI metastasis generally show iso or hypointense signal. Rarely hyperintense on DWI with decreased ADC may be seen, due to hypercellularity of the lesion, extracellular methemoglobin or increased protein concentration in the form of highly viscous mucin in cystic metastasis [15]. Ring enhancing metastases of adenocarcinoma have been reported with high signal on the diffusion weighted imaging sequence and low signal on ADC sequence. Restricted diffusion has been described in squamous cell carcinoma metastasis.

LYMPHOMAS

Lymphomas are highly cellular tumors and show diffusion restriction, have hyperintense signal on DWI and reduced ADC values [21].

MENINGIOMAS

Meningiomas are isointense on diffusion weighted images and ADC maps. Malignant Meningiomas have restricted diffusion probably due to high tumor cellularity, displaying high signal intensity on DW images and reduced ADC values [22].

MEDULLOBLASTOMA:

DWI demonstrates restricted diffusion because of densely packed tumor cells.

HAEMANGIOBLASTOMAS

The solid enhancing portion display high diffusibility.

ROLE OF DIFFUSION WEIGHTED IMAGING IN DIFFERENTIATION OF RESIDUAL OR RECURRENT TUMORS AND POST TREATMENT CHANGES

Residual or recurrent lesions and post-operative and post radiation changes show similar findings on conventional MR imaging and are difficult to distinguish. Residual or recurrent lesions demonstrate areas of low signal intensity on ADC map. Treatment induced changes display areas of high signal intensity on the ADC map [23] (Figure 7). Post radiation changes are usually demonstrated as areas of diffusion restriction.

DEMYELINATING DISEASES

Multiple Sclerosis is the most common demyelinating disease. The characteristic MR appearance of

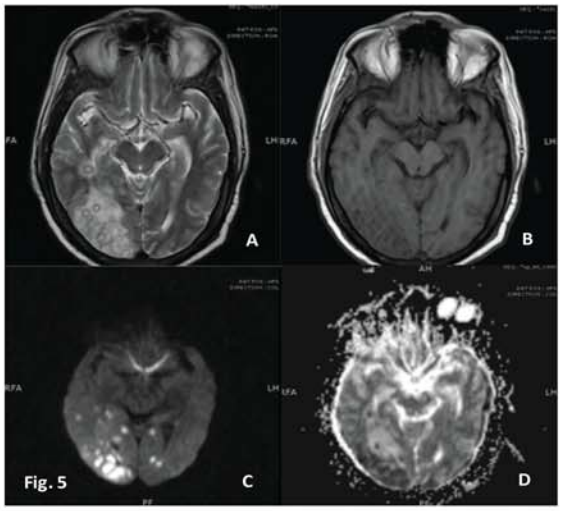

Figure 5 (A to D): Tuberculomas; T2 (A), T1 (B), DW (C) and ADC (D) images show multiple small nodular lesions showing diffusion restriction suggesting the diagnosis of tuberculomas.

MS plaques are multiple, ovoid, well circumscribed, T2 hyperintense foci. The activity of plaques can be evaluated by contrast enhanced magnetic resonance imaging. The presence of contrast enhancement represents blood brain barrier disruption in acute inflammatory lesions. On DWI acute multiple sclerosis plaques show restricted diffusion due to cytotoxic edema and increased inflammatory cellular infiltration. Chronic lesions do not show diffusion restriction [24]. In a study by Tsuchiya K et al, 94 plaques were demonstrated on T2-weighted and FLAIR images. A total of 13 of these plaques showed enhancement on contrast enhanced T1-weighted images and hyperintensity on diffusion weighted imaging, and five non-enhancing plaques showed hyperintensity on diffusion weighted imaging. Other non-enhancing plaques were isointense or slightly hypointense compared with normal white matter. Diffusion weighted imaging is different from contrast enhanced imaging and is a potential supplementary technique for characterizing multiple sclerosis plaques [25].

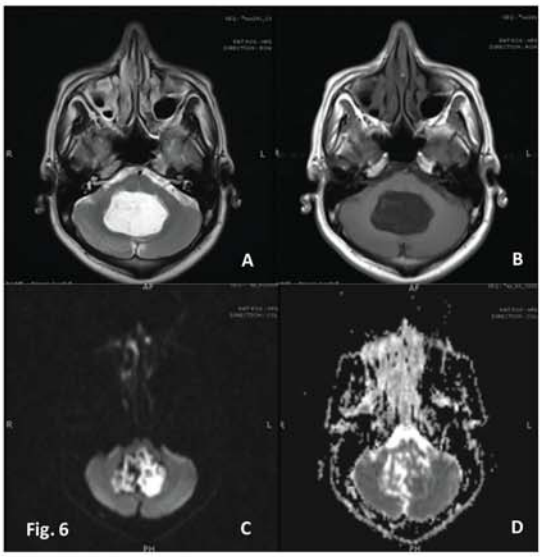

Figure 6 (A to D): Intraventricular Epidermoid; T2 (A), T1 (B), DW (C) and ADC (D) images through posterior cranial fossa show a diffusion restricted mass in fourth ventricle suggesting an epidermoid tumour.

LEUKODYSTROPHIES

Leukodystrophies refers to a pathological process, most commonly of metabolic origin, involving cerebral white matter. DWI showing restricted diffusion with low ADC. Evaluation of conventional diffusion weighted and ADC map images allows the detection of major diffusion abnormalities and various types of edema, of which the myelin edema is associated with leukodystrophies. Myelin edema present with high signals, and demyelinated white matter present with low signal

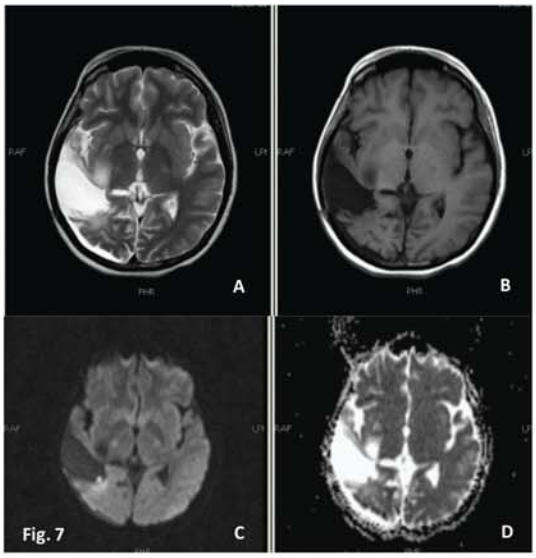

Figure 7 (A to D): Recurrent tumor; T2 (A), T1 (B), DW (C) and ADC (D) images through resection bed of a malignant glioma on follow-up shows a diffusion restricted nodule suggesting a tumour recurrence.

on diffusion weighted image [26]. Absent or low grade myelin edema is found in mucopolysaccharidosis, GM gangliosidosis, Zellweger disease, adrenomyeloneuropathy, L-2-hydroxyglutaric aciduria, non-ketotic hyperglycinemia, classical phenyl ketonuria, Van der Knaap disease and vanishing white matter. Medium grade myelin edema is seen in metachromatic leukodystrophy, x-linked adrenoleukodystrophy and HMG coenzyme liase defficiency. High grade edema is seen in Krabbe disease, Canavan disease, hyperhomocystinemias, maple syrup urine disease and leukodystrophy with brain stem and spinal cord involvement and high lactate [26].

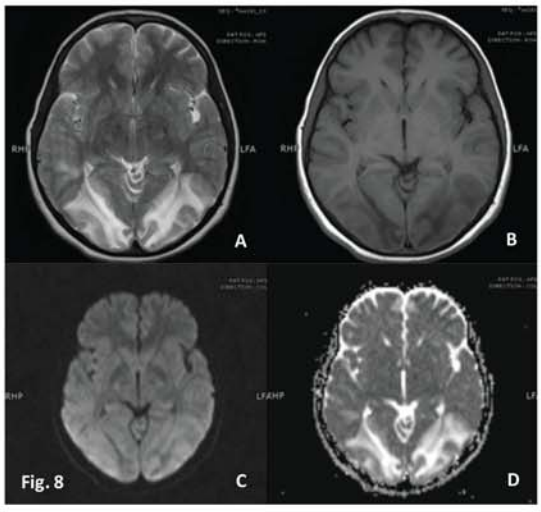

Figure 8 (A to D): PRES; T2 (A), T1 (B), DW (C) and ADC (D) Images show areas of abnormal signal intensities in parieto-occipital lobes bilaterally. In proper clinical scenario absence of diffusion restriction differentiate it from infarction.

TRAUMA

In post-traumatic patients with diffuse axonal injury MR imaging findings are T2-hyperintense lesions at grey-white matter junctions, in the white matter and in the brain stem. Shearing injuries which are not shown on T2-weighted, T2*-weighted gradient echo sequences and FLAIR images, can be picked at diffusion weighted images. Diffuse axonal injury usually demonstrated restricted diffusion as long as 18 days after injury 5. Lesions with increased ADC represents increased amount of extracellular water and lesions with decreased ADC may be due to trauma induced brain ischemia [27].

VASCULITIS

Magnetic resonance imaging shows lesions, commonly in the brain stem commonly as T2-hyperintense lesions with contrast enhancement. On diffusion weighted imaging the lesions are either iso or hyperintense with high ADC. The hyperintense signal on both Diffusion and ADC images is due to vasogenic edema due to disrupted blood brain barrier [28].

POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME

The typical MR findings are cortical and subcortical hyperintense lesions mainly in occipital lobes on T2W and FLAIR images. In eclampsia, hyperintense lesion on Diffusion Weighted Images are suggestive of cytotoxic edema, and hypointense areas on diffusion weighted images suggestive of vasogenic edema [29] (Figure 8).

EPILEPSY

The typical MR imaging on T2-weighted images in post-ictal period show unilateral or bilateral high signal in the cortical or limbic structures, mainly in the hippocampus. Diffusion Weighted Imaging can show hyperintensity in the cerebral cortex and a decrease in ADC on the side of epileptic focus [30].

ROLE OF DIFFUSION WEIGHTED IMAGING IN SKULL LESIONS

Diffusion Weighted Imaging is also helpful in the evaluation of skull
lesions. Prior studies indicate significant differences in ADCs between benign and malignant lesions. Recent studies have shown that ADC values in malignant skull lesions are significantly lower than ADC values in benign lesions [31.]

CONCLUSION

Diffusion Weighted Image has a high degree of sensitivity and specificity for diagnosing acute brain ischemia and differentiation of acute from chronic stroke. An accurate and early diagnosis of ischemic stroke is critical in ensuring patients receive prompt treatment, which, in turn, improves their chances of survival and increases their likelihood of recovery.

Diffusion Weighted Imaging is helpful in various other lesions of the brain including identification of abscess, differentiation of arachnoid from epidermoid cyst, grading of tumors. Generally lesions with decreased ADC, representing cytotoxic edema, suggest a worst prognosis and are more likely to be irreversible. Hence, diffusion weighted imaging remains a valuable tool in ischemic stroke and non-infarct lesions of the brain.

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